November 30, 2010

RESPONSIBLE CONDUCT OF RESEARCH (RCR)
A REFERENCE MANUAL FOR AFYA BORA CONSORTIUM (ABC) FELLOWS

INTRODUCTION

The Afya Bora Consortium is currently funded by an award from the U.S. National Institutes of Health (NIH). The NIH requires that all awards include training in "Responsible Conduct of Research" (RCR). NIH defines RCR as consisting of 9 topic areas, that are listed in a table below. We have limited our RCR program for this Fellowship to 6 of these 9 areas, focusing on those that are most pertinent to the goals of the Afya Bora Consortium.

THE FOLLOWING TOPIC NAMES ARE COPIED FROM THE U.S. NIH INSTRUCTIONS	THIS REFERENCE MANUAL
a. Conflict of interest – personal, professional, and financial	INCLUDED
b. Policies regarding human subjects, live vertebrate animal subjects in research, and safe laboratory practices	INCLUDED (omits animal subjects and laboratory practices)
c. Mentor/mentee responsibilities and relationships	OMITTED (included in Mentoring sessions)
d. Collaborative research including collaborations with industry	OMITTED (less relevant)
e. Peer review	INCLUDED
f. Data acquisition and laboratory tools; management, sharing and ownership (including copyrights and patents)	INCLUDED (omits laboratory tools)

g. Research misconduct and policies for handling misconduct	**INCLUDED**
h. Responsible authorship and publication	**INCLUDED**
i. The scientist as a responsible member of society, contemporary ethical issues in biomedical research, and the environmental and societal impacts of scientific research	**OMITTED (implicit in this Fellowship)**

To meet this NIH requirement, the ABC working group has developed the following plan for Fellows in training.

1. During the orientation at the commencement of the Fellowship, we will present an overview of the various topic areas, as an interactive session.

2. Many of the RCR topics are complicated and rather technical or legalistic. Therefore, we do <u>not</u> expect Fellows to master all of these details, nor will we examine Fellows about RCR specifics. Instead, we are supplying a "reference manual" of materials that provide much detail about these topics, in a digital version that will be included on the hard drive of each Fellow's laptop. As with other reference manuals, this materials will constitute a resource that Fellows can access if RCR issues arise, either during their Fellowship or thereafter.

3. What do we expect Fellows to know about RCR? We expect Fellows to be aware of each of the individual 6 topic areas, and know that supporting materials can be accessed on their hard drive if need arises.

Also, we expect Fellows to be aware of the complexities of many of these topics, some of which can be rather controversial. Therefore, it is important to realize that if issues arise, such as conflict of interest or authorship, individual health professionals are <u>not</u> expected to be able to deal with these on their own. Instead, we want Fellows to be aware that the ABC is a network that can offer consultation and support as needed. In other words, the network can provide access to a professional expert who can be consulted for advice on the technical details of policies and procedures.

4. Topics that are covered. The reference materials cover 6 of the 9 topics included in RCR. However, there are a few omissions, for areas that are presented elsewhere during the Fellowship (such as Mentoring), or areas that are not relevant to the ABC Fellowship (such as the use of experimental animals).

5. Source of documents. All these supporting materials are in the public domain. They have been sourced from a variety of sites which are credited. Many of the documents are from the University of Pennsylvania, which has developed these resources for faculty and

other members of its University community. The Penn documents are broadly representative of established practices in research Universities in the U.S. at this time, and conform with NIH guidelines.

6. Are these documents "definitive"? It should be recognized that these materials do not necessarily represent the "final word" in many of these areas. Established practices vary at different Universities, in different disciplines, in different countries, and are constantly evolving.

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HUMAN SUBJECTS PART 5	University of Pennsylvania. Reference manual for faculty and academic administrators. Human research protection program
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PEER REVIEW PART 1	Wikipedia. Peer review, a general overview
PEER REVIEW PART 2	NIH. Peer review of grant applications at the U.S. National Institutes of Health
PEER REVIEW PART 3	Nature magazine, 2010; 468: 29. A discussion of peer review of manuscripts
DATA PART 1	University of Pennsylvania. A Reference manual for Biomedical Graduate Studies Students and Research Fellows. Data Management and Ownership: pages 7, 37
DATA PART 2	Wikipedia. Copyright

TOPIC and HEADER	DOCUMENT Items in red provide basic orientation Items in black are mainly formal policies and procedures
DATA PART 3	University of Pennsylvania. Reference manual for faculty and academic administrators. Policy Relating to Copyrights and Commitment of Effort for Faculty
DATA PART 4	Wikipedia. Patents
DATA PART 5 (OMITTED)	University of Pennsylvania. Patent and Tangible Research Property Policies and Procedures
DATA PART 6	University of Pennsylvania. Roles, Responsibilities, and Expectations in Technology Commercialization at Penn
MISCONDUCT PART 1	University of Pennsylvania. A Reference manual for Biomedical Graduate Studies Students and Research Fellows. Procedures Concerning Misconduct: pages 2, 32, 38
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AUTHORSHIP PART 2	University of Pennsylvania. University policy. Fairness of authorship credit in collaborative publications

Update on the Requirement for Instruction in the Responsible Conduct of Research

Notice Number: NOT-OD-10-019

Key Dates
Release Date: November 24, 2009

Issued by
National Institutes of Health (NIH), (http://www.nih.gov)

Purpose

The purpose of this Notice is to update NIH policy on instruction in the responsible conduct of research, convey some of the consensus best practices that have evolved in the research training community over the past two decades, and to provide access to additional information that may be useful to institutions and individuals in meeting their obligations under NIH policy. Specifically this Notice: 1) develops principles based on 20 years' experience of providing instruction in responsible conduct of research by the scientific research community; 2) is more specific about who should participate, how often instruction should occur, and the form that instruction should take; 3) addresses issues that have arisen as the practice of biomedical, behavioral and clinical science has evolved; and 4) provides guidance to applicants, peer reviewers and NIH staff in determining how well specific plans for instruction in responsible conduct of research compare with the best practices accumulated over the past two decades by the research training community.

Applicability

This Notice applies to all NIH Institutional Research Training Grants, Individual Fellowship Awards, Career Development Awards (Institutional and Individual), Research Education Grants, Dissertation Research Grants, or other grant programs with a training component that requires instruction in responsible conduct of research as noted in the Funding Opportunity Announcement.

Background

In 1989, the NIH published its first Notice of policy concerning instruction in responsible conduct of research in the NIH Guide (Volume 18; Number 45. December 22). This Notice required that institutional training grant applications include a description of activities related to instruction about responsible conduct of research. A subsequent Notice (NOT-OD-94-200 NIH Guide Volume 23, Number 23, June 17), published in 1994, updated all previous Notices and required that applications for institutional research training grants lacking a plan for instruction in responsible conduct of research be returned without review, established review procedures, and established the minimum requirements for an acceptable plan. Similar requirements were subsequently adopted for instruction via research education grants, individual fellowships, and career awards as funding opportunity announcements for these programs were published.

In the ensuing years, there have been a number of developments related to instruction in responsible conduct of research. The scientific community has responded by developing innovative courses, workshops, research projects on instruction in responsible conduct of research, and instructional materials. Congress has enacted laws establishing the Office of Research Integrity to promote integrity in biomedical and behavioral research supported by the U.S. Public Health Service. The NIH Institutes and Centers (ICs), NIH peer review committees, and the scientific communities participating in NIH research have all evolved standards for what constitutes responsible conduct of research and an acceptable plan for instruction in this area. Legislation in this area initially focused on activities that fall under the formal definition of Research Misconduct. **Federal Regulations define Research Misconduct as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research or in reporting research results (http://ori.hhs.gov/documents/42_cfr_parts_50_and_93_2005.pdf).** It does not include honest error or honest differences in interpretations or judgments of data. However, it is well appreciated by all that responsible conduct, as opposed to misconduct, encompasses many other aspects of ethical behavior in the practice of scientific research.

The practice of biomedical research continues to evolve in terms of the interaction of participants (team research) and participating disciplines, emerging technologies in both the laboratory and in the publishing arena, and in the interactions of academic, medical, and for-profit enterprises. Acknowledging these changes, and drawing on the experiences of the past two decades, this Notice clarifies and updates NIH policy on instruction in responsible conduct of research.

Definition

For the purpose of this Notice, **responsible conduct of research is defined as the practice of scientific investigation with integrity. It involves the awareness and application of established professional norms and ethical principles in the performance of all activities related to scientific research.**

Basic Principles

The following principles are based on several key concepts about responsible conduct of research and best practices that have evolved over the past two decades' experiences:

1. Responsible conduct of research is an essential component of research training. Therefore, instruction in responsible conduct of research is an integral part of all research training programs, and its evaluation will impact funding decisions.
2. Active involvement in the issues of responsible conduct of research should occur throughout a scientist's career. Instruction in responsible conduct of research should therefore be appropriate to the career stage of the individuals receiving training.
3. Individuals supported by individual funding opportunities such as fellowships and career development awards are encouraged to assume individual and personal responsibility for their instruction in responsible conduct of research.
4. Research faculty of the institution should participate in instruction in responsible conduct of research in ways that allow them to serve as effective role models for their trainees, fellows, and scholars.
5. Instruction should include face-to-face discussions by course participants and faculty; i.e., on-line instruction may be a component of instruction in responsible conduct of research but is not sufficient to meet the NIH requirement for such instruction, except in special or unusual circumstances.
6. Instruction in responsible conduct of research must be carefully evaluated in all NIH grant applications for which it is a required component.

Policy

NIH requires that all trainees, fellows, participants, and scholars receiving support through any NIH training, career development award (individual or institutional), research education grant, and dissertation research grant must receive instruction in responsible conduct of research. This policy will take effect with all new and renewal applications submitted on or after January 25, 2010, and for all continuation (Type 5) applications with deadlines on or after January 1, 2011. This Notice applies to the following programs: D43, D71, F05, F30, F31, F32, F33, F34, F37, F38, K01, K02, K05, K07, K08, K12, K18, K22, K23, K24, K25, K26, K30, K99/R00, KL1, KL2, R25, R36, T15, T32, T34, T35, T36, T37, T90/R90, TL1, TU2, and U2R. This policy also applies to any other NIH-funded programs supporting research training, career development, or research education that require instruction in responsible conduct of research as stated in the relevant funding opportunity announcements.

Instructional Components

NIH recognizes that instruction in responsible conduct of research occurs formally and informally in educational settings and that informal instruction occurs throughout the research training experience. The guidance provided below is directed at formal instruction in responsible conduct of research. It reflects the accumulated experiences and the best practices of the scientific community over the past two decades. These practices have been incorporated into many of the best regarded programs of instruction in responsible conduct of research.

1. **Format:** Substantial face-to-face discussions among the participating trainees/fellows/scholars/participants; a combination of didactic and small-group discussions (e.g. case studies); and participation of research training faculty members in instruction in responsible conduct of research are highly encouraged. **While on-line courses can be a valuable supplement to instruction in responsible conduct of research, online instruction is not considered adequate as the sole means of instruction. A plan that employs only online coursework for instruction in responsible conduct of research will not be considered acceptable, except in special instances of short-term training programs (see below), or unusual and well-justified circumstances.**
2. **Subject Matter:** While there are no specific curricular requirements for instruction in responsible conduct of research, the following topics have been incorporated into most acceptable plans for such instruction:

    a. conflict of interest – personal, professional, and financial
    b. policies regarding human subjects, live vertebrate animal subjects in research, and safe laboratory practices
    c. mentor/mentee responsibilities and relationships

d. collaborative research including collaborations with industry
e. peer review
f. data acquisition and laboratory tools; management, sharing and ownership
g. research misconduct and policies for handling misconduct
h. responsible authorship and publication
i. the scientist as a responsible member of society, contemporary ethical issues in biomedical research, and the environmental and societal impacts of scientific research

While courses related to professional ethics, ethical issues in clinical research, or research involving vertebrate animals may form a part of instruction in responsible conduct of research, they generally are not sufficient to cover all of the above topics. Additional detail regarding subject matter is available under Resources.

3. **Faculty Participation:** Training faculty and sponsors/mentors are highly encouraged to contribute both to formal and informal instruction in responsible conduct of research. Informal instruction occurs in the course of laboratory interactions and in other informal situations throughout the year. Training faculty may contribute to formal instruction in responsible conduct of research as discussion leaders, speakers, lecturers, and/or course directors. Rotation of training faculty as course directors, instructors, and/or discussion leaders may be a useful way to achieve the ideal of full faculty participation in formal responsible conduct of research courses over a period of time.

4. **Duration of Instruction:** Instruction should involve substantive contact hours between the trainees/fellows/scholars/participants and the participating faculty. Acceptable programs generally involve at least eight contact hours. A semester-long series of seminars/programs may be more effective than a single seminar or one-day workshop because it is expected that topics will then be considered in sufficient depth, learning will be better consolidated, and the subject matter will be synthesized within a broader conceptual framework.

5. **Frequency of Instruction:** Reflection on responsible conduct of research should recur throughout a scientist's career: at the undergraduate, post-baccalaureate, predoctoral, postdoctoral, and faculty levels. Institutional training programs and individual fellows/scholars are strongly encouraged to consider how to optimize instruction in responsible conduct of research for the particular career stage(s) of the individual(s) involved. Instruction must be undertaken at least once during each career stage, and at a frequency of no less than once every four years. It is highly encouraged that initial instruction during predoctoral training occurs as early as possible in graduate school. Individuals at the early career investigator level (including mentored K awardees and K12 scholars) must receive instruction in responsible conduct of research at least once during this career stage. Senior fellows and career award recipients (including F33, K02, K05, and K24 awardees) may fulfill the requirement for instruction in responsible conduct of research by participating as lecturers and discussion leaders. To meet the above requirements, instruction in responsible conduct of research may take place, in appropriate circumstances, in a year when the trainee, fellow or career award recipient is not actually supported by an NIH grant. This instruction can be documented as described below.

Special Considerations by Type of Award

Institutional training and institutional career development programs (for example, T15, T32, T34, T90/R90, TL1, K12, or K30 programs): Institutional programs are encouraged to provide instruction in responsible conduct of research for all individuals associated with the program of training regardless of their source of support.

Short-term training and research education programs (for example, T35 and R25 programs lasting six or fewer months, short-term trainees supported on T15, T32 and T34 programs, and short-term participants in R25 programs): The NIH recognizes that the duration of an institutional training or research education program should be considered in the design, implementation, and review of plans for instruction in responsible conduct of research. The duration of such instruction within short-term institutional programs should be appropriate for the total duration of the program and should be justified in the application. This is an instance where on-line instruction could be appropriate. Such programs may also use innovative strategies to incorporate instruction in responsible conduct of research and to relate instruction in responsible conduct of research to the scientific focus of the short-term program.

Individual awards: In keeping with the individual nature of these programs, fellows and scholars, along with their institutions and sponsors/mentors, are encouraged to tailor instruction in responsible conduct of research to the needs of the individual. Thus, instruction may go beyond formal institutional courses and provide opportunities for the individual to develop their own scholarly understanding of the ethical issues associated with their research activities and their impact on society. An individualized plan would also be appropriate in the rare instance where an institution does not have an established formal mechanism for such instruction.

Application Procedures

1. **Institutional Applications**
    a. New (Type 1) applications must include a plan for instruction in responsible conduct of research. In addition to addressing the five instructional components, the plan must describe how participation in instruction in responsible conduct of research will be monitored.
    b. Renewal (Type 2) applications must, in addition, describe changes in formal instruction over the past project period and plans for the future that address any weaknesses in the current instruction in responsible conduct of research. All training faculty who served as course directors, speakers, lecturers, and/or discussion leaders during the past project period must be named in the application

2. **Individual Applications**

    a. New (Type 1) applications must include a section on instruction in responsible conduct of research, appropriate to the career stage of the applicant (instruction for applicants in the early stages of their careers; participation as course directors, lecturers, or discussion leaders for applicants in middle or senior stages of their careers), as part of the Research Training Plan or Candidate Information and Career Development Plan. This section will document prior participation or instruction in responsible conduct of research during the applicant's current career stage (including the date instruction was last completed) and propose plans to either receive instruction in responsible conduct of research or participate as a course lecturer, etc., depending on the applicant's career stage. Such plans must address the five instructional components outlined above. The plan may include career stage-appropriate, individualized instruction or independent scholarly activities that will enhance the applicant's understanding of ethical issues related to their specific research activities and the societal impact of that research. The role of the sponsor/mentor in instruction in responsible conduct of research must be described.
    b. Where applicable, renewal (Type 2) applications must describe instruction in responsible conduct of research activities undertaken during the past project period as well as future plans in order to meet the frequency requirement as outlined above in Instructional Components.

Applications lacking a plan for instruction in responsible conduct of research will be considered incomplete and may be delayed in the review process or not reviewed.

Peer Review

Reviewers will evaluate plans for instruction in responsible conduct of research as well as the past record of instruction in responsible conduct of research, where applicable. Reviewers will specifically address the five Instructional Components (Format, Subject Matter, Faculty Participation, Duration and Frequency) taking into account the characteristics of institutional programs or the unique circumstances outlined for short-term training programs, individual fellowships, career awards, and research education programs. The review will be guided ultimately by the principles set forth at the beginning of this Notice.

The plan for instruction in responsible conduct of research and the past record of instruction in responsible conduct of research, where applicable, will be discussed after the overall determination of merit of the application at large; the review panel's evaluation of the plan will not be a factor in the determination of the impact/priority score. Plans and past record will be rated as **ACCEPTABLE** or **UNACCEPTABLE.** The results of the review of the plan for instruction in responsible conduct of research and the past record of instruction in responsible conduct of research, where applicable, will be reported as an administrative note in the summary statement and will explain how the review panel determined its rating. Regardless of the impact/priority score, applications with unacceptable plans will not be funded until the applicant provides an acceptable, revised plan. Institute or Center staff will apply the principles set forth at the beginning of this Notice to determine the acceptability of the revised plan.

Reporting Requirements

For Institutional Training, Education, and Institutional Career Development Awards:

Continuation (Type 5) applications must describe the nature of the instruction in responsible conduct of research and the extent of trainee and faculty participation as required in the PHS 2590. This report must include a description of any enhancements and/or modifications to the five instructional components from the plan described in the awarded application. Specific training faculty members who were contributors to formal instruction in responsible conduct of research during the last budget period must be named.

For Individual Fellowships:

Continuation (Type 5) applications must report specifically on instruction for the fellow in responsible conduct of research. This report must include subject matter covered, format, frequency and duration of instruction, or indicate when during a previous or future budget period instruction in responsible conduct of research did or will take place. The report should discuss both formal and/or informal instruction in responsible conduct of research and should note the extent to which the sponsor or senior fellow participated in these activities.

For Individual Career Development Awards:

Continuation (Type 5) applications must include a description of instruction in responsible conduct of research as required in the PHS 2590. This report should describe instruction, or participation as a course director, etc. in the case of senior career awardees, in both formal and informal instruction in responsible conduct of research in the past budget period, if applicable. If instruction, or participation as a course director, etc., occurred in a prior budget period, the PI should note the date of occurrence. Any activities undertaken to individualize instruction appropriate to the career stage of the PI should be discussed.

For Dissertation Awards (R36):

Continuation (Type 5) applications must report on instruction in responsible conduct of research under a separate heading. This section should describe participation in both formal and informal instruction in responsible conduct of research in the past budget period, where applicable. If instruction occurred in a prior budget period, the PI should note the date when formal instruction was last completed. Any activities undertaken to individualize instruction appropriate to the career stage of the PI should be discussed. The report will describe how the mentor participated in these activities.

Compliance

NIH policy requires participation in and successful completion of instruction in responsible conduct of research by individuals supported by any NIH training/research education/fellowship/career award. It is expected that course attendance is monitored and that a certificate or documentation of participation is available upon course completion. NIH does not require certification of compliance or submission of documentation, but expects institutions to maintain records sufficient to demonstrate that NIH-supported trainees, fellows, and scholars have received the required instruction.

Resources

The NIH Research Training website (http://grants.nih.gov/training/extramural.htm) includes additional information on instruction in responsible conduct of research and links to the Office of Research Integrity (http://ori.hhs.gov/), links to instructional materials, and examples of programs that have been regarded as good models for instruction in responsible conduct of research (http://bioethics.od.nih.gov/researchethics.html). The National Academy Press has just published the 3rd. edition of the classic, *On Being a Scientist*, and is available online at http://books.nap.edu/catalog.php?record_id=12192.

Inquiries

Questions concerning this Notice should be directed to:

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NIH Research Training Officer
Director, Division of Scientific Programs
Office of Extramural Programs
National Institutes of Health
Phone: 301-496-3255
Email: ulanere@mail.nih.gov

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

Office of Extramural Research (OER)

Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892

of Health and Human Services (HHS)

Note: For help accessing PDF, RTF, MS Word, Excel, PowerPoint, Audio or Video files, see Help Downloading Files.

ORI

Introduction to the Responsible Conduct of Research

Nicholas H. Steneck

illustrations by David Zinn

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Message from the Secretary of Health and Human Services

Advances in scientific knowledge have provided the foundation for improvements in public health and have led to enhanced health and quality of life for all Americans. Many of these advances can be traced to the work of the U.S. Department of Health and Human Services (HHS), which supports the world's largest medical research effort.

Research conducted with support from HHS also helps to assure the safety of foods and health care products, is vital in the fight against drug and alcohol abuse, and in many other ways fosters the Department's mission to improve health and to help those in need of assistance.

As the custodian of the largest share of our Nation's resources devoted to biomedical and behavioral research, HHS takes seriously the challenge of ensuring these resources are used responsibly. Special programs already exist to oversee the protection of human and animal subjects in research, to review conflicts of interest, and to assure laboratory safety and responsible grants management.

With this publication, we hope to encourage researchers and research institutions to make a special effort to understand, discuss, and teach others about the responsible conduct of research.

Tommy G. Thompson
Secretary
U.S. Department of Health and Human Services

Foreword

The Office of Research Integrity (ORI) oversees and directs Public Health Service (PHS) research integrity activities on behalf of the Secretary of Health and Human Services and the American public. This responsibility extends to around $30 billion in Federal research support, devoted primarily to the biomedical and behavioral sciences through intramural and extramural programs, and to the thousands of researchers, research staff, and research administrators who work on PHS-funded research.

As part of its efforts to promote integrity in PHS-funded research, ORI is authorized to undertake activities and to support programs that enhance education in the responsible conduct of research (RCR). The *ORI Introduction to the Responsible Conduct of Research* is being issued to further this important mission.

The importance of formal RCR education was first explicitly recognized in the 1989 Institute of Medicine Report, *The Responsible Conduct of Research in the Health Sciences*, and has since been endorsed by other groups and members of the research community. Thanks to this support, researchers who want to learn about or help others understand responsible conduct in research have many resources available, from formal courses to web-based instruction programs, a growing array of challenging books, and the experience of established researchers conveyed through mentoring.

The *ORI Introduction to RCR* seeks to supplement existing resources by making a comprehensive overview of basic rules of the road for responsible research available to all PHS-funded researchers. It has been prepared with the needs of small and mid-size research institutions and beginning researchers in mind, since we have often been asked to provide resources for this community, but it may find use in other settings.

In issuing this publication, it needs to be stressed that ORI is not establishing or even recommending how RCR ought to be taught. We understand that responsible conduct in research can be and is learned in different ways, that the standards for responsible conduct can vary from field to field, and that in many situations two or more responses to a question about responsible research may be considered acceptable research practice. We hope the *ORI Introduction to RCR* will therefore be seen as the beginning and not the end of learning about this important aspect of professional life.

Chris B. Pascal, J.D.
Director
Office of Research Integrity

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Preface

Spurred by a growing belief in the importance of science and technology, public support for research increased dramatically over the course of the 20th century. A century ago, research did not play a major role in the average person's life. Today, few aspects of life are not touched in one way or another by the information and technologies generated through research.

With growing public support for research has come an understandable concern about the way it is conducted. Public funds support roughly one-third of all research and development (R&D) in the U.S. and half of all basic research. Many researchers, therefore, spend a significant portion of their time working for the public. As public servants and also professionals, researchers have clear obligations to conduct their research in a responsible manner.

In general terms, responsible conduct in research is simply good citizenship applied to professional life.

In general terms, responsible conduct in research is simply good citizenship applied to professional life. Researchers who report their work honestly, accurately, efficiently, and objectively are on the right road when it comes to responsible conduct. Anyone who is dishonest, knowingly reports inaccurate results, wastes funds, or allows personal bias to influence scientific findings is not.

However, the specifics of good citizenship in research can be a challenge to understand and put into practice. Research is not an organized profession in the same way as law or medicine. Researchers learn best practices in a number of ways and in different settings. The norms for responsible conduct can vary from field to field. Add to this the growing body of local, state, and Federal regulations and you have a situation that can test the professional savvy of any researcher.

Researchers learn best practices in a number of ways and in different settings. The norms for responsible conduct can vary from field to field.

The *ORI Introduction to the Responsible Conduct of Research* has been written primarily for researchers and research staff engaged in research supported by the Public Health Service but is applicable to scholarly research in general. As an "introduction," it seeks to provide a practical overview of the rules, regulations, and professional practices that define the responsible conduct of research. The coverage is not exhaustive and leaves room for continued reading and discussion in the laboratory and classroom, at professional meetings, and in any other setting where researchers gather to discuss their work.

The content is organized around two ways of thinking about research. The main sections follow the normal flow of research, from a consideration of shared values to planning, conducting, reporting, and reviewing. The chapters within the main sections cover nine core instructional areas that have been widely recognized as central to the responsible conduct of research. An opening chapter on rules of the road and a brief epilogue on responsible research round out the coverage.

Although designed to follow the normal flow of research, the chapters in this volume are all more-or-less self-contained and can be read in any order. Each opens with a short case in which students and researchers are faced with making decisions about the responsible conduct of research. Throughout

the chapters, important points are summarized in bulleted lists (✓) or noted in the margins (see left). Each chapter ends with a set of closing questions for further discussion (1 , 2 ...) and resources for reference and additional reading. The Web addresses given for the resources and elsewhere in this work were current at the time of printing.

While written with all researchers in mind, special consideration has been given to the needs of students, postdocs, and researchers who do not have easy access to responsible conduct of research materials or to colleagues who can explain the intricacies of responsible conduct in research to them. Two or three hours with this book should provide anyone in this position with a better understanding of the reasons for and the scope of the most important responsibilities researchers have.

Many colleagues have generously provided comments on parts or all of this work as it took shape over several drafts, including Ruth Bulger, Tony Demsey, Peggy Fischer, Carolyn Fassi, Nelson Garnett, Shirley Hicks, Erich Jensen, Mike Kalichman and his students, Nell Kriesberg, John Krueger, Tony Mazzaschi, Judy Nowack, Chris Pascal, Ken Pimple, Larry Rhoades, Fran Sanden, Mary Scheetz, Joan Schwartz, David Shore, Peggy Sundermeyer, and Carol Wigglesworth. Co-creator, artist David Zinn, patiently produced multiple versions of his drawings as we worked together to turn serious dilemmas into lighter but thought-provoking illustrations. ORI Director, Chris Pascal, and Associate Director, Larry Rhoades, deserve credit for initiating and carrying through on this project. If through promoting integrity and responsible conduct in research this work helps preserve the place of research in society today, it will have been a project well worth undertaking.

Nicholas H. Steneck
Ann Arbor, MI

Part I.

Shared Values

Part I: Shared Values

THERE IS NO ONE BEST WAY TO UNDERTAKE research, no universal method that applies to all scientific investigations. Accepted practices for the responsible conduct of research can and do vary from discipline to discipline and even from laboratory to laboratory. There are, however, some important shared values for the responsible conduct of research that bind all researchers together, such as:

- ✓ **HONESTY** — conveying information truthfully and honoring commitments,
- ✓ **ACCURACY** — reporting findings precisely and taking care to avoid errors,
- ✓ **EFFICIENCY** — using resources wisely and avoiding waste, and
- ✓ **OBJECTIVITY** — letting the facts speak for themselves and avoiding improper bias.

At the very least, responsible research is research that is built on a commitment to these and other important values that define what is meant by integrity in research.

The opening chapters of the *ORI Introduction to RCR* provide a framework for thinking about basic values in the context of the day-to-day practice of research.

Chapter 1, Rules of the Road, presents a brief overview of the different ways research responsibilities are defined, ranging from formal regulations to informal codes and common practices.

Chapter 2, Research Misconduct, describes research practices that must be avoided and the obligation researchers have to report misconduct.

Setting off on the road to the responsible conduct of research

Chapter 1. Rules of the Road

How should you conduct your research? What practices should you follow? The public and their professional colleagues expect researchers to follow many rules and commonly accepted practices as they go about their work advancing knowledge and putting knowledge to work. Responsible conduct in research is conduct that meets this expectation.

Society's expectations for the responsible conduct of research are complex and not always well defined. Becoming a responsible researcher is not like becoming a responsible driver. Responsible driving is clearly defined through laws and written down in drivers' manuals. Before individuals are allowed to drive, they are tested on both their knowledge of the rules of the road and their skills. Then, licensed drivers are constantly reminded of their responsibilities by signs, traffic signals, and road markings. They also know that their behavior as drivers is monitored and that there are specific penalties for improper behavior.

Guidance for the responsible conduct of research is not this well organized. Some responsible practices are defined through law and institutional policies that *must be followed.* Others are set out in non-binding codes and guidelines that *should be followed.* Still other responsible practices are commonly accepted by most researchers but not written down. Instead, they are transmitted informally through mentoring, based on the understandings and values of each mentor. This situation is further complicated by the fact that researchers are not routinely tested on their knowledge of responsible practices or licensed. Moreover, their behavior as researchers is inconsistently monitored and the penalties for irresponsible behavior vary considerably.

Researchers do, of course, care deeply about responsible behavior in research and pay a great deal of attention to best research practices. The fact remains, however, that it can take

some effort to find out what these practices are and how to act when the complex rules for responsible practice seem to conflict with one another.

This chapter describes the four basic sources of rules of the road for the responsible conduct of research:

- ✓ **professional codes,**
- ✓ **government regulations,**
- ✓ **institutional policies, and**
- ✓ **personal convictions.**

If you are primarily interested in learning more about your responsibilities rather than understanding their origin, skip ahead to the substantive chapters that follow, returning to this chapter later, when it might have more relevance.

Case Study

Katherine, a postdoc in Dr. Susan B.'s laboratory, has just had a manuscript accepted for publication in a prestigious research journal, conditional on a few important changes. Most importantly, the editor has requested that she significantly shorten the methods section to save space. If she makes the requested changes, other researchers may not be able to replicate her work.

Asked about the situation, Dr. B. recommends that Katherine go ahead with the changes. After all, if other researchers want more information they can always get in touch. She remains concerned that an inadequate explanation of her methods could lead other researchers to waste time and valuable research dollars attempting to replicate her work.

Should Katherine make the requested changes?

Should she be concerned about providing inadequate information to colleagues?

Is reducing detail in methods sections a reasonable way to go about saving valuable space in journals?

How can Katherine get definitive answers to these and other questions about the responsible conduct of research?

1a. Professional self-regulation

Prior to World War II, society provided little public support for research and did not expect much from researchers in return. Researchers were more or less left alone to run their own affairs, except when they assumed other roles, as teachers, physicians, or engineers.

As professionals, researchers have not been particularly concerned about rules for self-regulation. Since the goal of research is to advance knowledge through critical inquiry and scientific experimentation, it has commonly been assumed that the normal checking that goes on in testing new ideas is sufficient to keep researchers honest. Based on this assumption, research arguably does not need specific rules for self-regulation because it is, by definition, an activity that routinely monitors itself.

The lack of a perceived need for specific rules poses problems for researchers who want guidance on responsible research practices. Intellectually and professionally researchers organize their lives around fields of study. They are biologists, chemists, and physicists, increasingly working in specialized areas, such as biophysics, biochemistry, molecular biology, and so on. However, the societies that represent fields of study for the most part have not developed comprehensive guidelines for responsible research practices. Many do have codes of ethics, but most codes of ethics are simply general statements about ideals and do not contain the specific guidance researchers need to work responsibly in complex research settings.

Fortunately, there are a few important exceptions to this last generalization. Comprehensive descriptions of responsible research practices can be found in (see the resources listed at the end of this chapter for references):

National Academy of Sciences, On Being a Scientist (1995)

The scientific research enterprise, like other human activities, is built on a foundation of trust. Scientists trust that the results reported by others are valid. Society trusts that the results of research reflect an honest attempt by scientists to describe the world accurately and without bias. The level of trust that has characterized science and its relationship with society has contributed to a period of unparalleled scientific productivity. But this trust will endure only if the scientific community devotes itself to exemplifying and transmitting the values associated with ethical scientific conduct.

http://www.nap.edu/readingroom/books/obas/preface.html

- ✓ **reports and policy statements issued by the National Academy of Sciences, the American Association for the Advancement of Science, the Association of American Medical Colleges, and Sigma Xi;**
- ✓ **guidance on responsible publication practices published in journals; and**
- ✓ **a few comprehensive professional codes.**

When applicable, the guidance provided by professional societies is a good place to begin learning about responsible research practices.

American Chemical Society
The Chemist's Code of Conduct (1994)

Chemists Acknowledge Responsibilities To:

The Public.	Chemists have a professional responsibly to serve the public interest and welfare and to further knowledge of science....
The Science of Chemistry.	Chemists should seek to advance chemical science, understand the limitations of their knowledge, and respect the truth....
The Profession.	Chemists should remain current with developments in their field, share ideas and information, keep accurate and complete laboratory records, maintain integrity in all conduct and publications, and give due credit to the contributions of others. Conflicts of interest and scientific misconduct, such as fabrication, falsification, and plagiarism, are incompatible with this Code.
The Employer.	Chemists should promote and protect the legitimate interests of their employers, perform work honestly and competently, fulfill obligations, and safeguard proprietary information.
Employees.	Chemists, as employers, should treat subordinates with respect for their professionalism and concern for their well-being....
Students.	Chemists should regard the tutelage of students as a trust conferred by society for the promotion of the student's learning and professional development....
Associates.	Chemists should treat associates with respect, regardless of the level of their formal education, encourage them, learn with them, share ideas honestly, and give credit for their contributions.

http://www.chemistry.org/portal/a/c/s/1/acsdisplay.html?DOC=membership%5Ccode.html

1b. Government regulation

As public support for research grew after World War II, the public, through its elected officials, became more interested in the way research is practiced. Over time, concerns began to surface about some of these practices, focusing initially on the use of animals and humans in research and later on research misconduct. When it appeared that the research community was not doing enough to address these concerns, government turned to regulation.

Government regulations usually begin in Congress. When a potential problem is identified, Congress calls hearings to learn more about the problem and then passes legislation to fix it. The regulations covering the use of humans and animals in research as well as research misconduct stem from three acts passed by Congress:

- ✓ **the 1966 Animal Welfare Act (PL 89-544),**
- ✓ **the 1974 National Research Act (PL 93-348), and**
- ✓ **the 1985 Health Research Extension Act (PL 99-158).**

These and other research-related acts give the Federal Government the authority to regulate the research it funds.

Along with the authority to address problems, Congress usually provides guidance on general objectives, but it seldom drafts detailed regulations. This job falls to the Federal agencies in the Executive Branch of government, which are responsible for carrying out the law. Federal agencies translate Congressional directives into regulations (also called rules), policies, and guidelines.

In 1989, the Department of Health and Human Services (HHS) established the Office of Scientific Integrity (OSI) and the Office of Scientific Integrity Review (OSIR), in response to the 1985 Health Research Extension Act. The Office of Research Integrity (ORI) was established in 1992 and assumed the responsibilities previously assigned to

OSI and OSIR. In addition to responding to misconduct, ORI undertook a number of steps to promote integrity and responsible research practices. The *ORI Introduction to RCR* is a result of that effort.

Regulations. When Federal agencies translate Congressional directives into regulations, they must follow provisions set out in the Federal Administrative Procedure Act (5 USC 551-702). As its name implies, this act establishes procedures for developing new regulations, including steps for getting public input. Before establishing a new regulation, an agency must issue a draft regulation, obtain and consider public comment, and then issue the final regulation. Each step must be published in the *Federal Register*–the "official daily publication for rules, proposed rules, and notices of Federal agencies and organizations, as well as executive orders and other presidential documents" (http://www.gpoaccess.gov/fr/index.html). Objections raised during the public comment period must be addressed before the final regulation is adopted. After it is adopted, the final regulation is incorporated into the Code of Federal Regulations and becomes official government regulatory policy that must be followed.

Agency policies and guidelines. Executive Branch agencies have the authority to issue some policies as part of their normal operation. The National Institutes of Health (NIH), for example, has the authority to establish policies for grant awards. From time to time, it changes these policies to assure that its research funds are spent wisely and responsibly. It is in this capacity that NIH issued a special RCR "Training Grant Requirement" in 1989 and the more recent "Required Education in the Protection of Human Research Participants" (discussed in Chapter 3).

Federal agencies also issue Guidelines, which recommend but do not require a particular course of action. To help research institutions handle allegations of research

Required Education in the Protection of Human Research Participants

June 5, 2000 (Revised August 25, 2000)

National Institutes of Health

Policy: Beginning on October 1, 2000, the NIH will require education on the protection of human research participants for all investigators submitting NIH applications for grants or proposals for contracts or receiving new or non-competing awards for research involving human subjects.

Background: To bolster the Federal commitment to the protection of human research participants, several new initiatives to strengthen government oversight of medical research were announced by HHS Secretary Shalala on May 30, 2000. This announcement also reminds institutions of their responsibility to oversee their clinical investigators and institutional review boards (IRBs). One of the new initiatives addresses education and training. This NIH announcement is developed in response to the Secretary's directive.

http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html

misconduct (see Chapter 2), ORI issued as guidelines a Model Policy and Procedures for Responding to Allegations of Scientific Misconduct (http://ori.hhs.gov/policies/model_policy.shtml). In this case, the model policy is intended to provide guidance and does not impose binding requirements on institutions.

The plethora of Federal regulations, policies, and guidelines that affect research can be confusing. They do not always speak with one voice. The same aspect of a research project can be subject to regulations by more than one Federal agency, as for example the use of human or animal subjects. Common Federal regulations, such as the Federal Policy on Research Misconduct (discussed in Chapter 2) and the "Common Rule" for human subjects research (discussed in Chapter 3), are not truly common regulations until they have been adopted by all agencies. In addition, distinctions between regulations, policies, requirements, guidelines, and recommended practices can be difficult to understand.

Researchers are well advised to seek help when it comes to understanding Federal and state research regulations. The Federal agencies that regulate research have comprehensive Web pages that list and explain their policies and regulations and readily answer questions. For local advice, your institutional research administrators may be the best place to begin.

1c. Institutional policies

Research institutions (universities, hospitals, private research companies, and so on) are required by law to have policies that cover various aspects of their research programs if they accept Federal funds. They must have committees to review human and animal research (discussed in Chapters 3 and 4). They must have procedures for investigating and reporting research misconduct (Chapter 2) and conflicts of interest (Chapter 5). They must approve and manage all research budgets, ensure that laboratory safety rules are followed, and follow established practices for the responsible use of hazardous substances in research. They must also provide training for researchers who use animal or human subjects in their research and for individuals supported on NIH training grants.

To help manage their responsibilities, most research institutions have research offices/officers and institutional research policies. Both provide excellent sources of guidance for responsible conduct in research, since both are the products of the institution's efforts to clarify its own responsibilities. In addition, institutional policies are often more comprehensive than Federal and state policies since they must encompass the full panoply of institutional responsibilities. So, for example, many research institutions have more comprehensive definitions of research misconduct than the Federal Government to cover other practices that can undermine the integrity of research, such as the

deliberate violation of research regulations, abuses of confidentiality, and even the failure to report misconduct (discussed in Chapter 2). Most also require institutional review for more human subjects research than is required by Federal regulation.

Large research institutions usually have Web sites that contain some or all of the following information:

- ✓ **copies of institutional research policies,**
- ✓ **links to state and Federal policies,**
- ✓ **required forms and instructions for completing them,**
- ✓ **responsible conduct of research training programs, and**
- ✓ **lists of key personnel.**

There is, of course, little or no coordination across different research institutions, so the information on an institution's Web site pertains only to that institution. But if you are looking for a comprehensive set of rules of the road for responsible research, check your home institution's research administration Web site or one from a comparable institution.

Stanford University - Research Policy Handbook Document 2.1

Title:	Principles Concerning Research
Originally issued:	Dec 8, 1971
Current version:	Dec 8, 1971
Classification:	Stanford University Policy
Summary:	Presents broad principles to guide the research enterprise and assure the integrity of scholarly inquiry at Stanford University.

http://www.stanford.edu/dept/DoR/rph/2-1.html

1d. Personal responsibility

As important as rules of the road are for the responsible conduct of research, they have two important limitations. First, rules generally set minimum standards for behavior rather than strive for the ideal. The rules say that you can drive at 65 miles per hour over a stretch of road, but there may be times or circumstances when 55 would be better. If you use human subjects in research, you must follow specific rules, but there may be situations in which you should strive for a higher standard of conduct. Responsible research requires more than simply following rules.

Second, rules will not resolve some of the personal conflicts and moral dilemmas that arise in research. Journals have rules against listing undeserving authors on papers (individuals who have not made significant contributions to the research described in the paper). These same rules do not tell you what to do if the undeserving author can have a significant influence on your career. Rules also cannot replace the critical reasoning skills needed to assess ethically controversial human or animal experiments or conflicts of interest. Researchers will face ethical dilemmas in research. They should be able to recognize these dilemmas and know how to resolve them (discussed in Chapter 11).

The rules of the road for research therefore need to be supplemented with good judgment and a strong sense of personal integrity. When meeting deadlines, you can cut corners by filling in a few missing data points without actually running the experiments or adding a few references to your notes that you have not read. You can resist sharing data with colleagues or leave some information on method out of a publication to slow down the competition. You can ignore your responsibilities to students or a mentor in order to get your own work done. You can do all of these things and more, but should you?

In the final analysis, whatever decision you make when you confront a difficult decision about responsibility in research, you are the one who has to live with the consequences of that decision. If you are uncertain whether a particular course of action is responsible, subject it to one simple test. Imagine what you are preparing to do will be reported the next day on the front page of your local newspaper. If you are comfortable having colleagues, friends, and family know what you did, chances are you acted responsibly, provided, of course, you also understand your responsibilities as a researcher, as described in the rules of the road covered in the rest of the *ORI Introduction to RCR*.

Questions for discussion

1. **Is research a profession?**
2. **How do researchers learn about the responsible conduct of research?**
3. **How should researchers learn about the responsible conduct of research?**
4. **What factors influence researchers' attitudes toward the responsible conduct of research?**
5. **How is integrity in research monitored? Is self-regulation of integrity in research effective?**

Resources

Policies, Reports, and Policy Statements

Association of American Medical Colleges. *Developing a Code of Ethics in Research: A Guide for Scientific Societies*, Washington, DC: AAMC, 1997. (available at: https://services.aamc.org/Publications/index.cfm?fuseaction=Product.displayForm&prd_id=28&prv_id=17&cfid=1&cftoken=28C93522-2734-4BCC-92A8B871AE78AE22/)

Institute of Medicine. *The Responsible Conduct of Research in the Health Sciences*, Washington, DC: National Academies of Science, 1989. (available at: http://www.nap.edu/books/0309062373/html)

National Academy of Sciences. Committee on the Conduct of Science. *On Being a Scientist: Responsible Conduct in Research,* 2nd ed. Washington, DC: National Academy Press, 1995. (available at: http://www.nap.edu/readingroom/books/obas/)

National Institutes of Health. *Guidelines for the Conduct of Research in the Intramural Research Programs at NIH*, 1997. (available at: http://www.nih.gov/campus/irnews/guidelines.htm)

Sigma Xi. *Honor in Science*, New Haven, CN: Sigma Xi, 1984. (available at: http://www.sigmaxi.org/resources/publications/)

General Information Web Sites

American Association for the Advancement of Science. *Integrity in Scientific Research*. http://www.aaas.org/spp/video/ (Information on five videos on integrity in research.)

Bird, S, Spier, R, eds. *Science and Engineering Ethics*, 1995 ff. http://www.springer.com/east/home?SGWID=5-102-70-173705003-0&changeHeade/ (Includes articles on the responsible conduct of research.)

Collaborative Institutional Training Initiative (CITI), Course in the Responsible Conduct of Research. *Home Page.* https://www.citiprogram.org/rcrpage.asp?affiliation=100/

National Institutes of Health. *Research Conduct and Ethics Instruction Materials*. http://www1.od.nih.gov/oir/sourcebook/ResEthicsCases/cases-toc.htm

North Carolina State University. *Research & Professional Ethics Program*. http://www.fis.ncsu.edu/Grad/ethics/

Office of Research Integrity. *Home Page.* http://ori.hhs.gov/

Online Ethics Center for Engineering and Science. *Home Page.* http://onlineethics.org/

RCR Education Consortium. *Home Page*. http://rcrec.org/

Shamoo, AE, ed. *Accountability in Research: Policies and Quality Assurance*, 1994 ff. http://www.tandf.co.uk/journals/titles/08989621.html (Includes articles on research integrity and related issues.)

Additional Reading

Barnbaum, DR, Byron, M. *Research Ethics: Text and Readings*, Upper Saddle River, NJ: Prentice Hall, 2001.

Beach, D. *The Responsible Conduct of Research*, New York: VCH Publishers, 1996.

Bulger, RE, Heitman, E, Reiser, SJ. *The Ethical Dimensions of the Biological and Health Sciences*, 2nd ed. Cambridge, UK; New York: Cambridge University Press, 2002.

Elliott, D, Stern, JE. *Research Ethics: A Reader*, Hanover, NH: Published by University Press of New England for the Institute for the Study of Applied and Professional Ethics at Dartmouth College, 1997.

Frankel, M, Bird, S. eds. "The Role of Scientific Societies in Promoting Research Integrity," *Science and Engineering Ethics* 9, 2 (2003).

Grinnell, F. *The Scientific Attitude*, 2nd ed. New York: The Guilford Press, 1992.

Korenman, SG, Shipp, AC. *Teaching the Responsible Conduct of Research through a Case Study Approach: A Handbook for Instructors*, Washington, DC: Association of American Medical Colleges, 1994.

Macrina, FL. *Scientific Integrity: An Introductory Text with Cases*, 2nd ed. Washington, DC: ASM Press, 2000.

Penslar, RL. *Research Ethics: Cases and Materials*, Bloomington: Indiana University Press, 1995.

Resnik, DB. *The Ethics of Science : An Introduction, Philosophical Issues in Science*, London; New York: Routledge, 1998.

Shamoo, AE, Resnik, DB. *Responsible Conduct of Research*, New York: Oxford University Press, 2003.

Sigma Xi. *The Responsible Researcher: Paths and Pitfalls*, 1999.

Stern, JE, Elliott, D. *The Ethics of Scientific Research: A Guidebook for Course Development*, Hanover, NH: University Press of New England, 1997.

Whitbeck, C. *Ethics in Engineering Practice and Research*, Cambridge; New York: Cambridge University Press, 1998.

When research misconduct becomes public

Chapter 2. Research Misconduct

Public concern about misconduct in research first surfaced in the early 1980's following reports of cases of egregious misbehavior. One researcher republished under his own name dozens of articles previously published by others. Other researchers in one way or another falsified or fabricated research results. To make matters worse, it seemed as if research institutions sometimes ignored or deliberately covered up problems rather than investigate them. Eventually Congress stepped in and required Federal agencies and research institutions to develop research misconduct policies.

Research misconduct policies provide guidance on responsible conduct in three areas. They:

- ✓ **establish definitions for misconduct in research,**
- ✓ **outline procedures for reporting and investigating misconduct, and**
- ✓ **provide protection for whistleblowers (persons who report misconduct) and persons accused of misconduct.**

Together, the definitions of and procedures for handling allegations of misconduct in research form an initial foundation for effective self-regulation in research.

Although Federal policies technically apply only to federally funded research, many research institutions apply Federal research misconduct policies to all research. Many research institutions have also broadened the basic Federal definitions to include other inappropriate practices. In combination, Federal and institutional research misconduct policies define research practices that researchers must avoid. Failure to do so can result in the termination of employment or ineligibility to receive Federal funding.

Case Study

Dr. José M. is beginning his fifth year as an independent researcher. His work is going well. He has published a number of important articles and secured a large grant for future work. Based on this progress, he expects his pending promotion review to proceed without problems.

Late one afternoon a graduate student hands José two papers written by a senior colleague in his department. She has circled graphs in each of the papers that are clearly the same but reported as representing two different experiments. After checking the graphs carefully and reviewing the supporting data, José agrees that something is wrong. The senior colleague, who will almost certainly be a member of his promotion review, has either made a careless mistake or falsified information in a publication. What should he do?

Ask the senior colleague about the graphs?
Bring the publications to the attention of his department chair?
Report the problem anonymously to a research administrator?
Encourage the graduate student to report the problem?
Nothing, at least until after the promotion review is completed?

2a. Federal research misconduct definition and policies

After a decade of sometimes spirited debate, in December 2000 the Office of Science and Technology Policy (OSTP) in the Executive Office of the President adopted a Federal Policy on Research Misconduct. The OSTP Policy is in most respects similar to earlier ones adopted by the Public Health Service (PHS) and the National Science Foundation (NSF), but it did recommend some significant changes to the definition of research misconduct. When it is finally implemented by all government research agencies (the target date of December 2001 was not met), all federally funded researchers will be subject to a uniform definition of research misconduct.

Definition. The OSTP Policy defines "research misconduct" as "fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results" (see accompanying box for details). It also sets the legal threshold for proving charges of misconduct.

To be considered research misconduct, actions must:

- ✓ **represent a "significant departure from accepted practices";**
- ✓ **have been "committed intentionally, or knowingly, or recklessly"; and**
- ✓ **be "proven by a preponderance of evidence."**

These further stipulations limit the Federal Government's role in research misconduct (fabrication, falsification, or plagiarism) to well-documented, serious departures from accepted research practices.

When using the common Federal definition to discuss research misconduct, it is important to understand that it establishes a minimum standard for measuring acceptable behavior, not a standard for judging all research behavior. In particular, it does not imply that all other behaviors are acceptable. It also does not encompass criminal behavior, personal disputes, violations of grant management policies or other unacceptable behaviors not unique to research, such as discrimination or harrassment. The government's main concern in establishing this definition is to assure that publicly funded research is accurate and appropriately represented by clearly stating that three practices, commonly referred to as "FFP," are wrong.

Federal Research Misconduct Policy.

I. Research Misconduct Defined. Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- Research misconduct does not include differences of opinion.

http://ori.hhs.gov/policies/fed_research_misconduct.shtml

Reporting and investigation. Federal misconduct policy assumes that researchers and research institutions bear the primary responsibility for reporting and investigating allegations of misconduct. This assumption is consistent with the position, strongly supported by most researchers, that research is a profession and should regulate its own conduct (see Chapter 1).

Successful professional self-regulation depends on conscientious community participation. For individual researchers, this means they must assume responsibility for their own actions, take misconduct seriously, and report apparent misconduct by other researchers.

Every institution that receives PHS funding must have procedures in place for receiving and investigating reports of research misconduct. These procedures must include:

- ✓ **the designation of individuals who are authorized to receive and investigate allegations of misconduct,**
- ✓ **provisions for an initial inquiry to determine whether the allegations have any merit,**
- ✓ **provisions for a formal investigation to reach conclusions about the truth of the allegations,**
- ✓ **the designation of an individual who is authorized to weigh (adjudicate) the conclusions reached in the investigation and impose administrative actions to redress the misconduct (sanctions) or take steps to vindicate the person charged, and**
- ✓ **provisions for reporting findings to ORI.**

Researchers should be familiar with these procedures and their institution's definition of research misconduct (discussed below).

Basic protections. Researchers who commit misconduct place their careers at risk. The Federal Government can debar researchers who commit misconduct from receiving Federal funds for a specified period of time. In most

instances, research institutions also take their own actions, such as terminating a researcher's employment or requiring supervision of future research activities. By like token, making allegations of misconduct—blowing the whistle—can sometimes place a whistleblower's career at risk. Although by law institutions must not retaliate against whistleblowers who report in good faith, they sometimes do.

The new common Federal policy provides guidelines for protecting both parties—the whistleblower and the respondent—in research misconduct investigations. As a general rule, research misconduct allegations must not be made public until they have been fully investigated and confirmed. There are, however, exceptions to this rule. If the misconduct could pose a threat to public health or safety, such as misconduct in a clinical trial, it must immediately be brought to the attention of the person heading the trial, the person with oversight authority, or both. ORI and the Federal sponsor must also be notified immediately. In such cases, the names of the persons charged should remain confidential, but steps must be taken to safeguard the subjects in the trial.

Similarly, research institutions and researchers must not in any way penalize or take action against individuals who report research misconduct in good faith. Even if accusations are not sustained, as long as they are brought in good faith, informants must be protected and given support since they play a vital role in professional self-regulation.

2b. Institutional research misconduct policies

Institutional research misconduct policies generally follow the pattern recommended by the Federal Government, but almost always include some additional elements that for one reason or another are assumed to have local importance. This is particularly true for the definition of research misconduct. Institutional definitions must include some

University Research Misconduct Policies

Rice University. Research misconduct may include the fabrication/ falsification of data, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, reviewing, or reporting research. It also encompasses the failure to comply with federal requirements for protecting researchers, human and animal subjects, and the public. In general, gross negligence of research standards and any action taken with the intent to defraud are considered forms of research misconduct. It does not, however, include honest error or honest differences in interpreting or judging data.

http://professor.rice.edu/professor/Research_Misconduct.asp

University of New Mexico. A researcher commits research misconduct under UNM's policy if he or she fabricates or falsifies data or research results or plagiarizes another person's ideas or work. Research misconduct also occurs if a researcher wantonly disregards truth or objectivity or fails to comply or attempt to comply with legal requirements governing the research; however, other University policies and procedures will be followed in resolving such cases. It is important to understand that research misconduct is not a mistake in reasoning, disagreeing with recognized authorities, misinterpreting results, an error in planning or carrying out an experiment, or an oversight in attribution.

http://www.unm.edu/%7Ecounsel/research/policies/2464.pdf

version of FFP, but then sometimes add other practices that also constitute misconduct in the particular local setting. Thus, depending on where a researcher works, any of the following practices could be reported as misconduct in research.

Violation of Federal rules. As will be discussed in later chapters, research is subject to many rules or regulations other than research misconduct policies. Although the violation of a research rule or regulation is not considered misconduct under the common Federal definition of research misconduct, many research institutions explicitly state that the violation of any research regulation is research misconduct.

Abuse of confidentiality. Confidentiality plays a number of important roles in research. Most peer review is done confidentially (see Chapter 10). Researchers also share ideas

with colleagues with the understanding that they will not be used or made public without permission (see Chapter 8). Federal regulations, such as the Health Insurance Portability and Accountability Act of 1996 (see Chapter 3), impose confidentiality requirements on human subjects research. The abuse of confidentiality may not undermine the validity of research data, but it can undermine the integrity of the research process. Therefore, some institutions include such abuses under their definition of research misconduct.

Authorship and publication violations. As will be discussed in Chapter 9, there are well-established guidelines for getting credit for work done (authorship) and making research results known (publication). Some violations of these guidelines do not rise to the level of FFP, as defined in Federal policy. For example, the Federal Government usually does not get involved in disputes over authorship or investigate charges of trivial publication (dividing the results of a single experiment into multiple publications so that there are more to list on a résumé). However, given the importance of the integrity of the research record, some research institutions include authorship and publication violations in their misconduct policies.

Failure to report misconduct. Failure to report many crimes can be considered a crime and result in penalties. This is particularly true if failure to report a crime puts other individuals or society at risk. Research misconduct can put individuals at risk, if, for example, the misconduct affects information that is used for making medical or public decisions. Failure to report research misconduct also undermines professional self-regulation. Therefore, some research institutions include failure to report misconduct in their research misconduct policies.

Obstruction of investigations and retaliation. To emphasize the importance of research misconduct investigations, some institutions also include obstruction

of investigations and retaliation against whistleblowers under research misconduct.

Other practices. Early in the evolution of Federal research misconduct policies, the National Science Foundation (NSF) and the Public Health Service (PHS) included a broad provision in their definitions to catch other practices that "seriously deviate" from commonly accepted practices. NSF in particular felt that FFP left out behaviors that could undermine the integrity of the research it funded. While the "serious deviations" clause no longer exists in the common Federal definition, except as a standard for judging FFP, it can still be found in some institutional policies. Researchers therefore need to be aware of the fact that in some settings, actions that seriously deviate from commonly accepted practices can be considered research misconduct.

2c. Putting research misconduct into perspective

Research misconduct has understandably received considerable public attention. Researchers who act dishonestly waste public funds, harm the research record, distort the research process, undermine public trust, and can even adversely impact public health and safety. Research misconduct policies, whether Federal, state, institutional, or professional, identify seriously inappropriate behaviors and establish procedures for dealing with them.

Judged on the basis of the number of confirmed cases, misconduct apparently is not common in research. Over the last decade, PHS and NSF combined have averaged no more than 20 to 30 misconduct findings a year. This puts the annual rate of misconduct in research at or below 1 case for every 10,000 researchers. However, before making too much of this assessment, two important cautions need to be kept in mind.

First, the number of confirmed cases is probably less than the number of actual cases. Underreporting is to be

expected, as it is in criminal and other types of inappropriate behavior. Moreover, several studies have suggested that researchers do not report suspected misconduct, even though they should (see Korenman, Additional Reading). Since every case of misconduct can potentially undermine public support for research, researchers should take their responsibility to look out for and report research misconduct seriously.

Second, the responsibility to avoid misconduct in research is a minimum standard for the responsible conduct of research, so the fact that most researchers do not engage in research misconduct does not necessarily imply that the level of integrity in research overall is high. Responsible research requires careful attention to many other expectations for appropriate practice, as discussed in the remainder of the *ORI Introduction to RCR*.

Questions for discussion

1. **Should other practices besides fabrication, falsification, and plagiarism be considered misconduct in research?**
2. **Is it fair to use "significant departure from accepted practices" to make judgments about a researcher's behavior?**
3. **Should researchers report misconduct if they are concerned that doing so could adversely impact their career?**
4. **What evidence is needed to demonstrate that a researcher committed misconduct "intentionally, or knowingly, or recklessly"?**
5. **What are appropriate penalties for different types of misconduct?**

Resources

Policies, Reports, and Policy Statements

Department of Health and Human Services. Commission on Research Integrity. *Integrity and Misconduct in Research*, Washington, DC: Health and Human Services, 1995. (available at: http://ori.hhs.gov/documents/report_commission.pdf)

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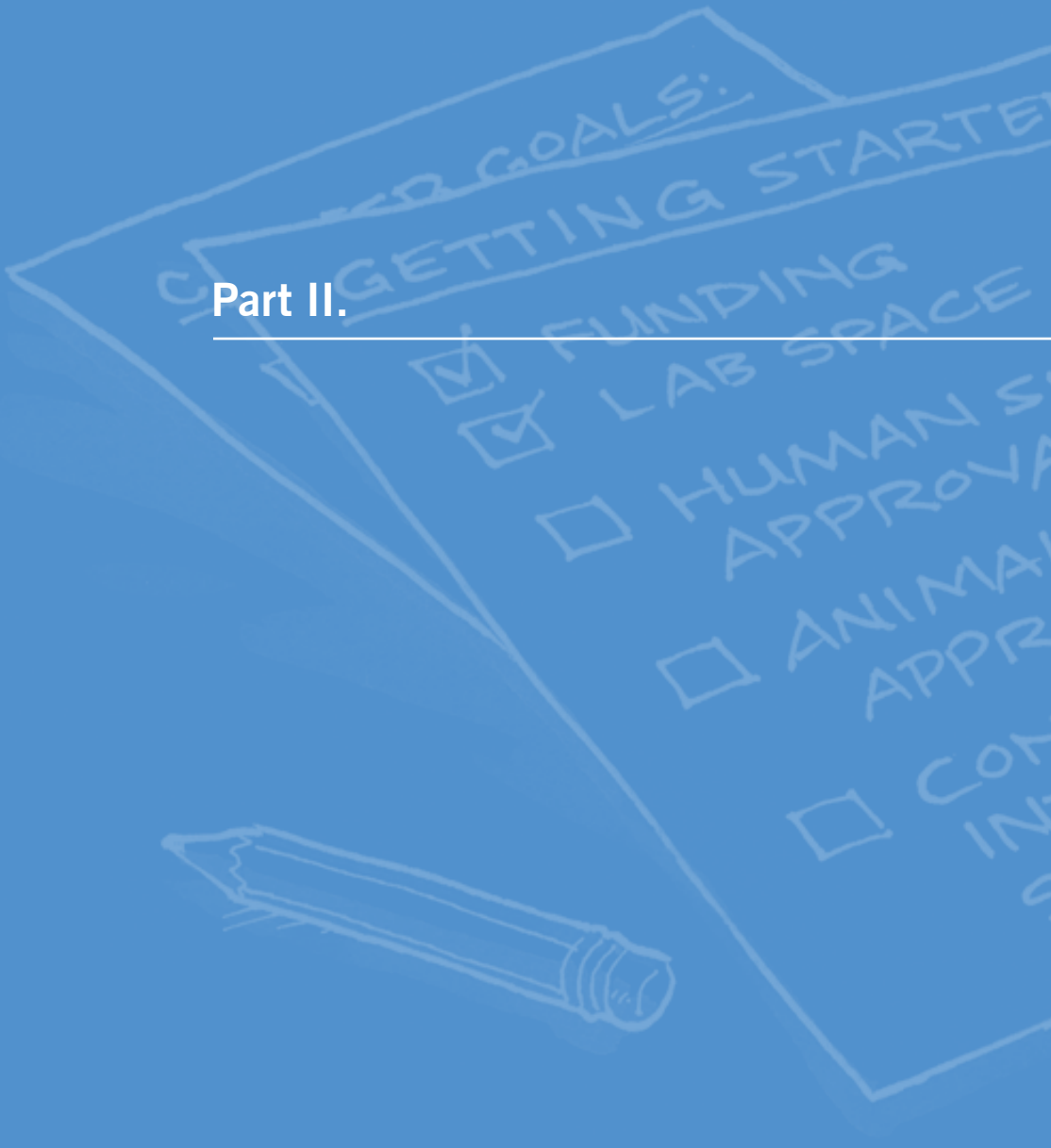
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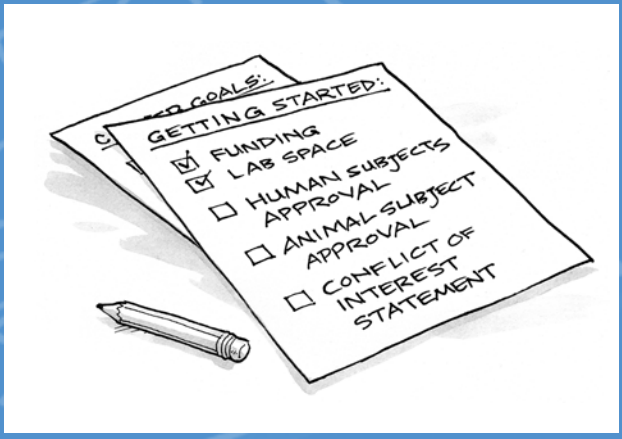
Part II.

Planning Research



Part II: Planning Research

RESEARCH BEGINS WITH IDEAS, QUESTIONS and hypotheses. What causes this particular phenomenon? What would happen if…? How can I find out…?

Researchers think first about problems and ways to solve them and about the resources they will need to perform experiments.

Planning for any project should include the consideration of responsibilities. In some cases, work cannot begin until it has been approved. In other cases, confronting potential problems before they arise can help ensure that they do not turn into real problems later.

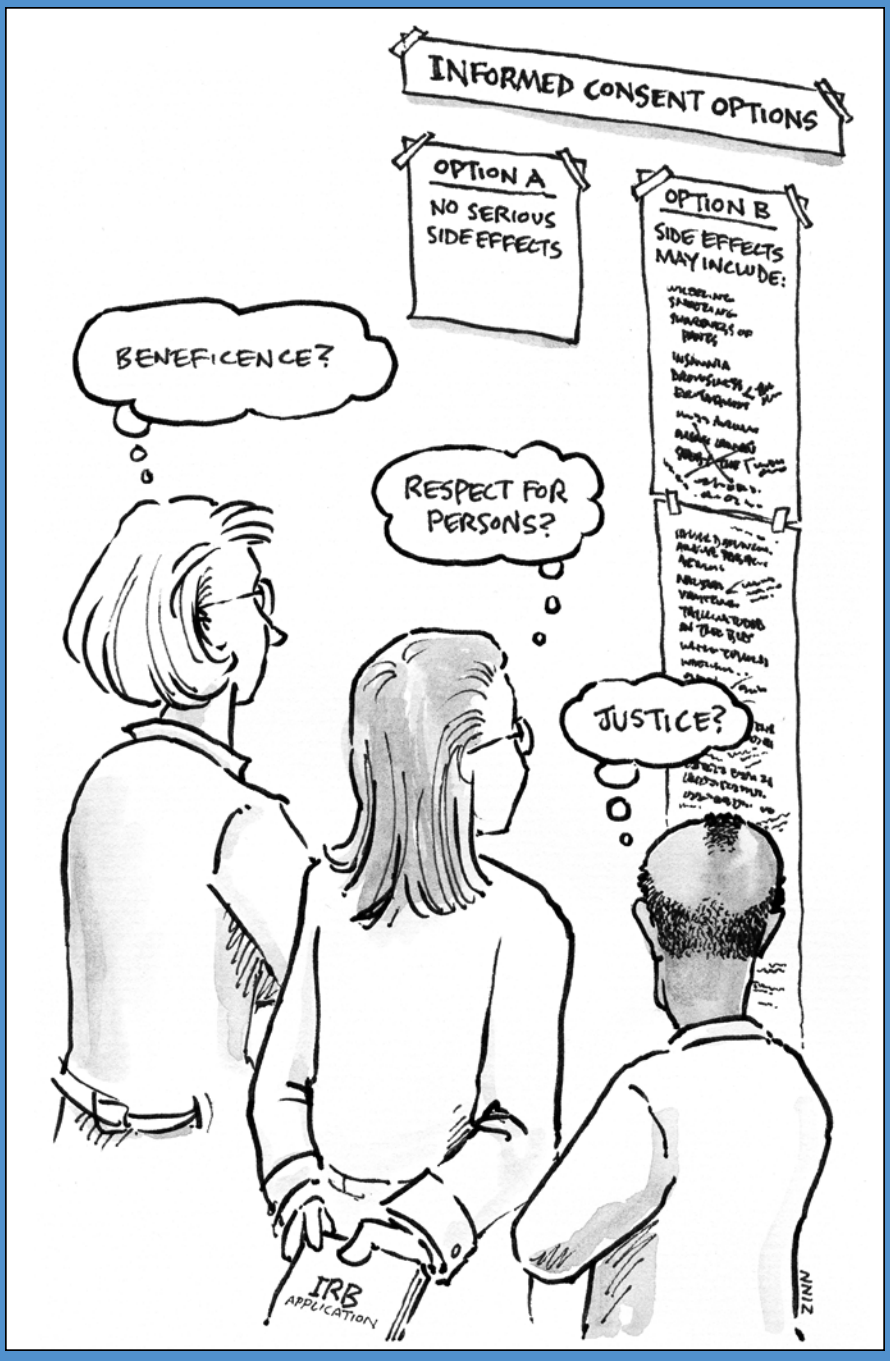
The chapters in this section cover three areas where appropriate planning and approval are essential:

Chapter 3, The Protection of Human Subjects, describes the regulations covering the use of humans in research.

Chapter 4, The Welfare of Laboratory Animals, describes similar regulations for animals used in research.

Chapter 5, Conflicts of Interest, discusses what researchers should do when their interests are or appear to be in conflict.

Planning is essential in other areas as well. Responsible research administration, the safe use of hazardous materials, and the fair treatment of students and employees should be addressed early in any project. However, with the use of humans and animals and, increasingly, the potential influence of conflicting interests, there is no choice. These responsibilities must be fully addressed before the first subject is contacted, the first animal purchased, or any agreement signed.



Designing a responsible informed consent form

Chapter 3. The Protection of Human Subjects

The use of human subjects in research benefits society in many ways, from contributing to the development of new drugs and medical procedures to understanding how we think and act. It also can and has imposed unacceptable risks on research subjects. To help ensure that the risks do not outweigh the benefits, human subjects research is carefully regulated by society.

Case Study

Two weeks into the new semester, the professor in Mary's course on family health gives the class a special assignment that was not on the course syllabus. Over the next week, everyone in the class is to talk with three classmates who are not in the course about the way their families deal with medical emergencies and chronic illness. Next week they should come to class prepared to report on their interviews. The Professor warns them, however, that in talking about their conversations they should not mention any names to protect the privacy of their classmates.

The assignment makes Mary uneasy. In her basic psychology course last semester she learned about some of the rules pertaining to the use of human subjects in research. However, when she raises her concerns with her professor, he assures her that her informal conversations with classmates are not research and therefore not subject to regulation. Moreover, since she will not be mentioning any names, there are no privacy issues to worry about.

Should Mary be content with these assurances and conduct the interviews?

If she still has concerns, where should she turn for advice?

Did the professor act properly in giving this assignment to the class?

Investigators who conduct research involving humans that is subject to regulation must comply with all relevant Federal regulations as well as any applicable state and local laws, regulations, and policies related to the protection of human subjects. They are also expected to follow other relevant codes that have been formulated by professional groups. To meet these responsibilities requires, among other things:

- ✓ **knowing what research is subject to regulation,**
- ✓ **understanding and following the rules for project approval,**

- ✓ getting appropriate training, and
- ✓ accepting continuing responsibility for compliance through all stages of a project.

If you expect to use or study living humans in your research, no matter how harmless that use may seem, and receive Federal funding, familiarize yourself with your responsibilities and check with someone in a position of authority before making any contacts or undertaking any work.

3a. Federal regulations

Society protects the welfare of individuals in many ways, but it did not specifically address the issue of the welfare of research subjects until after World War II. Following the War, widespread concerns about atrocities committed during the War in the name of research led to the formulation of a code for human subjects research known as the Nuremberg Code (1947). Although not binding on researchers, the Nuremberg Code and the later Declaration of Helsinki (1964; latest revision and clarification, 2002) provided the first explicit international guidelines for the ethical treatment of human subjects in research.

The Nuremberg Code and Declaration of Helsinki did not put an end to unethical human subjects research. During the Cold War, U.S. researchers tested the effects of radiation on hospital patients, children, and soldiers without obtaining informed consent or permission to do so. Through the 1950's and 1960's, well after antibiotics effective for the treatment of syphilis were discovered, scores of African-American males in a long-term syphilis study (conducted by the U.S. Public Health Service in Tuskegee, Alabama) were not offered treatment with the new drugs so that researchers could continue to track the course of the disease. These and other questionable practices raised serious public concern and led eventually to government regulation.

Excerpts, Nuremberg Code (1947)

1. The voluntary consent of the human subject is absolutely essential.
2. The experiment should be such as to yield fruitful results for the good of society.
3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

http://www.hhs.gov/ohrp/references/nurcode.htm

To prevent these and similar abuses from continuing, in 1974 Congress required the Department of Health, Education and Welfare (HEW, currently Health and Human Services—HHS) to clarify its rules for the use of human subjects in research. With this mandate in hand, HEW codified its procedures under Title 45 of the Code of Federal Regulations, Part 46 (45 CFR 46). (At roughly the same time, the FDA codified its rules for human subjects research under 21 CFR 50 and 56.)

Congress also called in 1974 for the creation of a National Commission for the Protection of Human Subjects of

Biomedical and Behavioral Research. During the 4 years it met, the Commission issued a number of reports on the protection of research subjects and recommended principles for judging the ethics of human subjects research (discussed below).

In 1991 most Federal departments and agencies that conduct or support human subjects research adopted a common set of regulations for the protection of human subjects referred to as the "Common Rule" (45 CFR 46, Subpart A). Additional requirements on three sensitive research areas are also included in 45 CFR 46:

- ✓ **Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research.**
- ✓ **Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects.**
- ✓ **Subpart D – Additional Protections for Children Involved as Subjects in Research.**

Together, 45 CFR 46, Subparts A-D, provide a comprehensive articulation of society's expectations for the responsible use of human subjects in research.

Authority for enforcing the HHS regulations for the protection of human subjects who participate in research conducted or supported by HHS now rests with the Office for Human Research Protections (OHRP) in the Office of Public Health and Science (OPHS). If you have specific questions about the Federal requirements for the protection of human subjects, contact your local institutional officials, OHRP (for research conducted or supported by HHS), or appropriate officials at the department or agency conducting or supporting the research.

3b. Definitions

Researchers are responsible for obtaining appropriate approval before conducting research involving human subjects. The need for approval rests on three seemingly obvious but not always easy-to-interpret considerations: 1) whether the work qualifies as research, 2) whether it involves human subjects, and 3) whether it is exempt. All three considerations are discussed in the Common Rule and guide decisionmaking about the use of human subjects in research. The authority to make decisions about the need for approval rests with the Institutional Review Board (IRB, discussed below) or other appropriate institutional officials.

Research. The Common Rule defines research as "systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge" (§ 46.102(d), see box, next page, for full definition). This means that a project or study is research if it:

- ✓ **is conducted with the intention of drawing conclusions that have some general applicability and**
- ✓ **uses a commonly accepted scientific method.**

The random collection of information about individuals that has no general applicability is not research. Scientific investigation that leads to generalizable knowledge is.

Human subjects. Human subjects are "living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information" (§ 46.102(f), see box, next page, for full definition). Humans are considered subjects and covered by Federal regulations if the researcher:

- ✓ **interacts or intervenes directly with them, or**
- ✓ **collects identifiable private information.**

45 CFR 46. 102
Protection of Human Subjects – Definitions

(d) **Research** means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

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(f) **Human subject** means a living individual about whom an investigator (whether professional or student) conducting research obtains

(1) data through intervention or interaction with the individual, or

(2) identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

If one of these two conditions applies and if the project or study qualifies as research, then institutional approval is needed before any work is undertaken.

Exempt research. Some studies that involve humans may be exempt from the requirements in the Federal regulations. Studies that fall into the following categories could qualify for exemptions, including:

- ✓ **research conducted in established or commonly accepted educational settings;**
- ✓ **research involving the use of educational tests;**

- ✓ **research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if unidentifiable or publicly available;**
- ✓ **research and demonstration projects which are conducted by or subject to the approval of department or agency heads; or**
- ✓ **taste and food quality evaluation and consumer acceptance studies.**

It is critically important to note, however, that decisions about whether studies are exempt from the requirements of the Common Rule must be made by an IRB or an appropriate institutional official and not by the investigator.

3c. IRB membership and deliberations

Federally funded research that uses human subjects must be reviewed and approved by an independent committee called an Institutional Review Board or IRB. The IRB provides an opportunity and place for individuals with different backgrounds to discuss and make judgments about the acceptability of projects, based on criteria set out in the Common Rule.

Under the Common Rule, IRBs must have at least five members and include at least one scientist, one non-scientist, and "one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution" (§ 46.107(d)). IRBs have authority to approve, require modification of (in order to secure approval), and disapprove all research activities covered by the Common Rule. They also are responsible for conducting continuing review of research at least once per year and for ensuring that proposed changes in approved research are not initiated

without IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subject.

IRBs weigh many factors before approving proposals. Their main concern is to determine whether (§ 46.111(a)):

- ✓ risks to subjects are minimized;
- ✓ risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result;
- ✓ selection of subjects is equitable;
- ✓ informed consent will be sought from each prospective subject or the subject's legally authorized representative;
- ✓ informed consent will be appropriately documented;
- ✓ when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects; and
- ✓ when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Researchers should consider each of these issues before completing their research plan and submitting it to an IRB for approval.

Making decisions about whether human subjects will be treated fairly and appropriately or given adequate information requires judgments about right and wrong (moral judgments). In the 1979 Belmont Report, the National Commission recommended three principles for making these judgments:

- ✓ **respect for persons** and their right to make decisions for and about themselves without undue influence or coercion from someone else (the researcher in most cases);
- ✓ **beneficence** or the obligation to maximize benefits and reduce risks to the subject; and

The Belmont Report (1979)
Ethical Principles and Guidelines for the Protection of Human Subjects of Research

SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, thereby creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles.

http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm

✓ **justice** or the obligation to distribute benefits and risks equally without prejudice to particular individuals or groups, such as the mentally disadvantaged or members of a particular race or gender.

While this list does not exhaust the principles that can be used for judging the ethics of human subjects research, it has nonetheless been accepted as a common standard for most IRB deliberations. Knowing this, researchers should spend time considering whether their work does provide adequate respect for persons, appropriately balances risks and benefits, and is just.

3d. Training

To help assure that researchers understand their responsibilities to research subjects, the National Institutes of Health (NIH) currently requires

> …education on the protection of human research participants for all investigators submitting NIH applications for grants or proposals for contracts or receiving new or non-competing awards for research involving human subjects. (http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html)

Many institutions, including NIH, provide this training through special Web-based programs that summarize essential information and in some cases require some evidence of mastery. A description of the education program and who was trained must be included in applications for grants and contracts before they will be considered.

3e. Continuing responsibility

Once a project has been approved by an IRB, researchers must adhere to the approved protocol and follow any additional IRB instructions. This, unfortunately, is where a few researchers and institutions have occasionally run into problems and temporarily had their "assurance" (FWA - Federalwide Assurance) suspended. The continuing responsibilities that researchers have include:

✓ **enrolling only those subjects that meet IRB approved inclusion and exclusion criteria,**

Federalwide Assurance (FWA)

The Federal Policy (Common Rule) for the protection of human subjects at Section 103(a) requires that each institution "engaged" in Federally supported human subject research file an "Assurance" of protection for human subjects. The Assurance formalizes the institution's commitment to protect human subjects. The requirement to file an Assurance includes both "awardee" and collaborating "performance site" institutions.

Under the Federal Policy (Common Rule) at Section 102(f) awardees and their collaborating institutions become "engaged" in human subject research whenever their employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain, release, or access individually identifiable private information for research purposes.

In addition, awardee institutions are automatically considered to be "engaged" in human subject research whenever they receive a direct HHS award to support such research, even where all activities involving human subjects are carried out by a subcontractor or collaborator. In such cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award. The awardee is also responsible for ensuring that all collaborating institutions engaged in the research hold an OHRP approved Assurance prior to their initiation of the research.

http://www.hhs.gov/ohrp/assurances/assurances_index.html

- ✓ **properly obtaining and documenting informed consent,**
- ✓ **obtaining prior approval for any deviation from the approved protocol,**
- ✓ **keeping accurate records, and**
- ✓ **promptly reporting to the IRB any unanticipated problems involving risks to subjects or others.**

While research institutions are increasingly monitoring the progress of human subjects research, the primary responsibility for conducting experiments as approved still lies with the individual researchers and staff who conduct the experiments.

3f. Ethical issues

Despite the many rules governing research with humans, tough choices continually arise that have no easy answers.

Informed consent. It is widely agreed that research subjects should be fully informed about experiments in which they may participate and give their consent before they enroll. However, some subjects, such as children, some adults with impaired decisionmaking capacity, and some critically ill patients, cannot give informed consent, either because they are not old enough to understand the information being conveyed or because they have lost their ability to understand.

These and other problems could be eliminated by forbidding researchers to do studies that raise difficult questions about respect for persons, beneficence, and justice, but this would make it difficult or even impossible to get some crucial information needed to make informed decisions about medicine and public health. Since children do not respond to medicines in the same way as adults, it is important to include children in some clinical trials. However, it is not easy to decide when they should be included and how consent can/should be obtained.

Right to withdraw. It is widely agreed that research subjects should have the right to withdraw from experiments at any time, but in some cases they cannot. In the final stages of development, mechanical hearts are tested on patients whose own heart is about to fail. But if it has not failed, and once the mechanical heart replaces the weakened heart, there is no turning back. The patient can technically withdraw from the experiment and undergo no further testing, but he or she cannot withdraw from the conditions imposed by the experiment, no matter how distressing living with the mechanical heart might be. Knowing this, under what conditions should these experiments be allowed?

Risk without benefit. In one recent experiment, researchers wanted to test whether a common surgical procedure used to relieve arthritis pain had any benefits. To gather information about benefits they designed a clinical trial in which subjects in the control group received sham surgery. An operation was performed, but the common surgical procedure was not performed.

The researchers in this case complied with all regulations, which included thorough IRB review. None of the patients experienced any adverse effects, and the study concluded that the common surgical procedure did not provide significant benefits. However, since surgery always involves some risk, the subjects in the control group were placed at risk without any expectation that they would benefit. Should this be allowed, and if so, under what circumstances?

These and other questions must ultimately be answered by IRBs during the review process. Researchers who serve on IRBs need additional training to help them deal with the growing complexities of biomedical, social, and behavioral research. Researchers who use human subjects in research should seriously consider having some formal training in bioethics so that they can participate in the critical reasoning process needed to respond to the complex moral issues raised by the use of human subjects in research.

Questions for discussion

1. Why should some research on humans be exempted from regulation?
2. What other criteria could be used to identify necessary members for IRBs?
3. What should subjects know about proposed research and their protection before they enroll as subjects?
4. What other principles could be used for evaluating the ethics of human subjects research besides respect for persons, beneficence, and justice?
5. Should subjects be allowed to enroll in experiments that either promise no direct benefit to them or cannot provide them with the opportunity to withdraw completely?

Resources

Policies, Reports, and Policy Statements

Directives for Human Experimentation: Nuremberg Code. 1949. (available at: http://www.hhs.gov/ohrp/references/nurcode.htm)

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How do researchers decide which animals are used in research?

4. The Welfare of Laboratory Animals

Animal research is as carefully regulated as human research, but for different reasons. With humans, regulation stems from the need to assure that the benefits all humans gain from human research do not impose unacceptable burdens on some research participants. Animals may benefit from the information gained through animal experimentation and some research with animals is conducted specifically for the purpose of improving animal health (veterinary medicine and animal husbandry research). But most animal research is conducted primarily for the benefit of humans, not animals. Moreover, unlike humans, animals cannot consent to participate in experiments or comment on their treatment, creating special needs that should be taken into consideration in their care and use.

The special needs of animals have evolved over time into policies for the appropriate care and use of all animals

Case Study

After many years using fish and frogs to study brain function, Dr. Ruth Q. encountered some problems that can be explored only using new animal models. For the near future, she plans to turn to mice or rats, but eventually may have to do some research using cats or dogs. To help prepare the way for this new research, she decides to put a note about her plans in the progress report for her current research grant, which runs out next year.

The day after she gave a draft of the progress report to her long-time research assistant, he came to her with a troubled look on his face. Although he never told her, the main reason he applied for the job in her laboratory many years ago was the fact that she did not use warm-blooded animals in her research. If she changed her animal models as planned, he would have to quit his job and had no prospects for getting another position that paid as well and was as rewarding.

Does Dr. Q. have any obligation to consider her research assistant's views before she redirects his research?

Why are objections raised to the use of some animals in research and how can those objections be answered?

Why are there more objections to using some animals in research compared to others?

involved in research, research training, and biological testing activities. Researchers can meet their responsibilities by:

- ✓ **knowing what activities are subject to regulation,**
- ✓ **understanding and following the rules for project approval,**
- ✓ **obtaining appropriate training, and**
- ✓ **accepting continuing responsibility for compliance through all stages of a project.**

If you expect to use or study living animals in your research, regardless of the level of invasiveness, familiarize yourself with your responsibilities and check with someone in a position of authority before making any plans or undertaking any work.

4a. Rules, policies, and guidelines

The current rules, policies, and professional guidelines for the responsible use of animals in research are the product of roughly 50 years of ongoing discussion between government, the public, animal care professionals, and

Animal Welfare Act as Amended (7 USC, 2131-2156)

Section 1.

(a) This Act may be cited as the **"Animal Welfare Act."**

(b) The Congress finds that animals and activities which are regulated under this Act are either in interstate or foreign commerce or substantially affect such commerce or the free flow thereof, and that regulation of animals and activities as provided in this Act is necessary to prevent and eliminate burdens upon such commerce and to effectively regulate such commerce, in order—

(1) to insure that animals intended for use in research facilities or for exhibition purposes or for use as pets are provided humane care and treatment;

(2) to assure the humane treatment of animals during transportation in commerce; and

(3) to protect the owners of animals from the theft of their animals by preventing the sale or use of animals which have been stolen.

http://www.nal.usda.gov/awic/legislat/awa.htm

PHS Policy on Humane Care and Use of Laboratory Animals (Amended, August 2002)

II. Applicability

This Policy is applicable to all PHS-conducted or supported activities involving animals, whether the activities are performed at a PHS agency, an awardee institution, or any other institution and conducted in the United States, the Commonwealth of Puerto Rico, or any territory or possession of the United States.

http://grants2.nih.gov/grants/olaw/references/phspol.htm

researchers. The conclusions reached through these discussions are laid out in two key sources of information for researchers who use animals in their work: Federal regulations and professional guidelines.

Federal regulations. Over the last 50 years, Congress has addressed the responsible use of animals in research on a number of occasions and drafted two important statutes:

- ✓ **the 1966 Animal Welfare Act (revised 1970, 1976, 1985, and 1990) and**
- ✓ **the 1985 Health Research Extension Act, Sec. 495.**

The former broadly assigns authority for the responsible transportation, care, and use of animals to the United States Department of Agriculture (USDA), as implemented by Title 9 of the Code of Federal Regulations. It covers animals used "in research facilities or for exhibition purposes or for use as pets." The latter law delegates authority for the responsible use of animals in "biomedical and behavioral research" to the Secretary of Health and Human Services (HHS), acting through the Director of the National Institutes of Health (NIH) and the Office of Laboratory Animal Welfare (OLAW), NIH.

Researchers who use animals in research, including observational research, or teaching, can come under the jurisdiction of the USDA animal welfare regulations and/or

the PHS Policy on Humane Care and Use of Laboratory Animals (hereafter, PHS Policy), which carries out the provisions of the 1985 Health Research Extension Act. They therefore should be familiar with both.

Guidelines. In the late 1950's, a group of animal-care professionals formed the "Animal Care Panel" (ACP) specifically for the purpose of establishing a professional standard for laboratory animal care and facilities. Their work led to the publication of a comprehensive and influential *Guide for Laboratory Animal Facilities and Care* (1963, revised 1965, 1968, 1972, 1978, 1985, and 1996). The current edition, now called the *Guide for the Care and Use of Laboratory Animals,* or *Guide*, as it is commonly referenced, was prepared by a committee appointed by the National Research Council of the National Academy of Sciences and provides guidance on:

- ✓ **Institutional Policies and Responsibilities;**
- ✓ **Animal Environment, Housing, and Management;**

Guide for the Care and Use of Laboratory Animals (1996)

The Guide for the Care and Use of Laboratory Animals (the Guide) was first published in 1963 under the title Guide for Laboratory Animal Facilities and Care and was revised in 1965, 1968, 1972, 1978, and 1985. More than 400,000 copies have been distributed since it was first published, and it is widely accepted as a primary reference on animal care and use. The changes and new material in this seventh edition are in keeping with the belief that the Guide is subject to modification with changing conditions and new information.

The purpose of the Guide, as expressed in the charge to the Committee to Revise the Guide for the Care and Use of Laboratory Animals, is to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate. The Guide is also intended to assist investigators in fulfilling their obligation to plan and conduct animal experiments in accord with the highest scientific, humane, and ethical principles. The recommendations are based on published data, scientific principles, expert opinion, and experience with methods and practices that have proved to be consistent with high-quality, humane animal care and use.

http://www.nap.edu/readingroom/books/labrats/preface.html

- ✓ **Veterinary Medical Care; and**
- ✓ **Physical Plant.**

The *Guide* is widely accepted by both government and research institutions as the most authoritative source of information on most animal care and use questions. The PHS Policy requires that PHS-funded institutions use the *Guide* as a basis for developing and implementing an institutional program for animal care and use.

4b. Definitions

The term "animal" is defined differently in the statutes, codes, policies, and guidelines that govern animal research. Federally funded research is guided by two key definitions:

- ✓ **The PHS Policy, which applies to all PHS-funded activities involving animals, defines "animals" as "any live, vertebrate animals used or intended for use in research, research training, experimentation, or biological testing or for related purposes."**
- ✓ **The Federal Code that implements the Animal Welfare Act (Title 9) covers warm-blooded animals but excludes "[b]irds, rats of the genus Rattus and mice of the genus Mus bred for use in research, and horses not used for research purposes and other farm animals…."**

Many institutions apply uniform and consistent standards to all activities involving animals regardless of the source of funding or legal requirements as a way of ensuring broad compliance with all regulations covering the care and use of animals in research.

Researchers are not authorized to make decisions about covered or excluded research themselves. Therefore, anyone who plans to use animals in research, teaching, testing and other covered activities is well advised to assume a broad definition and to consult with their institutional committee (see below) before ordering animals or beginning work.

4c. Institutional organization

The task of assuring that researchers adhere to the regulations and guidelines for the responsible care and use of animals is generally recognized to be an institutional responsibility. Institutions vest authority for animal care and use in an "institutional official" (IO), who in turn appoints the Congressionally mandated Institutional Animal Care and Use Committee (IACUC), administers institutional care and use units at institutions that are large enough to have such, and handles other general matters relating to the care and use of animals at that institution.

IACUCs. Following the provisions of the 1985 Health Research Extension Act, PHS Policy, USDA regulations, the *Guide*, and the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) require research institutions to establish an IACUC. IACUCs oversee and evaluate all aspects of the institution's animal program, procedures, and facilities. Its members must include a doctor of veterinary medicine, one researcher who uses animals in research, and one person who is not affiliated with the institution. Many IACUCs also have a researcher who does not use animals or a member who has some grounding in ethics.

IACUC Members are appointed by their institution, but they have considerable independent authority. Their responsibilities include:

- ✓ **reviewing and approving all animal use research proposals,**
- ✓ **reviewing the institution's animal care program,**
- ✓ **inspecting (at least twice a year) the institution's animal facilities,**
- ✓ **receiving and reviewing concerns raised about the care and use of animals, and**
- ✓ **submitting reports to the Institutional Official.**

IACUCs also have independent authority to suspend projects if they determine that they are not being conducted

in accordance with applicable requirements. This authority comes directly from Congress through the Health Research Extension Act and can be exercised independent of any other institutional administrative authority.

Animal care and use units. Research institutions with large animal research programs generally have centralized animal care and use units that provide veterinary support, training in procedures, and advice on analgesics, anesthesia, euthanasia, and occupational health and safety. While the staff employed in these units cannot approve research protocols for the institution or make decisions specifically assigned to the institutional IACUC, as animal care professionals they are an excellent local source of information about the responsible care and use of animals in research.

4d. Federal and voluntary oversight

OLAW, USDA, and a voluntary accreditation program (Association for Assessment and Accreditation of Laboratory Animal Care—AAALAC) are charged with or assume the task of assuring that research institutions live up to their responsibilities for the care and use of animals in research.

OLAW. OLAW relies on an "assurance" mechanism to monitor institutional compliance with the PHS Policy. An "Assurance" is a signed agreement submitted by a research institution confirming that it will:

- ✓ **comply with applicable rules and policies for animal care and use,**
- ✓ **provide a description of the institution's program for animal care and use,**
- ✓ **maintain an appropriate IACUC, and**
- ✓ **appoint a responsible IO for compliance.**

The Assurance is considered the cornerstone of a trust relationship between the institution and the PHS and grants considerable authority to institutions for self-regulation.

Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International

AAALAC International is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs. ...

More than 700 companies, universities, hospitals, government agencies and other research institutions in 29 countries have earned AAALAC accreditation, demonstrating their commitment to responsible animal care and use. These institutions volunteer to participate in AAALAC's program, in addition to complying with the local, state and federal laws that regulate animal research.

http://www.aaalac.org/about/index.cfm

An OLAW-approved Assurance and compliance with PHS policy are considered terms and conditions of receiving PHS funds. Compliance is monitored by OLAW through annual mandatory institutional reporting to OLAW and in the event of noncompliance, serious deviations from the *Guide*, or IACUC suspensions. OLAW conducts limited site visits and reviews, and if necessary conducts investigations of reported noncompliance. Institutions that fail to submit an Assurance or to live up to the terms of their Assurance can have their approval to use animals in research, teaching, and testing suspended.

USDA. The animal welfare regulations also have mandatory reporting requirements, but USDA is an inspection-based system carried out by USDA Veterinary Medical Officers. Rather than allowing institutions to "assure" their own compliance, USDA visits sites, either announced or unannounced, to check whether institutions are in compliance. If violations are found, the institution is then subject to administrative fines and penalties.

Accreditation programs. Animal use programs can be, and most large ones are, accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International. AAALAC is "a private nonprofit organization that promotes the humane treatment of animals in science through a voluntary accreditation

program." It is governed by a Board of Trustees representing scientific, professional, and educational organizations. Its Council on Accreditation is composed of animal care and use professionals and researchers who conduct the program evaluations that determine which institutions are awarded accreditation.

AAALAC relies on widely accepted guidelines, such as the *Guide*, and other peer-reviewed resources when evaluating an institution's animal research program. During the accreditation process, AAALAC accreditors evaluate all aspects of an institution's animal research program. If an institution meets AAALAC's standards, it receives an accreditation for a specified period of time and can use this accreditation to demonstrate its commitment to high standards for the care and use of animals.

4e. Principles for the responsible use of animals in research

There is a range of views about the morality of animal experimentation. Antivivisectionists hold that humans have no right to place their own welfare above the welfare of animals and therefore all animal experimentation is immoral. Many animal welfare organizations find that some scientifically necessary experimentation is acceptable, but that it should be kept to a minimum and conducted on animals low on the phylogenetic scale, in ways that minimize pain and suffering. Many scientists feel that extensive animal experimentation is necessary and moral, provided it is based on sound scientific practices and utilizes quality animal care, along with minimization of pain and distress.

To help researchers and IACUCs make decisions about the responsible and appropriate use of animals in research, the Federal government has adopted nine *Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research, and Training* (see box, next page). These principles specify requirements for planning and conducting research and are useful to investigators and IACUCs. When questions

arise, PHS policy and USDA regulations provide further criteria for researchers and IACUCs to consider in assessing protocols.

Further practical advice on ways to assure appropriate respect for animals can be found in the "three Rs of alternatives" devised by Russell and Burch in 1959:

- ✓ **Replacement—using non-animal models such as microorganisms or cell culture techniques, computer simulations, or species lower on the phylogenetic scale.**
- ✓ **Reduction—using methods aimed at reducing the numbers of animals such as minimization of variability, appropriate selection of animal model, minimization of animal loss, and careful experimental design.**
- ✓ **Refinement—the elimination or reduction of unnecessary pain and distress.**

US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training

[Researchers should:]

1. follow the rules and regulations for the transportation, care, and use of animals;
2. design and perform research with consideration of relevance to human or animal health, the advancement of knowledge, or the good of society;
3. use appropriate species, quality, and the minimum number of animals to obtain valid results, and consider non-animal models;
4. avoid or minimize pain, discomfort, and distress when consistent with sound scientific practices;
5. use appropriate sedation, analgesia, or anesthesia;
6. painlessly kill animals that will suffer severe or chronic pain or distress that cannot be relieved;
7. feed and house animals appropriately and provide veterinary care as indicated;
8. assure that everyone who is responsible for the care and treatment of animals during the research is appropriately qualified and trained; and
9. defer any exceptions to these principles to the appropriate IACUC.

http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples/

Although PHS Policy is not explicit in addressing refinements, the requirements to use appropriate animal models and numbers of animals and to avoid or minimize pain and distress are, for all practical purposes, synonymous with requirements to consider alternative methods that reduce, refine, or replace the use of animals. USDA animal welfare regulations require a written narrative of the methods used and sources consulted to determine the availability of alternatives.

Knowing the concerns society has about the use of animals in research, researchers should be prepared to explain why they are using a particular species in their research; why pain or discomfort cannot be avoided; why it may be necessary to sacrifice the animals; and why non-animal options cannot be used to gather the same information or to achieve the same ends, based on the principles set out in the *U.S. Government Principles* and other sources of guidance.

4f. Broader responsibilities

Even with all of the care and review that currently is used to assure the responsible use of animals in research, animal research is still controversial and raises concerns that cannot easily be set aside.

Pain and suffering. Some experimental information cannot be gained without subjecting animals to pain and suffering. Researchers who study the effects of severe trauma, such as child abuse, can learn a great deal about physiological change by subjecting animals to different levels of pain and suffering. This can be done by administering mild electric shocks, forcing animals such as rats to swim until they reach exhaustion, or subjecting them to other traumatic treatments. How much pain and suffering is acceptable in experiments is not easily determined.

Concern for different species. There is widespread agreement that some animals, such as primates and

household pets, deserve more protection than other animals, such as worms and clams. There is less agreement about the relative protection that is needed for species within general groups of animals, such as cats, dogs, pigs, rabbits, mice, and rats. What moral considerations set one species apart from another when making decisions about the use to which it can be put in experiments?

Unnecessary experiments. Members of the public disagree about the use to which animals can reasonably be put in research, testing, and teaching. Animals are used to test the safety of experimental drugs, but should they also be used to test the toxicity of chemicals or cosmetics (as once was common, but has largely been abandoned)? Should they be used to train surgeons to do elective surgery? Do researchers sometimes use more animals in an experiment than is absolutely necessary or use animals when other means of testing would provide the same information?

Discussions about the responsible use of animals in research are not likely to dissipate in the near future. If animals are essential to your research and cannot be replaced; if you cannot reduce the number without compromising the experiment; and if you cannot further refine your methods to reduce pain and suffering, then presumably you have done all you can to meet your responsibility. However, do not forget that society does not have to permit the use of animals in research. It can seek to protect animals through complex and expensive regulations if it loses confidence in the research community's ability to regulate itself.

Questions for discussion

1. Should all animals used in research be treated the same or are there reasons to treat some animals differently than others?
2. Are there some animals that should not be used in research?
3. What circumstances justify pain and suffering of experimental animals?
4. How should research animals be procured? How should they be housed and treated during experiments?
5. How should members of IACUCs be selected? What constituencies should be represented on IACUCs?

Resources

Policies, Reports, and Policy Statements

National Academy of Sciences. Institute of Laboratory Animal Resources Commission of Life Sciences. *Guide for the Care and Use of Laboratory Animals*, Washington, DC: National Academy Press, 1996. (available at: http://www.nap.edu/readingroom/books/labrats/)

National Institutes of Health. *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*, Bethesda, MD: National Institutes of Health, nd. (available at: http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples)

Public Health Service. *Public Health Service Policy on Humane Care and Use of Laboratory Animals*, Washington, DC: GPO, 2002. (available at: http://grants2.nih.gov/grants/olaw/references/phspol.htm)

United States. Congress. *Animal Welfare Act*, PL 89-544, 1966. (available at: http://www.nal.usda.gov/awic/legislat/awa.htm)

United States Department of Agriculture. *USDA Animal and Plant Health Inspection Animal Care Policy Manual*, Washington, DC: GPO, nd. (available at: http://www.aphis.usda.gov/ac/polmanpdf.html)

General Information Web Sites

Association for the Assessment and Accreditation of Laboratory Animal Care. *Home Page*. http://www.aaalac.org/

National Institutes of Health. Office of Laboratory Animals Welfare. *Home Page*. http://grants2.nih.gov/grants/olaw/olaw.htm

United States Department of Agriculture. Animal Care Program. *Home Page*. http://www.aphis.usda.gov/ac/

Additional Reading

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Hart, LA. *Responsible Conduct with Animals in Research*, New York: Oxford University Press, 1998.

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Smith, CP, Animal Welfare Information Center (U.S.). *Animal Welfare and Ethics: Resources for Youth and College Agricultural Educators*, Revised and enlarged ed. *AWIC resource series; no. 6*, Beltsville, MD: U.S. Department of Agriculture Agricultural Research Service National Agricultural Library Animal Welfare Information Center, 2000.

Whose interest comes first?

5. Conflicts of Interest

Researchers work hard, often spending long hours and sometimes weekends in the laboratory, library, or at professional meetings. Their motivation for working hard stems from many sources. Research:

- ✓ **advances knowledge,**
- ✓ **leads to discoveries that will benefit individuals and society,**
- ✓ **furthers professional advancement, and/or**
- ✓ **results in personal gain and satisfaction.**

Each of these incentives or *interests* is commonly recognized as responsible and justifiable.

Researchers are allowed to and even encouraged to profit from their work (see the discussion of the Bayh-Dole Act, below). Professional advancement as a researcher depends on productivity. Society expects researchers to use the

Case Study

Early in his undergraduate education, Dr. Sam M. decided to dedicate his studies to finding a cure for a psychological disorder that seemed to run in his family. As a biology major, he pursued independent research projects and worked long hours as a lab assistant. He then enrolled in a PhD program in psychopharmacology and is now completing a 3-year postdoc in the neurosciences.

During his postdoc he worked on a promising compound he first discovered during his graduate years. His work has gone well and he feels the time is right to explore clinical applications. After more than a decade of living on student and postdoc wages, he is also ready for a better paying job.

As Sam weighs the options of an academic versus an industry job, he begins to wonder about who owns or will own the useful applications of his work, if and when there are any. Will it be owned by:

his graduate institution, where he first worked on the promising compound?

his postdoc institution, where he refined his ideas?

his future academic or industry employer?

himself, based on his hard work and innovative ideas?

society, which funded parts of his education and most of his research?

Who has a legitimate interest in Sam's work and when do his own personal financial interests create a conflict of interest?

funds it supplies to advance knowledge and to make useful discoveries. Personal gain and satisfaction provide strong incentives for doing a good job and acting responsibly.

Researchers' interests can and often do conflict with one another. The advancement of knowledge is usually best served by sharing ideas with colleagues, putting many minds to work on the same problem. But personal gain is sometimes best served by keeping ideas to oneself until they are fully developed and then protected through patents, copyrights, or publications. Legitimate research interests can create competing responsibilities and lead to what is commonly called *conflicts of interest.*

It is important to understand that *conflicts of interest* are not inherently wrong. The complex and demanding nature of research today inevitably gives rise to competing obligations and interests. Researchers are expected to serve on committees, to train young researchers, to teach, and to review grants and manuscripts at the same time they pursue their own research. Conflicts of interest cannot and need not be avoided. However, in three crucial areas:

- ✓ **financial gain,**
- ✓ **work commitments, and**
- ✓ **intellectual and personal matters,**

special steps are needed to assure that conflicts do not interfere with the responsible practice of research.

5a. Financial conflicts

Personal interests and the prospect of financial gain should not, but unfortunately can, improperly influence a researcher's fundamental obligation to truth and honesty. Although researchers should not, they can find ways to delay unfairly a competitor's work in order to secure a patent or some other financial advantage for themselves. Financial interests can provide a strong incentive to overemphasize

or underemphasize research findings or even to engage in research misconduct (Chapter 2). *Financial conflicts of interest* are situations that create perceived or actual tensions between personal financial gain and adherence to the fundamental values of honesty, accuracy, efficiency, and objectivity (Section I).

Financial interests are not inherently wrong. Researchers are permitted to benefit financially from their work. A 1980 Congressional law known as the Bayh-Dole Act encourages researchers and research institutions to use copyrights, patents, and licenses to put research ideas to use for the good of the public. Prior to this time, there were no uniform policies regulating the ownership of ideas developed with public funding. Bayh-Dole essentially gives that ownership to research institutions as an incentive to put ideas to work for the overall good of society. It not only approves of but, in fact, strongly encourages researchers and research institutions to have financial interests as a way of ensuring that the public's investment in research is used to stimulate economic growth.

While financial interests should not and in most instances do not compromise intellectual honesty, they certainly can, especially if the financial interests are *significant*.

Bayh-Dole Act (Public Law: 96-517)
Policy and Objective
35 USC Part II, Chapter 18, Section 200

It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

http://www.law.cornell.edu/uscode/html/uscode35/usc_sup_01_35_10_II_20_18.html

Universities are currently starting hundreds of new businesses based on researchers' ideas. Some of these businesses will generate significant profits (hundreds of thousands to millions of dollars each year). If the difference between commercial success and failure rests on one key publication, the pressure to put the best face on that publication can be considerable.

Financial conflicts also arise from the ever-present pressure researchers have to secure funds to support their research. A private sponsor might withdraw support from a project if it does not produce the "right" results. Success in the stiff competition for research grants can rest on having the "right" preliminary results. Research is expensive, funding often in short supply. The pressure simply to survive, much less profit personally, can and does create financial conflicts of interest.

Federal policies. Concerns about the actual or potential adverse effect of financial interests on research prompted the Public Health Service (PHS) and the National Science Foundation (NSF) to adopt conflict of interest policies in the mid-1990's. These policies require research institutions to establish administrative procedures for:

- ✓ **reporting *significant* conflicts before any research is undertaken;**
- ✓ **managing, reducing, or eliminating *significant* financial conflicts of interest; and**
- ✓ **providing subsequent information on how the conflicts were handled.**

Significant financial conflict is defined as:

- ✓ **additional earnings in excess of $10,000 a year, or**
- ✓ **equity interests in excess of 5 percent in an entity that stands to benefit from the research.**

The financial interests of all immediate family members are included in these figures.

Department of Health and Human Services
Conflict of Interest Definitions
45 CFR 94.3

Significant Financial Interest means anything of monetary value, including but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights). The term does not include:

(1) Salary, royalties, or other remuneration from the applicant institution;

(2) Any ownership interests in the institution, if the institution is an applicant under the SBIR program;

(3) Income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities;

(4) Income from service on advisory committees or review panels for public or nonprofit entities;

(5) An equity interest that when aggregated for the Investigator and the Investigator's spouse and dependent children, meets both of the following tests: Does not exceed $10,000 in value as determined through reference to public prices or other reasonable measures of fair market value, and does not represent more than a five percent ownership interest in any single entity; or

(6) Salary, royalties or other payments that when aggregated for the investigator and the investigator's spouse and dependent children over the next twelve months, are not reasonably expected to exceed $10,000.

http://a257.g.akamaitech.net/7/257/2422/14mar20010800/edocket.access.gpo.gov/cfr_2002/octqtr/45cfr94.3.htm

State and local policies. Although the Federal requirements apply only to PHS- and NSF-funded research, many research institutions have adopted global policies that apply to all researchers. Many also use different values for defining *significant,* to as low as any financial interest. Researchers therefore should check their local conflict-of-interest policy to find out when and what they are required to report. They also need to keep in mind that many states have their own conflict-of-interest policies, which apply to all state-paid employees.

AAMC Task Force Recommendations
Financial Conflicts of Interest in Clinical Research
(December 2001)

B. In the event of compelling circumstances, an individual holding significant financial interests in human subjects research may be permitted to conduct the research. Whether the circumstances are deemed compelling will depend in each case upon the nature of the science, the nature of the interest, how closely the interest is related to the research, and the degree to which the interest may be affected by the research....

C. Institutional policies should require full prior reporting of each covered individual's significant financial interests that would reasonably appear to be affected by the individual's research, updated reporting of any relevant change in financial circumstances, and review of any significant financial interests in a research project by the institution's COI committee prior to final IRB approval of the research. COI committee findings and determinations should inform the IRB's review of any research protocol or proposal, although the IRB may require additional safeguards or demand reduction or elimination of the financial interest....

http://www.aamc.org/research/coi/firstreport.pdf

New England Journal of Medicine
Conflict of Interest Policy
June 13, 2002

[B]eginning with this issue of the Journal, we have modified the statement in Information for Authors to read as follows:

> Because the essence of reviews and editorials is selection and interpretation of the literature, the Journal expects that authors of such articles will not have any significant financial interest in a company (or its competitor) that makes a product discussed in the article.

The addition of the word "significant" acknowledges that not all financial associations are the same. Some, such as the receipt of honorariums for occasional educational lectures sponsored by biomedical companies, may be appropriately viewed as minor and unlikely to influence an author's judgment. Others, such as ownership of substantial equity in a company, are of greater concern. It is our intent to focus on the financial relationships that, in our judgment, could produce bias, or the perception of bias, in an article.

http://content.nejm.org/cgi/content/full/346/24/1901

Professional societies and journal policies. A number of professional societies have issued reports or made recommendations on appropriate ways to handle conflicts of interest. Similarly, more and more journals now require researchers to disclose real or potential financial conflicts. Sometimes disclosure must be made to the journal editor, who decides what, if any, action is needed. Sometimes disclosures must be included in the publication itself. Before submitting an article to a journal for publication, researchers should carefully check and make sure they have followed that publication's conflict of interest policies.

5b. Conflicts of commitment

Conflicts of commitment arise from situations that place competing demands on researchers' time and loyalties. At any time, a researcher might be:

- ✓ working on one or more funded projects;
- ✓ preparing to submit a request for a new project;
- ✓ teaching and advising students;
- ✓ attending professional meetings and giving lectures;
- ✓ serving as a peer reviewer;
- ✓ sitting on advisory boards; or
- ✓ working as a paid consultant, officer, or employee in a private company.

Each of these activities requires time and makes demands on a researcher's institutional commitments. Care needs to be taken to assure that these commitments do not inappropriately interfere with one another.

Allocation of time. Researchers must be careful to follow rules for the allocation of time. Federally funded researchers must follow the rules for cost accounting published by the Office of Management and Budget in a document known as *Circular A-21*. Most research

institutions also have rules for how researchers spend their time, particularly time serving as paid consultants, giving paid lectures, or working as an employee in a private company. At a minimum, these rules require that researchers:

- ✓ honor time commitments they have made, such as devoting a specified percentage of time to a grant or contract;
- ✓ refrain from charging two sources of funding for the same time; and
- ✓ seek advice if they are unsure whether a particular commitment of time is allowed under an institution's or the Federal Government's policies.

Although researchers will frequently work on several projects at the same time, in the final analysis primary work obligations must be met. In addition, the time devoted to one project ordinarily cannot be billed to another.

Relationships with students. Academic researchers involved in start-up ventures often have opportunities to hire students. This puts them in a situation where they can hire their own students. As mentors, they have a primary obligation to help students develop into independent researchers. As heads of start-up companies, their primary obligation is to see promising ideas commercialized. While the two responsibilities can complement one another, they can also be in conflict. Should an individual who is both the researcher's student and employee be advised to develop a promising idea that could lead to an independent career or to work on a more routine problem that will benefit the start-up company? Situations such as these create conflicts and should be avoided or appropriately managed.

Use of resources. Equipment and supplies purchased with public funds can easily be used to advance private research interests. While this might seem like a harmless practice, particularly if the equipment is not in constant use, unless a researcher has permission to use the equipment to support private research, this practice is not

Stanford University
Conflict of Commitment Policy

1. Outside consulting privileges are not normally available to Academic Staff. They may consult only with permission, as noted below. Under no circumstances may any Academic Staff member's outside consulting work exceed the limits imposed by the faculty consulting policy, i.e., 13 days per calendar quarter (that is, one day in seven) on a full-time equivalent basis.... Academic Staff may not use University resources, including facilities, personnel, equipment, or confidential information, except in a purely incidental way, as part of any outside consulting activities nor for any other purposes that are unrelated to the mission of the University.
2. Academic Staff must maintain a significant presence on campus (main or overseas) throughout each quarter in which they are employed by Stanford, consistent with the scope of their appointment.
3. Academic Staff must not allow other professional activities to detract from their primary allegiance to Stanford. For example, Academic Staff employed on a full-time basis must not have significant outside managerial responsibilities nor act as a principal investigator on sponsored projects that could be conducted at Stanford University but instead are submitted and managed through another institution.

http://www.stanford.edu/dept/DoR/rph/4-4.html

appropriate. The equipment can be used for other university work since this is allowed by the government. But it cannot be used for a personal project without permission. It also cannot be used for research that is explicitly prohibited by the Federal government, such as stem cell research using lines not authorized by the President's policy.

Disclosure of affiliations. It is widely agreed that outside affiliations that create conflicts of interest should be listed on academic publications, but should researchers list their academic affiliations on other publications? As president or CEO of a new company, is it appropriate for a researcher to also note in the end-of-the-year financial report that she or he is also a full professor at a prestigious university? Should researchers who serve on private boards list their academic affiliation? Researchers must be careful to separate their academic or institutional work from their

private work. In particular, they should not inappropriately use their institutional research affiliation to advance their private interests by implying, for example, that private work has the support of their research institution if it does not.

Representing outside entities. The results researchers commercialize in private ventures, such as drugs used in a university hospital, a software program used in an accounting office, or a consultation service for employees, might be used by their primary employer. In these cases, the researcher could be the resident expert on the goods and services in question. Each employer in this case presumably wants the best deal on the goods and services, whereas the researcher is also interested in personal profits, creating a conflict of commitment.

Since the situations described above are often not subject to specific policies or guidance, judgments about responsible conduct often rest with the researcher. In making judgments about the best way to deal with institutional conflicts, it is helpful to take into consideration:

- ✓ **how others will view your commitments and**
- ✓ **the judgment of someone who has no stake in the outcome.**

In addition, it is always a good idea, even if it is not required, to seek advice from an institutional official.

5c. Personal and intellectual conflicts

Researchers are also expected to avoid bias in proposing, conducting, reporting, and reviewing research. They therefore should be careful to avoid making judgments or presenting conclusions based solely on personal opinion or affiliations rather than on scientific evidence.

Personal conflicts are usually the easiest to identify and resolve. Researchers generally should not serve as reviewers for grants and publications submitted by close colleagues and students. Their presumed *interest* in seeing

their colleagues and students succeed could conflict with their obligation to makes judgments based solely on the evidence at hand. Most granting agencies require reviewers to disclose conflicts of interest, including personal conflicts, as a condition of service.

Intellectual conflicts are more difficult to identify, but are nonetheless important. If a researcher holds strong personal views on the importance of a particular area of research or set of research findings, those views should be disclosed so that others can take them into consideration when judging the researcher's statements. The same is true of strong moral convictions that could influence a researcher's scientific opinions. This is particularly true when researchers serve as expert witnesses or advisors. It is for precisely this reason that the National Academy of Sciences, which has provided essential science advice to the Federal Government since the Civil War, carefully considers all conflicts of interest when it sets up advisory panels (see box, below).

Federal Advisory Committee Act
Public Disclosure Requirements Applicable to the National Academy of Sciences
January 5, 1997

The Academy shall determine and provide public notice of the names and brief biographies of individuals that the Academy appoints or intends to appoint to serve on the committee. The Academy shall determine and provide a reasonable opportunity for the public to comment on such appointments before they are made or, if the Academy determines such prior comment is not practicable, in the period immediately following the appointments. The Academy shall make its best efforts to ensure that (A) no individual appointed to serve on the committee has a conflict of interest that is relevant to the functions to be performed, unless such conflict is promptly and publicly disclosed and the Academy determines that the conflict is unavoidable, (B) the committee membership is fairly balanced as determined by the Academy to be appropriate for the functions to be performed, and (C) the final report of the Academy will be the result of the Academy's independent judgment. The Academy shall require that individuals that the Academy appoints or intends to appoint to serve on the committee inform the Academy of the individual's conflicts of interest that are relevant to the functions to be performed.

http://www.nasonline.org/site/PageServer?pagename=ABOUT_FACA

5d. Reporting and managing significant conflicts

If a researcher has a significant conflict of interest, as defined by Federal, state, institutional, journal, or other policies, it must be reported and managed or eliminated. "Managing" a conflict means finding a way to assure that the interests do not adversely influence the research. Some options for managing conflicts of interest include:

- ✓ **requiring full disclosure of all interests so that others are aware of potential conflicts and can act accordingly;**
- ✓ **monitoring the research or checking research results for accuracy and objectivity; or**
- ✓ **removing the person with the conflict from crucial steps in the research process, such as the interpretation of data or participating in a particular review decision.**

These and other options are either worked out by a conflict of interest review committee or an administrator charged with overseeing conflicts of interest.

If the conflicts cannot be managed and could have an adverse impact on the research, then they must be eliminated, by divesting equity, reducing the income received from the research, assigning supervisory responsibilities to someone else, stepping out of the room when a particular proposal is discussed, or some other action.

Finally, it is important to note that research administrators, funding agencies, journal editors, and conflict of interest committees, not the researcher, should make final decisions about the management of conflicts of interest. This protects the researcher from charges of acting in her or his own interest and helps assure that the most responsible decisions are made.

Questions for discussion

1. Is $10,000 or a 5 percent equity stake an appropriate level for raising concerns about possible conflicts of interest or should other values be used?
2. Should researchers be allowed/encouraged to profit personally from their research apart from their normal compensation?
3. What are appropriate mechanisms for managing financial conflicts of interest?
4. What are appropriate mechanisms for protecting students from a mentor's conflict of commitment?
5. What are appropriate mechanisms for managing intellectual and personal conflicts of interest?

Resources

Policies, Reports, and Policy Statements

Association of American Medical Colleges. *Guidelines for Dealing with Faculty Conflicts of Commitment and Conflicts of Interest in Research*, Washington, DC: AAMC, 1990. (available at: http://www.iit.edu/departments/csep/codes/coe/assoc.amer.medical.colleges.guidelines.html)

_____. *Protecting Subjects, Preserving Trust, Promoting Progress II: Principles and Recommendations for Oversight of an Institution's Financial Interests in Human Subjects Research*, Washington, DC: AAMC, 2002. (available at: http://www.aamc.org/research/coi/start.htm)

Association of American Medical Colleges, Task Force on Financial Conflicts of Interest in Clinical Research. *Protecting Subjects, Preserving Trust, Promoting Progress–Policy and Guidelines for Oversight of Individual Financial Interests in Human Subjects Research*, Washington, DC: AAMC, 2001. (available at: http://www.aamc.org/research/coi/start.htm)

Association of American Universities. *Report on Individual and Institutional Financial Conflict of Interest*, Washington, DC: AAU, 2001. (available at: http://www.aau.edu/research/COI.01.pdf)

Council on Government Relations. *Recognizing and Managing Personal Conflicts of Interest*, Washington, DC: COGR, 2002. (available at: http://www.cogr.edu/docs/COIFinal.pdf)

Department of Health and Human Services. *Final Guidance Document: Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection*, Washington, DC: HHS, 2001. (available at: http://www.hhs.gov/ohrp/humansubjects/finreltn/fguid.pdf)

Drazen, JM, Curfman, GD. "Financial Associations of Authors," *The New England Journal of Medicine* 346, 24 (2002): 1901-1902. (available at: http://content.nejm.org/cgi/content/full/346/24/1901/)

Food and Drug Administration. *Guidance: Financial Disclosure by Clinical Investigators*, Washington, DC: FDA, 2001. (available at: http://www.fda.gov/oc/guidance/financialdis.html)

Institute of Medicine. National Academies of Science. *Study Conduct: Bias and Conflict of Interest*, Washington, DC: IOM, nd. (available at: http://www.iom.edu/subpage.asp?id=5350%0D)

National Institutes of Health. "Objectivity in Research," *Federal Register* 60, 132 (1995): 35809-35819. (available at: http://grants2.nih.gov/grants/guide/notice-files/not95-179.html)

National Science Foundation. "Investigator Financial Disclosure Policy," *Federal Register* 60, 132 (1995): 35820. (available at: http://www.nsf.gov/pubs/stis1996/iin118/iin118.txt)

Office of Management and Budget. *Circular A-21*, Washington, DC: OMB, 2000. (available at: http://www.whitehouse.gov/omb/circulars/a021/a021.html)

United States, Congress. 105th Congress. First Session. *Federal Advisory Committee Act Amendments of 1997*, PL 105-153 (1997). (available at: http://www.nasonline.org/site/PageServer?pagename=ABOUT_FACA)

General Information Web Sites

Association of American Universities. *Conflict of Interest and Misconduct*. http://www.aau.edu/research/conflict.cfm

Association of University Technology Managers. *Home Page*. http://www.autm.net/index_ie.html

National Institutes of Health. Office of Extramural Research. *Conflict of Interest*. http://grants1.nih.gov/grants/policy/coi/

Additional Reading

Boyd, EA, Bero, LA. "Assessing Faculty Financial Relationships With Industry: A Case Study," *Journal of the American Medical Association* 284 (2000): 2209-2214.

Campbell, TID. "Understanding the Potential for Misconduct in University-industry Relationships: An Empirical Study." In *Perspectives on Scholarly Misconduct in the Sciences*, edited by John M. Braxton, 259-282. Columbus, OH: Ohio State University Press, 1999.

Cho, MK, Shohara, R, Schissel, A, Rennie, D. "Policies on Faculty Conflicts of Interest at US Universities," *Journal of the American Medical Association* 284 (2000): 2203-2208.

Jefferson, T, Smith, R, Yee, Y, Drummond, M, Pratt, M, Gale, R. "Evaluating the BMJ Guidelines for Economic Submissions: Prospective Audit of Economic Submissions to BMJ and The Lancet," *Journal of the American Medical Association* 280, 3 (1998): 275-277.

National Institutes of Health. *Financial Conflict of Interest and Research Objectivity: Issues for Investigators and Institutional Review Boards*, Washington, DC: NIH, 2000. (available at: http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-00-040.html)

Shamoo, AE. "Role of Conflict of Interest in Scientific Objectivity: A Case of a Nobel Prize Work," *Accountability in Research* 2, 1 (1992): 55-75.

United States. Congress. House. Committee on Government Operations. Human Resources and Intergovernmental Relations Subcommittee. *Federal Response to Misconduct in Science, Are Conflicts of Interest Hazardous to our Health?: Hearing before a Subcommittee of the Committee on Government Operations, House of Representatives, One Hundredth Congress, second session, September 29, 1988*, Washington: U.S. G.P.O., 1989.


GETTING START
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Part III.

Conducting Research

Part III: Conducting Research

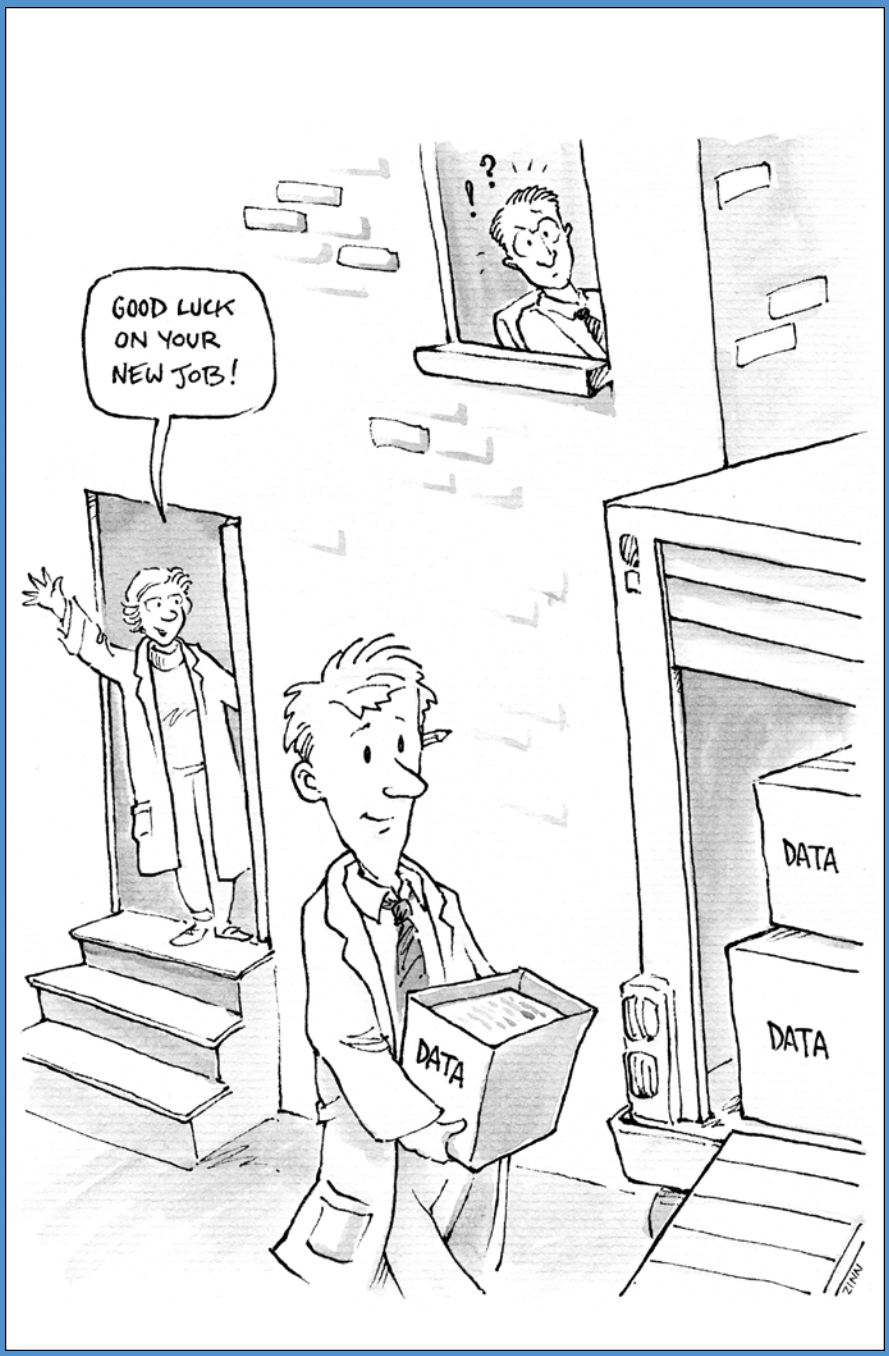
ONCE PLANNING IS COMPLETE, RESEARCHERS CAN finally get on with the work they presumably enjoy most—conducting research. This is when

hypotheses and new techniques are finally tested, when efforts get underway to solve problems and put new information to use. At this stage in any research project, three additional areas of responsibility become important:

Chapter 6, Data Management Practices, discusses how researchers should collect, store, protect, and share data, mindful of the need to maintain its integrity, validity, and accuracy. Ownership issues must be considered. Some data must be shared with colleagues; other data must be protected from unapproved use. Some data must be preserved for specified periods of time; some destroyed to protect confidentiality.

Chapter 7, Mentor and Trainee Responsibilities, covers the role of the researcher as teacher. The continued growth of research in all fields is vitally dependent upon a constant supply of well-trained researchers. New researchers learn many of the techniques of their profession as they work side by side with established researchers. Established researchers therefore should take their responsibilities as mentors seriously.

Chapter 8, Collaborative Research, explores special responsibilities that arise when researchers work with colleagues, whether in their own discipline or in other disciplines, at other institutions, and in other countries. When collaborating with colleagues, how should intellectual property agreements be worked out? Which country or institution's research policies should be followed? How should project funds and project responsibilities be managed?



Who owns research data?

6. Data Management Practices

Researchers spend much of their time collecting data. Data are used to confirm or reject hypotheses, to identify new areas of investigation, to guide the development of new investigative techniques, and more. We launch space probes to collect data that help us understand the origins of the universe and use gene databases as tools for understanding and curing disease. Science as we know and practice it today cannot exist without data.

Data management practices are becoming increasingly complex and should be addressed before any data are collected by taking into consideration four important issues:

- ✓ **ownership,**
- ✓ **collection,**
- ✓ **storage, and**
- ✓ **sharing.**

The integrity of data and, by implication, the usefulness of the research it supports, depends on careful attention to detail, from initial planning through final publication.

Case Study

Dr. Marion W. long ago learned that good data management practices are essential to responsible research. She therefore carefully supervises the work of her assistants and students, checking notebooks, backing up computer files, and from time to time verifing results for herself.

As she is wrapping up work on one project before starting another, the technology transfer officer at her university calls. A graduate student who previously worked in her laboratory has moved to another university and filed a patent for work that may have been done in Dr. W.'s laboratory on her research funds? If this is the case, the graduate student may not be able to lay claim to the patent.

What records will Dr. W. need to prove that the work was done in her laboratory?

Who owns and controls the data collected in her laboratory?

Do computer records pose any unique problems in this case?

6a. Data ownership

Research produces data. As a product, common sense might suggest that the person who conducts the research should own the product—the data. In fact, conditions imposed by funders, research institutions, and data sources may dictate otherwise.

Funders. Funders provide support for research for different reasons. Government is interested in improving the general health and welfare of society. Private companies are interested in profits, along with benefits to society. Philanthropic organizations are interested in advancing particular causes. These different interests translate into different ownership claims. Typically:

- ✓ **Government gives research institutions the right to use data collected with public funds as an incentive to put research to use for the public good (see the discussion of the Bayh-Dole Act, Chapter 5).**
- ✓ **Private companies seek to retain the right to the commercial use of data.**
- ✓ **Philanthropic organizations retain or give away ownership rights depending on their interests.**

Since the claims of funders can and do vary considerably, researchers must be aware of their obligations to them before they begin collecting data.

With government funding, it is important to distinguish between grants and contracts. Under grants, researchers must carry out the research as planned and submit reports, but control of the data remains with the institution that received the funds (see below). Contracts require the researcher to deliver a product or service, which is then usually owned and controlled by the government. If your research is supported with government funds, make sure you know whether you are working under a grant or a contract. The difference is significant and could determine who has the right to publish and use your results.

University of Pittsburgh
Guidelines on Data Retention and Access

Data Ownership and Access to Data

Both the principal investigator and the University have responsibilities, and hence, rights concerning access to, use of, and maintenance of original research data. Research data belongs to the University of Pittsburgh, which can be held accountable for the integrity of the data even after the researchers have left the University. Although the primary data should remain in the laboratory where it originated (and hence at the University), consistent with the precepts of academic freedom and intellectual integrity, the investigator may be allowed to retain the research records and materials created by him/her. In the event that the investigator leaves the University, an Agreement on Disposition of Research Data may be negotiated by the investigator and the Department Chair or Dean to allow transfer of research records. However, consistent with the same precepts, it should be specified in the agreement that the University has the right of access to all research records and materials for a reasonable cause after reasonable prior notice regardless of the location of the responsible investigator....

Some circumstances may warrant an exception, requiring that the primary data be retained by the University....

Split of collaborative team: When a collaborative team is dissolved, University of Pittsburgh policy states that each member of the team should have continuing access to the data and materials with which he/she had been working, unless some other agreement was established at the outset. The unique materials prepared in the course of the research should be available/accessible under negotiated terms of a transfer agreement.

http://www.pitt.edu/ ~ provost/retention.html

Research institutions. Support for research is typically awarded to research institutions, not to individual researchers. As the recipients of research funds, research institutions have responsibilities for budgets, regulatory compliance, contractual obligations, and data management. To assure that they are able to meet these responsibilities, research institutions claim ownership rights over data collected with funds given to the institution. This means that researchers cannot automatically assume that they can take their data with them if they move to another institution. The research institution that received the funds may have rights and obligations to retain control over the data.

Data sources. Increasingly research subjects and other entities that are the source of data are seeking some control over data derived from them. Countries with unique resources, such as tropical rain forests, individuals with rare medical conditions, and entities with unique databases, have at one time or another claimed ownership of research results based on their data. Research subjects and entities that have or can be the source of important data may no longer be willing to provide or be the source of data without some ownership stake in the end results.

Well before any data are collected, ownership issues and the responsibilities that come with them need to be carefully worked out. Before undertaking any work, make sure you can answer the following questions:

- ✓ **Who owns the data I am collecting?**
- ✓ **What rights do I have to publish the data?**
- ✓ **Does collecting these data impose any obligations on me?**

If you do not have firm answers for each of these questions, preferably in writing when financial interests are involved, you are not ready to begin your research.

It is also important to note that in most cases ownership provisions must be approved by the institution that receives and is responsible for the administration of research funds. Researchers therefore should not enter into agreements that affect the control and use of data without getting institutional approval. The results could be disastrous and expensive if ownership is disputed later.

6b. Data collection

There is no one best way to collect data. Different types of research call for different collection techniques. There are, however, four important considerations that apply to all data collection and that will help ensure the overall integrity of both the process and the information collected.

Appropriate methods. Reliable data are vitally dependent on reliable methods. If you use a test that can detect an effect in one of every 100 samples to find an effect that may not occur more frequently than 1 in every 1,000 cases, your results will not be reliable. Failure to find the effect could be due to either your experimental design or the lack of an effect, but you will not know which is true. The common saying, "garbage in, garbage out," applies to research methods.

Although the need for appropriate methods might seem obvious, studies have suggested that researchers sometimes use inappropriate statistical tests to evaluate their results (see articles by DeMets and Gardner, Additional Reading). Methods can also be compromised by bias—choosing one method or set of experimental conditions so that a particular conclusion can be drawn—or sloppy technique. Whatever the origin, the use of inappropriate methods in research compromises the integrity of research data and should be avoided. Responsible research is research conducted using appropriate, reliable methods.

Attention to detail. Quality research requires attention to detail. Experiments must be set up properly and the results accurately recorded, interpreted, and published. A failure to pay attention to detail can result in mistakes that will later have to be corrected and reported. Correcting the record takes time and resources that are better spent on the research itself.

Obviously, it is not possible to avoid all mistakes in research. However, take a look at the errata section of any scientific journal and ask yourself how the mistakes reported could have been avoided. Did the authors check to make sure that each figure was correctly labeled? Were the calculations double checked? Did someone check to make sure the authors were properly listed? Since others rely on their work, researchers have a responsibility to make sure their work is carefully undertaken and reported. Sloppy research wastes funds and should be avoided.

Authorized. Many types of data collection need to be authorized before they can proceed. Typically permission is needed to use:

- ✓ human and animal subjects in research;
- ✓ hazardous materials and biological agents;
- ✓ information contained in some libraries, databases, and archives;
- ✓ information posted on some Web sites;
- ✓ published photographs and other published information; and
- ✓ other copyrighted or patented processes or materials.

Researchers have a responsibility to know when permission is needed to collect or use specific data in their research. If you are not sure whether permission is needed, check before proceeding with data collection.

Recording. The final step in data collection is the physical process of recording the data in some type of notebook (hard copy), computer file (electronic copy), or other permanent "record" of the work done. The physical formats for recording data vary considerably, from measurements or observations to photographs or interview tapes. However data are recorded, it is important to keep in mind that the purpose of any record is to document what was actually done and the results that were achieved.

In recording data, keep two simple rules in mind to avoid problems later, should someone ask about or question your work:

- ✓ Hard-copy evidence should be entered into a numbered, bound notebook so that there is no question later about the date the experiment was run, the order in which the data were collected, or the results achieved. Do not use loose-leaf notebooks or simply collect pages of evidence in a file. Do not change records in a bound notebook without noting the date and reasons for the change.

- ✓ **Electronic evidence should be validated in some way to assure that it was actually recorded on a particular date and not changed at some later date. It is easy to change dates on computers and thereby alter the date a particular file seems to have been created. If you collect your data electronically, you must be able to demonstrate that they are valid and have not been changed.**

As you record your data, it may be helpful to think about them as the legal tender of research—the currency researchers cash in when they apply for grants, publish, are considered for promotion, and enter into business ventures. To have and hold their value, research data must be properly recorded.

6c. Data protection

Once collected, data must be properly protected. They may be needed later:

- ✓ **to confirm research findings,**
- ✓ **to establish priority, or**
- ✓ **to be reanalyzed by other researchers.**

Over time, data, as the currency of research, become an investment in research. If the data are not properly protected, the investment, whether public or private, could become worthless.

Data storage. The responsible handling of data begins with proper storage and protection from accidental damage, loss, or theft:

- ✓ **Lab notebooks should be stored in a safe place.**
- ✓ **Computer files should be backed up and the backup data saved in a secure place that is physically removed from the original data.**
- ✓ **Samples should be appropriately saved so that they will not degrade over time.**
- ✓ **Care should be taken to reduce the risk of fire, flood, and other catastrophic events.**

Properly store and protect your data. They are valuable.

Confidentiality. Some data are collected with the understanding that only authorized individuals will use them for specific purposes. In such cases, care needs to be taken to assure that privacy agreements are honored. This is particularly true of data that contain personal information that can be linked to specific individuals. It is also true of confidential information about protected processes and materials. If a company shares confidential data about a process with a researcher prior to seeking a patent on that process, the researcher must take care to make sure the data are kept confidential.

Data that are subject to privacy restrictions must be stored in a safe place that is accessible only to authorized personnel. Using random codes to identify individual subjects, rather than names or social security numbers, can also further protect private information. Access to these codes can then be restricted to provide a double layer of protection. Whatever the method used to protect private or confidential information, the researcher who collects or uses the information has the primary responsibility for its protection.

Period of retention. Data should be retained for a reasonable period of time to allow other researchers to check results or to use the data for other purposes. There is, however, no common definition of a *reasonable period of time.* NIH generally requires that data be retained for 3 years following the submission of the final financial report. Some government programs require retention for up to 7 years. A few universities have adopted data-retention policies that set specific time periods in the same range, that is, between 3 and 7 years. Aside from these specific guidelines, however, there is no comprehensive rule for data retention or, when called for, data destruction.

It is difficult to predict when data collected sometime in the past could be useful. When a new disease emerges, such

as AIDS, researchers use stored samples/data to pinpoint first occurrences and the likely course of development of the disease. Although the original data were not stored for this purpose, they nonetheless can be useful for tracking diseases years later. Stored data are also useful for understanding social questions. The Department of Energy committee that made recommendations on appropriate compensation for improper human radiation experiments conducted during the Cold War pulled together data collected as far back as the 1950's. Researchers also cannot predict when someone will challenge their work and ask to see the original data.

Given the different reasons data could be useful over long periods of time, researchers should give some thought to retaining data longer than some minimum period required by specific regulations. How long is reasonable will vary from field to field and institution to institution. Nevertheless, it is important to have a clear retention policy that balances the best interests of society with those of the research institution and the individual researcher. Before throwing out notebooks, cleaning out files, or erasing your computer memory, give careful consideration to who might benefit from or ask to see your data in the future.

6d. Data Sharing

It is widely agreed that research data should be shared, but deciding when and with whom raises questions that are sometimes difficult to answer.

Researchers are not expected to and in most instances should not release preliminary data, that is, data that have not been carefully checked and validated. The one exception to this rule would be preliminary data that could potentially benefit the public. A researcher who has strong preliminary indications of a major threat to public health, such as unexpected side effects from a drug or an unrecognized environmental health problem, may have good reason to

NIH Data Sharing Policy and Implementation Guidance
(Updated: March 5, 2003)

Goals of Sharing Data

Data sharing promotes many goals of the NIH research endeavor. It is particularly important for unique data that cannot be readily replicated. Data sharing allows scientists to expedite the translation of research results into knowledge, products, and procedures to improve human health.

There are many reasons to share data from NIH-supported studies. Sharing data reinforces open scientific inquiry, encourages diversity of analysis and opinion, promotes new research, makes possible the testing of new or alternative hypotheses and methods of analysis, supports studies on data collection methods and measurement, facilitates the education of new researchers, enables the exploration of topics not envisioned by the initial investigators, and permits the creation of new datasets when data from multiple sources are combined.

In NIH's view, all data should be considered for data sharing. **Data should be made as widely and freely available as possible while safeguarding the privacy of participants, and protecting confidential and proprietary data.** To facilitate data sharing, investigators submitting a research application requesting $500,000 or more of direct costs in any single year to NIH on or after October 1, 2003, are expected to include a plan for sharing final research data for research purposes, or state why data sharing is not possible.

http://grants1.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm

share this information with the public and other researchers before it is fully validated. Data that have no immediate public benefit, such as the discovery of a basic scientific process that could eventually lead to public benefits, in most instances is best held until the researcher is confident that the results will stand.

Researchers can withhold confirmed or validated data until they have had time to establish their priority for their work through publication or, in rare cases, a public announcement. They do not have to release data on a day-to-day or experiment-to-experiment basis for other researchers to use, even though this might speed the advance of knowledge. Provided no agreements have been made to the contrary, keeping data confidential prior to

publication is a commonly accepted practice that most researchers and funding agencies accept.

Once a researcher has published the results of an experiment, it is generally expected that all the information about that experiment, including the final data, should be freely available for other researchers to check and use. Some journals formally require that the data published in articles be available to other researchers upon request or stored in public databases. In the specific case of federally funded research that is used in setting policies that have the effect of law, research data must be made available in response to Freedom of Information Act (FOIA) requests (OMB, Circular A-110). There is, in other words, considerable support for sharing data with other researchers and the public unless there are compelling reasons for confidentiality.

6e. Future considerations

The continued evolution of data policies will likely be driven by a number of different issues, including the growing complexity of data and debates about proper control.

Complexity. Our capacity to generate data sometimes outstrips our capacity to store and share it. Data storage and sharing were major problems during the early years of the Human Genome project. They continue to pose problems for any research area that is able to generate massive amounts of information efficiently and inexpensively. DNA microarray chips can generate 10,000 bits of information with a single, easily conducted test. The logistics of storing and sharing this information presents a monumental challenge for everyone engaged in research. Even when researchers want to, it is not always clear how they should go about collecting, storing, and sharing data responsibly.

Control. In large projects, questions frequently arise about the control of data, particularly when financial interests are at stake. Should researchers participating in large,

Research Committee, Society for Academic Emergency Medicine
Guidelines for Clinical Investigator Involvement in Industry-sponsored Clinical Trials

IV. Trial Data Management

1. The industry sponsor and the investigators should have a firm commitment to thorough monitoring of the trial at every step.
2. All data collected in the trial should be open to scrutiny by both the investigators and the industry sponsor.
3. Clinical investigators should have substantial input into the initial analytic plan and also any subsequent amendments that occur during the trial period.
4. When possible, statistical analysis of the data should be conducted by an entity independent of the researchers and the sponsor. For trials using interim analysis, use of an independent entity is particularly important. Decisions to prematurely stop a trial should be based upon predetermined criteria.
5. Consideration should be given to the use of an unbiased, blinded "clinical evaluation committee" for trials that involve assessment of potentially subjective endpoints.
6. The industry sponsors must share the results of all data analyses with the principal investigators. Selective withholding or incomplete reporting of data analyses to the principal investigators is unacceptable.
7. Trial results and data analysis should be shared with the principal investigators as soon as they become available. Delays by the industry sponsors for marketing or related purposes are unacceptable.

http://www.saem.org/download/edward.pdf

multi-site clinical trials have the right to publish their own findings, that is, retain some control over their own data, or should the collection, storage, and interpretation be centralized? This issue is currently unresolved and the subject of intense public debate.

National security. Recent events have heightened concerns about the possible use of data from publicly supported research by terrorists and nations that could pose a threat to national security. Efforts are underway to address these concerns through voluntary policies and new

Federal regulations (e.g., USA Patriot Act of 2001) that will assure reasonable control without unduly restricting the ability of researchers to share their work and ideas freely with one another (see the recent report, *Biological Threats and Terrorism,* Additional Reading). Researchers whose work could be affected by these concerns should keep abreast of ongoing policy development and regulation.

However these issues are resolved, researchers have been the most important component of responsible data management practices in the past and will likely remain so as long as the public feels the majority of researchers can be trusted. With this in mind, ask yourself how someone funding your research would feel if he or she had a chance to take a close look at your data management practices.

Questions for discussion

1. **Should research data belong to researchers rather than to research institutions?**
2. **Should data recording practices be standardized to facilitate sharing and monitoring? What recording practices could be standardized?**
3. **What interpretation practices could be standardized? How does your laboratory verify the accuracy and validity of data before its disclosure or use in grant proposals and publications?**
4. **Who should pay the cost of sharing data? Who should have access to the data?**
5. **How long should researchers be able to withhold data to allow time to protect ownership claims? How long should research data be stored?**

Resources

Policies, Reports, and Policy Statements

American Statistical Association. *Ethical Guidelines for Statistical Practice*, Alexandria, VA: American Statistical Association, 1999. (available at: http://www.amstat.org/profession/index.cfm?fuseaction=ethicalstatistics/)

Council on Government Relations. *Policy Considerations: Access to and Retention of Research Data*, Washington, D.C.: 1995. (available at: http://206.151.87.67/docs/DataRetentionIntroduction.htm)

Food and Drug Administration. *Good Laboratory Practices for Designing Toxicology Studies for Petition Submissions and Notifications*, 21 CFR Part 58 (2002). (available at: http://www.cfsan.fda.gov/~dms/opa-pt58.html)

Harvard University, Office of Technology Licensing. *Record-Keeping Procedures*, 2000. (available at: http://www.otd.harvard.edu/inventions/ip/patents/recordkeeping/)

National Institutes of Health. *NIH Data Sharing Policy and Implementation Guidance*, 2003. (available at: http://grants1.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm)

Society for Clinical Data Management. *Good Clinical Data Management Practices*, Version 2, Hillsborough, NJ: Society for Clinical Data Management, 2002. (available at: https://www.scdm.org/GCDMP/Default.asp)

United States. Congress. *USA Patriot Act of 2001*, PL 107-56, 2001. (available at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_cong_public_laws&docid=f:publ056.107.pdf)

University of Pittsburgh. *Guidelines on Data Retention and Access*, Pittsburgh, PA: University of Pittsburgh, 1997. (available at: http://www.pitt.edu/~provost/retention.html)

General Information Web Sites

National Institutes of Health. Office of Extramural Research. *NIH Data Sharing Policy*, Washington, DC: National Institutes of Health. http://grants.nih.gov/grants/policy/data_sharing/

Society for Clinical Data Management. *Home Page*. http://www.scdm.org/

Additional Reading

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Council on Government Relations. *Materials Transfer in Academia*, Washington, DC: Council on Government Relations, 1997.
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Gardner, MJ. "An Exploratory Study of Statistical Assessment of Papers Published in the British Medical Journal," *Journal of the American Medical Association* 263, March 10 (1990): 1355-1357.

Kanare, HM. *Writing the Laboratory Notebook*, Washington, DC: American Chemical Society, 1985.

Knobler, SL, Mahmoud, AAF, Pray, LA, eds. *Biological Threats and Terrorism: Assessing the Science and Response Capabilities: Workshop Summary*. Washington, DC: National Academy Press, 2002.

Stevens, AR. *Ownership and Retention of Data*, Washington, DC: National Association of College and University Attorneys, 1997.

Mentor-trainee working relationships?

7. Mentor and Trainee Responsibilities

While conducting investigations, researchers often assume the added role of mentors to trainees.* The mentor-trainee relationship is complex and brings into play potential conflicts. How much time—training time for the mentor, research time for the trainee—should each devote to the other? Who gets credit for ideas that take shape during the course of a shared experiment? Who *owns* the results? When does a trainee become an *independent researcher?*

The essential elements of a productive mentor-trainee relationship are difficult to codify into rules or guidelines,

Case Study

At a recent meeting, several faculty in a large, research-oriented science department raised concerns about their mentoring program. While mindful of the many demands they all faced, they wondered whether changes were needed in the way the department assigned, trained, and oversaw mentors. The ensuing discussion raised some potentially good suggestions, which most agreed were best referred to a special committee for further discussion and recommendations. With a little arm twisting, Susan D., an advanced graduate student; Dr. Linda L., a postdoc; and Dr. Bill K., an established researcher, were recruited to serve.

At their first meeting, the three colleagues quickly agreed to tackle first the question of goals. If they knew what mentoring was expected to achieve, they could then assess the strengths and weaknesses of their current program and make suggestions for change. With this settled, they decided to spend some time talking with their peers and then get back together to compare notes. When they met the next time:

What goals would you expect each member of the committee to recommend?

Why might different members of the committee recommend different goals?

Assuming they came to the conclusion that some improvements were needed, what avenues are open to change the way mentors and trainees interact?

* The term "trainee" is used in this chapter to refer to anyone learning to be a researcher under an established researcher's supervision. This includes principally graduate students and postdoctoral fellows (postdocs), but may also include undergraduate and high school students working on research projects or junior research faculty, research scientists, and research staff.

leaving most of the decisions about responsible mentoring to the individuals involved. Common sense suggests that good mentoring should begin with:

- ✓ **a clear understanding of mutual responsibilities,**
- ✓ **a commitment to maintain a productive and supportive research environment,**
- ✓ **proper supervision and review, and**
- ✓ **an understanding that the main purpose of the relationship is to prepare trainees to become successful researchers.**

Understandings and agreements, however, will count for little if they are not backed up by firm commitments to make a relationship work.

Knowing the importance of personal commitments, researchers should carefully consider what responsibilities they have to trainees before they take on the essential task of training new researchers. Trainees, in turn, should be we aware of their responsibilities to mentors before accepting a position in a laboratory or program.

7a. Basic responsibilities

Mentor-trainee relationships begin when an experienced and an inexperienced researcher agree to work together. Each brings something to the table under such an arrangement. The experienced researcher has knowledge and skills that the inexperienced researcher needs to learn. She or he may also provide support for the trainee's research and education. Inexperienced researchers, whether graduate student, postdoctoral student (postdoc), research staff, or junior researcher, provide labor and fresh ideas. Under a productive relationship, the two work together to advance knowledge and put ideas to work. When the relationship breaks down, it is often because one of the parties is not getting from the relationship what she or he expected.

National Academy of Sciences
On Being a Mentor to Students in Science and Engineering

What is a Mentor?

In the broad sense intended here, a mentor is someone who takes a special interest in helping another person develop into a successful professional. Some students, particularly those working in large laboratories and institutions, find it difficult to develop a close relationship with their faculty adviser or laboratory director. They might have to find their mentor elsewhere—perhaps a fellow student, another faculty member, a wise friend, or another person with experience who offers continuing guidance and support.

In the realm of science and engineering, we might say that a good mentor seeks to help a student optimize an educational experience, to assist the student's socialization into a disciplinary culture, and to help the student find suitable employment. These obligations can extend well beyond formal schooling and continue into or through the student's career.

http://www.nap.edu/readingroom/books/mentor/

One way to avoid problems is to establish basic understandings about important issues early in the relationship. Trainees need to know:

- ✓ **how much time they will be expected to spend on their mentor's research;**
- ✓ **the criteria that will be used for judging performance and form the basis of letters of recommendation;**
- ✓ **how responsibilities are shared or divided in the research setting;**
- ✓ **standard operating procedures, such as the way data are recorded and interpreted; and, most importantly,**
- ✓ **how credit is assigned, that is, how authorship and ownership are established.**

Clarifying these issues early in a mentor-trainee relationship can prevent problems from arising later.

The need for early understanding is not one sided. Mentors need to know that a trainee will:

- ✓ **do assigned work in a conscientious way,**
- ✓ **respect the authority of others working in the research setting,**
- ✓ **follow research regulations and research protocols, and**
- ✓ **live by agreements established for authorship and ownership.**

Mentors invest time and resources in trainees. Trainees should respect this time and use resources responsibly, keeping their mentors informed about changing research interests or other circumstances that could affect their work.

A Guide to Training and Mentoring in the Intramural Research Program at NIH

A mentor is a person who has achieved career success and counsels and guides another for the purpose of helping him or her achieve like success. Research supervisors should always be mentors; they have the responsibility to discuss with and advise a trainee on aspects of his or her work and professional development. The trainee may find additional mentors informally—or the training institution may designate them. They are very important in the overall experience of the trainee and may contribute to research productivity as well....

Training in the skills of mentorship itself is important, especially for those who plan careers in research or teaching. Postdoctoral trainees should learn to train and guide others, for example, by working with more junior individuals, supervising technical staff, or training students. The characteristics considered important by a fellow in selecting a supervisor and other mentors—interest in contributing to the career development of another scientist, research accomplishments, professional networking, accessibility, and past success cultivating the professional development of fellows—are characteristics that trainees may eventually strive to emulate in their own careers.

Although this Section has emphasized the responsibilities of supervisors and others in research institutions to provide mentoring to trainees to facilitate their professional development, trainees also have responsibilities. Collaborative research frequently requires productive interactions among fellows themselves as well as recognition of their roles as part of a team effort. In addition, fellows must have a commitment to the work of the laboratory and Institute and to the achievement of their goals. They cannot be passive participants in their training; they should appropriately make known their satisfactions, dissatisfactions, and needs clearly and often.

http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/mentor-guide.htm

Arriving at basic understandings early in a mentor-trainee relationship is not easy, given the unequal power relationship between them. Mentors are in a position to lay out expectations, but it can be difficult for a trainee to raise questions early in a relationship about credit and authorship practices. To avoid putting trainees in the awkward position of having to raise these issues, mentors should be prepared to take the lead in raising issues that are of concern to the trainee as well as those that are of interest to the mentor. Developing written guidance on a laboratory's authorship and publication practices should also be considered.

7b. Research environment

Different mentors establish different research environments. Some laboratories are highly competitive; others emphasize cooperation. Some mentors are intimately involved in all aspects of the projects they supervise; others delegate authority. Similarly, different researchers like to work in different environments. Some enjoy independence; others like to have close working relationships with colleagues. Some thrive in competitive environments; others prefer cooperative working relationships. Although there is no single formula for a "good" research environment, there are some fundamentals that mentors and trainees should keep in mind.

Equal treatment. Research ability is not tied to race, gender, ethnicity, or sexual orientation. These factors have no bearing on one's success as a researcher. Therefore, research environments should not put someone at a disadvantage based on who they are. If competition is encouraged in a way that puts any distinguishable group at a significant disadvantage, it is not acceptable. All students should be subject to the same level of supervision and scrutiny. Aside from legal obligations to avoid discrimination in the workplace, researchers have a

University of Michigan
Mentoring within a Diverse Community

Need for Role Models

Students from historically underrepresented or marginalized groups have a harder time finding faculty role models who might have had experiences similar to their own. As some students say, they want to find "someone who looks like me;" "someone who immediately understands my experiences and perspectives;" "someone whose very presence lets me know I, too, can make it in the academy."

Feelings of Isolation

Students from historically underrepresented groups can feel particularly isolated or alienated from other students in their departments, especially if the composition of a program is highly homogenous.

Burden of Being a Spokesperson

Students from underrepresented groups often expend a lot of time and energy speaking up when issues such as race, class, gender, or sexual orientation arise or are being ignored. These students point out how most of their peers have an advantage in not carrying such a burden.

Seeking Balance

Students observe that professors need to devote large parts of their lives to their work in order to be successful in the academy. Students from all disciplines tell us that they feel faculty expect them to spend every waking minute on their work. This perception of faculty expectations, accurate or not, is of grave concern to students who have children or wish to, as well as for those who want to balance their lives with their other interests.

http://www.rackham.umich.edu/StudentInfo/Publications/FacultyMentoring/contents.html

professional obligation to work to assure equal access to their profession, particularly if their work is publicly supported.

Professional practice. Researchers should maintain research environments that respect accepted practices for the responsible conduct of research. Trainees learn by example as well as formal training. They assume, not unreasonably, that the practices they observe are *appropriate* practices. Mentors therefore have an obligation to maintain research environments that set appropriate examples. They should not themselves make unreasonable authorship demands, fail to honor agreements made with

trainees, inappropriately cut corners in research, or engage in other practices that run counter to accepted practices for the responsible conduct of research.

Training in the responsible conduct of research. Beginning in 1989 and in line with recommendations made by the Institute of Medicine (IOM, 1989), the National Institutes of Health (NIH) required recipients of National Research Service Institutional Training Program awards (training grants) to offer instruction in the responsible conduct of research (RCR). The National Science Foundation (NSF) has a similar requirement for recipients of its Integrative Graduate Education and Research Traineeship (IGERT) Program awards. Later reports, notably by the 1995 Commission on Research Integrity, called for broadening this requirement to all PHS-funded research, but such a requirement has not been implemented. Nonetheless, there is widespread agreement that RCR training should be integral to the research environment, with heavy emphasis given to the role the mentor plays in providing this training.

7c. Supervision and review

When mentors accept trainees, they assume responsibility for assuring that the persons under their supervision are appropriately and properly trained. This responsibility is particularly important in research since for the most part there are no other checks on the qualifications of new researchers. Researchers do not take licensing exams. They are judged primarily by the quality of their research, which should be best known to the person directly supervising their work, that is, to their mentor.

Proper supervision of a trainee takes time. In one way or another a mentor needs to:

- ✓ **assure proper instruction in research methods,**
- ✓ **foster the intellectual development of the trainee,**

- ✓ **impart an understanding of responsible research practices, and**
- ✓ **routinely check to make sure the trainee develops into a responsible researcher.**

Mentors do not need to check all aspects of a trainee's work directly. In large laboratories, postdocs often supervise graduate students and laboratory technicians might teach specific laboratory skills. Training in the responsible use of animals is often done through an animal care program. However, the ultimate responsibility for training rests with the mentor.

Proper supervision and review play an important role in quality control. Trainees can make mistakes. Some have deliberately falsified or fabricated data. Mentors should review work done under their supervision carefully enough to assure that it is well done and accurate. This can be accomplished by:

Emory University School of Medicine
Policy for Postdoctoral Fellows

Mentor Obligations

Postdoctoral research opportunities at Emory University School of Medicine are intended to foster the training of basic and clinical research scientists. Included within this goal is the concept that postdoctoral fellows, with the guidance of their mentors, will develop a scientific project that utilizes the creativity and independence of the fellow. In this spirit, the mentor will provide adequate facilities, funds, and the appropriate guidance to achieve the agreed-upon goals of the project. In addition, mentors should provide guidance in critical review of scientific information, grant writing, manuscript writing and preparation, presentation of scientific information, and in the art of performing research. Mentors should also advise and as possible, aid fellows in decisions regarding future employment potential and career paths. Mentor review of fellow performance and career development should be conducted at least once per year. A member(s) of the departmental senior faculty should be designated to serve as liaison with departmental post-doctoral fellows, faculty, and the Office of Postdoctoral Education and its advisory committees.

http://www.med.emory.edu/POSTDOC/Web%20Forms/Adobe%20Forms/Policy%20for%20Postdoctoral%20Fellows%207.1.05-1.pdf

- ✓ reviewing laboratory notebooks and other compilations of data;
- ✓ reading manuscripts prepared by trainees carefully to assure that they are accurate, well-reasoned, and give proper credit to others;
- ✓ meeting with trainees on a regular basis to keep in touch with the work they are doing; and
- ✓ encouraging trainees to present and discuss data at laboratory meetings.

Some of this responsibility can be delegated to others, but as with all other matters regarding training, the mentor should assume ultimate responsibility.

7d. Transition to independent researcher

The ultimate goal of research training is to produce independent researchers who can establish their own research programs, take on trainees, and help research-dependent disciplines grow. This means that the mentor's final responsibility to trainees is to help them get established as independent researchers.

History has repeatedly shown that experienced researchers often do not give over control to the next generation easily. They have a difficult time seeing ideas they planted grow in another person or having someone they trained head out in new directions. And yet in many fields, it is well documented that researchers are most productive early in their careers, when they are first making their way as independent researchers.

The problem of trainee versus independent researcher is most apparent in postdoctoral training. Postdocs, as they are commonly known, are usually well prepared to undertake independent work, and yet they are still working under someone else's supervision. The fact that they are neither official students nor official faculty gives them few rights and protections. The fact that they are usually supported by

someone else's funding leaves them open to exploitation. To protect against such exploitation, a new organization, the National Postdoctoral Association, has recently been established "to address national issues relevant to postdocs and focus public debate on how to improve the lives of postdocs at all levels."

Researchers who supervise postdocs should carefully work out their relationship with this unique and important group of researchers in training. Some supervision is still necessary, but not as much as for graduate students. Postdocs may have their own funding and assume all the duties of a principal investigator, even if for administrative purposes their funding comes through their mentor. They may deserve first authorship on all of their papers, even though the mentor was involved in the research. Most importantly, they should be encouraged to develop the independence and record needed to get a regular research appointment, thereby paying back society's investment in years of research training and the student's investment in her or his own career.

Questions for discussion

1. Can elements of the mentor-trainee relationship be reduced to a written agreement that both parties would sign at the beginning of the relationship?
2. What are the qualities of a good mentor? A good trainee?
3. What are the qualities of a good research environment and how can they be fostered?
4. What is the purpose of postdoctoral training and how long should it last?
5. Can good mentoring be taught, monitored, and evaluated?

Resources

Policies, Reports, and Policy Statements

Commission on Research Integrity. *Integrity and Misconduct in Research: Report of the Commission on Research Integrity*, Washington, DC: Health and Human Services, 1995. (available at: http://ori.hhs.gov/documents/report_commission.pdf)

Gottesman, MM. *A Guide to Training and Mentoring in the Intramural Research Program at NIH*, Bethesda, MD: National Institutes of Health, 1999. (available at: http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/mentor-guide.htm)

Institute of Medicine. *The Responsible Conduct of Research in the Health Sciences,* Washington, DC: National Academies of Science, 1989. (available at: http://search.nap.edu/books/0309062373/html/)

National Institutes of Health. Alcohol, Drug, and Mental Health Administration. "Requirement for Programs on the Responsible Conduct of Research in National Research Service Award Institutional Training Programs," *NIH Guide for Grants and Contracts* 18 (1989): 1. (available at: http://grants.nih.gov/grants/guide/historical/1989_12_22_Vol_18_No_45.pdf)

National Science Foundation. *Integrative Graduate Education and Research Traineeship (IGERT) Program*, Washington, DC: NSF, 2002. (available at: http://www.nsf.gov/pubs/2002/nsf02145/nsf02145.pdf)

General Information Web Sites

Association for Women in Science. *Home Page*. http://www.awis.org/

MentorNet. *The E-Mentoring Network for Women in Engineering and Science*. http://www.mentornet.net/

National Postdoctoral Association. Home Page. (available at: http://www.nationalpostdoc.org/site/c.eoJMIWOBIrH/b.1388059/k.DBBE/NPA_Home.htm)

Additional Reading

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University of Michigan. Horace H. Rackham School of Graduate Studies. *How to Mentor Graduate Students: A Guide for Faculty in a Diverse University*, Ann Arbor, MI: University of Michigan, 2002. (available at: http://www.rackham.umich.edu/StudentInfo/Publications/FacultyMentoring/contents.html)

Collaboration or competition?

8. Collaborative Research

Researchers increasingly collaborate with colleagues who have the expertise and/or resources needed to carry out a particular project. Collaborations can be as simple as one researcher sharing reagents or techniques with another researcher. They can be as complex as multi-centered clinical trials that involve academic research centers, private hospitals, and for-profit companies studying thousands of patients in different states or even countries.

Any project that has more than one person working on it requires some collaboration, i.e., working together. In most projects, however, one person, commonly called the "principal investigator" or PI, is in charge. Others work under the PI's direction. In this chapter, the focus will be on groups of researchers who are all more or less equal partners working on a common, "collaborative" project.

In collaborative projects, researchers continue to have the responsibilities discussed in other chapters in the *ORI*

Case Study

Sharon, Ben, and Terra met during a late-night discussion at a professional meeting. They share a common interest in learning disorders but come from different scientific backgrounds. Sharon works at the cutting edge of brain imaging technology. Ben is an educational psychologist interested in pre-school children in inner cities. Terra has been putting her knowledge as a physiologist to work exploring the effects of alternative medicines.

As late night turns to early morning, the newly met trio begins to see benefits from working together and starts sketching out a grant proposal. The scientific ideas quickly fall into place, but some of the logistics raise questions that need answers.

Who should submit the proposal, through which university?

Do all three need to get IRB approval to work on the project?

What will happen if their work has practical applications?

How should they go about answering these questions? Are there other important questions that should be asked as well?

Introduction to RCR, but they assume some additional responsibilities stemming from collaborative relationships. These additional responsibilities arise from the added burdens of:

- ✓ **the increasingly complex roles and relationships;**
- ✓ **common, but not necessarily identical, interests;**
- ✓ **management requirements; and**
- ✓ **cultural differences**

inherent in any large project but especially in collaborative projects. Special attention to these added burdens can help keep collaborative projects running smoothly.

8a. Roles and relationships

Effective collaboration begins with a clear understanding of roles and relationships, which should begin the day the collaboration is established by discussing and reaching agreement on the details of the collaborative relations. Before any work is undertaken, there should be some common understanding of:

- ✓ **the goals of the project and anticipated outcomes;**
- ✓ **the role each partner in the collaboration will play;**
- ✓ **how data will be collected, stored, and shared;**
- ✓ **how changes in the research design will be made;**
- ✓ **who will be responsible for drafting publications;**
- ✓ **the criteria that will be used to identify and rank contributing authors;**
- ✓ **who will be responsible for submitting reports and meeting other requirements;**
- ✓ **who will be responsible for or have the authority to speak publicly for the collaboration;**
- ✓ **how intellectual property rights and ownership issues will be resolved; and**

- ✓ how the collaboration can be changed and when it will come to an end.

Clear understandings in advance are the best way to avoid complications and disagreements later in a collaboration.

Obviously, situations can arise during a collaboration that could not have been anticipated in advance. For this reason, it is important for effective communication to continue throughout any collaborative project. Collaborators should:

- ✓ share findings with colleagues in the collaboration and pay attention to what others are doing;
- ✓ report and discuss problems as well as findings;
- ✓ make other collaborators aware of any important changes, such as changes in key personnel; and
- ✓ share related news and developments so that everyone in the collaboration is equally knowledgeable about important information.

All of these points may seem obvious, but they can easily get lost in the day-to-day details of doing research. However, if you are working with collaborators, keep in touch. Without effective communication, collaborations can easily run into problems and dissolve.

8b. Management

In addition to effective communication, collaborative projects should have effective management plans that cover:

- ✓ financial issues,
- ✓ training and supervision,
- ✓ formal agreements, and
- ✓ compliance.

When a PI is in charge of all of the work done on a project, the lines of responsibility are clear. The PI is ultimately responsible for all aspects of the project, from financial

expenditures to staff training, data collection, reporting, and wrapping up the project. In collaborative research, the partners in the collaboration share responsibilities. Under these circumstances, an effective management plan is essential.

Financial management. The expenditure of Federal research funds is subject to financial management rules issued by the Office of Management and Budget in Circulars A-21 and A-110 (see boxes, below and next page). A-21 covers all aspects of financial management, from accounting procedures to reporting requirements. For example, one section carefully describes, in fairly technical terms, allowable and unallowable expenses. Some travel costs are allowed; others are not. A-110 sets out rules for issuing government grants and contracts. It explains how equipment should be purchased and used, even after the project has come to an end.

Office of Management and Budget Circular A-21

48. Travel costs.

a. **General.** Travel costs are the expenses for transportation, lodging, subsistence, and related items incurred by employees who are in travel status on official business of the institution. Such costs may be charged on an actual basis, on a per diem or mileage basis in lieu of actual costs incurred, or on a combination of the two, provided the method used is applied to an entire trip and not to selected days of the trip, results in reasonable charges, and is in accordance with the institution's travel policy and practices consistently applied to all institutional travel activities.

b. **Lodging and subsistence.** Costs incurred by employees and officers for travel, including costs of lodging, other subsistence, and incidental expenses, shall be considered reasonable and allowable only to the extent such costs do not exceed charges normally allowed by the institution in its regular operations as a result of an institutional policy and the amounts claimed under sponsored agreements represent reasonable and allocable costs.

c. **Commercial air travel.** Airfare costs in excess of the lowest available commercial discount airfare....

http://www.whitehouse.gov/omb/circulars/a021/a021.html

Office of Management and Budget Circular A-110

34. Equipment.

(c) The recipient shall use the equipment in the project or program for which it was acquired as long as needed, whether or not the project or program continues to be supported by Federal funds and shall not encumber the property without approval of the Federal awarding agency. When no longer needed for the original project or program, the recipient shall use the equipment in connection with its other federally-sponsored activities, in the following order of priority: (i) Activities sponsored by the Federal awarding agency which funded the original project, then (ii) activities sponsored by other Federal awarding agencies.

http://www.whitehouse.gov/omb/circulars/a110/a110.html

Every federally funded research project must adhere to the rules set out in A-21 and A-110. Therefore, collaborative projects must be managed in ways that assure that all expenditures are in compliance, from those incurred by the primary investigators working at major research institutions to survey workers or clinicians working in the field.

Training and supervision. Wherever they work, research staff should be properly trained and supervised. In some instances the training is mandatory. Anyone who works with research animals or human subjects must have formal training. The same is true of staff who work with hazardous substances or biohazards. These requirements extend to everyone working on a collaborative project, whether they are at a different institution, in another state, or even another country. Management plans for collaborative projects therefore should include the training and supervision of all researchers and staff working on the project.

Formal agreements. Some aspects of collaborative projects must be worked out in advance in formal agreements. For example, when research is carried out in more than one place, it is sometimes necessary to transfer

materials from one institution to another. Since many materials are carefully controlled, to protect either safety or ownership, the terms of transfer should be carefully spelled out, including (see NIH-recommended provisions below):

- ✓ **who owns the materials,**
- ✓ **the use to which they can be put, and**
- ✓ **proper acknowledgment of the source.**

These agreements help protect the interests of the collaborators by assuring that ownership will be respected and that the materials will be properly used.

Compliance. Increasingly, research institutions must in one way or another certify that they are in compliance with specific research regulations. When research institutions are involved in collaborative projects, an institution's responsibility for compliance can extend to other institutions. If the other institution is a U.S. university with a large

National Institutes of Health
Recommended Provisions for a Materials Transfer Letter

1. The [supplied] MATERIAL is the property of the PROVIDER and is made available as a service to the research community.
2. THIS MATERIAL IS NOT FOR USE IN HUMAN SUBJECTS.
3. The MATERIAL will be used for teaching or not-for-profit research purposes only.
4. The MATERIAL will not be further distributed to others without the PROVIDER's written consent....
6. Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties....
7. The RECIPIENT agrees to use the MATERIAL in compliance with all applicable statutes and regulations.
8. The MATERIAL is provided at no cost, or with an optional transmittal fee solely to reimburse the PROVIDER for its preparation and distribution costs. If a fee is requested, the amount will be indicated here: [insert fee]

http://www.ott.nih.gov/pdfs/MTA.pdf

research portfolio, that institution most likely already has a compliance plan in place. However, if the other institution does not do a great deal of research or is located in another country, it may not have thought about its compliance responsibilities. Management plans for collaborative projects must take into account the need for meeting compliance responsibilities throughout the project sites and not just at one institution.

8c. Different research settings

Most researchers devote their careers to one field of research and spend their time talking with colleagues with similar interests. However, science is increasingly best served when researchers work with colleagues in other fields. Physicians and engineers have teamed together to develop miniature wireless devices that can gather information while passing normally through the body. Computer scientists are working with organic chemists and biologists to develop faster computers and more flexible display devices. Collaborative projects encourage researchers to pursue interdisciplinary research.

For the most part, interdisciplinary research follows the same rules and practices as disciplinary research. There are times, however, when researchers in different fields bring different practices or expectations to a project. When this happens, researchers might think of adopting two common-sense rules:

- ✓ **do not ignore any responsibilities, and**
- ✓ **when there are choices about appropriate action, select the most demanding option.**

When in doubt, it makes sense to seek the highest rather than the lowest denominator.

Different expectations can enter a project in a number of ways, especially when judgments about responsible practice are involved. The government and some research

institutions allow researchers to earn up to $10,000 through consulting or other outside employment before they have to declare a potential conflict of interest (discussed in Chapter 5). Others institutions use lower thresholds, in some cases requiring researchers to report conflicts of interest if they have any outside financial interests. Different institutions also manage conflicts of interest in different ways, from supervision or reporting to outright prohibition. When there are differences in reporting policy, the prudent course of action is to go with the lowest financial threshold and accept the most stringent management plan, even though some researchers working on the collaborative project may not be required to do so.

Ownership issues also raise questions about which rules to follow. One party to a collaboration may have no interest in reporting a promising idea for development; another may feel under an obligation to do so, following either a university's or Federal policy. There may also be different understandings among the different institutions that are part of a collaboration about what constitutes disclosable information and who owns the information once it is disclosed. Given the consequences of disputes that can erupt in these situations, it is essential that every collaborative project settle disclosure and ownership issues early in the project before disputes arise. Waiting longer opens the door for misunderstandings and disputed claims when one of the parties in the collaboration makes a valuable discovery.

Finally, there are significant differences in the way researchers in different fields and even different laboratories carry out the routine business of collecting data and publishing results. Some still collect data in bound laboratory notebooks; others use computers. In some fields, it is common practice to circulate early results in newsletters and/or abstracts; in other fields, journal publications are the preferred mode of communication. Different fields have

different ways and standards for listing authors. These and other differences should be addressed openly and early in any collaboration to assure that misunderstandings do not arise later over data collection and publication.

Questions for discussion

1. **Why should collaborative research be encouraged?**
2. **When should research collaborations be formalized?**
3. **Are there any drawbacks to collaborative research? What problems can they raise?**
4. **Which country's rules should be used in collaborative projects that are carried out in different countries?**
5. **What steps should be taken when a collaborative project comes to an end or a collaboration is dissolved?**

Resources

Policies, Reports, and Policy Statements

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GETTING RECOGN
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Part IV.

Reporting and Reviewing Research

Part IV: Reporting and Reviewing Research

RESEARCH HAS NO VALUE IF IT IS NOT MADE public. Results are shared with colleagues so they can be tested, used to advance knowledge, and put to work. They are shared with the public and policymakers so that they can be used to make decisions about funding and practical application.

While researchers might engage in research simply for their own satisfaction, if their work receives public support, they have a responsibility to share that work with others.

Chapter 9, Authorship and Publication, covers the responsibilities researchers have when they share results with others through informal communications, oral presentations, scholarly publications, and public statements. Whatever mechanism is used, research results should be shared honestly, efficiently, and without bias. Dishonesty and bias undermine the usefulness of research publications; inefficiency (publishing the same research several times) wastes public funds and the valuable time of reviewers and journal editors.

Chapter 10, Peer Review, describes the responsibilities researchers have when they review the work of other researchers. Non-peers—individuals who do not have equal training and knowledge—cannot evaluate the quality and importance of research. Peers can and therefore play a crucial role in many important decisions about the funding, publication, and use of research.

Responsible authorship?

9. Authorship and Publication

Researchers share the results of their works with colleagues and the public in a variety of ways. Early results are usually shared during laboratory meetings, in seminars, and at professional meetings. Final results are usually communicated to others through scholarly articles and books. Public communication takes place through press releases, public announcements, newspaper articles, and public testimony. Some of these ways of communicating research results (i.e., of publication) are well structured and controlled; others are informal and have few controls.

Whether structured or informal, controlled or free ranging, responsible publication in research should ideally meet some minimum standards. All forms of publication should present:

Case Study

As his first major grant is coming to an end, several important elements of Dr. Sanjay K.'s research suddenly fall into place. The last series of experiments his graduate student ran clearly link the gene they are studying to a particular type of cancer. His postdoc's work on the proteins associated with this gene could pave the way for possible cures. With these results in hand, he is finally ready to make a strong case for continued support and, happily, his pending promotion. All he has to do now is publish the results.

A week later, Sanjay's optimism starts to fade. As might have been expected, his department chair was delighted with his progress, but then suggested that the first paper announcing the results come out under her name to give it broader circulation. Meanwhile, his postdoc and graduate student have gotten into a heated debate about the order their names should appear on the paper; the university's public affairs office has asked for a summary of the results for a press release; and the technology transfer office has called telling him to hold all publications until they can evaluate the commercial potential of his work.

What should Sanjay do?

Which of these problems should Sanjay tackle first?

Is there anything he could have done to assure that things went more smoothly when he was ready to publish his results?

- ✓ a full and fair description of the work undertaken,
- ✓ an accurate report of the results, and
- ✓ an honest and open assessment of the findings.

In assessing the completeness of any publications, researchers should ask whether they have described:

- ✓ what they did (methods),
- ✓ what they discovered (results), and
- ✓ what they make of their discovery (discussion).

It is, however, not as easy as one might anticipate to meet these expectations.

9a. Authorship

The names that appear at the beginning of a paper serve one important purpose. They let others know who conducted the research and should get credit for it. It is important to know who conducted the research in case there are questions about methods, data, and the interpretation of results. Likewise, the credit derived from publications is used to determine a researcher's worth. Researchers are valued and promoted in accordance with the quality and quantity of their research publications. Consequently, the authors listed on papers should fairly and accurately represent the person or persons responsible for the work in question.

Contribution. *Authorship* is generally limited to individuals who make significant contributions to the work that is reported. This includes anyone who:

- ✓ was intimately involved in the conception and design of the research,
- ✓ assumed responsibility for data collection and interpretation,
- ✓ participated in drafting the publication, and
- ✓ approved the final version of the publication.

There is disagreement, however, over whether authorship should be limited to individuals who contribute to all phases

ICJME Statement on Authorship

An "author" is generally considered to be someone who has made substantive intellectual contributions to a published study... .

Authorship credit should be based on 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

All persons designated as authors should qualify for authorship, and all those who qualify should be listed.

Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

http://www.icmje.org/

of a publication or whether individuals who made more limited contributions deserve authorship credit.

The widely accepted *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, authored by the International Committee of Medical Journal Editors (ICMJE), sets a high standard for authorship. It recommends limiting authorship to persons who contribute to the conception and design of the work or to data collection and interpretation and, in addition, play an important role in drafting and approving the final publication. Anyone who plays a lesser role can be listed under *acknowledgments* but not at the beginning of the paper as an *author*.

As influential as they are, the ICMJE recommendations on authorship are not uniformly followed, even in journals that subscribe to the ICMJE *Requirements*. Practices for determining authors vary considerably by discipline and even from laboratory to laboratory. This places most of the responsibility for decisions about authorship on the researchers who participated in the work reported in each

publication. These decisions are best made early in any project, to avoid misunderstandings and later disputes about authorship.

Importance. Authors are usually listed in their order of importance, with the designation *first* or *last author* carrying special weight, although practices again vary by discipline. Academic institutions usually will not promote researchers to the rank of tenured faculty until they have been listed as first or last author on one or more papers.

As with the principle of contribution, however, there are no clear rules for determining who should be listed as first author or the order in which other authors should be listed. The ICMJE *Requirements* simply note that:

> The order of authorship on the byline should be a joint decision of the coauthors. Authors should be prepared to explain the order in which authors are listed.

Some journals have specific rules for listing authors; others do not, again placing most of the responsibility for this decision on the authors themselves.

Corresponding or primary author. Many journals now require one author, called the *corresponding* or *primary* author, to assume responsibility for all aspects of a publication, including:

- ✓ **the accuracy of the data,**
- ✓ **the names listed as authors (all deserve authorship and no one has been neglected),**
- ✓ **approval of the final draft by all authors, and**
- ✓ **handling all correspondence and responding to inquiries.**

In accepting this responsibility, *corresponding authors* should take special note of the fact that they are acting on behalf of their colleagues. Any mistakes they make or fail to catch will affect their colleagues' as well as their own careers.

9b. Elements of a responsible publication

Each element of a publication serves an important purpose and must be carefully prepared to make sure it serves that purpose.

Abstracts. Abstracts summarize the content of publications in sufficient detail to allow other researchers to assess relevance to their own work. Abstracts, therefore, should neither understate nor overstate the importance of findings. Negative results that might be important to other researchers or the public should be mentioned. The data presented in the abstract should be the same as the data presented in the body of the publication—an obvious requirement, but one that studies of publication practices show some authors do not follow (see Pitkin, Additional Reading).

Standards for Reporting Research Results
The CONSORT Statement

Abstract

To comprehend the results of a randomized controlled trial (RCT), readers must understand its design, conduct, analysis, and interpretation. That goal can be achieved only through complete transparency from authors. Despite several decades of educational efforts, the reporting of RCTs needs improvement. Investigators and editors developed the original CONSORT (Consolidated Standards of Reporting Trials) statement to help authors improve reporting by using a checklist and flow diagram. The revised CONSORT statement presented here incorporates new evidence and addresses some criticisms of the original statement.

The checklist items pertain to the content of the Title, Abstract, Introduction, Methods, Results, and Discussion. The revised checklist includes 22 items selected because empirical evidence indicates that not reporting the information is associated with biased estimates of treatment effect, or because the information is essential to judge the reliability or relevance of the findings. We intended the flow diagram to depict the passage of participants through an RCT. The revised flow diagram depicts information from four stages of a trial (enrollment, intervention allocation, follow-up, and analysis). The diagram explicitly shows the number of participants, for each intervention group, included in the primary data analysis. Inclusion of these numbers allows the reader to judge whether the authors have done an intention-to-treat analysis.

http://www.consort-statement.org/Statement/revisedstatement.htm

To ensure completeness and accuracy, many journals now use *structured* abstracts. This assures that all of the key elements of the publication are mentioned and easily identified. With scientific publications now running in the millions per year in well over 100,000 journals, researchers cannot read all seemingly relevant publications in detail. They must rely on abstracts to point them to important developments and findings.

Methods. Researchers cannot check and build on the work of others without knowing how it was conducted. Methods therefore should be described in sufficient detail to allow other researchers to replicate them. When researchers use well-established methods, this section of a publication can be shortened, provided appropriate references are given to a full description of the methods along with any changes that have been made. New or unique methods should be described in more detail to allow other researchers to replicate the work.

Results. Research results should be reported in sufficient detail to allow other researchers to draw their own conclusions about the work. This does not mean that every piece of recorded data should be reported. Researchers can and must process their raw data before publication (to keep publications to a reasonable size if for no other reason). However, results should not be left out just because they do not agree with the conclusions the authors would like to reach. The results section should represent a complete summary of what was discovered, leaving interpretations for the closing discussion.

Discussion. Researchers can and should evaluate the significance of their findings under *discussion*—also called *conclusion* or *summary*. This portion of a publication helps those who are less familiar with the field understand the importance of the findings. It also provides a venue for identifying unresolved problems and future research needs.

Since the *discussion* is read by individuals who may not be able to evaluate its validity, it is particularly important that authors avoid bias and one-sided reporting in this section. Cautions and other interpretations should be mentioned along with the limitations of the study to provide a balanced view of the reported results. Review articles (articles that survey research findings in particular areas) should make an honest effort to cover all relevant work. It is not always easy to recognize one's own biases, which is a good reason to ask colleagues to read and comment on manuscripts before they are submitted for publication.

Notes, bibliography, and acknowledgments. *Notes, bibliography, and acknowledgments* should be used to place publications in context and to give credit to others for their ideas, support, and work. They serve to:

- ✓ **provide support for important statements of fact or assumptions,**
- ✓ **document the work of others used in the publication,**
- ✓ **point to additional reading and resources, and**
- ✓ **recognize the support of funding agencies or colleagues and staff who do not qualify as authors.**

Since others rely on and trust this information, it, along with every other element of a responsible publication, should be fair and accurate.

9c. Practices that should be avoided

Competition in research for funding and recognition places considerable pressure on researchers to publish. Ideally, quality should matter more than quantity, but in reality quantity—the number of articles published—is often used as a measure of productivity and ability. However, no matter how important it may be to publish, some publication practices should be avoided.

The Council of Science Editors
A New Standard for Authorship (1998 proposal)
Paul J. Friedman, MD

Publication has become the essential achievement for academic advancement for both clinical and basic scientists, although the type and number of publications demanded may vary widely. Despite a recent increased emphasis on teaching as a meritorious activity, faculty and trainees realistically feel intense pressure to publish. One unfortunate result has been a proliferation of papers and journals and a variety of abuses of trainees, junior colleagues, and patients, and of integrity.

To help restore a sense of proportion and confidence in the validity of biomedical publication, this conference proposes a new step in the evolution of the concept of authorship. We propose to publish the contributions of the individuals associated with a manuscript. The information will be solicited on a modified copyright form, which will be filled out and signed by all the authors. We propose a check-off list, such as the following:

- ☐ Concept
- ☐ Design
- ☐ Supervision
- ☐ Writing
- ☐ Resources
- ☐ Data collection and/or processing
- ☐ Analysis and/or interpretation
- ☐ Literature search
- ☐ Critical review
- ☐ Material

http://www.councilscienceeditors.org/services/friedman_article.cfm

Honorary authorship. The practice of listing undeserving authors on publications, called "honorary" authorship, is widely condemned and in the extreme considered by some to constitute a form of research misconduct. However, common agreement notwithstanding, honorary authorship is a significant problem in research publication today (see articles by Drenth and Flanagin, Additional Reading). Researchers are listed on publications because they:

- ✓ **are the chair of the department or program in which the research was conducted,**
- ✓ **provided funding for the research,**
- ✓ **are the leading researcher in the area,**
- ✓ **provided reagents, or**
- ✓ **served as a mentor to the primary author.**

Persons in these positions can make significant contributions (see left) to a publication and may deserve recognition. However, they should not be listed if these are the only contributions they made.

Salami publication. *Salami publication* (sometimes called bologna or trivial publication) is the practice of dividing one significant piece of research into a number of small experiments (least publishable units or LPUs), simply to increase the number of publications. This practice may distort the value of the work by increasing the number of studies that appear to support it. It also wastes valuable time and resources. Before an article is published it is reviewed, edited, and in one form or another prepared for publication. After publication it is entered into indexes and databases, such as the National Library of Medicine's *PubMed*®. Libraries and individuals purchase the journal in which it is published. If the same information could be summarized in one article as opposed to two, three, or more, everyone involved, from the publishers to libraries and the researchers who have to keep up to date on current information, benefits. Researchers therefore should avoid trivial or salami publication.

Duplicate publication. Duplicate publication is the practice of publishing the same information a second time without acknowledging the first publication. This practice not only wastes time and resources but can also distort the research record and endanger public health.

Researchers rely on meta-analyses (analyses of a group of similar experiments or *studies of studies*) to improve their understanding of difficult problems. One clinical trial or epidemiological study may not produce clear evidence, but the pooled results of many related studies can. However, if some of the studies in the pooled study (meta-analysis) have been published two or more times without proper notice, the results of the meta-analysis will be unfairly weighted in the

direction of the duplicate publication. Therefore, duplicate publication is not only deceptive but poses real dangers to public health and safety (see articles by Jefferson and Tramer, Additional Reading).

Premature public statements. Academic or scholarly publication practices are designed to assure that the information conveyed to broader audiences through these practices is accurate and fairly presented. While the system is not foolproof and erroneous or biased information is from time to time published, standard publication practices do serve an important quality control role in research. Accordingly, researchers should follow standard publication practices when making research results public and not issue premature public statements about their work before it has been reviewed. From time to time there may be overriding circumstances, such as early indications of a significant threat to public health or safety, but for the most part research results should be made public only after they have been carefully reviewed and properly prepared for publication.

Questions for discussion

1. What are the accepted criteria for authorship in your field of research? If there are none, what should they be?
2. Should researchers be allowed to omit some details from the methods section of their publications until they have had time to patent their methods?
3. What should a researcher do if the journal that has accepted a publication will not let the researcher publish the method or results in as much detail as the researcher feels is necessary?
4. What should a researcher do if an undeserving author in a position of some authority demands authorship status on a paper?
5. What factors should be considered when making a decision to publish the results of a study in one article versus several articles?

Resources

Policies, Reports, and Policy Statements

Council of Biology Editors. *Scientific Style and Format*, CBE, 2006. (available at: http://www.councilscienceeditors.org/publications/style.cfm)

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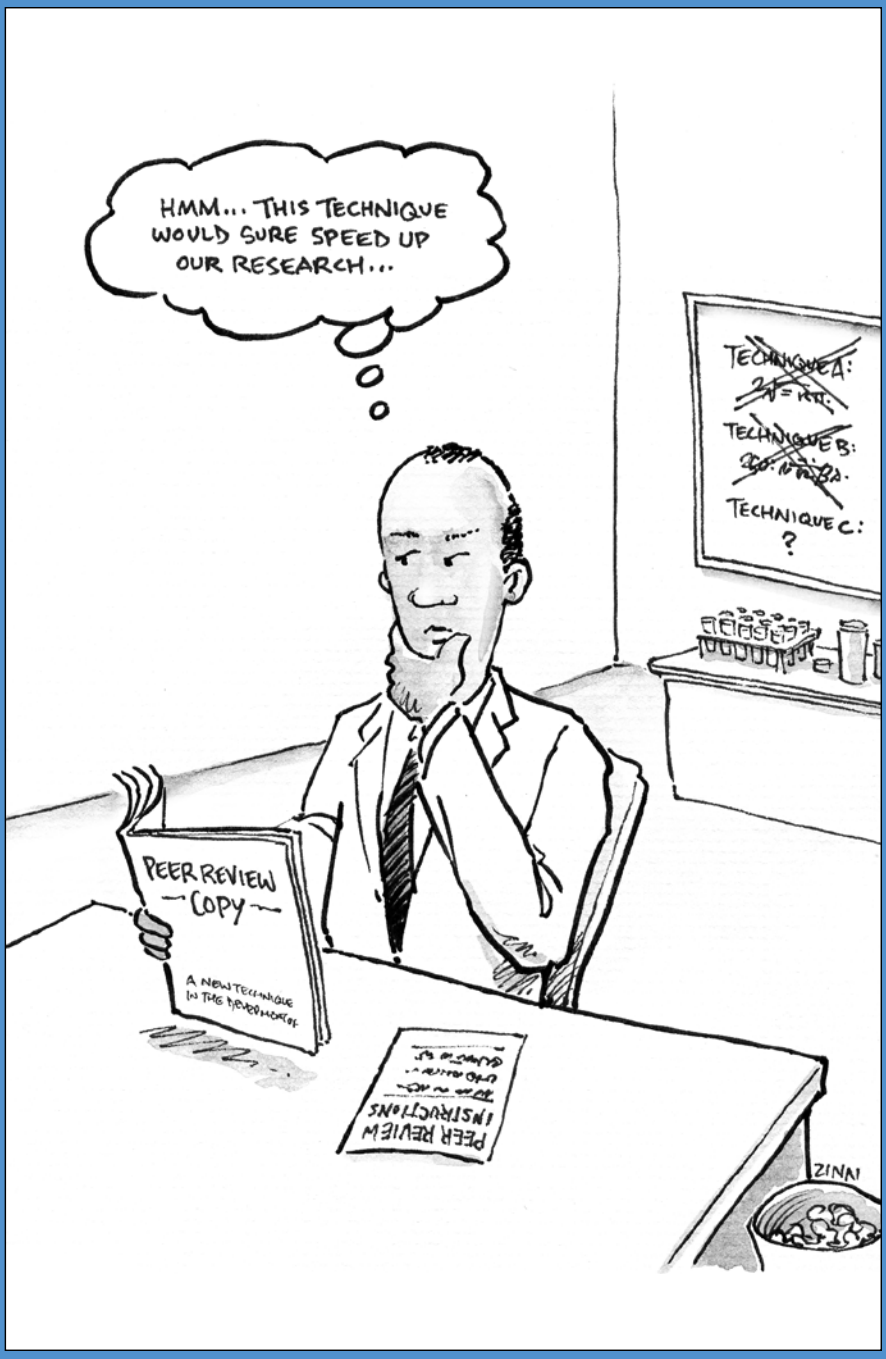

One of the benefits of serving as a peer reviewer?

10. Peer Review

Peer review—evaluation by colleagues with similar knowledge and experience—is an essential component of research and the self-regulation of professions. The average person does not have the knowledge and experience needed to assess the quality and importance of research. Peers do. Therefore many important decisions about research depend on advice from peers, including:

- ✓ **which projects to fund (grant reviews),**
- ✓ **which research findings to publish (manuscript reviews),**
- ✓ **which scholars to hire and promote (personnel reviews), and**
- ✓ **which research is reliable (literature reviews and expert testimony).**

The quality of the decisions made in each case depends heavily on the quality of peer review.

Case Study

Dr. Sung L. is struggling with the decision whether to agree to review the work of an advanced graduate student at another university for publication in the major journal in his field. He is familiar with the student's work and attended a session several months ago at which she presented a brief report on her work. It clearly overlaps with his research in a number of ways, which is one reason he has been asked to serve as a reviewer.

Dr. L. knows he is qualified to do the review and is confident he can provide an objective, constructive judgment of the students's work. However, since his students are working on similar problems, he is concerned about the appearance of a conflict of interest. In addition, he is not sure he wants to learn more about the work in question until he publishes his own work, to avoid later charges that he unfairly used some of the student's ideas. Finally, there is the matter of yet another lost weekend doing the review, when his department chair has already told him to cut down on unpaid professional service.

Should Dr. L. agree to do the review?

If he is uncertain about his responsibilities, where can he get advice?

Would the situation be different if he had been asked to review the student's work for an appointment or promotion decision?

Peer review can make or break professional careers and directly influence public policy. The fate of entire research programs, health initiatives, or environmental and safety regulations can rest on peer assessment of proposed or completed research projects. For peer review to work, it must be:

- ✓ **timely,**
- ✓ **thorough,**
- ✓ **constructive,**
- ✓ **free from personal bias, and**
- ✓ **respectful of the need for confidentiality.**

Researchers who serve as peer reviewers should be mindful of the public as well as the professional consequences of their evaluations and exercise special care when making these evaluations.

10a. Meeting deadlines

The effort researchers put into peer review is for the most part not compensated. Researchers may receive reimbursement for travel and per diem when they attend special grant-review sessions and occasionally are paid a basic daily stipend, but this seldom covers the true cost of reviewing a manuscript or a stack of grant applications. As uncompensated effort, the time researchers devote to peer review can easily take second place to other obligations. Running a crucial experiment or submitting a grant application on time understandably is more important than reviewing someone else's work.

However pressed you are for time, if you agree to do a review, you should find the time to meet your obligation in a timely manner. Research is competitive. Researchers are rewarded for discoveries. They should not lose their priority for a discovery due to the tardiness of a reviewer sending comments on a manuscript. Research is also useful. The

Editors of the Publications Division
American Chemical Society

Ethical Obligations of Reviewers of Manuscripts

1. ...every scientist has an obligation to do a fair share of reviewing.
2. A chosen reviewer who feels inadequately qualified to judge the research reported in a manuscript should return it promptly to the editor.
3. A reviewer (or referee) of a manuscript should judge objectively the quality of the manuscript, of its experimental and theoretical work, of its interpretations and its exposition, with due regard to the maintenance of high scientific and literary standards. A reviewer should respect the intellectual independence of the authors.
4. A reviewer should be sensitive to the appearance of a conflict of interest....

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6. A reviewer should treat a manuscript sent for review as a confidential document....
7. Reviewers should explain and support their judgments adequately....
8. A reviewer should be alert to failure of authors to cite relevant work by other scientists,...
9. A reviewer should act promptly, submitting a report in a timely manner.
10. Reviewers should not use or disclose unpublished information, arguments, or interpretations contained in a manuscript under consideration, except with the consent of the author....

http://pubs.acs.org/ethics/eg_ethic2000.pdf

announcement of discoveries that can benefit the public should not be delayed because someone who agreed to review a manuscript does not have the time to do the review.

Editors, program managers, and others who rely on peer review to make decisions generally provide a deadline for getting the review done when they first contact reviewers. Anyone who agrees to take on a peer review assignment under these conditions should meet the proposed deadline. If the time frame is not reasonable, either decline to do the review or ask for more time in advance. Do not delay someone else's work just because you are short on time.

10b. Assessing quality

Journal editors, grant administrators, and others rely on peers to assess the quality of proposed and published research. Some parts of an application or manuscript can be checked fairly easily. Are the calculations correct? Is the method that has been used or proposed appropriate? Do the reported results support the conclusions? Other parts are more difficult to confirm. Have the data been accurately recorded and reported? Were the experiments run? Did the subjects give consent? Do the articles cited in the references and bibliography contain the information they are said to contain?

Peers who are asked to make judgments about the quality of a proposed or completed project must do their best to determine whether the work they have been asked to review is internally consistent and conforms to the practices of their field of research. This certainly includes:

- ✓ **assessing whether the research methods are appropriate;**
- ✓ **checking calculations and/or confirming the logic of important arguments;**
- ✓ **making sure the conclusions are supported by the evidence presented; and**
- ✓ **confirming that the relevant literature has been consulted and cited.**

At the very least, peer reviewers should be expected to assess whether the manuscript or proposal under review makes sense and conforms to accepted practices, based on the information presented.

Research that conforms to accepted practices can still have problems. Research quality can be compromised by:

- ✓ **careless mistakes made in reporting data and/or listing citations;**
- ✓ **the deliberate fabrication and falsification of data;**
- ✓ **improper use of material by others (plagiarism);**

- ✓ **inaccurate reporting of conflicts of interest, contributors/ authors; and**
- ✓ **the failure to mention important prior work, either by others or by the researcher submitting a paper for publication.**

However, how much peer reviewers can or should do to detect these and other deceptive or sloppy practices remains subject to debate.

There are limits to the amount of checking that is both reasonable and practical. Unless given permission to do so, reviewers should not discuss the work they are reviewing with the authors. In many cases, reviews are "blind" (no author identification), so reviewers could not check with

Society for Neuroscience
Responsible Conduct Regarding Scientific Communication (1998)

2. Reviewers of Manuscripts

2.1. Thorough scientific review is in the interest of the scientific community.

2.2. A thorough review must include consideration of the ethical dimensions of a manuscript as well as its scientific merit.

2.3. All scientists are encouraged to participate if possible when asked to review a manuscript.

2.4. Anonymity of reviewers should be preserved unless otherwise stated in the guidelines for authors and for reviewers, or unless a reviewer requests disclosure.

2.5. Reviewers should be chosen for their high qualifications and objectivity regarding a particular manuscript.

2.6. Reviews should not contain harsh language or personal attacks.

2.7. Reviews should be prompt as well as thorough.

2.8. Reviewers must not use non-public information contained in a manuscript to advance their own research or financial interests.

2.9. Information contained in a manuscript under review is confidential and must not be shared with others.

http://www.sfn.org/index.cfm?pagename=responsibleConduct_reviewersOfManuscripts/

authors even if they wanted to. In addition, it is not reasonable to expect reviewers to check every reference and detail. The fact remains, however, that peer reviewers frequently miss problems that might have been detected had the reviewer checked a little more carefully.

If you agree to serve as a peer reviewer, remember that you have essentially been asked to provide your stamp of approval for someone else's work. In such circumstances, it is wise to do your homework. Do not give your stamp of approval too easily.

10c. Judging importance

In addition to quality, peer reviewers are also asked to make judgments about the importance of proposed or published research. They are asked to answer questions such as:

- ✓ **Assuming a researcher could carry out a proposed research project, is it important to do so?**
- ✓ **Are these research results important enough to publish?**
- ✓ **Has a researcher made important contributions to a field of study?**
- ✓ **Is this evidence important enough to be used in setting policy?**

Along with quality, judgments about importance essentially determine which research is funded or published and which researchers are hired and relied upon for advice.

Peer reviewers do not always make judgments about importance with an open mind. Studies have shown that they can be swayed by:

- ✓ **the stature of the researcher who conducted the research or the institution at which the research was conducted;**
- ✓ **country of origin;**
- ✓ **a preference for one research method over another, e.g., a clinical versus a laboratory approach; and**
- ✓ **the outcome of the studies under review.**

For the most part, these factors should not have a bearing on judgments about importance and yet they do. Each has been shown to influence the judgments peer reviewers make about the publication of research results (see articles by Callaham, Cho, Dickersin, Godlee, Jadad, and Link, Additional Reading).

There is no simple solution to the problem of bias in peer review. Peers frequently are not of one mind about what is or is not important. One reviewer may feel that a field of research should move in one direction, a second in an entirely different direction. Often, it takes time and more research to find out whether a line of investigation or a particular set of findings is *important*. Nonetheless, researchers can take steps to lessen the impact of bias on their judgments and to help others judge for themselves whether a researcher has biases.

One way to lessen the impact of bias is to write *transparent* reviews. By "transparent" is meant laying out clearly for anyone reading the review how it was prepared, the literature that was used, and the reviewer's own possible biases. If reviewers fully and carefully explain how their judgments about importance were made, others can assess whether they want to accept those judgments.

A second way that has been proposed to lessen the impact of bias is to eliminate anonymous reviews. Some argue that this would lessen the candor and rigor of reviews; others that it would make reviewers more accountable. For the present, most reviews are anonymous, which places the burden for fairness on the reviewer. If you have strong feelings about a person or particular line of investigation, tell the person who asked you to do the review and consider whether you can, in fact, provide an impartial assessment.

10d. Preserving confidentiality

Some information that is shared during peer review is shared confidentially, that is, with the understanding that it will not be shared with anyone else without permission. Confidentiality is generally required during:

- ✓ grant reviews,
- ✓ manuscript reviews, and
- ✓ personnel reviews.

During grant and manuscript reviews, confidentiality helps protect ideas before they are funded or published. In personnel reviews, confidentiality is important to protect personal privacy.

Peer reviewers have an obligation to preserve confidentiality during the review process if they have been asked to do so. While this obligation might seem obvious, it can be compromised in some seemingly harmless and other more harmful ways. For example, although researchers sometimes do, it is *not acceptable* to do any of the following without getting permission:

- ✓ ask students or anyone else to conduct a review you were asked to do;
- ✓ use an idea or information contained in a grant proposal or unpublished manuscript before it becomes publicly available;
- ✓ discuss grant proposals or manuscripts you are reviewing with colleagues in your department or at a professional meeting;
- ✓ retain a copy of the reviewed material (generally manuscripts and grant proposals should be shredded or returned after the review is complete); and
- ✓ discuss personnel and hiring decisions with colleagues who are not part of the review process.

There may be times when some added advice during a review may be helpful, but reviewers should not seek this

advice without getting permission. It may also be tempting to use information in a grant application or manuscript to speed up your own research, but until it has been made public, confidential information is not available for use, even to reviewers. If you are not comfortable protecting confidential information, then do not agree to be a peer reviewer.

Researchers who are in a position to pass judgment on the work of colleagues have significant power. They can hasten or slow that work; credit or discredit it. They have the power to shape entire fields of research and to influence public policy. If you have that power, make sure you use it responsibly and with some compassion, knowing that what you say and do directly affects the careers of other researchers.

Questions for discussion

1. **What should researchers or students do if a colleague or mentor asks them to take a look at a manuscript they have not been authorized to review?**
2. **What information contained in a manuscript or proposal should reviewers be expected to check?**
3. **Should peer review be anonymous?**
4. **How can researchers who sit on committees that advise on research directions separate their own interests from the best interests of the field they are helping shape?**
5. **What would happen if the public lost confidence in peer review and looked for other mechanisms to judge the quality and importance of research?**

Resources

Policies, Reports, and Policy Statements

International Committee of Medical Journal Editors. *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, 2006. (available at: http://www.icmje.org/)

National Institutes of Health. *NIH Guide – Objectivity in Research*, Bethesda, MD: NIH, 1995. (available at: http://grants2.nih.gov/grants/guide/notice-files/not95-179.html)

University of Michigan Medical School. *Guidelines for the Responsible Conduct of Research: Right and Responsibilities of Peer Review*, Ann Arbor, MI: UM, 1999. (available at: http://www.responsibility.research.umich.edu/UMMSpeer.html)

General Information Web Sites

International Congress on Peer Review and Biomedical Publication. *Home Page*, 2005. http://www.ama-assn.org/public/peer/peerhome.htm

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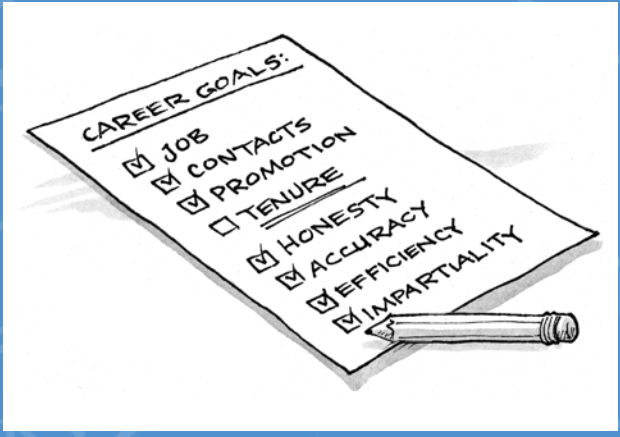
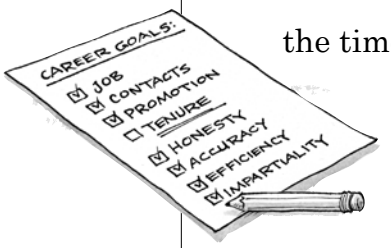
Part V.

Safe Driving and Responsible Research



Part V: Safe Driving and Responsible Research

IT IS NOT EASY TO GO THROUGH LIFE DOING everything we must or should do all of the time. It should therefore come as no surprise that in many small and some significant ways, researchers do not always follow the rules of the road for responsible conduct in research. They roll through stop signs when they clean up their data more than they



should, accept honorary authorship, purchase something with grant funds that is not strictly allowed, or give colleagues more favorable reviews than they deserve. From time to time, they drive faster than the posted speeds to arrive at their destination—a grant, a publication, new knowledge—a little more quickly.

We ignore *musts* and *shoulds* in life for different reasons. For one, society sends mixed messages about obeying rules. Should you turn in someone for cheating or "mind your own business"? Rules also can conflict with one another. Should you report misconduct if doing so puts your career at risk? And finally, we are amazingly adept at "bending" or "stretching" the rules by thinking up good reasons why a questionable course of action is acceptable under a particular set of circumstances, that is, at justifying our actions, whatever they are.

The ease with which rules can be bent or ignored is particularly evident early in the career track the majority of researchers traditionally follows. Studies consistently suggest that well over half and probably closer to three-quarters of college students cheat during their undergraduate years. In two separate studies, 1 in 10 research trainees reported a willingness to break the rules to get grants funded or papers published. Roughly the same number of students applying for research fellowships and residencies in medicine significantly misrepresents their research publications on résumés, as confirmed in studies conducted

in six medical specialties. Presumably most individuals who cheat or inflate résumés know that it is wrong to do so, but they nonetheless find reason for engaging in these practices.

The same patterns of behavior can easily spill over into other aspects of research. The pressures that prompt students to bend or ignore the rules do not disappear after graduation. Getting into good schools is replaced by getting a good job and promotions. Competition for grades is replaced by competition to get funded and published. Too little time to study for tests is replaced by too little time to teach, mentor, provide service, and do research. The stakes may even increase later in careers, as family responsibilities are added into the mix and personal ambitions grow, making it even easier to put more pressure on the accelerator to get to your destination a little faster.

There are many quick-and-easy reasons that can be called up to justify bending or ignoring some of the rules of the road for responsible research:

- ✓ **I already have enough information to know what the results will be, so there is no need to run the controls again, even though they did not give me the expected results the first time.**
- ✓ **No one funds truly exploratory research, so the only way to test new ideas is to use funds from an existing grant, even though these funds are for other work.**
- ✓ **If my bosses read my research papers rather than counting them, I wouldn't have to publish the same research twice or chop it up into small, insignificant pieces.**
- ✓ **Given the competition in this field, you cut your own throat if you share your methods and information with colleagues too freely.**

- ✓ They will cut off my funds if I report these results, so for the good of my laboratory and staff I should sit on them for a while longer.
- ✓ I know my research is not going to harm anyone, so why waste my time and the time of the IRB getting permission.

Rules are not always reasonable or rationally applied. Life and colleagues are not always fair. Good guys do sometimes seem to come in last.

However, the problem with quick-and-easy justifications and catchy phrases is they fail to take into consideration the larger consequences of our actions. What would happen if everyone decided, for one "good" reason or another, to run stop signs, drive on the wrong side of the road, or ignore the speed limit? Obviously, chaos would quickly ensue and driving would no longer be safe (or become even more hazardous than it is already). The same would be true of research if researchers routinely ignored responsible research practices and did what they thought was necessary simply to achieve some end, whether the discovery of truth, the development of something useful, or personal success.

As stated at the beginning of the *ORI Introduction to RCR*, there is no one best way to undertake research, no universal method that applies to all scientific investigations. Accepted practices for the responsible conduct of research can and do vary from discipline to discipline and even laboratory to laboratory. There are, however, some important shared values for the responsible conduct of research that bind all researchers together, including honesty, accuracy, efficiency, and objectivity. There are no excuses for compromising these values. Their central role in research is the responsibility of each and every researcher. Drive safely and be a responsible researcher.

Resources

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Notes

Notes

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From the Vice Provost for Research

A Layman's Guide to Conflict of Interest

Introduction

The University of Pennsylvania supports the translation of research results into practical applications for the public good. To this end, the University encourages faculty to patent and license inventions arising from their research, to participate in the establishment of industry partnerships designed to commercialize novel technologies, to accept company-sponsored research funding, and to consult for private companies. Faculty involvement in commercial activities carries many advantages, including the practical application of new technologies, the receipt of royalty income for the University and the faculty, and the provision of an additional source of research funding. Contemporary attitudes are best captured by the fact that the Federal government has mandated that universities seek to commercialize the results of federally supported research for the public good.

However, the increasing involvement of faculty with commercialization ventures carries with it certain intrinsic dangers, which have the potential for diverting the University and its faculty from their primary educational, research, and service missions. Conflicts of interest can arise when the interests of the commercial venture differ from the interests and primary obligations of the University and its faculty, or when the commercial ventures consume an undue share of the faculty members attention.

This primer describes commonly observed conflicts of interest. In addition, illustrations are provided of some approaches to manage potential conflicts so that faculty can pursue ventures in the commercial arena without compromising their academic responsibilities. The University has established policies that define potential conflicts and provide guidelines and procedures for limiting and managing them. Commercialization ventures and licenses of technology are negotiated by the Center for Technology Transfer (CTT) on behalf of both the faculty member and the University. CTT staff are alert to potential conflicts and refer them to the University Conflict of Interest Standing Committee (CISC) for review and advice. The CISC reviews potential conflicts and recommends management strategies to the Vice Provost for Research.

Individual Conflicts of Interest

Conflict of Commitment

Principle: Faculty owe their primary commitment and allegiance to the University.

Non-University activities include involvement with commercial ventures in roles such as serving on the board of directors or on the scientific advisory board, acting as a manager or scientific director, consulting, and the like. These activities create commitments with the potential to compete with the primary commitment to the University--teaching, research, and service during the academic year (which is 9 months for some faculty and 11 months for others).

Management strategy. Faculty may not engage in non-academic commitments that, in the aggregate, exceed one day in seven during the academic year. This is a limitation imposed by University policy. There is a good faith assumption that faculty will accurately estimate the time devoted to non -academic activities regardless of where they are conducted. This policy applies to the time involved in extramural activities, and not to the dollar amount that is paid for such services.

If a faculty member is involved in founding a new company, he/she may be induced to dedicate excessive

time to the myriad issues associated with new ventures. Under these circumstances, a potential conflict of commitment can be reduced by ensuring that qualified individuals are recruited to manage the business and scientific aspects of the company, so that the faculty member has limited fiduciary and other responsibilities, and is able to provide scientific consultation without getting immersed in the day-to-day supervision of research and development. Alternatively, the faculty member may take an unpaid leave of absence for a period of time to dedicate her/himself full time to the new company. Another strategy is to license a patent to an established company that then undertakes product development while paying royalties to the faculty member and the University, rather than attempt to establish a new company to develop a novel technology.

Conflict of Financial Interest

Principle. A faculty member has a responsibility to respect the financial well-being of the University.

Through various relationships with a commercial entity, a faculty member could assume responsibility for the financial well-being of that commercial entity that might produce a conflict of interest by competing with the financial interests of the University. Fiduciary responsibility for a company is created when a faculty member is appointed to the Board of Directors of the company or becomes an officer or manager in the company. If the company is a supplier to the University or holds a patent license from the University, the potential for conflict is augmented.

Management strategies. Faculty members must negotiate technology commercialization proposals through the Center for Technology Transfer. In most cases, contracts for research at the University must be administered through the Office of Research Administration (or other administrative branch) of the University. To protect the intellectual property rights of the University, discoveries made using University resources and facilities must be disclosed to the Center for Technology Transfer, which may file a patent for the University. Only if the University declines to protect the disclosed technology, may a faculty member apply for a patent without University involvement.

If a faculty member has a fiduciary responsibility or an equity interest in a company that does business with the University or holds patent licenses from the University, the faculty member must disclose these relationships (usually done as part of the required annual disclosure form described below). Faculty sign consulting agreements, involving intellectual property or the right to do work in certain areas, at their own risk. If not written properly, such agreements may unduly restrict the research activities of the faculty and the intellectual property rights of the University. Upon request, the Center for Technology Transfer will review consulting agreements.

Conflict of Research Integrity

Principle. Faculty should maintain the highest level of scientific integrity in the conduct of research. The complete, objective, and timely dissemination of new findings through publications and presentations, is essential for research integrity.

The potential for personal gain must not jeopardize or appear to jeopardize the integrity of the research process, including the choice of research, its design, the interpretation of results, and the reporting of results. If an investigator has a significant financial interest in a commercial venture, then there may be a temptation to dedicate research effort to development of saleable products or processes for that company. A faculty member is particularly at risk of conflict if he/she has a sponsored research agreement (SRA) from the company in which he/she has a financial interest. Furthermore, the possible conflict may increase in proportion to the impact the company-sponsored research could have upon the value of the faculty member's financial interest.

Management strategies. A plan must be individually tailored to protect against potential conflicts of research integrity.

One troublesome problem encountered by the Conflict of Interest Standing Committee is the request for a

sponsored research agreement from a company in which a faculty member has an equity interest or a fiduciary responsibility. One option is to identify another investigator, with no financial interest, to undertake the research project. Another option is to involve a disinterested faculty member as a co-investigator with control over the design and analysis of research projects, to certify integrity of all aspects of the research program. Finally, in rare cases, it may be justified to create an oversight committee of disinterested scientists who certify the integrity of the program by an appropriate review process. In some instances, a proposed sponsored research project is more appropriately performed at the company itself rather than at the University. In all instances, presentations or publications must clearly disclose the sources of funding and any financial interest that could influence the perception of research integrity.

Conflict of Educational Mission

Principle. Students and post-doctoral fellows must be assured of an educationally appropriate training program.

Education is a salient mission of the University, and training programs should be designed to give priority to the educational needs of students and research trainees such as postdoctoral fellows. Sometimes the goals of a commercial entity that sponsors research at the University may be in conflict with the goals of an optimal training program.

Management strategies. Usually, it is inappropriate to support the stipends or research ex- penses of students or postdoctoral fellows through sponsored research funding from commercial entities in which the faculty member has a financial interest. In those cases where a student or postdoctoral fellow is involved in research that is supported by a company-funded SRA, the SRA should state that the presentation of results will not be controlled by the company.

Conflict of Interest Standing Committee (CISC)

The Conflict of Interest Standing Committee (CISC) reviews and makes recommendations on the resolution of cases of potential or real conflict of interest which arise from technology transfer activities or from sponsored projects of the University or its faculty. The recommendations of the CISC are transmitted to the Vice Provost as advice on the disposition of cases involving potential conflicts of interest, including a determination whether a real or potential conflict exists, and proposals on how such conflicts should be eliminated, reduced, or managed.

Cases involving potential conflict of interest may be referred to the CISC by the Center for Technology Transfer (CTT), by the Office of Research Administration (ORA), by University or School administrators, Department Chairs, or individual faculty. The staff of the Center for Technology Transfer (CTT) is responsible for referring to the CISC cases which arise from commercialization efforts under consideration by the CTT. The ORA staff is responsible for referring to the CISC cases which arise from applications for sponsored research support.

In its deliberations, the CISC depends upon University policies for guidance since it acts in a regulatory and advisory rather than a policy making capacity. University policies are promulgated in several documents which are listed at far right.

Procedures

Cases referred from the CTT. Upon learning of a potential conflict of interest, a CTT staff member prepares a brief descriptive memorandum which includes background, current status, proposed financial arrangements, and the nature of the potential conflict. After review by the individual who is the subject of the memorandum, it is distributed to members of the CISC, and to the appropriate Dean and departmental Chair, preferably at least one week in advance of the meeting of the CISC.

Cases referred from the ORA. The staff of ORA will review all grant and contract applications, identify those where the applicants have indicated a potential conflict, and screen these to determine which ones should be referred to the CISC. The staff will prepare a brief synopsis of the issues involved in each case referred to the CISC.

Cases from other sources. Deans, Department Chairs, or individual faculty may refer cases of potential conflict of interest to the Chair or staff of the CISC, who will review them, determine whether they are appropriate for consideration, and present them for review by the committee.

The CISC discusses the potential conflict and makes recommendations, including a determination whether a potential conflict of interest exists, and how it should be managed. A draft of these recommendations is circulated to all members of the CISC for comment. The final version is then circulated to the committee members for a mail/FAX/email ballot. After approval, the final recommendations are sent to the Vice Provost as advice. The Vice Provost may accept the recommendations or may return them to the CISC for further consideration, revision, or clarification. Once the recommendations have been accepted, the Vice Provost informs the faculty or staff member involved, with copies to the concerned Chair, Dean, and CISC.

The Department Chair and Dean are responsible for insuring that there is compliance with the recommendations of the Vice Provost. The Dean is responsible for reporting by letter to the Vice Provost, with a copy to the CISC, that compliance has been achieved.

If the conflict involves an application for sponsored research, the award will not be accepted until the Vice Provost for Research has conveyed a decision on compliance.

Confidentiality. The proceedings of the CISC are confidential, including all documents, drafts, and discussions.

Membership

The CISC consists of about 10 members of the standing faculty appointed by the Vice Provost for Research. Faculty members serve as citizens of the University and not as advocates for specific schools or constituencies. There are three ex-officio members, the Executive Director, Sponsored Programs, the Managing Director, Center for Technology Transfer, and an attorney from the Office of the General Counsel. In addition, invitations to meetings are extended to professional staff of the Center for Technology Transfer and to selected professional staff from the Schools. The CISC is chaired by a faculty member appointed by the Vice Provost. Staff support for the CISC will be provided by the Office of Research Administration and/or the Center for Technology Transfer, which will designate an individual to serve as Secretary of the Committee.

All faculty members, plus the Director, Office of Research Administration, and the Director, Center for Technology Transfer have voting rights. Other attendees participate in discussion but do not vote. Voting membership implies a commitment to attend all meetings unless the member is out of town or has other overriding obligations.

Meetings

Attendance. Meetings are limited to CISC members, invited staff, and other invitees, and are not open to the public.

Quorum. A quorum consists of over half of all voting members. In general, an attempt will be made to insure that there is a quorum present at all meetings. The CISC Chair, at her/his discretion, may require that certain decisions be approved by a majority of all voting members not just a majority of those attending a specific meeting. Final versions of recommendations will usually be approved by mail/FAX in order to insure that all voting members have an opportunity to register their opinions.

Conflicts for Committee Members

A CISC member is recused from discussion of a particular case under the following conditions: (1) The case involves a member of the same department; (2) The CISC member has a personal interest because of inter-departmental relationships, such as collaboration with the faculty member whose case is under consideration; (3) The CISC member has a fiscal interest in the case under discussion. Special exceptions to these guidelines may be made but only with the prior approval of a majority of the voting members.

Appeal Process

In the event of a disagreement between the responsible administrator(s) or investigator(s) and the Vice Provost regarding the management of a potential conflict, an appeal may be made to the Provost. The decision of the Provost is final.

University Policies

University policies relevant to conflict of interest are set forth in the sources listed below. A booklet which includes copies of these policies can be obtained from the Center for Technology Transfer, 3700 Market St, Suite 300, Philadelphia, PA 19104-3147, phone 215-573-4500; FAX 215-898-9519.

1. *Policy for faculty members* University of Pennsylvania: Conflict of Interest Policy for Faculty Members, *Almanac* March 8, 1983; and Handbook for Faculty and Academic Administrators, Section II.E.1.

2. *Extramural activities:* University University of Pennsylvania: Guidelines for Extramural Activities, Associations, and Interest for Staff, *Human Resources Policy Manual*, February 1, 1990.

3. *Extramural activities:* School of Medicine University of Pennsylvania Medical Center and Health System: Guidelines for Extramural Activities of Faculty, revised, 1995.

4. *Financial disclosure University of Pennsylvania:* Financial Disclosure Policy for Sponsored Projects; (Appendix 3, Conflict of Interest Standing Committee Procedures) *Almanac,* September 12, 1995.

5. *Student protection University of Pennsylvania:* Guidelines for Student Protection in Sponsored Research Projects and Student Access to Information Regarding Sources of Financial Support, *Almanac* October 21, 1986.

6. *Commercial sponsors University of Pennsylvania:* Policy Information for Potential Commercial Sponsors of Research at the University of Pennsylvania, *Almanac* May 17, 1983.

7. *Patent policy University of Pennsylvania:* Patent and Tangible Research Property Policies and Procedures of the University of Pennsylvania, *Almanac* March 15, 1994.

Where Do I Find More Information? Whom Do I Consult If I Have Questions?

The University has policies and procedures for reviewing and managing conflict of interest issues. A formal set of guidelines regarding conflict of interest and related matters appears in the *University of Pennsylvania Handbook for Faculty and Administrators* and in several other University documents. A booklet entitled *Information on Conflict of Interest* that brings these guidelines together in one place can be obtained from the Center for Technology Transfer.

At any time, faculty members may consult their department chairs and deans for advice about potential conflicts of interest. The University Conflict of Interest Standing Committee (CISC) reviews potential conflict of interest questions referred to it by the Center for Technology Transfer, by administrators, or by the

faculty. The CISC can be contacted through the Center for Technology Transfer.

In addition, faculty members are required to disclose all external activities and financial interests on a form that is distributed annually by all departments. This regular disclosure of all potential conflicts of interest serves to help the University monitor possible conflicts, and helps the faculty by providing them with assurance that they are acting in conformity with the spirit and guidelines of the University.

Contact information:

Center for Technology Transfer

3700 Market St, Suite 300

Philadelphia, PA 19104-3147

phone 215-573-4500

FAX 215-898-9519

http://www.upenn.edu/CTT

(Check University directory for names and email addresses of CTT staff members.)

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RESPONSIBLE CONDUCT OF BIOMEDICAL RESEARCH:

A Handbook for Biomedical Graduate Studies Students

Fourth Edition

BIOMEDICAL GRADUATE STUDIES PROGRAM
UNIVERSITY of PENNSYLVANIA

PREFACE TO THE FOURTH EDITION

Scientists agree that a trainee in biomedical research should be taught to maintain the highest standards of scientific integrity and ethical behavior in all phases of the conduct of research. Scientists and trainees should also be aware of the potential for subjectivity, unconscious bias and conflicts of interest that accompany the collection and treatment of data, the attribution of responsibility and credit, the mentoring of students and fellows, and the use of human and animal subjects for research. Scientific data collected and reported with the greatest care and ethical considerations may yet contain unrecognized errors due to the limitations of knowledge or technology. The requirement for high standards of scientific integrity and ethical behavior is important for a number of reasons. Scientists must be able to trust one another's work, since advances in science rely on the integrity of the research record. Furthermore, most research is carried out using public funds and thus the public should have confidence that this is money well-spent.

The goal of BGS's training in Responsible Conduct of Research (RCR) is to make graduate students aware of the rules, regulations and guidelines governing research and to minimize the potential problems associated with carrying out research. While these problems cannot be totally eliminated, they should be recognized, openly acknowledged and constructively addressed by discussions among scientists and with trainees. The incidence and consequences of misconduct can be sharply reduced by both good habits of research and by an increased understanding of what constitutes accepted responsible conduct. Education of this nature is the major goal of the RCR training program at the University of Pennsylvania.

The fourth edition of the handbook on RCR has been modified considerably, and is intended as a companion to the excellent publication, *ON BEING A SCIENTIST: third edition* (National Academy Press, Washington, DC 2009) and *Teaching the Responsible Conduct of Research Through a Case Study Approach (*a handbook prepared by the Association of American Medical Colleges, Korenman and Shipp, eds., 1994). These documents utilize a case study approach to initiate discussions of relevant issues in the conduct and training of biomedical research. The revised handbook includes additional material unique to the training of young investigators, provides practical information on the guidelines and procedures regarding alleged misconduct at the University of Pennsylvania, and includes examples of perspectives on the ethical conduct of research from the scientific community.

I would like to thank the faculty and staff of the University who assisted in editing this handbook and in developing the RCR training program. I am particularly grateful to Drs. Jane Glick and Glen Gaulton for compiling the previous three editions, to Dr. Hillary Nelson for providing material for this edition and for identifying the best available sources for RCR training and case studies and to Colleen Dunn and Judy Jackson in the BGS office for the many hours they spent executing the revised BGS RCR training and for proof-reading this document. I am also grateful to Dr. Stanley Korenman, UCLA Health System and the Association of American Medical Colleges for granting permission touse case studies and text from *Teaching the Responsible Conduct of Research through a Case Study Approach,* Korenman, S.G. and Shipp, A., eds. (AAMC, Washington, DC 1994), and to the U.S. Department of Health and Human Services, Office of Research Integrity, Nicholas Steneck, Ph.D., *ORI Introduction to the Responsible Conduct of Research (2007)* (http://ori.hhs.gov/documents/rcrintro.pdf).

Susan R. Ross, Ph.D.
University of Pennsylvania School of Medicine

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Question:

1. What do you think should be done?

E. Conflicts of Interest (Much of the material here was adapted from the University of Minnesota's website- http://www.research.umn.edu/ethics/curriculum/conflict_interest.html - and is used with permission). The research community is committed to conduct itself in accordance with the highest standards of integrity and ethics and in compliance with applicable state and federal laws related to conflict of interest and objectivity in research. COI are situations where two or more competing interests create the perception or the reality of an increased risk of bias or poor judgment. Because trust is one of the core ethical values of science, COI involves the abuse, actual, apparent, or potential, of the trust that people have in scientists. COI are not always inherently bad and can be expected to occur. It is how they are handled that can lead to improper, inappropriate, or bad outcomes.

DEFINITIONS

There are many areas in which a potential conflict of interest may arise. These include the following. (See Scientific Integrity by F. L. Macrina for a more detailed discussion.)

Financial conflict of interest: Although the legal definition varies from state to state, financial conflict of interest basically involves any situation in which an individual exploits his or her position for personal or financial gain. This is probably the most important type of conflict because of its visibility and the potential for damage to the reputation of the University and all concerned. A conflict of interest occurs when an academic employee or student compromises his or her professional judgment in carrying out University teaching, research, outreach, or public service activities because of an external relationship that directly or indirectly affects the financial interest of the academic employee or student, their family members, or any associated entity. An obvious example would be the ownership of, or a major interest in, a private firm by a faculty member or student who also has the decision-making responsibility in awarding a contract to that firm. Sponsorship of research by commercial firms in which the faculty member or student has a significant interest is another obvious example. However, many potential conflicts of interest can be more complex and not so clearly discernible.

Potential conflicts of interest due to financial involvements with commercial institutions may not be recognized by others unless specific information is provided. Therefore, the scientist must disclose all relevant financial relationships, including those of the scientist's immediate family, to the University, Department, Center or Division during the planning, conducting and reporting of research studies, to funding agencies before participating in peer review of applications for research support, to meeting organizers before presentation of results, to journal editors when submitting or refereeing any material for publication, and in all written communications and oral presentations.

Scientific conflict of interest: This type of conflict involves participation in journal reviews, review panels or other groups that make decisions regarding the allocation of resources or the publication of papers or someone who offers scientific testimony as an expert witness. Possible conflicts in review panels or refereeing are usually handled by excusing the person with the potential conflict. The situation with expert testimony is not so clear but the individual's background and connections should be revealed before the testimony.

Academic conflict of interest: This involves utilization of the name and/or the resources of the University for personal gain.

Conflict of commitment or effort: Most of the University rules about conflict of interest apply to faculty, and they strictly limit how much time, money, and energy that a faculty member can spend on outside interests: (http://www.hr.upenn.edu/policy/policies/005.aspx). Non-University activities that require considerable time and effort could lead to a significant decrease in the time and effort devoted to the employer, the University. The University has a policy that basically allows faculty the equivalent of one day per week for outside consulting or other professional activities. The policy requires approval in advance for activities that demand more than one day per month (on average) and reporting of all activities in which more than three days per term are spent.

BGS requires students on fellowships to devote all of their time to the educational program. Any outside jobs must be approved by BGS and must pertain to the education of the student. This is usually limited to teaching assistantships and other activities that are related to their educational goals.

Conflict of conscience: Such a conflict can arise when an individual's personal convictions (e.g., religious, ethical, or moral) are so strong that they influence the decision being made. Another type of conflict can arise for individuals working on a particular disease that affects a family member or friend. There are no widely accepted procedures for dealing with conflicts of this type.

Nepotism: In the past, the employment of two related individuals (e.g., a married couple) in the same department was not allowed by anti-nepotism rules. Now, the matter is handled by a rule that simply states such individuals cannot participate in any decisions affecting the other person.

Case Studies on Conflicts of Interest

Case #14 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled “Teaching Research Ethics: A Workshop at Indiana University”. © 1995 by Indiana University).

Marty Brown, a plant biologist at a major research university, is investigating the potential utility of transgenic tobacco plants as “factories” for the production of foreign proteins. The potential benefit of this research to human medicine is clear. For instance, the non-plant gene that Brown is working with right now is human Factor VIII, a protein essential for blood clotting and the protein that most people with hemophilia lack.

In his current experiment, Brown has introduced a construct of the Factor VIII gene into tobacco and has 100 transgenic plants that he is studying in a developmental time course. He is following both Factor VIII production and the plants’ growth to assess the effect of the foreign gene on the plants’ development, and vice versa. Brown is excited about the success of his experiment thus far, and he feels that the potential uses for his findings make it imperative that he publish as soon as possible. A disease-free, inexpensive source of Human Factor VIII would be of great benefit to hemophiliacs, who run the risk of contracting disease from plasma-derived sources and who must find a way to pay about $300,000 per year for their treatment. The urgency is all the more real to Brown, whose infant son is a hemophiliac. The sooner Brown’s promising results are published, the sooner other scientists will be able to follow his line of work, and the sooner his discovery can have a practical, clinical impact.

One Friday, late in January, Brown checks on the 100 transgenic tobacco plants that have now been in the greenhouse for about a month. He discovers that twelve of them are beginning to look sickly. Their leaves are drooping a bit and turning yellow on the edges. He records this in his notebook, and also notes that all of these plants are close to the door. Later, in the lab, when he checks his previous results, he finds that these twelve plants have been producing Factor VIII at a consistently higher level than the other plants. Only one other plant had Factor VIII in this range, although quite a few came close. Feeling pressed for time, Brown decides not to investigate the cause of the poorer growth of the twelve plants any further. He concludes that because they happen to be near the greenhouse door, they have been repeatedly exposed to lower temperatures than the other plants, and that this is the problem. He records this conclusion in his notebook along with the other entries.

Early the following week, Brown is working on integrating his most recent transgenic plant data into the first draft of the manuscript on which he is working. He has entitled it "Human Factor VIII Production in Transgenic Tobacco Has No Deleterious Effect on Plant Growth." When Brown comes to the data on the twelve sickly plants, he considers whether he should exclude these plants from his analysis. He thinks that doing so would be justified because of the plants' proximity to the greenhouse door. In addition, the paper would be more impressive without the uncertainty associated with the data from these plants. He weighs the relevance of the data from those twelve plants against the principle that there is nothing wrong with excluding outliers and irrelevant data. Besides, he thinks these results are too important to risk letting them get held up in the review process.

Questions

1. Should Brown leave out the data from those twelve plants? Why or why not?
2. What if it was just one plant out of 100 plants instead of 12 plants out of 100?
3. How can Brown deal with the potential conflict of interest that occurs from the fact that his infant son is a hemophiliac?

Case #15 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*)

Cynthia Walsh, M.D., an associate professor of medicine, is a prominent academic cardiologist. Her personal financial investments include significant stock holdings in three publicly traded biotechnology firms. She is approached by one of these firms to be a lead investigator in a therapeutic trial of a novel agent for preventing tissue damage from myocardial infarction (MI). This will be a randomized double-blinded, placebo-controlled clinical trial (neither patient nor physician will know whether the drug under investigation or a placebo is being used in a given patient). Dr. Walsh is quite familiar with the preliminary animal and cell biology work in the area and believes that there is an excellent chance that this new drug will result in a significant improvement in survival and reduce damage to the heart muscle. She even thinks this novel agent may reduce the risk of heart failure and irregular beats.

Dr. Walsh's group is one of the few cardiology groups fully prepared to carry out this investigation, which is why she was contacted, and a clinical fellow suited to manage the study is available. She cares for a large number of patients with MI and believes that she could enroll

numerous patients efficiently. The drug will only be available to her patients if her group participates in the trial. The company is offering $5,000 for each patient enrolled and the money would really help both her salary and the division budget. As a lead investigator, she will become much better known and will likely experience an increase in referrals if the trial succeeds.

Questions

1. Is Dr. Walsh's participation in this study appropriate? Justify your position.
2. Does Dr. Walsh have a conflict of interest? If so, what is the nature of the conflict? How could it be mitigated? Would the nature of the conflict of interest be different had she not already owned stock, but instead had been offered stock as a form of compensation for conducting the study?
3. If Dr. Walsh already believes the drug is an improvement based on the literature emanating from animal experiments, can she honestly assign patients randomly to treatment or placebo? What if she believes the drug is deleterious because of its adverse effects on the kidney late in the course of treatment?
4. What should the role of the university be in this case?
5. During study of the first few patients, it becomes apparent to Dr. Walsh that she can tell who is on the active drug because the patients get a facial flush. Might that further influence her ability to remain objective? What considerations apply in answering that question?

Case #16 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*)

Dr. Simon Goldberg is a dermatologist and a tenured faculty member at a research-intensive medical school. When not attending to his clinical and educational responsibilities, he conducts research into the mechanisms by which skin tissue heals and repairs itself. Recently, Dr. Goldberg received a contract from Vanite, a large cosmetics company whose products are sold worldwide. The U.S. Food and Drug Administration (FDA) has questioned claims the company makes concerning one of its leading products, Creme de Jouvence, which Vanite asserts can repair damage to the skin caused by aging and exposure to the sun. Vanite stands by this claim, although it is uncertain which of the many ingredients in the product actually produces the rejuvenating effect. Therefore, it would like to hire Dr. Goldberg to investigate this matter. Dr. Goldberg's findings will be used in Vanite's response to the FDA. As it is under some pressure to respond in a timely manner, Vanite would like to have the results of this study as quickly as possible. Whatever Dr. Goldberg finds, he will receive $250,000 to cover the expenses and salary associated with the project. However, if he can identify an ingredient that proves active within nine months, a company representative has assured Dr. Goldberg that Vanite will hire him again to study the safety of a new cosmetic ingredient the firm has developed.

Questions:

1. What kinds of incentives are created by the promise of future employment?
2. Assume that in order to make the deadline, Dr. Goldberg enlisted two predoctoral students to assist with the project. To recruit them for this effort, he told the students that they would gain valuable exposure and experience from their participation. What problems might be posed by this situation?

3. Vanite is clearly under pressure to support its claims and Dr. Goldberg is conscious of Vanite's desire to acquire data to help the company make its case. If you were Dr. Goldberg, what would you do to retain your objectivity in this study?
4. The FDA will scrutinize Dr. Goldberg's research findings. What impact does this independent review by a government agency have on your concerns about this contract?

Case #17 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Professor Widom files for a patent on a novel antisense strategy for knocking out genes. The technique is potentially applicable to the treatment a variety of genetic diseases. Rather than licensing the technology to a company, Prof. Widom has decided to create a Biotech start-up company. There are still a lot of issues to address before a drug based on this strategy will be ready to go to clinical trials, including optimizing chemical synthesis, target site specificity and drug delivery. The start-up company awarded Prof. Widom a grant of $50,000/year to fund developmental research in her own lab at the University. Prof. Widom assigns two graduate students to the project.

1. Who besides the PI should know about the relationship between the company and Prof. Widom. How much does each party need to know?
2. Is it OK for Prof. Widom to manage an NSF grant involving the same chemistry as funded by her company? If so, under what circumstances would this be OK and when would it not be OK?
3. What are some of the concerns of the graduate students assigned to this project?
4. What are some of the benefits to the graduate students assigned to this project? Benefits to the PI? Benefits to the University?
5. One day Prof. Widom receives a manuscript to review from the editor of a major journal in the antisense field. The article is written by two scientists who are employed by a company working in the same area as Prof. Widom's. In fact, the two companies will compete in the same market if they are successful in developing products. The paper reports interesting advances in drug delivery. Should Prof. Widom agree to review the paper? If so, what steps should she take before agreeing to review the paper?
6. Prof. Widom needs a certain supply (cost = $2000) and she wants to buy it from her own company, which she claims is the sole supplier. Is this allowed? Are any restrictions placed on this transaction?

F. Publication Practices, Responsible Authorship and Peer Review (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)*, Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health, and the Federal Policy on Research Misconduct*) (http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/Conduct%20Research%206-11-07.pdf)

Authorship: Authorship refers to the listing of names of participants in all communications, oral and written, of experimental results and their interpretation to scientific colleagues. Authorship is the fulfillment of the responsibility to communicate research results to the scientific community for external evaluation.

HANDBOOK FOR FACULTY AND ACADEMIC ADMINISTRATORS
Revised 2009

A SELECTION OF POLICIES AND PROCEDURES OF THE UNIVERSITY OF PENNSYLVANIA

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II.E.10. Conflict of Interest Policy for Faculty Members

(Source: 1979 Handbook for Faculty and Administration; revised, Office of the Provost, Almanac, March 8, 1983; revised 1991)

(See also, Human Resources Policy Manual, Policy No. 003 on Use of University Property.)

I. Introduction

This policy applies in full to all Standing Faculty, Standing Faculty-Clinician-Educators, and all full-time members of both the Associated Faculty and Academic Support Staff, hereinafter simply designated as "faculty members." Parts of it also apply to those with part-time faculty appointments; these cases are noted in the appropriate sections. The details of this policy derive from the following general obligations:

- All employees are required to conform to the mores and ethical standards of the University and the rules promulgated to enforce them.

- Employment as a faculty member presumes a primary commitment of time and intellectual resources to the academic mission of the University and its functioning as a community.

The following sections cite specific types of activity that have commonly been found to conflict with these obligations, and the procedures and regulations that have been devised to identify and resolve such conflicts. They are intended to serve as examples and not as a comprehensive compilation. Situations not covered by them will be judged in the light of the above general obligations.

Examples of actions that run counter to the first general obligation include nepotism, discrimination on the basis of irrelevant characteristics, inappropriate use of the University's name, and exploitation of any aspect of association with the University for unacceptable purposes or private gain. They are proscribed at all times for all faculty members, extending to those in part-time employment as noted in the relevant sections of this document. Excessive commitment of time or mental effort to extramural engagements or other non-University activities during the academic year constitutes a violation of the second general obligation. As used in this policy, the academic year is defined for each faculty member as that portion of the year during which he or she receives a salary from the University for services.

II. Conflict of Interest in the Allocation of Time and Effort to Extramural Activities

The University recognizes that its faculty members are not employees in the usual sense, and that a precise allocation of academic time and effort is inappropriate. Their pursuit of knowledge in their areas of competence is

presumed to be a lifelong commitment. A limited association of faculty members with government, professional agencies, and public or private organizations is appropriate, especially when it may enhance their competence as scholars.

Policy on Extent of Extramural Activities. Forms of extramural activity include part-time engagement for a fee as a technical or professional consultant or practitioner and formation or association with business enterprises or non-profit organizations.* In principle, both such associations are approved under the following conditions:

1. Faculty members should not engage in such extramural associations to an extent that detracts significantly from their availability for normal academic duties. These commitments in aggregate should not exceed one day per seven-day week during the academic year. Exceptions to this shall be permitted only in unusual circumstances and require the specific approval of the President or Provost, the academic dean and the department chair.

2. Faculty members shall make known to their department chairs and academic deans the prospect of each continuing engagement, including, at least, all engagements expected to extend for a substantial portion of an academic term. Faculty members should decide to enter a relationship only if, after discussion with their department chairs and academic deans, there is concurrence that the proposed engagement will not conflict with the faculty members' professional obligations to the University, or with the University's outstanding or prospective commitments for teaching and research.

3. In addition to the prospective disclosure cited above, all faculty members must report on the extent of their extramural activities of all types as detailed below.

*Including part-time employment by another academic institution. Such employment may be inappropriate for a faculty member whose primary commitment of time and intellectual resources is to the academic mission of the University of Pennsylvania and its functioning as a community. A full-time faculty member who considers employment for research or teaching at another academic institution during the period of his or her employment by the University should treat this prospective employment as a continuing engagement and follow the procedures below.

III. Conflict of Financial Interest between the University and Extramural Organizations

Members of the faculty or of their immediate families (including parents, children, siblings, spouse) may have significant investments or interests or hold official positions in extramural business organizations, whether or not they have undertaken to perform continuing work or services for them. Such economic or

official relationships are of concern if:

1. The organizations are engaged in activities that parallel activities in which the University is currently or prospectively engaged, and in which faculty members play (or might appropriately play) a role in their academic capacity; or

2. The organizations have a present or prospective relationship with the University, e.g., as suppliers of goods or services or as parties to research contracts, and the conduct of those relationships may involve faculty members in their academic capacities; or

3. The engagements undertaken by faculty members under the aegis of extramural business organizations might be suitable and appropriate activities for execution within the University.

A. Policy on Disclosure of Relationships with Organizations that are Suppliers or Potential Competitors of the University. In any of the situations outlined above, faculty members shall be required to report the facts and circumstances of the potential conflict to their department chairs and academic deans so that appropriate steps may be taken to avoid conflicts of interest, especially ones in which faculty members may benefit from a knowledge of confidential information.

It is generally assumed that those with part-time faculty appointments shall not normally participate in University decisions that could engender conflicts of interest for them. Where part-time faculty might encounter a conflict, the policy stated above extends to them. Furthermore, in any circumstances in which part-time faculty members are engaged in externally sponsored research projects contracted with the University, or where they stand to benefit from a knowledge of confidential information, full disclosure of their relationships with relevant extramural organizations and of the facts pertaining to any potential conflict is required.

B. Policy on Acceptance of Engagements through Extramural Organizations. Faculty members with positions or connections in extramural organizations who wish to undertake engagements through those organizations rather than through the University are obliged to offer first to the University each such engagement (grant, contract, client, etc.) in which they would assume one or both of the following relationships to the engagement:

1. Owner, executive or other principal decision-making position responsible for the conduct of that business enterprise; and/or

2. Principal investigator or other substantial responsibilities for the satisfaction of the engagement.

By requiring that each engagement be offered to the University, the following ends are served:

1 The disclosure of the type, scope and extent of extramural activities is achieved, in accordance with University policy;

2 The decision as to whether an engagement is appropriately undertaken as a University or extramural activity is shared with the University administration, thereby avoiding possible conflicts of interest, and the appearance of such conflicts.

Faculty members intending to conduct engagements in business enterprises with which they are associated shall disclose in writing to their department chairs and deans:

1. The nature and terms of the proposed enterprise, and

2. The reasons why it should be conducted as an extramural activity.

If the chairs and deans agree that the engagements are not appropriate as a University activity, and if they conclude that the other conditions of the extramural consulting policies of the University will be met, then they will advise the faculty members to proceed. Otherwise, they may require that the engagements be conducted within the University.

IV. Disclosure of University Affiliation in Publications of Extramural Organizations

Faculty members who form or associate with extramural business enterprises or non-profit organizations should exercise particular care that their University affiliation is appropriately cited in publications of such organizations. Problems that can arise from failure to observe this injunction include:

1. Such an organization, by reason of the participation of faculty members, might be considered to have some formal or informal relationship to the University.

2. Faculty members by reason of their positions in such organizations might be expected to discharge duties and responsibilities for those organizations that would be inconsistent with their primary duty to the University.

A. Disclaiming University Relationships. A business enterprise or non-profit organization with which a faculty member has a connection may release to the public from time to time publications concerning itself and its activities. In all

such publications it may be desirable and, in many cases, required by law that a faculty member's affiliation with the University be disclosed.

The impact of such disclosure will depend on the circumstances. At one extreme a faculty member might serve as a member of the board of directors of an established business or non-profit organization, where there is not even a remote implication that such organization is in any way connected with the University of Pennsylvania. At the other extreme, all or a large number of the principals of an organization (officers, directors, promoters and substantial shareholders) may be faculty members. In such cases, there is a strong implication that the organization may be connected with the University of Pennsylvania, even that the University bears some responsibility for its activities and success. In these cases, an express statement of the form,

> The _____ has no connection, directly or indirectly, with the University of Pennsylvania.

in prominent type, should be included in all publications released by such organization. The Provost shall have the power to require that such a statement be included in all organizational publications that refer to faculty members, when it is in his or her judgment necessary.

The foregoing rules extend to part-time faculty members, when their association with the University is mentioned in an organizational publication.

B. Affirmation of Obligations to the University. A faculty member may have a position of responsibility (continuing or temporary) with an extramural business organization. In such cases it should be made clear in any publications of the organization that the obligations, in terms of both time and responsibility, of the faculty member to the extramural organization are limited by and subject to the policy of the University of Pennsylvania. This alerts both the public and the faculty member's business associates that duties to the extramural organization are thus limited. This is especially necessary in the case of corporate officers who are normally regarded as owing a comprehensive fiduciary duty to the corporation and its shareholders. The suggested format for such a disclosure is:

> J. Smith, a Vice President of this corporation, is a member of the faculty of the University of Pennsylvania and as such is subject to limitations by the University on the time that may be devoted to the affairs of this corporation. In any instance where the interest of this corporation may conflict with the interest of the University of Pennsylvania, J. Smith will resolve such conflict in favor of the University of Pennsylvania.

The Provost shall have the power to require such a disclosure in any instance where he or she adjudges it necessary.

V. Conflict of Interest in Externally Sponsored Research

Regulations concerning sponsored research may be found in the *Sponsored Projects Handbook.* (*See* http://www.upenn.edu/researchservices/, available from the Office of Research Services, and Guidelines for Extramural Activities of Faculty of the University of Pennsylvania Medical Center and Health System. The Office of Research Services can be reached at 3451 Walnut Street, Room P-221, Philadelphia PA 19104-6205, tel: 215-898-7293.)

The University encourages its faculty members, including those in part-time employment, to participate in externally sponsored research projects, whether supported by government agencies, foundations, associations, or other non-profit organizations; or by corporations, partnerships or other for-profit entities. In any sponsored project, faculty members are expected to avoid use of the project for their private financial gain other than in the form of salary support or of royalties resulting from commercialization of intellectual property rights in accordance with University policies. However, there may be unusual circumstances under which the interests of the University would be served if a faculty participant in a sponsored project were to assume an entrepreneurial role; for example, if a faculty member participates directly in a private enterprise providing funds to Penn in support of the project. Assumption of such a role would not be a violation of these guidelines if approved in advance and reviewed periodically by the relevant dean and the Vice Provost for Research. Examples of situations from which conflicts of interest may arise include, but are not limited to, the following:

1. Undertaking or orientation of sponsored research to serve the needs of a private agency or enterprise in which a responsible staff member has an interest.

2. Purchase of major equipment, instruments, materials or other items for externally sponsored research from any agency or enterprise in which a responsible staff member has an interest.

3. Acceptance of any limitations on the free publication of and access to the results of any sponsored research. Exceptions may be granted by the Provost for privileged information, but only in the form of a delay in the release of such information. The delay shall only on rare occasions exceed three months. Those wishing to engage in research of a kind whose results cannot be so disseminated may only do so as an extramural consulting activity under the conditions previously described.

4. Transmission to any private agency or enterprise, use for personal gain, or other unauthorized use of the work product, results, materials, records, or information gathered from sponsored research that is not made generally available through publication or other free access.

5. Acceptance of gratuities or special favors from a private agency or

enterprise with which the University conducts business in connection with a sponsored research project.

A. Disclosure to Responsible University Officials. Before participating in any sponsored research project, all faculty members must give written notice of their extramural consulting relationships or other sponsored research projects that may relate in any way to the project to the appropriate department chairs and through them to the deans and Vice Provost for Research. Any significant financial or managerial interests that may relate in any way to the project must be disclosed in writing to the Vice Provost. Any faculty members engaged in sponsored research projects must disclose in the same manner any change in their outside activities or interests. In the light of such disclosures, the University shall take appropriate steps to neutralize or eliminate potential conflicts of interest.

B. Distribution of Effort. The sponsoring agency supporting research must not be misled as to the amount of intellectual effort that faculty members are actually devoting to these research projects. A system of precise time accounting is incompatible with the inherent character of the work of faculty members, because the various functions that they perform are closely interrelated and do not conform to any meaningful division of a standard work week. However, if externally sponsored research agreements provide that faculty members shall devote a definite fraction of effort to the projects, or if it is agreed that they shall assume specified responsibilities in relation to such research, demonstrable relationships between the stated efforts or responsibilities and the actual extent of their involvement are to be expected. Each faculty member, in such circumstances, shall confirm the fraction of effort devoted to the projects in the effort reports required of all faulty members who are so engaged.

C. Advice and Guidance. Any questions concerning potential conflicts of interest, appropriate distribution of effort, or other problems associated with externally sponsored research, should be addressed to the office of the Vice Provost for Research.

VI. Requirements for Reporting Extramural Activities and Obligations

At the end of each academic year, each faculty member shall submit to his or her department chair and dean a report of his or her extramural activities during that year, containing the following information:

1. Number of days (or hours, if preferred) of extramural activities for fee (include consulting, professional practice, and outside teaching commitments).

2. Names of organizations (government agencies, private firms, partnerships) for which the extramural activities conducted represented a continuing engagement.

3. Number of days (or hours, if preferred) of extramural activities on behalf of business enterprises in which the faculty member has a financial interest or official position.

4. Names of business organizations in which the faculty member is a significant owner, partner, officer, director, or staff member.

The last item shall also be reported by all part-time faculty members for whom any of the following conditions obtain:

1. The organization is a supplier of the University and the part-time faculty member participates in the decision to engage its services.

2. The organization supplies goods or services to the University to be used in the performance of externally sponsored research projects in which the part-time faculty member participates.

3 The part-time faculty member is privy to confidential University information that could be used to the business advantage of the organization.

4. The affiliation of the part-time faculty member with the University may be mentioned in any publication of the organization.

Forms for the reporting of extramural activity are available from the Office of the Provost.

All faculty members must also report on a continuing and timely basis to the appropriate administrators the relevant circumstances, as noted in the sections cited, whenever any of the following conditions are met:

1. They have or wish to initiate a relationship with an extramural business organization that is or may become a supplier or competitor of the University (*see* section II.E.10.A. on Policy on Disclosure of Relationships with Organizations that are Suppliers or Potential Competitors of the University).

2. They wish to undertake an engagement (grant, contract, client, etc.) through an extramural organization (*see* section II.E.10.B. on Policy on Acceptance of Engagements through Extramural Organizations).

3. They intend to participate in a sponsored research project that may be related to their other sponsored research projects, to any of their extramural consulting relationships, or to any organization in which they have significant managerial or financial interests (see section II.E.10 on Policy on Acceptance of Engagements through Extramural Organizations).

VII. Employment of More than One Family Member

(Source: Office of the President, July 1, 1964; revised, 1969 Handbook for Faculty and Administration; revised, Office of the Provost, Almanac, March 8, 1983; revised, Almanac, December 16, 1997)

University policy permits the employment of more than one member of a family (defined as being related by blood, marriage and former marriage, or adoption, or defined as partners recognized under University benefits policy), whether or not the persons concerned are in the same academic or administrative department. The University's primary concern in such cases of appointment, as in all others, is that faculty or staff members are the best candidates with respect to the requisite qualifications for employment. The University has a parallel concern, however, in the avoidance of a conflict of interest or the appearance of such conflict, where an employee's professional decisions or actions pertaining to the performance of his or her job would be colored by considerations arising from a family relationship with another employee. The University also recognizes that the appointment of two or more family members, especially within the same department, could generate pressures and prejudice among colleagues. To guard against such conflicts and abuses, the following rules must be observed:

A. Family Members Appointed to the Faculty

1. No faculty member shall participate in any way whatsoever in the decision to employ, promote, reappoint, or terminate the appointment of a member of his or her family on the Standing Faculty or the Associated Faculty.

2. Any proposal to employ as a faculty member a person who is related to a member of the faculty or administration must be brought to the attention of the dean before an offer of appointment is made. In cases where there is a potential conflict of interest in the professional relationships of family members or with respect to other employees of the University arising from the family relationship, the department chair must outline in writing the steps being taken to avoid or manage conflicts of interest or the appearance of such conflicts, subject to approval by the dean. Deans will report such arrangements to the Provost in the course of normal administrative oversight.

3. No faculty member shall participate in any other decision, including determining the salary, teaching and/or administrative assignments, and space assignments, directly and individually affecting a member of his or her family on the Standing Faculty or Associated Faculty.

B. Family Members Appointed to Non-faculty Positions

Faculty members should take care to avoid conflicts of interest or the appearance of such conflicts in the employment of, and in any ongoing University-related professional relationship with, a family member in a non-

faculty position. All decisions regarding such employment should be conducted in strict conformance with Human Resources Policy.

C. Reporting

In the course of normal administrative oversight, department chairs or other heads of departments shall report periodically to deans, and deans shall report to the Provost, on steps that have been taken to avoid or manage conflicts of interest or the appearance of such conflicts among faculty members and/or academic administrators who are related as family. In each case, the faculty members and/or academic administrators who are subject to such reports shall receive copies of such reports on a timely basis.

These requirements extend to part-time faculty appointments whenever such a person may exercise decision-making power over the employment and/or administration of a family member employed by the University.

II.E.11. Decreases in Salary

(Source: Standing Resolution of the Trustees, October 16, 1959; revised September 9, 1983; revised, Office of the Provost, Memorandum No. 190, June 8, 1990)

Academic base salaries of faculty members may be decreased only in accordance with an expressed agreement between the faculty member and the University or because of financial exigency. Decreases for financial exigency shall be limited to the following:

- Simultaneous uniform percentage decreases in the academic base salaries of all faculty members in the University; and

- Simultaneous uniform percentage decreases in the academic base salaries of a class of faculty members such as a particular rank, department or school.

No decrease for financial exigency shall be made except after consultation, initiated by the President, with the Executive Committee of the Faculty Senate or with representatives selected by the class of faculty members subject to a proposed decrease. Consultation shall cover such issues as the existence in fact of a financial exigency, the appropriateness of the selection of the particular class for salary decrease, alternative actions and the like.

If after such consultation the academic base salaries of faculty members are decreased, with or without the concurrence of the Senate or the representatives of the class of faculty members, the President shall notify the affected faculty members, in writing, of (a) the fact that the academic base salaries of all of the faculty members in the University, or of a described class of faculty members,

POLICY NO: 005
EFFECTIVE DATE: 03/31/2010

CONFLICT OF INTEREST

This policy on conflict of interest is divided into two parts, the first dealing with faculty and the second dealing with other employees of the University.

005.1 FACULTY

Certain categories of potential conflict of interest as to faculty are addressed in existing University policies, including the Conflict of Interest Policy for Faculty Members adopted by the Faculty Senate on November 17, 1982, approved by the Provost on March 1, 1983 and printed in the 1983 Handbook for Faculty and Academic Administrators. University Council also recommended a Policy on Outside Financial Interests on September 24, 1969 which is as follows:

1. A member of the faculty may have a significant investment or interest, or hold an official position, in an outside firm or organization but has not undertaken to perform continuing work or services for it. Such an economic or official relationship is of concern if 1) the firm or organization is engaged in activities which parallel activities in which the University is currently or prospectively engaged and in which the faculty member plays (or might appropriately play) a role in an academic capacity; or 2) the firm or organization has a present or prospective relationship with the University, e.g., as a supplier of goods or services or as a party to a research contract, and the conduct of that relationship may involve the faculty member in his academic capacity. In either of these situations, the faculty member shall be required to report the facts and circumstances to the Department Chairman and the Academic Dean or Director so that appropriate steps may be taken to avoid a conflict of interest.
2. These policies are recognized to govern those areas of potential conflict of particular concern to faculty.
3. A number of other existing University policies pertaining to conflict of interest apply to faculty members unless they are intended by their terms to apply only to other employees. These policies include but are not limited to policies on patent and copyright, purchasing, nepotism, and sexual harassment.

005.2 UNIVERSITY EMPLOYEES OTHER THAN FACULTY AND OFFICERS ("EMPLOYEES")

Employees of the University shall avoid any conflict between their personal interests and the interests of the University; furthermore, they shall avoid any situation where it would be reasonable for an objective observer to believe that the person's judgment or loyalty might be adversely affected. For purposes of Paragraphs III(a) and (b) below, reference to the University is intended to include also reference to all entities controlled or owned in substantial part by the University.

a. If an employee has any power of influence to approve or disapprove a transaction proposed to be entered into between the University and that person or between the University and any entity or individual having a significant relationship to that person, he or she has a potential conflict of interest and may not participate in the process leading to the approval or disapproval of the transaction unless the underlying facts giving rise to the potential conflict of interest are disclosed and approval for participation is obtained pursuant to the procedures described below in paragraph (e).

b. An employee also has a potential conflict of interest if that person, or any entity or individual having a significant relationship to that person may benefit from information considered by the University to be confidential and learned in his or her capacity as an employee of the University.

c. A significant relationship exists as to an entity if a person is a director, trustee, officer, or employee of, a partner or member in, or has a material financial interest in, the entity in question.
    1. An entity is a corporation, partnership, unincorporated association, or any similar group.
    2. Determination of a material financial interest is a matter of personal judgment but, at a minimum, would be required for an aggregate interest for the person and for all entities or individuals having material relationships with the person of more than:
        - 1 percent of any class of the outstanding securities of a firm or corporation, or
        - 10 percent interest in a partnership or association, or
        - 5 percent of the total direct and beneficial assets or income of the person.

d. A significant relationship exists as to an individual if that individual is in the immediate family of a person subject to this policy. The immediate family includes parents, siblings, spouse and offspring.

e. An employee who has a potential conflict of interest covered by this policy shall immediately disclose the potential conflict in writing to a superior. The employee may continue participation in the transaction only on terms approved in writing by the superior.

f. A number of other University policies pertaining to conflict of interest remain in effect and may, depending on their terms, apply to employees of the University. These policies include but are not limited to policies on extramural consulting by administrative staff, purchasing, sponsored research, patent and copyright, nepotism, and sexual harassment.

    Note: Contact the Office of the Secretary of the University Conflict of Interest Policy for Trustees and Officers of the University.

Applicability: All Faculty & Staff
Cross-reference: Policy 006
Supersedes Policy Number(s): N/A

Confidential Financial Disclosure Statement
This form should be submitted with a grant application or human subjects protocol. Alternatively, a signed copy may be submitted electronically as a PDF file to COI@exchange.upenn.edu

Name _____ **Date**_____

Academic Title _____ **Department/Division**_____

Email Address _____ **Phone**_____

Name of Department Chair & Email address: _____

Title of Research as listed in PennERA_____

_____

Does this Research involve an IRB Protocol? NO _____ **YES** _____ **IRB #**_____

Does this Research involve a grant, contract, or other sponsored agreement? NO _____ **YES** _____ **ORS #**_____

Sponsor or other sources(s) of support (list all) _____ _____ _____

Part I: Financial Interests / Relationships (Check all appropriate boxes).

- **For any Intellectual Property that is being tested, evaluated or developed in this research and / or**
- **For any personal financial interests that may affect or be affected by this research; and / or**
- **For any financial interests in/with one or more Outside Organizations* whose interests may affect/be affected by this research, including companies that compete with the sponsor of the research or the manufacturer of investigational products being used in this research****

Over the past 12 months to the present and anticipated over the next 12 months, do you, your spouse or dependent children:

	YES	NO
a. Own **any** shares of stock, options, partnership or LLC interest, or other ownership interest in the Outside Organization that is not publicly traded? (This includes the proceeds of the sale of stock, options or other equity)		
b. Own shares of stock, options, partnership or LLC interest, or other ownership interest of greater than 5% or >$10,000 in the Outside Organization that is publicly traded? (This includes the proceeds of the sale of stock, options or other equity)		
c. Receive or expect to receive >$10,000 in compensation for consulting or other personal services from the Outside Organization?		
d. Receive or expect to receive >$10,000 in compensation for any position in the Outside Organization?		
e. Serve as Management, on the Board of Directors, or in some other fiduciary capacity for the Outside Organization? (This does not include service on an Advisory Board)		
f. Serve on an Advisory Board of the Outside Organization?		
g. Have an interest in a patent (including any patent application), copyright or licensing agreement whose value may be affected by this research?		
h. Have assigned your interest in any invention, patent application etc. to an Outside Organization?		
i. Receive or expect to receive >$10,000 in personal income directly from this Outside Organization for licensing your discoveries?		
j. Receive or expect to receive >$10,000 in honoraria or royalties for book, publications or lectures from this Outside Organization?		
k. Does the sum of c, d, i and/or j for any one Outside Organization exceed $10,000?		

* Any organization other than the University of Pennsylvania, the Health System or its corporately owned entities (e.g., Pennsylvania Hospital, Clinical Care Associates, CPUP, etc.), as well as education affiliations or research relationships with CHOP-PA, VAMC, and HHMI.

****AAMC Guidelines** recommend that if an investigator has an interest in and has actual knowledge that a competing Outside Organization's interests would reasonably appear to be affected by the research, then the investigator should disclose such interests in the competing Outside Organization.

IF THIS RESEARCH INVOLVES HUMAN SUBJECTS RESEARCH, YOU MUST COMPLETE ALL PARTS OF THIS FORM (Parts II-VI).
For research <u>other</u> than Human Subjects Research, if you answered "YES" to any of the above, please complete Parts II, III, V& VI.

Part II: Financial Interests that May Relate to, Affect, or Be Affected by this Research Project or Protocol

II. A. Do you, your spouse or dependent children receive **personal income**, **honoraria or other compensation for services** (e.g. consulting, lecturing/speaking, [including CME for a commercial CME provider but funded by an Outside Organization], SAB service, DSMB service, expert witnessing) provided on behalf of any Outside Organization whose interests might reasonably be expected to be affected by the outcome of this research? **According to University Policy you may be required to provide a copy of the consulting agreement**.

Outside Organization	Income received past 12 months (estimate to the nearest dollar e.g., $1,000.00).	Income expected over next 12 months (estimate to the nearest dollar e.g., 1,000.00).	Written Consulting Agreement?	Time spent: Hours / Week or Days / Month
	$	$	Y/N	
	$	$	Y/N	
	$	$	Y/N	

II. B. Do you, your spouse or dependent children hold **equity positions** whose value might reasonably be expected to be affected by the outcome of this research?

Outside Organization	Publicly Traded?	Value of stock held or optioned (estimate to the nearest dollar, e.g., 1,000.00).	= >5% Ownership	Options only?
	Y/N	$	Y/N	Y/N
	Y/N	$	Y/N	Y/N
	Y/N	$	Y/N	Y/N

II. C. Do you, your spouse or dependent children have a **proprietary interest** in products or processes (IP Interests), including but not limited to, a patent, trademark, copyright or licensing agreement, or right to receive compensation in connection with the development or sale of the product, whose current or future value or income stream might reasonably be expected to be affected by the outcome of this research?

Description of Product or Process	Nature of Interest			
_____	Name of Patent Inventor, Owner or Licensee	Copyright author, owner or licensee	Right to receive compensation from commercialization?	Other Interest? (please specify)
			Y/N	
			Y/N	

II. D. Do you, your spouse or dependent children receive **revenues related to Intellectual Property** identified under Part IIC whose value might reasonably be expected to be affected by the outcome of this research, including royalties, licensing fees, milestone payments or anything of value?

Paid to you by Penn?	Paid to you by Outside Organization?	Revenues received over the past 12 months (estimate to the nearest dollar, e.g., 1,000.00).	Revenues anticipated over the next 12 months (estimate to the nearest dollar, e.g., 1,000.00).
Y/N	Y/N	$	$
Y/N	Y/N	$	$

II. E. Do you participate in other research that may affect or be affected by your financial interests/ relationship with this Outside Organization? Please list below.

If you have not previously done so, you must submit a separate financial disclosure for this other research.

Sponsor	ORS/ IRB #	Grant #	Title	Disclosure Submitted Y/N?

Part III: Students and Post Doctoral Fellows

Do students or trainees participate in this research? Y_____ N_____

If you have identified an Outside Organization above, does this Outside Organization provide salary support for students or post-doctoral fellows participating in this research? Y_____ N_____

Outside Organization's name(s) _____ _____

Part IV: Human Subjects Research

In order to fully evaluate whether there are circumstances to permit your participation in human subjects research, respond to the following questions (Include a separate page if not enough room below).

1. Are there any other Penn Investigators involved? Do any of them have a potential financial conflict of interest?
2. Did/do you receive any consulting income for the design of this or other clinical studies from the sponsor?
3. What role will you have in: the study design, subject recruitment, enrollment, consent, administration of study intervention(s), data collection, data analysis and publication?
4. Will subjects be recruited from your clinical practice?
5. What Phase Trial is this?
6. Will there be a Data Safety Monitoring Board?
7. Is this a multi-site clinical trial? Yes_____No_____ (if no, skip to Question 9).
8. If so:
   a. Who is the overall Principal Investigator?
   b. How many subjects will be enrolled at Penn? _____ Overall? _____
9. Describe any unique qualifications, training or other compelling circumstances that would argue for your participation in the trial.

Part V: Research Projects Affecting an Outside Organization in which you have a Financial Interest

In order to fully evaluate whether this financial interest constitutes a conflict of interest that would need to be managed, reduced or eliminated, describe more fully the relationship of the work being proposed to the scientific interests of the Outside Organization and any role you have in the Outside Organization. Please add any information which would help to clarify any of the sections above. Prepare and attach a statement to address the following:

- Does any scope of work that you perform for the Outside Organization as an extramural activity overlap with the scope of work of this research or other research in which you participate, whether internally or externally funded? If yes, describe the overlap.

- If Outside Organization is a start-up company, describe your role, if any, in the founding of the new company and your continuing involvement. Describe the specific scientific interest(s) of the company and its research capabilities.

- Please add any information which would help to clarify these issues and include possible management strategies to safeguard against conflicts of interest and commitment.

Part VI: Certification & Signature of Faculty Member

I certify that the above information is complete and true to the best of my knowledge and that I have read the University's policies related to conflict of interest as described in the Handbook for Faculty and Academic Administrators Section II.E.1., Conflict of Interest Policy for Faculty and the supplementary Financial Disclosure Policy for Research and Sponsored Projects, Almanac February 6, 2001 and the Financial Disclosure and presumptively Prohibited Conflcits for Investigators Participating in Clinical Trials, Almanac July 17, 2007. This information is provided with the understanding that its review shall be conducted in confidence by appropriate University Officials. The information may only be released by the University 1) in statistical or aggregate form that protects my privacy, or 2) to comply with the requirements of the sponsors of my research, or 3) as may be required to comply with University policies and procedures or any applicable legal requirements, or 4) with my written permission.

I acknowledge my obligation to submit an updated disclosure statement **at least annually** or **when there is any change** in my activities or financial interests that would affect or be affected by the outcome of this research project or protocol.

_____ _____

Signature of Investigator **Date**

UNIVERSITY OF PENNSYLVANIA

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Associate Provost for Faculty Affairs: Vincent Price

Dr. Vincent Price, the Steven H. Chaffee Professor of Communication and Political Science at the Annenberg School for Communication, has been named associate provost for faculty affairs at the University of Pennsylvania. He assumed his new position on July 1.

Photo by Kyle Cassidy

Vincent Price

As Associate Provost, Dr. Price will be responsible for the overall management of the academic personnel process, including recruitment, retention, and retirement; appointments and promotions; enhancement of faculty diversity; and resolution of individual faculty issues, including grievances.

Several University offices will report to him, including the Office of the Chaplain, the Annenberg Center for Performing Arts, the Institute for Contemporary Art, the Office of the Curator, and the Arthur Ross Gallery. In addition, he will work closely with both the University Ombudsman and the University's Affirmative Action Office.

"Faculty recruitment, retention, and diversity are among our highest priorities at Penn," said Provost Ronald J. Daniels. "We are seeking to create a climate that is welcoming, inspiring, and conducive to our faculty's professional growth and advancement."

"Vince will be a wonderful partner in this endeavor. His experience—as chair of Penn's Faculty Senate and chair of the department of communication studies at the University of Michigan—makes him distinctly qualified to oversee the office of faculty affairs."

Dr. Price's research examines mass communication and public opinion, social influence processes, and political communication, including the ways in which media frame issues. He has been editor of the flagship journal *Public Opinion Quarterly*, and his pioneering book *Public Opinion* (Sage 1992) has been published in five languages.

He earned a Ph.D. in communications from Stanford University in 1987 and a B.A. in English from Santa Clara University in 1979.

Dr. Price succeeds Deputy Provost, Dr. Janice Bellace, the Samuel A. Blank Professor of Legal Studies and Business Ethics and Professor of Management at the Wharton School (*Almanac* November 21, 2006).

Dean of Wharton School: Thomas Robertson

Dr. Thomas S. Robertson, executive faculty director of the Institute for Developing Nations at Emory University and former dean of Emory's Goizueta Business School, has been named dean of the University of Pennsylvania's Wharton School.

The appointment, effective August 1, was announced by President Amy Gutmann and Provost Ron Daniels.

Dr. Robertson, the Asa Griggs Candler Professor of Marketing at Emory, is an expert in marketing strategy and innovation with extensive international experience in higher education and the business community. He was dean of Goizueta from 1998 to 2004 and is widely credited with building it into one of the strongest schools at Emory, positioning it as a leading international business school.

From 1971 to 1994, Dr. Robertson was a faculty member at Wharton, where he was the Pomerantz Professor of Marketing and chair of the marketing department. He also served as associate dean for executive education and led the effort that built a major conference center on campus, designed an innovative set of new senior-management programs and sub-

(continued on page 8)

Thomas Robertson

Death of President Emeritus Martin Meyerson

President Emeritus Martin Meyerson passed away on Saturday, June 2 at the age of 84. He was president of the University of Pennsylvania from 1970 to 1981. A memorial will be held in October. See a tribute on page 3 and an obituary on the back page of this issue.

Associate Vice Provost for Research and Executive Director of Technology Transfer: Michael Cleare

Michael Cleare

Dr. Michael J. Cleare has been named associate vice provost for research and executive director of the Center for Technology Transfer.

Dr. Cleare will join Penn August 1 from Columbia University, where he is executive director of Science and Technology Ventures.

Working closely with vice provost for research, Dr. Steven J. Fluharty, and other senior administrators, Dr. Cleare will help reorganize and guide Penn research-commercialization activities to improve service offerings to investigators while yielding new resources to sustain, diversify and grow the research enterprise. He will directly oversee Penn's technology transfer office.

In addition, Dr. Cleare will help guide Penn's industry-sponsored research collaborations, particularly as University intellectual property plays an increasingly important role in the formation of academic-industry partnership agreements.

"President Amy Gutmann and Provost Ronald J. Daniels join me in expressing great pleasure over the opportunity to engage Mike Cleare on behalf of the University," Dr. Fluharty said. "Mike is very well regarded by peers, has a stellar track record as a commercialization leader in both academia and industry and will bring to the position his expert ability to form meaningful collaborations between seemingly disparate constituencies. We consider ourselves fortunate to be in a position to call upon his expertise."

Dr. Cleare has managed Columbia's successful research-commercialization endeavors for seven years. He was previously employed for 30 years by Johnson Matthey, a world leader in advanced materials technology. He has held a number of senior positions in research and development, new business development and division-level management. From 1995 to 1999, Dr. Cleare served as a parent board director for Johnson Matthey.

He received his B.S. and M.S. in chemistry from Imperial College in 1965 and his Ph.D. in chemistry from the University of London in 1970. He pursued post-doctoral studies at Michigan State University from 1970 to 1972 with a focus on platinum anti-cancer research. Dr. Cleare was a named inventor of Carboplatin, one of the most widely used anti-cancer drugs. He has published over 40 articles and papers and holds 10 patents.

IN THIS ISSUE

OF RECORD

It has been four years since the University promulgated a Conflict of Interest Policy setting forth particular requirements and prohibitions in the area of Clinical Trials. The Vice Provost for Research and the University Conflict of Interest Standing Committee which advises the Vice Provost for Research, rely upon this Policy in their evaluation of proposed clinical trials, and have interpreted the Policy in the context of a broad range of clinical research. This experience has identified several areas in which the language could be clarified to more clearly communicate the relevant requirements to the University community. The following revised policy was approved by the Tri-Chairs of the Faculty Senate on June 15, 2007. This policy becomes effective immediately.

—Ronald Daniels, Provost
—Steven J. Fluharty, Vice Provost for Research

Financial Disclosure and Presumptively Prohibited Conflicts for Investigators Participating in Clinical Trials

Preamble

Clinical trials represent a special area of research, which is distinguished by the involvement of human subjects who are often particularly vulnerable because they suffer from serious illness, may be searching desperately for treatments, and are being asked to participate in research that carries unknown risks and indeterminate benefits. Under these circumstances, it is particularly important that clinical research be insulated from potential conflicts of interest that might be perceived to influence its conduct or outcome. Therefore, for investigators *(see Definitions)* involved in clinical trials, the University has implemented an additional set of requirements involving disclosure and prohibition of financial interests, which supplement the standard conflict of interest policies.

These guidelines are consistent with the provisions of the AAMC white paper issued in December, 2001, "Protecting Subjects, Preserving Trust, Promoting Progress—Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research."

Investigators are expected to comply with all other relevant Conflict of Interest and Disclosure policies of the University *(see Appendix)*.

In order to be eligible to conduct clinical trials, investigators are required to complete a patient oriented research certification program and to sign a document indicating that they agree to comply with the University policies regarding human subject research. In addition, in connection with each clinical trial in which an investigator intends to participate, the investigator must submit a Financial Disclosure Form that discloses relationships the investigator has with any entity that sponsors or has a financial interest in the outcome of the trial and interests the investigator has in the product or procedure being evaluated in the trial.

I. Presumptive Prohibitions and Significant Financial Interests

Presumptive prohibitions refer to prohibited participation in clinical trials on the part of investigators who have Significant Financial Interests *(defined below)* that constitute potential conflicts of interest. Significant Financial Interests require review by the University Conflict of Interest Standing Committee (CISC), which will consider the circumstances in each instance and will determine whether the participation of the investigator should be prohibited, or whether there are either (a) compelling circumstances or (b) ameliorating circumstances that justify an exception to the presumptive prohibition. If the CISC determines that an exception is justified, it will recommend a management plan. This process is described below in more detail.

Significant Financial Interests include:

1. Service by the investigator or any member of his or her immediate family on the Board of Directors or as an officer *(see Definitions)* of any company or entity that sponsors or has a financial interest in the outcome of the clinical trial in which the investigator is engaged.

2. Ownership by the investigator, any member of his or her immediate family or any related entity, of a significant equity interest *(see Definitions)* in a company or entity that sponsors or has a financial interest in the outcome of the clinical trial, or receipt by the investigator, any member of his or her immediate family or any related entity, of significant payments *(see Definitions)* from or on behalf of a company or entity that sponsors or has a financial interest in the outcome of the clinical trial.

3. Ownership of a proprietary interest in the tested product or a related (i.e., either competing or complementary) product by the investigator, any member of his or her immediate family or any related entity.

II. Definitions of Terms

a. *Investigator* means any faculty, professional staff, support staff, students, fellows, trainees, or administrators who are engaged in the conduct, design, or reporting of the study.

b. *Significant equity interest* means:

i. any ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices (generally, interests in a non-publicly traded corporation);

ii. or, any equity interest in a publicly traded corporation that exceeds 5% ownership during the time the investigator is engaged in the study and for 1 year following the completion of the study;

iii. or, any equity interest in a publicly traded corporation that exceeds $10,000 during the time the investigator is engaged in the study and for 1 year following the completion of the study, wherein the equity interest was acquired less than 1 year prior to the commencement of the study or was provided at any time by any company or entity that has a financial interest in the outcome of the study;

iv. or, any equity interest in a publicly traded corporation that exceeds $50,000 during the time the investigator is engaged in the study and for 1 year following the completion of the study.

Interest in any publicly traded mutual fund or blinded trust is excluded.

c. *Significant payments* means payments (e.g., retainers for ongoing consultation, honoraria, or gifts) that have a monetary value of more than $10,000 per year, exclusive of the costs of conducting the clinical study or other clinical studies, during the period beginning 1 year before commencement of the clinical trial and ending 1 year following the completion of the study. Excluded are payments to a department or school from the sponsor of a covered study.

d. *Proprietary interest in a product* means property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement, or right to receive compensation in connection with the development or sale of the product. "Proprietary interest" does not include authorship of a work or inventorship of a patent where the author or inventor has no right to receive compensation in connection with the use or exploitation of the work or patent.

e. *Officers of a company or entity* are the named officers and any other individuals with fiduciary responsibility to the company or entity.

f. *Participation in a trial* includes sponsoring or holding the IND (investigational new drug) for a trial, the recruitment of patients, patient selection, the informed consent process, design of the study, conduct of the trial, patient visits, procedures, the analysis and interpretation of data, and the reporting of results.

g. *Compelling circumstances* are facts that convince the CISC that an investigator is uniquely positioned, and should be permitted to participate in a specific trial under appropriate management in spite of a Significant Financial Interest. Relevant information to be considered by the CISC includes the uniqueness of the investigator's position with respect to the study (for example, whether safety or other factors will be diminished if the investigator does not participate), the nature of the research; the magnitude of the financial interest; the extent to which the financial interest could be influenced by the research; the degree of risk to human subjects; and whether the interest is amenable to management.

h. *Ameliorating circumstances* are facts that convince the CISC that an investigator cannot influence the recruitment and enrollment of subjects or the results of the study, and should be permitted to participate in a specific trial under appropriate management in spite of a Significant Financial Interest. Relevant information to be considered by the CISC includes the

role of the investigator in the study, the overall study structure, the nature of the research; and whether the interest is amenable to management.[1]

i. *Clinical trial* means any research involving human subjects that is designed to evaluate the safety and/or efficacy of an intervention to diagnose, treat, or prevent disease, including research involving drugs or devices that are FDA approved. For the purposes of this policy, this definition usually excludes investigations involving the consented use of human tissue or participant information used for analysis of disease mechanisms.

j. *Disclosure* is described below.

k. *Member of the immediate family* includes the spouse, children, and parents of the investigator.

l. *Related entity* means any corporation, foundation, trust or other entity controlled or directed by the investigator or his or her spouse.

III. Process

1. In connection with the submission to ORS (Office of Research Services) of an application for grants and contracts for a clinical trial, or for IRB (Institutional Review Board) approval of a clinical trial, investigators must submit a completed Financial Disclosure Form.

2. The Financial Disclosure Form and other available information will be referred to the Conflict of Interest Standing Committee (CISC). The CISC will determine whether the investigator has a Significant Financial Interest. If so, the investigator may not participate in the clinical trial unless the CISC determines that there are compelling circumstances that justify the investigator's participation in the trial. If the CISC determines that there are compelling circumstances, it will develop a plan for managing the conflict.

3. The CISC will report its findings to the Vice Provost for Research, with a recommendation for appropriate action, including a management plan when appropriate. The Vice Provost for Research may accept or reject the CISC's findings or resubmit the matter to the CISC for additional consideration or clarification. The Vice Provost for Research shall decide whether the investigator will be permitted to participate in the clinical trial and, if so, shall also decide the terms of an appropriate management plan. The Vice Provost for Research shall communicate his or her decision and the terms of any required management plan to the investigator, the Principal Investigator, the CISC and other parties as appropriate.

4. An investigator may request that the Vice Provost for Research reconsider his or her decision. If the investigator is not satisfied with the decision of the Vice Provost for Research after such reconsideration, the investigator may appeal to the Provost, whose determination is final.

5. Every attempt will be made to make this process as expeditious as possible.

IV. Implementation of Conflict of Interest Management Plans

1. The Vice Provost for Research is responsible for the implementation of the approved management plan, in conjunction with the appropriate Deans and other administrative officials of the University.

2. Implementation begins with a signed agreement by the investigator and the study's Principal Investigator to accept the required management plan, with copies to the CISC, IRB, ORS, Dean and department chair. In instances where there is a conflict of interest issue, final IRB approval is contingent upon signed agreement by the investigator and the Principal Investigator of the COI management plan.

3. The Office of the Vice Provost for Research will obtain written assurance from the investigator and others as appropriate of continued compliance with the management plan, at least once a year. Such records will be maintained on file for reference by the Vice Provost for Research, in accordance with institutional record retention policy.

In the instance of complex management plans, such as those involving a committee charged to oversee the management plan, more detailed reports at intervals no less than once a year, may be required.

The Office of the Vice Provost for Research is responsible for maintaining an up-to-date file that documents the monitoring of all COI management plans. Any lapses in documentation must be reported to the Vice Provost for Research and the appropriate Dean.

4. Investigators shall also notify the Vice Provost for Research of any changes in their financial interests or relationships, so that it can be determined if further management or recommendations are appropriate.

V. Disclosure

1. The Principal Investigator must disclose the existence of as well as the nature of all Significant Financial Interests related to the study: to subjects participating in a clinical trial; on all presentations and publications of the data emanating from the trial; and to all other investigators engaged in the trial. More detailed guidelines for disclosure are set forth in the existing University of Pennsylvania policy, Financial Disclosure Policy for Research and Sponsored Projects, available at *www.upenn.edu/almanac/v47/n21/ORdisclosure.html*.

2. An investigator's Significant Financial Interest must be disclosed to trial participants in the informed consent documents in the manner and format approved by the IRB. It is the responsibility of the Principal Investigator to be sure that the IRB is aware of the Significant Financial Interests related to the study and explicitly approves the presentation of the disclosures within the informed consent from.

3. An investigator's Significant Financial Interest must be clearly disclosed in any published paper emanating from the clinical trial, consistent with the editorial practices and format of the specific journal, and it is the responsibility of the authors to insure that this takes place.

4. The Principal Investigator shall inform all investigators engaged in the study both of the existence of Significant Financial Interests and of the essential elements, as determined by the Vice Provost for Research, of the approved management plans, with a written record of the information transmitted.

VI. Sanctions

1. If it is suspected that an investigator has deliberately violated this policy by, for example, failing to disclose a Significant Financial Interest or failing to comply with an accepted management plan, the Vice Provost for Research, in conjunction with the appropriate Deans and other administrative officials of the University, will investigate the circumstances and take appropriate action. Depending on the circumstances, such action may include initiation of proceedings under other University policies, including the Procedures Regarding Misconduct in Research, the Procedure Governing Sanctions Against Members of the Faculty, and relevant Human Resources policies.

Appendix

Other University policies relevant to conflict of interest may be accessed on the University web site at *www.upenn.edu/research/Detailed-Policies.htm#COI*. Existing conflict of interest policies include: (1) Financial Disclosure Policy for Research and Sponsored Projects; and (2) UPHS Guidelines for Extramural Activities of Faculty. The AAMC white paper is available at *www.aamc.org/research/coi/firstreport.pdf*.

[1] For example, an investigator's only role in a trial may be to provide recognized standard of care procedures in the clinical treatment of patients enrolled in the trial. Depending on the study design, type of procedure and other factors the CISC may determine that under specified conditions the investigator cannot influence the results of the study and should be permitted to participate in the trial under an appropriate management plan.

Defining Clinical Research

Human Subject Research

This manual was written for human subject researchers. Human subject research encompasses a diverse array of activities including epidemiological studies, evaluations of therapeutic interventions, behavioral investigations, translational research, cell line development, and so on.

Human Research is defined as any activity that:

- Meets the DHHS (Health and Human Services) definition of “Research” and involves one or more “Human Subjects” as defined by DHHS regulations
  – or –
- Meets the FDA (Food&Drug Administration) definition of “Research” and involves one or more “Human Subjects” as defined by FDA regulations

Health and Human Services ("Common Rule") Definitions:

Research

45 CFR 46.102(d) defines research as a *systematic investigation*, including research development, and testing and evaluation, designed to develop or contribute to *generalizable knowledge*.

Human Subject

45 CFR 102(f) defines a human subject as an individual about whom an investigator conducting research obtains data through intervention or interaction with individual or identifiable private information.

- **Intervention** or **Interaction** includes physical procedures performed on an individual, manipulation, communication or interpersonal contact with an individual or manipulation of an individual's environment.
- **Private information** includes information that an individual can reasonably expect will not be made public, and information about behavior that an individual can reasonably expect will not be observed or recorded.
- **Identifiable** means that the identity of the individual is or may be readily ascertained by the investigator or associated with the information.

Food and Drug (FDA) Definitions:

Research

21 CFR 50.3(c) defines research as an experiment that involves a test article and one or more human subjects that is subject to the IND or IDE regulations or which collects data to be submitted to or held for inspection by FDA.

Research is subject to the IND regulations when it involves any use of a drug except for the use of a marketed drug in the course of medical practice (21 CFR §312.3)

Human Subject

21 CFR 50.3(e) defines human subject as an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. In the case of research involving a medical device, a human subject also includes an individual on whose specimen a medical device is used.

Test Article

21 CFR 50.3(j) defines test article as any drug (including a biological product for human use ,medical device for human use, human food additive, color, adaptive, electronic product, or any other article subject to regulation under the jurisdiction of the FDA.

Certain activities that meet the Common Rule definition of “research” may be exempt from some oversight or regulatory requirements (see IRB Submission: Determining Review Type). The Office of Regulatory Affairs (ORA) will make the final determination of exemption. In certain cases, the line delineating research may be blurred (for example an anthropologist gathering oral histories or a physician using medications off-label). In these instances, a consultation with Penn’s Institutional Review Board (IRB) can help to determine whether a project is considered human subject research.

The Institutional Review Board provides additional guidance on determining whether or not an activity meets the definition of human research. This guidance can be found at:
www.med.upenn.edu/ohrobjects/PM/1_IRBReviewRequired.pdf

Research Roles

This manual contains information that is relevant to all researchers, but also contains information specific to certain types of roles within research. Each role determines the responsibilities that an individual will have for the conduct and management of the study.

Principal Investigator (PI)

The **Principal Investigator (PI)** conducts the investigation and is responsible for the study at his/her site. The PI is responsible for following federal regulations and meeting Good Clinical Practice (GCP) standards. The PI is ultimately responsible for the conduct of the study and is held accountable for his/her study team.

The principal investigator's responsibilities include the following:

- Ensure self and staff are qualified
- Have adequate resources
- Comply with the protocol
- Ensure informed consent is obtained
- Provide medical care and follow-up to subjects
- Notify IRB and sponsor of safety information
- Communicate with the IRB and study sponsor
- Manage and maintain subject data
- Inventory and dispense investigational product

A detailed listing and description of the Principal Investigator's responsibilities can be downloaded for reference (PDF document).

Sponsor

The **Sponsor** is the individual, company, or organization who takes the responsibility for the initiation, administration and management of an investigation. A Sponsor is responsible for assuring that the study is conducted in accordance with federal regulations and GCP standards.

The Sponsor's responsibilities may include the following:

- Design research project
- Define and allocate study-related duties
- Provide finances
- Select and train qualified investigators
- Assure protocol adherence by principal investigators
- Monitor quality assurance and quality control
- Confirm IRB approval

- Notify regulatory authorities and study sites of safety information
- Manage and maintain study data
- Submit and maintain Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications to the FDA
- Oversee manufacturing, packaging, labeling, and handling of investigational agents

A detailed listing and description of the Sponsor's responsibilities can be downloaded for reference (PDF document).

Sponsor-Investigator

The **Sponsor-Investigator** is the person who holds the regulatory responsibilities of a Sponsor and both initiates and conducts a study. The Sponsor-Investigator has the same responsibility as the Sponsor in terms of upholding federal regulations and GCP standards and is also the Principal Investigator responsible for study conduct at the site level. Sponsor-Investigator's protocols are often referred to as Investigator-Initiated research.

You may be considered a sponsor-investigator if you:

- Holds an IND or IDE
- Has been granted an exemption from IND/IDE requirements
- Evaluates the pre-clinical data
- Holds primary responsibility for a multi-center study
- Develops the data and safety monitoring plans for the project
- Controls the manufacture and distribution of an investigational product

Institutional Review Board (IRB)

The **Institutional Review Board (IRB)** is an independent group within the University of Pennsylvania who reviews clinical research studies for adequate protection of the rights and safety of human subjects. The IRB encompasses national, local, and community ethical standards. A research project cannot be implemented without IRB approval.

The IRB's responsibilities include the following:

- Protect the rights and welfare of human research subjects
- Review new and ongoing research
- Obtain/maintain applicable regulatory documents
- Review qualifications of investigators
- Determine that research adequately addresses ethical concerns
- Determine that research meets regulatory requirements
- Develop and evaluate institutional policies
- Educate investigators and the community

Clinical Research Coordinator (CRC)

The **Clinical Research Coordinator (CRC)** is the individual who assists the investigator with the conduct of the study by overseeing the day-to-day responsibilities of the project. The CRC helps ensure that the study is conducted in accordance with federal regulations and GCP standards.

The CRC's responsibilities may include the following:

- Recruit subjects
- Participate in the informed consent process
- Organize and maintain regulatory documentation

- Coordinate study procedures and follow-up visits
- Serve as liaison for subject, investigators, IRB, sponsor,&health care providers
- Maintain investigational drug/device accountability
- Capture and report study data
- Collect information on adverse events

Clinical Research Nurse

The **Clinical Research Nurse** performs the same functions as the CRC noted above. Typically, a nurse specific to the area of research under study fills this position. In addition, he or she may additionally perform clinical activities related to the study, such as:

- Provide oversight of admin of meds, study drugs, study interventions
- Conduct assessment and collect medical history
- Monitor patient care, assess patient status, monitor treatment effects
- Coordinate activities of team in caring for patients

Research Project Manager

The **Research Project Manager** provides strategic planning and coordination of the research project. Often, a Research Project Manager is utilized in multi-site studies in which Penn is the coordinating center. The Research Project Manager may also be engaged critical study management activities, such as to liaise between the sponsor and the site, and be involved in contractual and budgetary activities.

A Research Project Manager's responsibilities may include:

- Strategic Planning for the project
- Supervises day to day operations of study
- Develop new business strategies to increase University revenue through research and grant opportunities
- Primary contact/liaison for study operations
- Multisite coordination of team members
- Implementation of group and individual investigator, study initiation and study closeout meetings
- Assists finance department in initiating contract with sites
- Reports study status, identifies challenges, and proposes solutions.
- Proactively tracks budget, may generate billing and identifies and coordinates with vendor or industry sponsor
- Monitor study parameters across multi-site studies, such as enrollment, dropout, adverse events, etc.
- Training and development of staff at sites
- Develops protocol with a team and PI and ensures compliance
- Prepare quarterly and annual reports to Sponsors
- Ensures adequate staffing, monitoring for PI initiated studies and multi-site studies
- Develop case Report forms and SOPs
- Ensure regulatory compliance at all sites
- Audit participating sites for protocol compliance
- May be responsible for overseeing data management and sites

Clinical Research Assistant

A **Clinical Research Assistant** is typically used to assist the CRC, Clinical Research Nurse and Research Project Manager in performing routine administrative activities. A Clinical Research Assistant's responsibilities may include:

- Assist in organizing and maintaining all documentation, case report forms and study binders

Assist in obtaining appropriate signature for regulatory forms
- Assist in the preparation of documents needed for initiation, monitoring and close-out visits with sponsors and/or clinical research organization
- Assist in preparation and submission of regulatory documents (including continuing review, amendments and adverse event reporting) to the University of Pennsylvania Institutional Review Board
- Assist in mailings and other clerical duties
- Maintain telephone follow-up with all study patients
- Screen for potential patients for research studies, in collaboration with the PI, clinical research nurse or clinical research coordinator
- Schedule clinical research study patient appointments
- Processing and shipping of blood, urine and serum specimens for clinical trails
- Assist in resolving regulatory related queries with, IRB, CRO and sponsors
- May be required to perform technical duties such as blood draws, EKG or blood pressure

Additional Roles

Additional roles in research include the following. These roles are explained in the Glossary.

- Co-investigator
- Sub-investigator
- Monitors (e.g. Clinical Research Associate)
- Data manager
- Statistician
- Medical monitor
- Data And Safety Monitoring Board (DSMB)
- Safety Monitoring Committee
- Site Management Organization (SMO)
- Clinical Research Organization (CROs)

- IACUC
  Penn's Animal Care and Use Committee reviews all research and training activities involving animals
- **IRB**
  The Institutional Review Board (IRB) reviews research involving human research participants.
- Human Research Participants
  Learn more about research participation
- ERA Help
- News
  Keep up to date with the ORA
- Links
  Listing many important Links related to the ORA
- Site Map
  Quickly find site content
- Contact
  How to get in touch with our staff

Application Procedures

Activities that Do Not Meet the Regulatory Definition of Human Research
The first question one should consider when assessing the requirement for IRB review is whether the activity meets the regulatory definition of human research**.** Anyone unsure about IRB review requirements and whether their proposed activity constitutes "human research" requiring IRB review should contact the Office of Regulatory Affairs. The IRB staff will determine if the activity is human research. If an activity does not meet the regulatory definition of human research, the IRB will, upon request, issue a letter stating that the project does not require IRB review or approval.
Refer to the IRB Guidance: Is IRB Review Required?

IRB REVIEW
Human research must be reviewed by a convened meeting of the IRB unless the research is determined to be exempt or is eligible for expedited review. Go to the Forms Page for IRB applications and templates. Final review category and submission requirements will be determined by the IRB.

Convened Board Review
The work of reviewing submissions is divided among 8 IRBs. IRBs 1-5 & 7 review general medical research. IRB 8 reviews social and behavioral research. IRB 6 serves Pennsylvania Hospital. If the protocol requires review by the full IRB at a convened meeting, the PI will be notified of the assignment of the protocol to an appropriate IRB within two days of receipt by the IRB.

In general, this assignment will be to the next scheduled meeting of an appropriate IRB (provided that the submission is complete). The IRB will review no more than 25 agenda items at each meeting (including new submissions, continuing reviews, amendments, unanticipated problems posing risks to subjects or others, or previously tabled protocols). Agenda items in excess of 25 will be assigned to the next scheduled meeting of an appropriate IRB.

Expedited Review
Federal regulations (45 CFR 46.110, 21 CFR 56.110) allow the IRB to review certain applications on an expedited basis if they meet specified criteria. All expedited protocols must be reviewed by the IRB at least once per year. Additionally, the standard requirements for informed consent (or its waiver, alteration, or exception) apply to all IRB approvals regardless of the type of review - expedited or convened IRB.

An expedited review consists of a review of research involving human subjects by the appropriate IRB Executive Chair or his/her designee. In reviewing the research, the reviewer may exercise all of the authorities of the convened IRB except that the reviewer may not disapprove the research. Additionally, the reviewer may refer the application to the convened IRB for a standard review as warranted.

Minor modification or amendment of previously approved research may be reviewed using an expedited review mechanism. The following are examples of the kinds of research modifications requiring either expedited or convened board review. Specific decisions on the level of review are made on a case-by-case basis.

- Adding research activities that qualify for exemption or fall under an expedited review category
- A minor increase or decrease in the number of participants
- Narrowing of inclusion
- Broadening of exclusion criteria
- An increase in the number of safety visits for the purpose of increased safety monitoring
- A decrease in the number of visits, provided the decrease does not affect the collection collection of information related to safety evaluations
- Changes in remuneration
- Changes to improve clarity of statement or correct typographical errors provided the change does not significantly alter the content or intent of the statement
- The deletion of investigators study staff, the addition of qualified investigators or study staff
- The addition or deletion of study sites
- Minor changes specifically requested by other University committees with jurisdiction over the research
- Qualifying protocols will be reviewed and the investigator will be informed of the IRB's decision within 10 business days following receipt of the submission.

Exempt Research
Federal regulations at 45 CFR 46.101(b) and 21 CFR 56.104 describe categories of research that may qualify for exemption from IRB review. The IRB makes the final determination of exemption.

If a study qualifies for exemption, the research protocol will be approved for a three years. At the end of the three year period, the PI may request renewal of the protocol.

Research activities may commence as soon as the letter granting exempt status is received from the IRB. Investigators are required

to submit to the IRB changes in the protocol that may change the level of review.

Within approximately 10 business days following receipt of the submission, the investigator will be notified of the IRB's decision; or the IRB will request additional information needed to determine the exempt status.

Refer to the Claim of Exemption Form Instructions and the Claim of Exemption Form for further guidance.

You may also submit a request for exemption electronically by using the Penn Request for Exemption (RFE) Application. Instructions on how to access the application can be found here.

Continuing Review
The IRB Application for Continuing Review must be submitted no later than six weeks prior to the expiration date for full board review and no later than two weeks for expedited review.

NOTE: No research related activities may occur after the protocol expiration date unless the PI contacts the IRB and the IRB Executive Chair (or authorized designee) determines that it is in the best interest of subjects to continue during the lapse in IRB approval.

Modifications to a Research Protocol

- Federal regulations require that no modifications in approved research, during the period for which approval has already been given, may not be initiated without prior IRB review and approval except where necessary to eliminate apparent immediate hazards to human subjects. Sometimes modifications are noted or recognized after they occur. These changes will be reviewed by the IRB as events that may represent unanticipated problems involving risks to participants or others and to determine whether the change was consistent with ensuring the participants' continued welfare.
- The IRB categorizes modifications into 3 types: Amendments, Deviations, and Exceptions.

Amendment
An amendment is a permanent, intentional action or process that revises/amends/modifies a previously approved research protocol. Information relating to protocol amendments will be provided to research subjects when the information may relate to their willingness to continue to be a part of the research. Investigators or sponsors must submit requests for changes to the IRB in writing. Upon receipt of the protocol amendment, an IRB Administrator with the assistance of the IRB Executive Chair, or Senior IRB Administrative staff will determine the appropriate level of review.
Minor modifications are defined as those that do not materially affect an assessment of the risks and benefits of the study and do not substantially change the specific aims/design of the study. Submit all modifications using the Modification Submission Form.

Exception
A one time, intentional action or process that departs from the IRB approved study protocol, intended for one occurrence.
If the action disrupts the study progress, such that the study design and results would be compromised, and the action compromises the safety and welfare of study subjects, prior documented IRB approval is required.

Deviation
A one time, unintentional action or process that departs from the IRB approved study protocol, involving one incident and identified retrospectively, after the event occurred. If the impact on the protocol disrupts the study design or compromises the safety and welfare of the subjects, the deviation must be reported to the IRB within 10 business days.
When the IRB reviews the exceptions and deviations, a determination will be made as to whether information related to protocol changes should be provided to participants when such information might relate to their willingness to continue to take part in the research. The investigator will be advised if subjects need to be informed.

School District of Philadelphia approval required to conduct research within the school district:
The School District of Philadelphia frequently receives requests from outside individuals and agencies to conduct research studies. While it is District policy to cooperate with researchers whose projects might benefit education, it is incumbaent on the District to ensure that such activities do not interfere with the instruction, or require excessive pupil or staff time. For this reason, all requests to conduct studies research studies in schools, utilizing questionnaires, surveys, interviews, focus groups, and/or requests for student data, are screened by the Office of Research and Evaluation's Research Review Committee. Ultimate responsibility for authorization rests with the Director of the Office of Research and Evaluation and the Chief Accountability Officer. Policies, procedures, & forms may be found on the School District of Philadelphia, Office of Research & Evaluation's website . Additional information

- IACUC
  Penn's Animal Care and Use Committee reviews all research and training activities involving animals
- IRB
  The Institutional Review Board (IRB) reviews research involving human research participants.
- Human Research Participants
  Learn more about research participation
- ERA Help
- News
  Keep up to date with the ORA
- Links
  Listing many important Links related to the ORA
- Site Map
  Quickly find site content
- Contact
  How to get in touch with our staff

Required Training

CITI Training Requirements: Investigators, Research Staff, & Students Engaged in Human Research

The CITI-Protection of Human Subjects Research Training courses fulfill the University's requirement for training in human research protections.
You must follow the instructions below in order to receive credit for completing the CITI course.

1. Open the www.citiprogram.org web site. It is recommended that you keep this page open so you can refer to it as you complete the registration process.
2. From the login and registration page, select “New users-Register here”.
3. Choose the University of Pennsylvania as the participating university.
   - **NOTE for VA and CHOP Affiliates**: If you have an appointment at the VA or CHOP, you should register under the VA or CHOP. Upon completion of the training, please send your certificate to Kadeda Burgess (burgess4@upenn.edu) to credit your training in Knowledge Link.
   - NOTE: Penn requires CITI training every 3 years. If you previously completed the School of Medicine's POR training or CITI training, the CITI Refresher 101 course satisfies the training requirement.
4. Select a user name and password. Provide all requested contact information.
5. You must enter your correct PennID in the PennID field in order to receive credit for completing a course. (Your Penn ID is the group of 8 numbers prominently displayed under your name on your Penn Card).
   If you do not have a Penn ID, enter your date of birth MMDDYYYY. If your data does not appear in Knowledge Link after one week, or if you have any other questions, contact Kadeda Burgess burgess4@upenn.edu or call 215-573-2540.
6. Select the Learner Group that is most appropriate for your research activities. If you are a Faculty/Staff member, please select your appropriate group below. You will be enrolled in the basic course for that group.
   - Biomedical Research
   - Social/Behavioral Research
   - IRB Member
   - Students - Class projects
   - Refresher 101 - Biomedical Research
   - Refresher 101 - Social & Behavioral Research
7. Under My Courses, click Enter next to the course "Human Research"
8. You must complete all modules in order to get a certificate of completion.

Fall 2010 Educational Series

To register for an IRB Fall Educational Series Workshop, please visit KnowledgeLink at http://knowledgelink.upenn.edu The Fall Workshops are available under the "Optional Training" tab.	Workshop Descriptions
Social & Behavioral Research – What Review Level is Appropriate & Application Basics	Date/Time: Tues October 5, 2010 10:00 a.m. – 11:30 a.m. Location: Class of 55 Conference Room Van Pelt Library
Working with Subjects: IRB Tips for Recruitment Plans & Materials, Compensation/Reimbursement and Information Sharing	Date/Time: Fri October 15, 2010 10:00 a.m. – 11:30 a.m. Location: HUP Flyers/Sixers Auditorium

Comprehensive Walk-Through of the IRB Application	Date/Time: Mon October 25, 2010 1:00 p.m. – 3:00 p.m. Location: HUP Flyers/Sixers Auditorium
Inside the IRB: What happens to your submissions after they are received by the IRB?	Date/Time: Thurs November 4, 2010 10:00 a.m. – 11:30 a.m. Location: HUP Flyers/Sixers Auditorium

IRB Member & Administrative Staff Tools & Resources

Title	*Link*
IRB Staff Contact List	
IRB Member • IRB Confidentiality Statement • IRB Member Self-Evaluation Form	
IRB Chairs • IRB Chair Self-Evaluation Form	
Declaration of Helsinki	
The Belmont Report	
The Nuremberg Code	
Primary Reviewer Worksheet	
Primary Reviewer Reference	
Vulnerable Populations Checklists • Pregnant Women • Prisoners • Children	
Informed Consent Worksheet	
Completeness Check & Appendices • Completeness Check • Drugs & Biologics/Devices • Significant Risk/Nonsignificant Risk Device Determinations	
Continuing Review Worksheet	
Continuing Review: Criteria for Approval Reference	WRK-17-1
Modification Review Worksheet	
Modification Review Reference	WRK-16
Human Research/Exemption Determination Worksheet	WRK-3
Expedited Review Worksheet	
Expedited Review Categories	
Standard Operating Procedures	
Guide to Daily Operations	
Categories of Action from IRB Review of Research	
DHHS Regulations (45 CFR 46)	
FDA Regulations	
Office of Human Research Protections (OHRP)	
Federal Wide Assurances	

OHRP Guidance Documents	
Center for Drug Evaluation and Research (CDER) -- ◦ CDER Home ◦ Regulatory Guidance ◦ Drug Development & Approval Process	
Center for Devices and Radiological Health (CDRH) -- ◦ CDRH Home ◦ Device Advice ◦ IDE - Guidance on how to obtain an investigational device exemption (IDE).	
Center for Biologics Evaluation and Research (CBER) -- ◦ Vaccines, Blood, & Biologics Home ◦ Guidance and Guidelines	
Clinical Trials & GCP -- ◦ Home ◦ Guidance and Information Sheets	
Guidance for Institutional Review Boards and Clinical Investigators • Compilation of current FDA Guidance documents for IRBs, including investigator responsibilities. Includes information on both drug and device studies.	

Study Preparation

This section of the manual covers those activities that are conducted during the process of preparing a research study, from assessing the feasibility of the research project through protocol and study document development, submission and approval, and initiating the research site.

Project Feasibility Assessment

When developing a potential research study, there are several aspects that require careful consideration to determine whether or not the project is feasible. This section attempts to outline some of the initial questions that need to be answered early in the study planning stage.

This section will expose the researcher to the various areas that need to be assessed:

Scientific Validity

Is there sufficient scientific validity to proceed with the project?

Conduct a thorough literature review to evaluate the merit of a proposal with these questions in mind:

- Will the project contribute to the field?
- Will the project replicate or challenge existing findings in the literature?

What type of study will be conducted?

A critical step early in the feasibility phase is to determine and clearly define the type of project being considered. The complexity of the project will impact the resources that will be needed.

Potential project types include:

Resource Assessment

Is there department/institute/center support?

Discuss the project with key persons in the department, center, or institute with the following questions in mind:

- Is there an experienced mentor, collaborator, or consultant that can be involved in the project?
- Is there institutional support from the divisional chief or department chairperson?
- Does the study reflect the values and principles of the department and institution?
- Is the institution willing to accept responsibility for the level of risk involved?
- Are there departmental resources that can be used to support the project?
- Who are the key persons and staff who will contribute to the effort?
- Do the faculty & staff have the ability and qualifications to carry out the methods and procedures of the project?

What is the length of time required to obtain approval of a study?

The length of time for approval depends upon several factors including the type of project, the amount of time the investigator and study team can dedicate to preparing the study for approval, whether or not contract negotiation is required, etc. Obtaining approval to commence a study involves more than just the IRB submission. There are multiple processes involved, each with their own time lag. However, many of the processes can be conducted simultaneously, as illustrated below.

INVESTIGATOR-INITIATED STUDY

INDUSTRY-SPONSORED STUDY

Recruitment Potential

Are there enough subjects available to complete the project?

It is important to ascertain whether or not there exist enough subjects eligible to be enrolled into the research study to achieve the proposed aims. To do this, first identify how many people will meet the study's eligibility criteria. Next, estimate what percentage of the targeted population can be accessed and realistically be expected to participate and use this information to decide whether there are enough subjects to meet the enrollment objectives.

The University of Pennsylvania Health System (UPHS) has an extensive network of physicians, hospitals, clinics, treatment centers, and community practices. All of these sites can be viewed as potential sources for research subjects with specific diagnoses. Healthy volunteers will need to be recruited from the population at large. Regardless, investigators must identify methods for recruiting from their targeted audience via medical records review, advertisements, word of mouth, or referrals.

Patient Database Query Tool

One option available to Penn researchers is to utilize the PICARD patient database. PICARD (Pennsylvania Integrated Clinical and Research Database) is comprised of diagnostic, treatment, and personal health information for over 1.5 million patients who have sought care within the UPHS since 1977. This database can provide valuable information for estimating a study's recruitment potential by providing counts of patients by diagnosis, visit dates, gender, and/or race, and a number of laboratory and Radiologic information.

For example, running a query of patients who have a diagnosis of both Parkinson's Disease (ICD-9 332, 332.0, or 332.1) AND Macular Degeneration (ICD-9 362.5, 362.50, 362.51, 362.52, 362.53, 362.54, 362.55, 362.56, or 362.57) returned the following results:

The PICARD database is available to Penn researchers to run simple queries through an application called Patient Database Query Tool. A PICARD Search can be accessed at http://somapps.med.upenn.edu/ohr/diag. **To access this site, you must either by connected directly to hupnet or accessing HUPNET through the UPHS virtual private network (VPN). To request access to the VPN, please access the following site: https://remedy.fcgis.com/UPHS%20Service%20Request**. Classroom sessions are offered periodically through the Office of Human Research (OHR) website (www.med.upenn.edu/ohr). In addition, the Office of Human Research Patient Informatics staff can assist in running more detailed queries.

The results that are returned from a simple PICARD search do not contain protected health information, but rather display the number of "hits", grouped by gender and ethnic group. Providing investigators full patient data sets that include patient identifiers normally requires IRB approval.

Financial Feasibility

Funding for a study can come from a variety of internal and external sources. External sources include federal agencies, pharmaceutical companies, public charities, or foundations.

The website for the Office of the Vice Provost for Research has a variety of links to possible funding sources at http://www.upenn.edu/research/funding.htm.

The following databases are available to Penn researchers:

- SPIN --(Sponsored Program Information Network) -- funding opportunities from the federal government and 1,700 other sources. Investigators can use a customized automated alert system called SMARTS (SPIN Matching and Research Transmittal Service) that allows investigators to receive email notifications about funding opportunities http://www.upenn.edu/research/smarts.htm
- Grants Advisor Plus -- funding opportunities for grants persons and faculty in higher education
- COS (Community of Science) -- scientific funding database
- GrantsNet - funding programs for young biomedical researchers, faculty, and administrators from the American Association for the Advancement of Science (AAAS) and the Howard Hughes Medical Institute

It is important to analyze the financial feasibility to determine whether there is enough funding to support the project. A thorough analysis of financial feasibility can be accomplished by preparing a study cost budget. Refer to Study Budget Development for more information.

Research Coordinator Staffing Issues

Career Paths

The School of Medicine, in collaboration with the Abramson Cancer Center, put forth a new series of job titles in 2007 that aim to provide a clearer career path for Clinical Research Coordinators and Clinical Research Nurses. By using these titles, it provides the research coordinator with direction for advancing their career, improves retention, and guides the manager in hiring new research coordinators and promoting deserving employees.
Sample job descriptions for these positions are available for download below. These job descriptions are intended to be used as a guide for hiring officers to consider the needs of the department and proposed position, or to consider a more appropriate job title to transition a current staff member into. It is expected that these job descriptions will be customized to the specific duties of the department and position.

Clinical Research Coordinator

- Clinical Research Coordinator A (Grade 25)
- Clinical Research Coordinator B (Grade 26)
- Clinical Research Coordinator C (Grade 27)
- Supervisor, Clinical Research Coordinators (Grade 28)

Clinical Research Nurse

- Clinical Research Nurse B (Grade 26)
- Clinical Research Nurse C (Grade 27)
- Clinical Research Nurse D (Grade 28)
- Supervisor, Clinical Research Nurses (Grade 29)

Clinical Research Assistant

- Clinical Research Assistant A (Grade 23)
- Clinical Research Assistant B (Grade 24)

An additional role to consider is the **Research Project Manager**. The Research Project Manager provides strategic planning and coordination of the research project. Often, a Research Project Manager is utilized in multi-site studies in which Penn is the coordinating center. The Research Project Manager may also be engaged critical study management activities, such as to liaise between the sponsor and the site, and be involved in contractual and budgetary activities.

The following charts attempts to identify the key distinctions in job responsibilities and qualifications among the Clinical Research Coordinator and Clinical Research Nurse positions (click to view).

- Clinical Research Coordinator Career Paths
- Clinical Research Nurse Career Paths

All new hiring requests for clinical research coordinators and clinical research nurses in the School of Medicine will use these job titles. Before these were available, a variety of other job titles have been used for clinical research coordinators, which may or may not have been the most appropriate reflection of the job. For example, Research Coordinator and Senior Research Coordinator are broader and not specific to clinical research. It is recommended that the managers consider reclassification of those employees into one of the new job titles. Human Resources can assist managers with the reclassification process. More information can be found in Human Resources Policy No 304: Position Reclassification and Salary Adjustments (http://www.hr.upenn.edu/Policy/Policies/304.aspx).

Other advantages exist for using these new job titles, as these are the only job titles that are exclusively used for research coordinators and nurses who are involved in clinical research (as opposed to basic science or other types of research). By being able to identify these individuals, it improves the ability for relevant offices, such as the Office of Human Research and the Institutional Review Board, to communicate important updates to these individuals that is necessary for performing their job. It also becomes possible to more reliably track clinical research coordinator retention and attrition data through the Clinical Research Registry, which can be useful for improving those staffing issues.

Recruitment & Selection

Sources for CRC Recruitment

Effective CRC recruitment requires a clear understanding of the position being filled and related qualifications. The job description must accurately reflect the expectations of the position; required experience and education. This will ensure that the position is properly graded and that a competitive offer can be made to the final candidate. Successful recruitment requires the manager to understand the area market for the specific positions and who else is competing for these same individuals (i.e. pharmaceutical companies, contract research organizations, colleges and universities, temporary agencies), and area salary information (if available).

There are many sources for CRC recruitment including national clinical research associations, internet based career sites, area colleges and universities, area newspapers, hospitals, employment agencies. The posting should reflect the essential elements of the job description along with characteristics unique to the position (i.e. full-time, part-time, temporary, permanent, prior experience in clinical trials, etc.).
National Clinical Research Associations:

1. Association of Clinical Research Professionals http://careers.acrpnet.org/
2. Society of Clinical Research Associates http://www.socra.org/

Area colleges and universities can be a source for CRC recruitment. Contact the college or university career placement office to post positions. If the CRC position requires a nursing background contact the college or university nursing program. The nursing programs can be a good source for part-time positions requiring individuals with a medical background. Community hospital nursing programs can also be a source of CRC recruitment as well.
Networking with similar research programs on campus can be an effective source for CRC recruitment. Within Penn, the Society for Clinical Research Coordination and Management has a career postings website (http://www.med.upenn.edu/crc/jobs.shtml). Active participation in this group's activities may lead to networking opportunities for recruitment purposes.

Area newspapers have on-line job postings in addition to the daily/Sunday classified sections. Consider career specific trade journals and sites (i.e. Nursing Spectrum - (http://nsweb.nursingspectrum.com/classifieds/employers.cfm?REGION=Northeast).

Networking among fellow employees can be an effective method of CRC recruitment. Physicians and other health care staff can be effective at identifying nurses working in a hospital with an interest in research.

Key Characteristics & Skills

The role of the CRC and CR Nurse is multi-faceted with a wide range of responsibilities, from patient care to administrative. The following skills are essential for success in this role:

1. Organizational skills
2. Ability to multi-task
3. Detail-oriented
4. People-oriented
5. Self-confident
6. Flexible
7. Able to manage time well
8. High energy level
   ("Becoming a Successful Clinical Research Investigator", Dr. David Ginsberg, 2005 Thompson CenterWatch)

Retention Strategies

Turnover of Clinical Research Coordinators (CRC) presents a costly impact on study operations. A recent Thomson CenterWatch survey of 256 hiring decision makers found that only 56% of Clinical Research Coordinators (CRC) have been in their positions for less than 3 years, and that many CRCs were switching to careers in industry as study monitors (CenterWatch Monthly, July 2004). This trend affects the study site with a loss of productivity, money and time spent training replacements, and an overall less experienced staff.

The most commonly encountered reasons for the high rate of turnover among CRCs include:

- Heavy Workload (>40 hours per week)
- Compensation
- Personal Life Changes
- Competitive hiring by other sites as CRC
- Transition from CRC to study monitor in search of higher compensation and flexibility
- Lack of recognition and professional respect
- Loss of funding on the part of the site

Burnout is a commonly reported occurrence among CRCs. Burnout is associated with perceived daily workload, job satisfaction and low endurance and nurturance personality traits. Aside from turnover, burnout can also affect productivity, data quality and subsequently may have a financial impact on the clinical trial.

Several strategies are recommended for improving CRC retention and preventing burnout. It is anticipated that implementation of the career paths identified earlier in this section will contribute to improvement of CRC retention by providing a clear path for the CRC and CR Nurse to advance within their profession.

Preventing Burnout
Respecting a realistic and flexible schedule for CRCs is another critical step toward preventing burnout. It is recommended that CRCs be expected to work no more than 40 hours per week, with the exception of emergency situations. The hours may vary to accommodate patient recruitment and visit needs, but the CRC should not routinely be expected to work beyond 40 hours. Investigators who set these expectations should consider that while the extra hours may reward the investigator with benefits such as professional recognition, tenure, and other opportunities, there are very few such career benefits for the CRC. If the workload is such that extra hours are required for the CRC to accomplish necessary duties, it may be prudent to hire another CRC, or at minimum a Clinical Research Assistant to reduce to burden on the CRC.

In addition to maintaining a realistic number of hours the CRC is expected to work, offering a flexible work schedule can also help retain staff. For example:

- Offer four 10-hour days to allow CRC to take care of medical appointments, well visits for their children and other family members or other personal needs.
- Stagger work times so that CRC can work around patient enrollments if they are working extra long days in the office to compensate for the time.

Professional Recognition
The CRC has long been an underappreciated role. Promoting a perception of being appreciated and recognized for their contributions can greatly improve CRC retention. This can be accomplished in several ways:

- Supporting membership in professional organizations such as ACRP or SoCRA
- Providing continuing education opportunities such as attendance at professional conferences
- Supporting pursuit of professional certification

Monetary Rewards

- **Bonuses**: A department may set up a paid bonus program that may be structured around retention, performance, or other factors. Bonus programs must be approved by Human Resources and must be applied equally across the department.
- **Salary Adjustments**: Salary adjustments can be made in conjunction with a reclassification into a more appropriate job title (see Career Paths). In addition, a salary adjustment can be made based on market data.

Low Cost /No Cost

- Monthly Lunches
- Team Building Strategies
- Attendance to seminars to build skills
- Acknowledgement for good or exceptional work email, certificates, gift cards

Education and Training

Required Research Training

Collaborative IRB Training Initiative (CITI) Training

All personnel - faculty, research fellows, students, and staff - engaging in human research must have documented discipline-appropriate training in human research protections. The Collaborative Institutional Training Initiative (CITI) web-based modules satisfy this requirement. The "CITI Protection for Human Subjects Training" course is available in Knowledge Link (http://knowledgelink.upenn.edu).
NOTE: The Patient Oriented Research Certification Program is no longer offered or required by the School of Medicine Office of Human Research. SOM faculty and staff involved in the design, conduct or reporting of human subjects research are required to complete the CITI Training program per IRB requirements.

Health Insurance Portability and Accountability Act (HIPAA) Training

All University and UPHS staff having contact with patient information are required to complete HIPAA training. However, HIPAA regulations include specific rules about how protected health information is used and protected in research. Researchers must complete either of these 2 versions of the online HIPAA training (available at http://knowledgelink.upenn.edu):

- HIPAA109 & HIPAA110: HIPAA Privacy Education for UPHS Physicians, House Staff and Penn School of Medicine Faculty (both 109 and 110 required)
- HIPAA111: HIPAA Privacy Education for Penn School of Medicine Staff and Students

Environmental Health & Radiation Safety (EHRS) Training

EHRS provides a number of training programs that are required by the Occupational Safety & Health Administration (OSHA) and the Nuclear Regulatory Commission (NRC). This training is required for all employees who work with or ship hazardous substances including:

- Chemicals
- Human blood, blood products, fluids, and human tissue specimens
- Radioactive materials or radiation producing equipment

To determine which training programs are required and how the training can be completed , review the section "Training Requirements" at http://www.ehrs.upenn.edu/training/index.html

Required Training for UPHS Employees

UPHS Annual Mandatory Education

http://www.uphs.upenn.edu/hr/training/ame/ame.htm

UPHS HIPAA Privacy Education
http://www.uphs.upenn.edu/hr/training/hipaa/hipaa.htm

UPHS Patient Safety
http://www.uphs.upenn.edu/hr/training/safety

EHRS- Shipping Requirements
http://www.ehrs.upenn.edu/programs/bio/transporting.html

Other Available Training Opportunities

Penn Clinical Research Coordinator Certification Program
This program is designed to provide a comprehensive training and education program for research staff at Penn, focusing on standards and techniques for performing job functions typical of a Clinical Research Coordinator (CRC) from an operational and regulatory compliance perspective. For more information and registration information, visit http://www.med.upenn.edu/penn/ohr/crc.shtml.

Penn Clinical Research Investigator Retreat
This training program is designed to provide a comprehensive training and education program for investigators at Penn who conduct clinical research, focusing on standards and techniques for managing research projects and conducting clinical research that is efficient, effective, and compliant. For more information and registration information, visit www.med.upenn.edu/penn/ohr/investigator.shtml

Human Subjects Research Workshops
This joint effort between the Office of Human Research, the Institutional Review Board, and members of the CRC Retreat Planning Committee is an ongoing seminar series that targets anyone working in human subjects research, including research coordinators, investigators, IRB staff and IRB members. The topics address a variety of study operational and compliance issues. For more information and registration information, visit http://www.med.upenn.edu/ohr/workshops.shtml.

Software/Computer Training
Various software training is available to UPHS and Penn staff including:

- *Sunrise*- The medical charting system used by UPHS has training programs available at https://www.uphs.upenn.edu/scm/educ
- *Technology Training*- University training is available for Penn-supported software including Microsoft programs (Word, Excel, Acess, etc.), Filemaker Pro, and Photoshop http://www.tts.isc.upenn.edu

One Year Certificate in Patient Oriented Research
This one year program is available to junior faculty and MDs interested in conducting clinical research. The program involves weekly lectures and the implementation of an independent research project. The program requires registration and a course fee and provides trainees with an introduction to biostatistics, study design, regulatory affairs, and the mechanics underlying the drug approval process. For more information visit http://www.med.upenn.edu/por/por.html

Clinical Research Certificate Program
This certificate program, managed by the Center for Clinical Epidemiology and Biostatistics, is designed for clinicians without clinical research training who desire a training experience less intense than degree-granting programs, but are interested in a solid basis for proposal development and research collaboration. For more information visit www.cceb.upenn.edu/education/non-degree/certificate.php

Master of Science in Translational Research
A graduate program in translational research is available for MDs and faculty enrolled in the Penn fellowship program. The coursework covers the fundamental skills, methodology, and principles necessary for the physician-researchers pursuing a career in translational research. An application is required to enroll in the program. For more information visit http://www.med.upenn.edu/mtr

Master of Science in Clinical Epidemiology
This two- to three-year clinical research training program, managed by the Center for Clinical Epidemiology and Biostatistics, includes didactic courses and the development and completion of a clinical research project. The program is designed for clinicians interested in academic careers as independent clinical research investigators. For more information visit www.cceb.upenn.edu/education/epi-degree/msce.php

Professional Research Associations

The following organizations offer training and certification programs for clinical research.

- Association of Clinical Research Professionals (ACRP) http://www.acrpnet.org
- Drug Information Association (DIA) http://www.diahome.org/diahome/
- Society for Clinical Research Associates (SoCRA) http://www.socra.org

Grant Writing

Grants are written to obtain research funding from federal agencies, private foundations, pharmaceutical companies, etc. Each agency has its own requirements for grant writing. This section will concentrate upon the requirements for the National Institute of Health (NIH).

Deadlines for new NIH grant applications vary depending on the type of grant. Information on NIH grant deadlines can be found at: http://grants.nih.gov/grants/funding/submissionschedule.htm

New investigators should estimate that the writing process will take between 2-6 months. Applications for NIH research support are made on Grant Application Form PHS 398. For detailed submission information, the School of Medicine 's Grant Writing Manual can be found at www.med.upenn.edu/rpd/grants.html. NIH also provides a Grant Writing information and tutorials, available at: www.nlm.nih.gov/ep/Tutorial.html

General writing tips include:

- Write clearly and concisely
- Proofread
- Write for technically diverse reviewers
- Avoid unnecessary complexity
- Collect preliminary data
- Follow instructions carefully
- Obtain outside opinions

Grant Writing Services
The Office of Research Program Development (RPD) has a dedicated grant writer and scientific editor who can provide assistance with writing and editing large, multidisciplinary proposals, such as program project (P01), center (P30) and specialized center (P50) grants. The RPD scientific writer/editor will help ensure:

- Integration of distinct projects to create a cohesive proposal
- Consistency of style and tone throughout the proposal
- Clarity in the presentation of ideas, goals, and strategies
- Polished grammar for maximum readability

Please contact RPD at: RPD@mail.med.upenn.edu to learn more about this service.

Components of an NIH Grant

Abstract
: An abstract is a summary of the grant written for the educated non-specialist. It is a concise description of the background, specific aims, the research methods, and significance. The abstract is used to assign a grant to a study section. Study section members (who are not primary reviewers) will rely heavily on the abstract. The researcher may choose to write the abstract last to ensure the content of the entire proposal is well summarized.

Specific Aims
: The specific aims section is generally a page explaining the long-term goals, the hypothesis, and the specific aims or objectives (Specific Aim #1, Specific Aim #2, Specific Aim #3, etc.). The hypothesis should be clear and focused. The aims should be related. Explain how the specific aims will be used to support the hypothesis.

Background/Significance
: The background/significance section is generally 3 pages describing the problem, current knowledge, remaining questions, and importance of the research. The investigator should provide a balanced review of the literature. Elaborate upon how the knowledge gained from the hypothesis and specific aims will improve the field and/or other related areas.

Preliminary Results/Progress Report

The Preliminary Studies/Progress Report: Limit to 12 pages describing what current and prior work has done to support the feasibility of the study. Identify how each of the specific aims in the work has been addressed and interpret the results critically. Demonstrate that the investigator has the experience and capabilities to conduct the proposed project. The investigator may include unrelated studies if they demonstrate his/her competence to perform the experimental techniques.

Experimental Design/Methods

The research design and methods section is no more than 25 pages (items "a" through "d") providing a concrete explanation of how the study aims will be accomplished. A detailed and technical description of the study procedures and methods should be incorporated. Avoid "shot gun" approaches or fishing expeditions. This section should address potential problems or limitations in the experimental design and, if possible, provide alternatives or solutions.

Reference Section

The reference section should accurately reflect the citations used throughout the grant.

Consortium and/or Consultant Arrangements

Describe collaborators at other institutions or other local experts who may be providing support or advice. This should include documentation substantiating their participation.

The grant application may also include:

- A biographical sketch
- Budget and justification
- A description of other research support
- Conflict of interest disclosures
- Assurances/regulatory (IRB) approval
- A description of resources and environment and letters from the department chair.

The grant will be assigned to an Institute or Center (IC) who then sends it to a scientific review group or "study section." The study section will review the grant and assign it a priority score for funding.

Grant Revisions

Approximately 40% of the grants reviewed by a study section are resubmissions. Do not be discouraged if you receive a poor priority score and need to resubmit your grant.

- Review the NIH information on application for renewal (www.niaid.nih.gov/ncn/grants/cycle/default.htm) and other resources that assist with grant writing

- Read the summary statement or "pink sheet"

- Identify the problems. **The most common criticisms include:**
  - Grant is poorly written- the plan is unclear, incorrect, or incomplete
  - Aims cannot be supported- the sample size is inadequate or uncertain
  - Plan is not well conceptualized- the methods are incomplete
  - Insufficient expertise- missing talent, usually statistical
  - Poorly chosen population of inference - poor subject selection, usually controls
  - Not enough evidence to support the planned response rates- need pilot data
  - Plan is unfocused- hypothesis is absent or unclear

- Ask for advice from experienced researchers

- Address the problems
  - Use the pink sheet to make revisions
  - If there are problems with the review (reviewers were not interested, did not have suitable expertise, or were biased), revise, resubmit, and request a new study section

Research Methods and Statistical Design

It is beyond the scope of this manual to provide information on various statistical approaches and models. The following is meant as a high-level overview of the basic elements of study

The researcher's goals influence the size, scope, and direction of the investigation. The intended purpose of biomedical research varies and usually falls along a continuum:

Basic research is research to advance scientific knowledge and understanding across a wide variety of areas such as physiology, pathophysiology, chemistry, etc., but is not focused on a specific practical application of that knowledge.

Translational research, often called "bench-to-bedside research," focuses on assessing the feasibility of translating basic research findings and knowledge into clinical therapies. The interface between basic research and clinical application includes elements of bench research necessary to support application to human medical care (e.g. biologic mechanism of action, pharmacokinetics, toxicology, etc.) and early stage research in humans.

Clinical application/development produces and evaluates materials, devices, systems, or methods as they apply to human healthcare. Clinical trials and certain translational research activities are components of this category.

A **clinical trial** is any investigation involving human subjects intended to identify the clinical, pharmacological or other effects of an investigational product (drug or device) to measure its safety and/or efficacy. The overall objectives of a clinical trial vary with the phase of investigation:

- *Phase I* - first study of a drug in humans, most commonly healthy adults; safety and dose ranging tolerability; basic metabolism or mechanism studies (generally small studies of 20 or less subjects)
- *Phase II* - first study of drug in target populations (patients); safety, dose ranging in patients; preliminary efficacy assessment (generally >100 subjects)
- *Phase III* - larger study to prove efficacy and increase experience with safety (generally large studies ranging from >100 to >1000 subjects ---- Phase III cardiovascular studies have enrolled higher than 40,000 subjects)
- *Phase IV* - post-marketing studies; vary in size; often to provide ongoing safety data.

If a researcher is conducting research in human subjects, a clear hypothesis is necessary in order to choose the study design. The study design, in turn, will impact which techniques will be used to minimize bias and how the statistical analysis will be conducted. The involvement of a statistician in the preparation of the statistical plan and analysis is an indispensable part of this process and has been described in A General Guide to Statistical Consultation.

Basic Elements of Study Design

Once the purpose of the investigation is understood and the hypothesis and objectives have been formulated it is necessary to identify the study design to be used for the project.

To help determine the appropriate research design:

- Identify the condition and outcome of interest.
  - Will manipulation of the variable(s) occur or will observational methods be used?
- Select the type, order and frequency of observations and measurements.
  - What methods will be used to obtain data? How, when, and in what order will these observations and measurements occur?
- Identify the nuisance variables.
  - Are there any identifiable sources of variation which can confound the results? Can their impact be minimized or controlled?
- Identify the population of interest.
  - What sample size will be needed? How will sampling occur? Is there only one group or will multiple groups be used for comparison?

Basic Types of Study Design

Study designs can be classified into two broad categories: experimental studies and observational studies.

Experimental Studies

In an experimental study, the selection and allocation or assignment of individuals for the experiment is under the control of the investigator. The controlled conditions help validate a cause-and-effect relationship between the treatment and the outcome within the population enrolled in the study (internal validity). However, it is important to remember that findings from experimental studies do not always accurately reflect findings under real-world conditions (external validity) since there are many factors in the real-world that cannot be fully captured in a carefully controlled experiment (e.g. natural variations in physiology and concomitant diseases or medications, patient compliance with the treatment, etc.).

General characteristics that differentiate experimental research designs from each other include the use of a control group, random assignment, and blinding. When used correctly, these characteristics can significantly strengthen the ability to infer cause and effect from experimental research.

Control Groups

Controls are subjects who are included in an investigation for comparison to the intervention/treatment group. Controls are not given the intervention, or are given a different intervention, or, depending on the type of experiment, do not have the condition, background, or risk factor under investigation. A control group may be enrolled concurrently with

the intervention group, study at the same location as the intervention group, or may be studied independently (as an external or historical control). Some common examples of control-group designs include:

1. A **cross-over design** is a type of experimental study where subjects act both as a control and as an actively treated subject. Generally, subjects are enrolled into one treatment group, then after a waiting or wash-out period (i.e. time for the treatment effect to be eliminated or "washed-out"), are enrolled into an alternate treatment group. In this type of design the subjects act as both the comparator group and the active treatment group. This approach reduces the variability in comparing active to treated subjects, but it is susceptible to bias if carry-over effects from the first treatment occur.
2. A **parallel groups design** is a type of study where different treatment groups are running simultaneously. The parallel-groups approach is susceptible to non-comparability between groups if the subjects are not properly allocated or assigned (i.e. the baseline characteristics may not be equal between the two groups to such a degree that the groups are not truly comparable).
    - A **matched pairs group** is a type of parallel study design in which subjects with similar, pre-determined traits are first paired and then randomized into different study arms for comparison.

3. A **series group design** assesses exposure to the study treatment in phases- one treatment group is completed before beginning the next treatment group. This design is most commonly used in Phase I dose-escalations studies as a safety measure, allowing full evaluation of the results from the first treatment group before subjecting another treatment group to the next higher dose.

Random Assignment

Non-randomized

In a non-randomized investigation, subjects are assigned to a treatment group as they appear for the study or based upon certain characteristics.

Randomized

In a randomized investigation, subjects are assigned to treatment groups on the basis of chance. The process of assigning subjects to treatment or intervention groups affects internal validity. The overall goal of randomization is to produce comparable groups across the study. Randomization strengthens the foundation for statistical procedures and, when properly executed in an experimental study, provides the strongest empirical evidence of any study design.
The following summarizes some typical methods of randomization.

1. **Simple randomization** - This type of randomization does not involve any restrictions. Since the treatment assignment is totally random there is no way to guarantee that there will be an even distribution between groups. For example, one site of a randomized multi-center drug trial may receive a majority of active drug rather than placebo simply by random chance. This type of randomization scheme can result in an unequal numbers of subjects receiving a specific treatment at a given site or over a given period of time.

2. **Random permuted blocks** - This type of randomization compensates for potential of simple randomization to unbalance treatment assignment. With this approach a randomization block size is chosen (e.g. 4, 8, or more subjects) in which the BALANCE OF TREATMENT ASSIGNMENTS is kept proportional according to study design. For example if a block size of 4 is chosen and the protocol defines two study groups, 1 active vs. 1 placebo drug group, then the block will contain 2 active study drug kits and 2 placebo study drug kits. Since the entire block of 4 kits is randomly assigned a treatment number, the subjects will receive their treatment assignment randomly over a given period of time.
3. **Stratified randomization** - This type of randomization assigns study treatment on the bases of certain baseline characteristics such as gender, age, weight, etc. (i.e. a specific 'stratum' of the population being studied). The goal of this approach is to balance the number the subjects with the characteristic of interest in each treatment group to ensure comparable groups. This type of randomization is most commonly used in smaller studies where fully random assignment of study treatment could result in an imbalance of subjects with a given baseline characteristic (e.g. the majority of obese subjects in one treatment group vs. non-obese in the other, or the majority of females in one treatment vs. males in the other.). Large-scale studies, due to their size, usually have balance of baseline characteristics and therefore less often require stratified randomization.

There are a variety of programs available to generate random allocation sequences. An example of an on-line program can be found at: www.randomization.com.

Blinding and Placebo Control

Blinded

Blinding is the act of keeping the identity of a study intervention secret (in other words, it would not be known if a study treatment was active treatment or placebo). Single-blind means only the research subject is blind to the actual intervention. Double-blind means two parties (usually the subject and the investigator/research team) are blind to the actual intervention. Occasionally the less-frequently used term of triple-blind is used to emphasize that non-study personnel are also blind to the study intervention (e.g. study monitors/auditors, end-point assessment committees, etc.). Blinded studies involving investigational products may use placebos and double-dummy treatments to disguise treatment assignment. A **placebo** is a study intervention designed to look like the active treatment but having no active properties. A **double-dummy treatment** is a method of blinding two treatments whose appearances are dissimilar by administering both treatment forms - one active and one placebo. For example, in designing a study comparing heparin (intravenously delivered) vs. a low molecular weight heparin (subcutaneously delivered) if the study were to be double-blinded, it would be necessary to have two types of placebo (two "dummy" treatments), an intravenous placebo and a subcutaneous placebo.

Un-blinded

In an un-blinded study **,** the subject, investigator and evaluator are aware of the actual study treatment. Un-blinded studies involving investigational products are referred to as **open-label**.

Observational Studies

In an observational study, specific events or findings within the study-defined population are collected without any intervention by the researcher. In other words, the researcher observes and studies findings in a setting outside of a randomized, blinded or placebo-controlled design. This type of design is usually used in investigations where it would be unnecessary, infeasible or unethical to assign factors (e.g. smoking in pregnant women). Like experimental studies, observational studies often use control groups for comparison, but because a treatment is not assigned randomization is not possible. Observational studies have the potential for introducing confounding biases due to the risk of an unknown association between the factor under study and the outcome.

Analytical

Cohort study: A cohort study examines specific events or outcomes in a group of subjects who are followed over time. This study design compares the incidence of a given event/outcome in exposed and unexposed groups in an effort to determine an association. The common association measurement for a cohort study is relative risk (see definition below).

Cohort studies can be prospective or retrospective. Prospective cohort studies are expensive and time-consuming, but because of their prospective nature, cohort studies can provide stronger empirical evidence than case-control studies. Retrospective cohort studies are often less expensive to conduct, but may be subject to data collection obstacles (e.g. the investigator has no mechanism of ensuring documentation of a specific type of event or outcome).

Case-control study: A case-control study is a type of retrospective observational study comparing persons with a disease, condition, or exposure (the cases) and persons without the disease, condition or exposure(the control), assessing differences in events or outcomes between the groups. The two groups are otherwise comparable across all the relevant baseline characteristics. The common association measure for a case-control study is the odds ratio (see definition below). Case-control studies are usually used for broad-based, inexpensive evaluation of risk factors and are also useful for evaluating rare conditions or risk factors with long induction periods.

Descriptive

Cross-sectional study: A cross-sectional study is a descriptive study of the relationship between diseases and other factors at one point in time in a defined population. Cross-sectional studies determine the prevalence (presence) of an exposure and disease, but lack information on timing of exposure. Cross-sectional studies generally cannot be used to draw causal inferences and are usually used for hypothesis generation.

Case reports and Case series: A case report is a description of a single patient and usually includes a discussion of medical conditions and treatments along with adverse events and outcomes. A case series is a group of case reports describing patients that have been exposed to a specific treatment or agent. Due to the typically small numbers of cases in a case series and the lack of a control group, the value of interpreting the reported findings is limited. These types of presentations are best used for hypothesis generation.

General Guide to Statistical Consultation

The importance of early involvement of a statistician in the design of a clinical study cannot be overstated.

> *To consult a statistician after an experiment is finished is often merely to ask him to conduct a post mortem examination. He can perhaps say what the experiment died of.*
> - R.A. Fisher (in his 1938 address to the First Indian Statistical Congress)

Most often the assistance of a statistician will be required for the selection of an experimental design, the development of the corresponding analysis plan and the subsequent interpretation of parameter estimates and test results. Meaningful involvement of a statistician in study development can permit significant contributions to the following study elements:

• Problem Formulation • Background and significance • Methods and materials • Experimental design • Study flowcharts • Study schema	• Feasibility of design • Sample size or power estimates • Statistical analysis plan • Data management plan • Case Report Form design • Choice of statistical software	• Choice of Database Software • Implications of probable/possible results • Responses to reviewer comments • Help with resubmission • References

Even when the analytic needs of the investigator seem obvious, review of the research plan by the "new eyes" of the statistician may lead to alternative methods that should improve efficiency or lead to new insights. Since statistics is evolving science, not static technology, new advances may replace or change analysis recommendations over time. Dialogue between investigator and statistician will almost always help to clarify research objectives, prioritize study aims, and lead to more informed and appropriate selection of tests of hypotheses. Ideally, such exchanges will lead researcher to view statistician as collaborator, rather than consultant, which should lead to improved research designs, more comprehensive analyses and better scientific insight.

The initial meeting with the biostatistician

Preparation for an initial meeting with a statistician should include a written description of the proposed project (refer to Executive Summary of Elements of a Study Protocol), stating the general objectives of the study and the questions that the investigator hopes to answer. The following are the key elements of the researcher's proposed study that the statistician will need in order to best assess study design and statistical approach:

- Study Objectives
- Population(s) targeted by the study (e.g. healthy volunteers, patients with a specific disease or combination of diseases, etc.)
- Response variables of interest
- Relevant classification (e.g. gender, race, severity type, smoking status, etc.)
- Important variables associated with the response variable of interest (i.e. covariates)
- Background information from a variety of sources:
  - pilot studies (i.e. a small version of the full study being proposed)
  - previous studies (i.e. similar study population or intervention)
  - scientific literature (i.e. theoretical basis for proposal, animal studies)
  - collegial exchanges (e.g. scientific meetings, workshops, e-mail)
  - anecdotal observation (e.g. poor sense of smell in schizophrenics)

Construction of a *Study Flowchart*, often called a Time and Events Chart (refer to Study Flowchart), and/or study schema diagrams can summarize and communicate the study design, most effectively. From the above information, the statistical consultant can assist with development of a list of specific aims, which the researcher will classify as primary, secondary or exploratory aims. These aims will give rise to null and alternative hypotheses (see definitions in Basic Statistical Terms), which may be subjected to statistical tests of significance.

The statistical consultant needs to understand the purpose and context of the proposal, rather than viewing the research as an abstract statistical problem. In addition to general and technical details of the proposed study, the researcher should be prepared to provide answers to the most basic questions concerning the study and core discipline. These questions might require explanation of fundamental elements of the disease, disorder or biological process being studied. For example, the statistician may not know whether the origins of a process to be studied are genetic, environmental or both and such information is important to the analysis approach to be used. Attention to this upfront planning for a study will lead to a solid development of clear and comprehensive narratives that will comprise the background, methods and other sections of a researcher's protocol.

Investigators with no access to statistical support are encouraged to contact the Biostatistics and Epidemiology Consulting Center (BECC) (http://www.cceb.upenn.edu/main/center/becc.html) and to complete and submit a Collaboration Request Form. This form provides information necessary to assess the availability of a statistician to assist the researcher in meeting project goals. Once the investigator has completed the 3-page request form, the request will be assigned a Project Identification Number and the investigator can expect to be contacted by a member of the BECC within three business days.

Basic Statistical Terms

To facilitate interaction with the biostatistician, the investigator should be familiar with some basic statistical terminology. The following defines some basic terms.

Alpha error: A statistical error in testing an hypothesis, often referred to as type I error (the "first type of error"), which incorrectly concludes that a treatment or intervention is proven effective when it is actually is not effective; sometimes referred to as a false positive result . (last clause from "MedTerms" from MedicineNet.com)

Beta error: A statistical error, often referred to as type II error (the "second type of error"), which incorrectly concludes that a treatment or intervention is proven ineffective when it is actually effective; often referred to as a false negative result.

Confidence Intervals (CI): Confidence intervals are a way of expressing a level of confidence in a specific statistical finding. If a study were repeated, the results of the repeated study would not be exactly the same as the first study. If a study were repeated many times, one would eventually establish a particular range of results in which the "real" result that would prove (or disprove) the study are likely to be found. This range is called the confidence interval. Therefore a 95% confidence interval would mean there is a 95% chance that the "real" result of the study analysis falls within the stated interval or range. The wider the confidence interval the greater the variability of the result, and the narrower the confidence interval, the lesser the variability of the result, though there are other factors to consider in determining whether the result likely proves or disproves the study hypothesis. For example, in a study of a treatment vs placebo, if the study outcome showed the treatment to have a 10% decrease in events, and the calculated range of likely values in which this result lies is found to be -1.2% to 12%, it would generally be expressed as: endpoint reduction in the treatment arm of 10% (95% CI -1.2% to 12%). In this case, since the lower range of the confidence interval crosses over 0% (i.e. a value showing no difference in the treatment arm from placebo) if the result was being viewed as either proving or disproving a difference in the study treatment arms, it could be argued that the trial was negative since a result of 0% lies within the range of possible results given the confidence interval. However, adopting a "likelihood" approach to the study finding, the majority of the range of the confidence interval extends in the positive direction beyond 0% (i.e. most of the likely values are greater than 0%), one could argue that it is more likely that the study does show a reduction in events by the treatment. (excerpted from: T. Greenhalgh, BMJ No 7105 Volume 315, August 16, 1997)

Null hypothesis (H0): A mathematical statement of the converse of (one of) the specific aims of the study. Following the example used in the definition for the alternative hypothesis, the corresponding null hypothesis would be that the proportion of children who play video games and exhibit at least one violent incident is equal to or less than (i.e. no worse than) the proportion of children who do not play video games. The null hypothesis is the converse of the alternative hypothesis.

Odds ratio: An odds ratio compares the odds of an event in one group with the odds of an event in a comparator group. Odds ratios are a common way to express outcomes in observational studies. For example, a case-control study of two cohorts, one with an exposure to a presumed noxious element and one without, included 100 subjects in each group and looked at death rates after 5 years. In this example there were 20 subjects that died in the exposed group (case group) vs. 5 who died in the unexposed group (control group). The odds of dying in the case group is the ratio of subjects who died to subjects who did not die, i.e. 20/80, or 1/4, which can be expressed as 0.25. The odds of dying in the control group

would the value of the odds ratio of the event rate comparing the case group to the control group would be displayed as: 0.25/0.05, or 5. Thus the odds of death in exposed group are 5 times the odds of death in the unexposed group.

Outlier: An extreme deviation from the mean (i.e. a data point that lies an abnormal distance away from other values).

P value: A way of expressing statistical significance. Standard practice (which was arbitrarily decided) is that a 5% likelihood that the study outcome is due to chance (i.e. a 95% likelihood the study outcome is not due to chance) is statistically significant. This 5% likelihood is expressed as P=0.05. A 1% likelihood that a study outcome is due to chance (i.e. 99% likelihood that study outcome is not due to chance), is expressed as P=0.01 and considered highly statistically significant. A criticism of the use of a P value test of significance is that it relies on an arbitrary cut-off in answering a yes-no question on a finding. An alternative approach is to look at a range of likelihood that a statistical finding expresses reality (see Confidence Intervals).

Power: Power is defined to be equal to 1- ß; that is the probability of not committing a Beta (Type II) error. Power is an index of sensitivity, since it is the probability of rejecting a false null hypothesis. An analogous index of specificity is 1- ?, the probability of not rejecting a true null hypothesis; although there is no common statistical name for this probability.

Risk, relative risk, and risk reduction

Risk is a simple calculation of the number of subjects in a group that experience an event divided by the total number of subjects in that group. The equation is: (number of subjects with event/total number of subjects assessed for the event).

Relative risk compares the risk of an event in one group to the risk in a comparator group. To show the relative risk of an event in a control group vs. a treatment group, the equation is: (risk of event in control group/risk of event in the treatment group).

Absolute risk reduction shows the absolute amount of reduction in the risk of an event in one group vs a comparator group. To show the absolute risk reduction in a treatment group vs a control (non-treatment) group the equation is: (control group risk - treatment group risk).

Relative risk reduction expresses the reduction in risk as the difference in the risk of an event in one group vs a comparator group divided by the overall risk of the event in the first group (i.e. the amount of risk reduction relative to the overall risk). To show the relative risk reduction in a treatment group vs a control (non-treatment) group the equation is: ([Control group risk - treatment group risk]/control group risk).

To illustrate the above definitions of risk, relative risk and risk reduction, consider the following example:

A study of a target disease compares usual care to a new treatment by measuring the number of deaths in each group. Two hundred subjects are enrolled in each study arm and results are measured over the five-year duration of the study. The table below shows the number of deaths in each group at 5 years.

Treatment intervention	Total number of patients	Number of Deaths
Control Group	200	40
Treatment Group	200	10

Risk: (subjects with events/total number subjects studied)
In the placebo group, the risk of death is 40/200, which is 0.20 or 20%. For the treatment group, the risk of death is 10/200, which is 0.05 or 5%. In other words, at five years, there is a 20% risk of dying in patients with the target disease if not treated compared to a 5% risk of dying if treated.

Relative Risk: (risk in control group/risk in treatment group)
Relative risk compares the risk in one group relative to the risk in the other group. The relative risk between the control group and the treatment group is .020/0.05, which is 4, meaning patients who do not receive treatment are at 4 times the risk of death than similar patients who receive the active treatment.

Absolute risk reduction: (risk in control group - risk in treatment group)
The control group risk of death is 20%, the treatment group risk of death is 5%, therefore the absolute amount of risk that was reduced by treatment is 20% - 5%, which is 15%. In other words, out of 200 patients treated 15% (or 30 patients) avoided death at five years.

Relative Risk reduction: [(risk in control group - risk in treatment group)/risk in control group]
In the example noted above the relative risk reduction would be [(20% - 5%)/20%], or 15/20, or 0.75, most often expressed as a percent: 75%. Relative risk reduction is usually more clinically useful than absolute risk reduction when trying to conceptualize the benefit of a treatment. In other words, while the control grouped showed 40 patient deaths and the treatment group showed 10, the relative risk reduction illustrates that this reduction of 30 deaths represents 75% of the overall risk of death; i.e. the treatment reduced the overall risk of death by 75%.

Statistical significance: The likelihood that a particular study outcome has arisen by chance. This is commonly expressed as a P value. **Note:** Statistical significance does not necessarily mean a finding is clinically significant.

Study arm: The different groups in a study. Each group represents an arm of the study. A single-arm study would have only one group; a double-arm study would have two groups, and so on.

Protocol Design/Review

The protocol is a document that describes the objectives, design, methodology, statistical considerations, and organization of a research study. The protocol explains the specific procedures of the study and outlines the scientific, organizational, administrative, and financial aspects of the research study.

The protocol is distinct from the research grant. While the grant provides a broad overview of the study procedures, the protocol clearly defines and operationalizes the details of study implementation.

The required elements of a study protocol are dictated in the Good Clinical Practice (GCP) standards.

Elements of a Study Protocol

The following sections describing the elements of a GCP standards protocol are contained in a downloadable template. The template uses functionalities in Microsoft Word to create automated formatting and generation of a table of contents. Various sections also contain suggested language that is compliant with federal regulations (e.g. safety section, adverse event reporting requirements, etc.). The available downloads are:

- Protocol Design Template with Annotated Guidelines (Word)
- Sample Study Protocol
- Please reference Tips for Using Protocol Design Template to learn how to use the automated table of contents feature.

  HINT: It is recommended to Right-Click on the link above, select Save Target As..., and choose a location to save the document on your computer. Then open the file from that location or from within Microsoft Word.

Note: This template was developed for drug studies, but can be adapted for other types of studies. The National Cancer Institute also has protocol templates available for cancer studies at http://ctep.info.nih.gov/guidelines/templates.html .

Title Page

The protocol title page is the "front cover" of the study protocol and displays the title prominently. Other information to include on the title page:

- Principal Investigator name
- Sponsor name
- Protocol version/version date

Table of Contents

Very short protocols of only a few pages may not require a table of contents. Larger protocols should have a table of contents to aid study personnel in easily finding a specific protocol section or item.

Executive Summary

It is useful to develop a brief protocol summary and include it as part of the protocol, typically located after the protocol table of contents. Generally only 1-3 pages in length, the protocol summary provides a way to quickly grasp the key elements of the protocol. This is a useful tool when trying to communicate with various parties about the study. The Executive Summary can be written with headings and associated text, or summarized succinctly in table form. The key elements of a protocol summary follow:

Title	Full title of protocol
Short title	Shortened title, if one is typically used by you or your Center/Dept.
Protocol number	The standard protocol number used to identify this study.
Phase	Clinical study phase (e.g. Phase 1, 2, 2a, 2b, 3, 3a, 3b or 4)
	Design attributes such as single blind, double blind or open label;

Methodology	Randomized, placebo or active placebo control; cross-over design, etc.
Study duration	Estimated duration for the main protocol (e.g. from start of screening to last patient processed and finishing the study)
Study centers	Single-center or multi-center. If multi-center, note number of projected centers to be involved.
Objectives	Brief statement of primary study objectives
Number of subjects	Number of subjects projected for the entire study (e.g. not for simply one site, rather for entire study, all sites combined)
Diagnosis and main inclusion criteria	Note the main clinical disease state under study and the key inclusion criteria (i.e. not the entire list that will appear later in the protocol -rather only the key inclusion criteria)
Study product, dose, route, regimen	Study drug name (generic name, though can also state marketed name if name-brand used in the study). Also dose, dose route and dose regimen
Duration and administration	Total duration of drug product administration (including any open-label lead-in, if applicable).
Reference therapy	Note if there is a standard reference therapy against which the study product is being compared, or if the reference is a placebo
Statistical Methodology	A very brief description of the main elements of the statistical methodology to be used in the study. (As few lines as possible).

1. **Introduction**

The introduction should open with remarks that state that this document is a clinical research protocol and the described study will be conducted in compliance with the protocol, Good Clinical Practices standards and associated Federal regulations, and all applicable University research requirements. The rest of the introduction should include the following subsections.

1.1 Background
This section should contain a background discussion of the target disease state to which the investigational product(s) hold promise, and any pathophysiology relevant to potential study treatment action.

1.2 Investigational Agent
This section should contain a description of the investigational product, its make-up, chemical properties and any relevant physical properties, including any available pharmacologic data. (A good example for this section is the "Description" and "Pharmacology" sections for drugs listed in the Physicians' Desk Reference)

1.3 Preclinical Data
Summarize the available non-clinical data (published or available unpublished data) that could have clinical significance.

1.4 Clinical Data to Date
Summarize the available clinical study data (published or available unpublished data) with relevance to the protocol under construction -- if none is available, include a statement that there is no available clinical research data to date on the investigational product.

1.5 Dose Rationale and Risk/Benefits
Describe the rationale used for selection of the dose for the protocol under construction. This should be based on non-clinical and clinical data available to date. It should include justification for route of administration, dosage, dosage regimen, and dosage period. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and/or knowledge that might reasonably be expected from the results.

2. **Study Objectives**

Describe the overall objectives and purpose of the study. This should include both primary and any secondary objectives, e.g.:

2.1 Primary Objective
To assess the efficacy of XXXX on decreasing infarct size as measured by Sestamibi scanning.

2.2 Secondary Objective
To assess the safety and tolerability of two doses of XXXX in subjects with acute myocardial infarction.

3. **Study Design**

3.1 General Design
Include:
- The type/design of the study (e.g. Phase, randomized, double-blind, parallel group, etc.)
- A schematic diagram of the trial design, procedures and stages is advisable
- Expected duration of subject participation
- A description of the sequence and duration of all trial periods including follow-up, if any

3.2 Primary Study Endpoints
Describe the primary endpoint to be analyzed in the study (e.g. could be safety or efficacy, depending on the main objective of the study).

3.3 Secondary Study Endpoints
Describe any secondary endpoints to be analyzed in the study

3.4 Primary Safety Endpoints
All studies should include the primary safety endpoints to be measured. If the primary objective of the study is a safety study and therefore the Primary Endpoint(s) of the study are safety endpoints, then it should be noted in section 3.1 above and this subsection 3.3 can be deleted.

4. **Subject Selection and Withdrawal**

4.1 Inclusion Criteria
Create a numbered list of criteria subjects must meet to be eligible for study enrollment (e.g. age, gender, target disease, concomitant disease if required, etc.) Generally should include items such as: "subjects are capable of giving informed consent", or if appropriate, "have an acceptable surrogate capable of giving consent on the subject's behalf."

4.2 Exclusion Criteria
Create a numbered list of criteria that would exclude a subject from study enrollment. If appropriate, should generally include that subjects cannot be homeless persons, or have active drug/alcohol dependence or abuse history. If exposure to certain medications or treatments at screening is prohibited, that must be noted in the exclusion criteria-if these are also prohibited concomitant medications during the study period that should be noted here as well.

4.3 Subject Recruitment and Screening
Describe how subjects will be recruited for the study, e.g. from investigator or sub-investigator clinical practices, referring physicians, advertisement, etc. Note in this section that information to be disseminated to subjects (handouts, brochures, etc.) and any advertisements must be approved by the EC/IRB for the site; include a sample of such information in the attachment section of the protocol. Also in this section, list any screening requirements such as laboratory or diagnostic testing necessary to meet any noted inclusion or exclusion criteria (greater detail of timing, etc. can be included later in section 6 "Study Procedures" section of the protocol).

4.4 Early Withdrawal of Subjects

4.4.1 When and How to Withdraw Subjects
Describe the scenarios under which a subject may be withdraw from the study prior the expected completion of that subject (e.g. safety reasons, failure of subject to adhere to protocol requirements, subject consent withdrawal, disease progression, etc.) Also, if abrupt termination of study treatment could affect subject safety (e.g. in an antihypertensive study, abrupt withdrawal without other intervention might cause hypertensive rebound), describe procedure to transition subject off the study drug or to alternate therapy. Refer to Withdrawing a Subject for more information.

4.4.2 Data Collection and Follow-up for Withdrawn Subjects

If any subject may be withdrawn prematurely from the study, it is imperative to collect at least survival data on such subjects throughout the protocol defined follow-up period for that subject (though careful thought should be give to the full data set that should to be collected on such subjects to fully support the analysis). Such data is important to the integrity of the final study analysis since early withdrawal could be related to the safety profile of the study drug. If a subject withdraws consent to participate in the study, attempts should be made to obtain permission to record at least survival data up to the protocol-described end of subject follow-up period. IT MUST BE A HIGH PRIORITY TO TRY TO OBTAIN AT LEAST SURVIVAL DATA ON ALL SUBJECTS LOST TO FOLLOW-UP AND TO NOTE WHAT METHODS SHOULD BE USED BEFORE ONE CAN STATE THE SUBJECT IS TRULY LOST TO FOLLOW-UP (e.g. number of phone calls to subject, phone calls to next-of-kin if possible, certified letters, etc.).

5. **Study Drug**

5.1 Description

This section should be a very brief synopsis of section 1.2 "Investigational agent", along with how the how the drug product will appear (e.g. as tablets or capsules of "X"mg, as a liquid with "X"mg dissolved in 10ml 5% dextrose and water, etc.)

5.2 Treatment Regimen

Describe dose, route of administration, and treatment duration.

5.3 Method for Assigning Subjects to Treatment Groups

Describe how a randomization number and associated treatment assignment will be made. This could be selection of a sequentially numbered drug kit/box, or communication with a randomization center that assigns a number associated with a specific treatment kit/box, etc.

5.4 Preparation and Administration of Study Drug

Describe in detail all the steps necessary to properly prepare study treatment. Include whether the drug preparation will be done in a pharmacy or by a study team member. Fully describe how the study treatment is to be administered. If study drug is stored, mixed/prepared or dispensed from the Investigational Drug Service, that should be noted here, including the contact number to that service office. Refer to Investigational Product Inventory for more information.

5.5 Subject Compliance Monitoring

Describe how the study team will assess and track subject compliance with the study treatment regimen, and what procedures must be followed for any subject who is significantly non-compliant with the study treatment regimen.

5.6 Prior and Concomitant Therapy

In this section, describe:

- What prior and/or concomitant medical therapy will be collected (if applicable).
- Which concomitant medicines/therapies (including rescue therapies) are permitted during the study
- Which concomitant medicines/therapies are not permitted during the study (if applicable)

5.7 Packaging

- Describe how the study drug and any comparator agent will be packaged along with the amounts (e.g. "20 ml vials containing 30 mg", or "bottles containing 30 tablets of .", etc.) along with any associated labeling
- Describe if drug is to be shipped in bulk (e.g. Study drug will be shipped in boxes of 30 vials each, etc.) or as separate subject-specific kits/boxes
- When subject drug kits are constructed describe all the contents of the kit/box and associated labeling. Refer to Product Labeling for more information.

5.8 Blinding of Study Drug

Describe how the drug is blinded (refer back to Section 8.4 "Unblinding Procedures").

5.9 Receiving, Storage, Dispensing and Return

5.9.1 Receipt of Drug Supplies

Describe how drug will be obtained i.e. what entity will ship the drug to the investigative site, and to what location at the site, (e.g. investigational pharmacy, etc.)

5.9.2 Storage

Describe storage temperature requirements, whether supplies must be protected from light, and the location of the supplies (e.g. study pharmacy). Describe any special handling requirements during storage

5.9.3 Dispensing of Study Drug

Describe how the drug will be assigned to each subject and dispensed. This section should include regular drug reconciliation checks (i.e. how much drug was assigned and whether subjects actually received assigned dose or received dose properly, how much remains, how much drug was inadvertently damaged, etc. --- eg. "Regular study drug reconciliation will be performed to document drug assigned, drug consumed, and drug remaining. This reconciliation will be logged on the drug reconciliation form, and signed and dated by the study team."). Refer to Dispensing for more information.

5.9.4 Return or Destruction of Study Drug

This section should note the procedures for final reconciliation of the site's drug supply at the end of the study, and whether study drug is to be shipped back to a source or destroyed on site. If drug is to be shipped back to a source, note the address and contact information here. Refer to Reconciling Investigational Product Inventory for more information.

6. **Study Procedures**

In this section, describe all the procedures and treatments required at each visit, broken out by visit. Create a study procedures flowchart/table that describes the activities and

procedures to be followed (a Study Flowchart). Include this flowchart/table in the Attachment section and refer to that attachment in this section.

7. **Statistical Plan**

7.1 Sample Size Determination
Describe the statistical methods for determining the sample size for the study

7.2 Statistical Methods
Summarize the overall statistical approach to the analysis of the study. The section should contain the key elements of the analysis plan, but should not be a reiteration of a detailed study analysis plan. The full Statistical Analysis Plan can then be a "stand-alone" document that can undergo edits and versioning outside of the protocol and therefore not trigger an IRB re-review with every version or edit -AS LONG AS THE KEY ELEMENTS OF THE ANALYSIS PLAN DO NOT CHANGE.

Be clear on primary as well as any applicable secondary analyses

7.3 Subject Population(s) for Analysis
This section should be very specific in defining the subject populations whose data will be subjected to the study analysis - both for the primary analysis and any applicable secondary analyses. Examples of such populations include:
- *All-randomized population:* Any subject randomized into the study, regardless of whether they received study drug
- *All-treated population:* Any subject randomized into the study that received at least one dose of study drug
- *Protocol-compliant population:* Any subject who was randomized and received the protocol required study drug exposure and required protocol processing

8. **Safety and Adverse Events**

Procedures for eliciting reports of, recording, and reporting adverse events should be specified. **Note** : See the downloadable protocol template for GCP-compliant standard language examples for subsections 8.1 though 8.3. The subsections include:

8.1 Definitions
8.2Recording of Adverse Events
8.3Reporting of Serious Adverse Events
Include the following (refer to Reporting Adverse Events for more information)
- Sponsor Reporting by Investigator
- IRB Notification by Investigator
- FDA Notification by Sponsor

8.4 Unblinding Procedures
While the safety of the subject always comes first, it is still important to seriously consider if unblinding the study therapy is necessary to ensure a subject's safety. This section should clearly describe the procedures for unblinding study therapy on a subject, including documentation of this in the subject's source document. For investigators, other than the sponsor-investigator, state that the investigator must inform the sponsor of all subjects whose treatment was unblinded - and describe the timelines for such reporting. In most cases, the unblinding will be part of managing an SAE, and will be reported with the SAE, however, in cases where unblinding was not associated with an SAE, such actions should be reported in a timely manner. While there is no regulation governing this timeline, it is suggested to use the same timeline requirements for investigator reporting of SAEs, (i.e. notification of sponsor within 24 hours by phone or fax, followed by a written narrative of the event within 48 hours.)

8.5 Stopping Rules
In studies with a primary safety endpoint or studies with high risk to study subjects, rules should be developed that clarify the circumstances and procedures for interrupting or stopping the study. If a central Data and Safety Monitoring Board (DSMB) or Committee (DSMC) is set up for the study, the stopping rules should be incorporated into their safety analysis plan as well.

8.6 Medical Monitoring
Refer to Monitoring Plan Development for more information about Medical Monitoring.

9. **Data Handling and Record Keeping**

Specifics should be provided for the handling of data to ensure the proper handling of data and records. **Note**: See the downloadable protocol template for GCP-compliant standard language examples for subsections 9.1 though 9.4. The subsections should include:

9.1 Confidentiality
9.2 Source Documents
9.3 Case Report Forms
9.4 Records Retention

10. **Study Monitoring, Auditing, and Inspecting**

It is recommended that the monitoring plan be referred to as a separate attachment. Include a statement that direct access to source data/documents will be provided for monitoring, audits, IRB review, and regulatory inspections. Monitoring plan development is covered in more detail in Monitoring Plan Development. Include specific provisions for the following:

10.1 Unblinding and Breaking
10.2 Study Monitoring Plan

11. **Ethical Considerations**

    Include a statement that the study will be conducted in accordance with the protocol, GCP, and applicable regulatory requirements. Provide specific reference as to how consent will be obtained, and that IRB approval will be obtained before the study is initiated. Standard language for this section is provided in the protocol template.

12. **Study Finances**

    12.1 Funding Source
    This section should describe how the study will be financed, but should not contain specific dollar amounts (e.g. "This study is financed through a grant from the US National Institute of Health", or ". a grant from the American Heart Association", etc.)
    12.2 Conflict of Interest
    Reference adherence to the University conflict of interest policy.
    12.3 Subject Stipends or Payments
    Describe any subject stipend or payment here. Refer to Considerations for Subject Payment for more information

13. **Publication Plan**

    This section should include the requirements any publication policies of the University, Department, Division or Research Center. If, in addition to the sponsor-investigator, other investigators are involved with the study, identify who holds the primary responsibility for publication of the any results of the study. Also define the need to first obtain approval from the primary responsible party before any information can be used or passed on to a third party.

14. **References**

    This is the bibliography section for any information cited in the protocol. It should be organized as any standard bibliography.

15. **Attachments**

    This section should contain all pertinent documents associated with the management of the study. The following list examples of potential attachments:

    - Investigator Agreement (for any investigator, other than sponsor-investigator, who participates in the study)
    - Sample Consent Form
    - Study Procedures Flowchart/Table
    - Core Lab Instructions To Investigators
    - Specimen Preparation And Handling (e.g. for any specialized procedures that study team must follow to process a study specimen, and/or prepare it for shipment)
    - Drug Conversion Plan (e.g. if there is a special regimen for transitioning a subject from their baseline medication over to study medication)
    - Antidote Preparation And Delivery (e.g. special instructions for preparing and delivering any therapy designed to reverse the effects of the study drug, if applicable)

Protocol Review

Review of Protocol from Sponsor

For industry-sponsored studies, the protocol is written by the sponsor and provided to the on-site investigator. It is the responsibility of the investigator to be thoroughly familiar with the protocol, and to conduct the study in strict accordance with the protocol.

If the investigator meets the prescribed qualifications, the sponsor will forward a confidentiality agreement. The confidentiality agreement is a legally binding document that prohibits the investigator from disclosing the proprietary and confidential information found within the protocol. The confidentiality agreement must be signed and returned to the sponsor. Once the agreement is executed, the sponsor will forward a study protocol (and Investigator's Brochure, if applicable) to the investigator for review.

The investigator and his or her study team will read and review the proposed protocol. An overall evaluation of the study will include clinical interest and feasibility (see Project Feasibility section of this manual).

The process of evaluating the feasibility of conducting a research trial is complex and multi-factorial. Some considerations that determine the difficulty of a protocol are summarized below:

IRB Protocol Summary

The IRB requires a separate, stand-alone protocol summary as part of the IRB submission. The IRB issued a new version of the Protocol Summary in June 2006, which is section II of a 3 part Biomedical Sciences Application for Review of Human Research. This document includes much of the information from the Executive Summary (noted in the Elements of a Protocol section).

The IRB provides detailed guidance on constructing the IRB protocol summary within the Biomedical Sciences Application for Review of Human Research (accessed from the Office of Regulatory Affairs website IRB Forms).

Study Flowchart

The Study Flowchart (also known as the Time and Events Chart or Schedule of Events) is a table that is created to display the schedule of study procedures. It outlines the planned chronological occurrence of events that research subjects will undergo during their study participation. The unified, visual format of a Study Flowchart helps promote organization and communication.

A Study Flowchart facilitates several study processes including:

- Project feasibility assessment
- Statistical design
- Case Report Form and Informed Consent Form development
- Institutional Review Board (IRB) and other Penn reviews
- Site orientation and in-service presentation
- Database construction
- Subject enrollment and follow-up

The Study Flowchart can be included as an element of the protocol or presented as an appendix to the study protocol. An example of a Study Flowchart is available to view.

Study Schematic

The Study Schematic is a diagram illustrating key concepts of the study design, such as sampling, randomization, and/or blinding. The unified, visual format of a Study Schematic helps promote organization and communication.

A Study Schematic facilitates several study processes including:

- Protocol design and implementation
- Statistical design and analysis
- IRB and other Penn reviews
- Site orientation and in-service presentation

The Study Schematic can be included as an element of the protocol or presented as an appendix to the study protocol. See example below.

Research Involving Drugs and Devices

Investigational Drug Studies

Background

One of the Food and Drug Administration's (FDA) primary mechanisms for ensuring the safety of research subjects is through an **Investigational New Drug Application (IND)**. An IND Application is a request for authorization from the FDA to administer an investigational drug or biological product to humans. The IND provides assurance that the investigational product has sufficient preclinical safety data *before* it is used.

The **IND holder** is the person or company who has filed the IND with the FDA. The IND Holder, often referred to as the **Regulatory Sponsor**, holds an additional set of responsibilities (covered in the Research Roles section). Essentially, the IND holder is responsible for keeping the FDA informed of safety data from the study. This is critical for monitoring the safety of a drug. The FDA may be receiving multiple safety reports of a drug from several IND studies being conducted across the country and this allows them to identify safety trends more quickly.

Clarifying the "New" in IND

The term IND can be misinterpreted, leading researchers to conclude that if the drug they are studying is already approved by the FDA, it is not a "new" drug and, therefore, does not need an IND Application. THIS IS INCORRECT!

There are many other considerations for whether a drug being investigated is "new". The FDA approves a drug as safe with any or all of the following specifications. Altering these specifications could result in the FDA determining the drug to be "new".

- "New" route of administration
- "New" dose or duration of exposure
- "New" form of the drug (e.g. capsule vs. tablet)
- "New" treatment indications (e.g. target disease, age, gender)
- "New" use with concomitant meds

The FDA-approved labeling includes chemical structure, preclinical and human safety information, as well as dosing information.

A study that uses a "new" aspect of the drug's use (i.e. different indication, dose, population, etc.) usually requires the filing of an IND. Therefore, an IND can be required for studies of a drug that is already approved for marketing.

In most situations where the study is sponsored by a pharmaceutical company, the sponsor holds the IND with the FDA for the investigational product. In this case, the PI holds responsibility for communicating with the sponsor in a timely manner so the sponsor can communicate in turn with the FDA.

However, even though a pharmaceutical company is providing funds for a study, this does not necessarily mean that the pharmaceutical company has filed an IND for that study. If the pharmaceutical company does not hold an IND , it is the responsibility of the Penn investigator to determine whether or not an IND is needed.

Consider the following example: a pharmaceutical company is providing an unrestricted grant and/or a supply of the investigational drug for your study. The company does not hold an IND , and the drug is already approved for marketing. Your contract with the company states that the company can use the results of your study data to submit to the FDA in support of an NDA (New Drug Application). This study could very likely require an IND because the results of your data could be used to change the labeling of the study drug.

When there is not an IND in place for a drug study sponsored by a pharmaceutical company, the researcher should consult with the Office of Human Research.

Any investigator-initiated research study involving a drug or device should consult with the Office of Human Research (OHR) to determine whether or not an IND application needs to be filed. Researchers can also use the IND Decision Tool (www.med.upenn.edu/penn/ohr/ind/tool.html). If it is possible that an IND exemption is appropriate for a study, the researcher should complete the IND Determination Assessment Form and submit it to the Office of Human Research for final determination.

For investigator-initiated clinical research involving drugs, the IRB requires either an IND or Documentation of Exemption through a written communication from the FDA or the OHR.

IND Facts

Did you know?

- A single IND can have multiple projects/studies running under it.
- For investigator-initiated research in which an IND is required, the investigator may be able to reference an existing IND to support the preclinical requirements of their application.
- The FDA grants INDs, but does not "approve" specific studies. Therefore, an IND study should never be referred to as "FDA-approved."
- "Acknowledgement" (rather than approval) of IND research comes in the form of non-objection to a study.
- Unless otherwise noted, a study may proceed 30 days after the receipt date on the FDA's IND acknowledgement letter. The letter acknowledges receipt of an IND application.

IND Submission

The IND application is prepared using FDA Forms 1571 and 1572. The required information includes:

- Sufficient preclinical data, including toxicity data
- Details of the chemistry, manufacturing and controls to provide adequate quality control information for the production of the agent and to describe the mechanism of action of the agent
- Background and rationale for intended clinical use
- Proposed protocol for Phase I human use

The instructions and FDA forms for IND and IDE can be found online at www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html.

The Office of Human Research has made available for download two template for IND submissions which provide essential elements, guidance and a formatted document in which to prepare an IND submission to the FDA.

- IND Submission Template for drugs not yet marketed
- IND Submission Template for marketed drugs

IND Holder Responsibilities

The IND holder is responsible for:

- Selecting qualified investigators
- Ongoing monitoring of all studies under the IND
- The validity of the data from all sites conducting research under the IND
- Maintaining adequate records of receipt, shipment, and disposition of the investigational drug
- For multi-site studies, ensuring that all sites are kept informed of adverse events and safety updates
- Communication with the FDA of any protocol changes, drug changes, and safety data.

The Office of Human Research provides a detailed outline of IND holder responsibilities, available for download.

Investigational Device Studies

An Investigational Device Exemption (IDE) is the medical device equivalent of an IND Application for drug studies. The IDE application is a request to the FDA for authorization to use an unapproved medical device in humans. An Investigational Device Exemption is required when the study poses a Significant Risk to participants. This categorization is determined by the IRB, although the FDA makes the ultimate decision in determining whether a device study poses a Significant or Non-Significant Risk.

The risk determination should be based on the proposed use of a device in a study, NOT on the device alone.

Significant Risk (SR) Device Study

An SR Device presents a potential risk to the health, safety, or welfare of a subject AND is

- An implant -- or --
- Used in supporting or sustaining human life -- or --
- Of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise prevents impairment of human health, -- or --
- Otherwise presents a potential serious risk to the health, safety, or welfare of a subject.
- An IDE Submission to the FDA AND IRB approval is required prior to initiation of an SR device study.

An IDE Submission to the FDA AND IRB approval is required prior to initiation of an SR device study.

Non-Significant Risk (NSR) Device Study

For device studies that do not meet the criteria of Significant Risk, the IRB can approve the study without an IDE. The study may begin immediately after IRB approval

Penn's Institutional Review Board has issued guidance to assist in determining Is an IDE Required? (PDF), available for download.

Additional IDE Resources from FDA:

- IDE Requirements: www.fda.gov/cdrh/devadvice/ide/approval.shtml#sig_risk
- Instructions for IDE Application: www.fda.gov/cdrh/devadvice/ide/application.shtml

Penn's Investigational Drug Service

A critical component of study preparation is determining the methods and procedures by which the investigational product will be stored, prepared, and dispensed, as well as how inventory will be tracked. It is the investigator's responsibility to ensure this is done per federal regulations.

The Investigational Drug Service (IDS) is the only UPHS research pharmacy and is located on the ground floor of the Maloney Building in the Hospital of the University of Pennsylvania

(HUP). The IDS also provides support to the Presbyterian Medical Center (PMC) and Pennsylvania Hospital (PAH), in collaboration with those hospitals' pharmacies.

All inpatient and outpatient research involving investigational products are required to register with the IDS . For more information, refer to Investigational Drug Service (IDS). Please note that the IDS will need a copy of any protocol-specific documentation (inventory logs, unblinding worksheets, etc.) prior to enrolling subjects.

The Investigational Drug Service (IDS) is available on a fee-for-service basis and provides the following services:

- Study initiation: evaluate study drug management feasibility, methodology of drug assignment and distribution, and costs for IDS involvement in the study
- Secure storage
- Manufacturing
- Assistance with IND submissions
- Inventory management
- Blinded assignments and dose adjustments
- Record-keeping
- Preparation and labeling
- Dispensation of investigational product
- Coordination of activities between investigators, sponsors, and satellite sites
- Meetings with monitors, auditors, and FDA inspectors
- Special compounding
- Randomized schematics
- Assistance with writing drug-related sections of the protocol

Information relating to this service can be found at http://www.itmat.upenn.edu/welcome.shtml.

To determine if a study/site can benefit from IDS assistance refer to Investigational Product Inventory.

Investigator's Brochure

The Investigator's Brochure is a compilation of all preclinical, clinical and non-clinical data on the investigational product that are relevant to human subjects. Its function is to assist investigators in understanding the rationale behind the protocol, particularly dose, dose frequency/interval, methods of administration, overdosing information, and safety reporting/monitoring.

The type and extent of information available will vary with the stage of development of the investigational product.

While there is no federal regulatory requirement that the Investigator's Brochure be submitted to the Institutional Review Board (IRB), there are regulatory requirements for submission of specific product information that can normally be found in the Investigator's Brochure. If, for instance, a study involves an approved drug that does not require an IND , the FDA-approved labeling found in the Physician's Desk Reference (PDR) or package insert can be used to provide the required regulatory information to the IRB.

Special Provisions for Drug/Device Research

In certain research and clinical practice scenarios, investigational products may be used to try to treat serious or life-threatening conditions either for a single subject or for a group of subjects. Individuals may accept greater risks from investigational products that offer the possibility of treating life-threatening, rare, or debilitating illnesses when they have no viable alternatives. Under these circumstances, federal regulations provide mechanisms to expand access to promising investigational products without compromising subject protection measures.

These mechanisms include:

- Humanitarian Device Exemption (HDE)
- Treatment IND
  - Group C Treatment IND
- Compassionate Use / Single Patient Use
- Emergency Use

Comparison of Special Research Provisions

	Humanitarian Device Exemption (HDE)	Treatment IND	Compassionate Use	Emergency Use
IND/IDE Number	Yes from sponsor, manufacturer, or FDA;			
Prospective IRB approval required	Yes		No	

Retrospective Data Collection	N/A	Yes	
Informed Consent	Yes** ** exception found under emergency use		
# of Patients	multiple	single subject (in rare instances may be multiple subjects)	

Humanitarian Device Exemption (HDE)

A Humanitarian Device Exemption (HDE) is a mechanism used by the FDA to provide access to devices that are developed to treat rare diseases and conditions. These devices are listed on the FDA website (www.fda.gov/cdrh/index.html) and are termed Humanitarian Use Device (HUD). By definition a HUD is intended to treat or diagnose a disease or condition that affects less than 4,000 individuals in the United States per year.

HUDs are exempt from the effectiveness requirements normally required by the FDA for approval. Investigations involving HUDs usually occur through standard research protocols, which must be IRB approved. If an investigator wishes to use a HUD for treating a single individual, the investigator must follow the procedures outlined below for compassionate use or emergency use.

Treatment INDs

A Treatment IND is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments.

A Treatment IND may be granted by the FDA after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. A sponsor applies a Treatment IND to an existing IND . Treatment protocols are planned and cover an unspecified number of patients.

There are four requirements:

1. The drug is intended to treat a serious or immediately life-threatening disease
2. There is no satisfactory alternative
3. The drug is already under investigation
4. The sponsor is actively pursuing marketing approval

Treatment IND protocols require full IRB review. The process for obtaining IRB approval is the same as that for standard research protocols.

GROUP C TREATMENT IND

The "Group C" treatment IND was established through an agreement between the FDA and the National Cancer Institute (NCI). The Group C program is a means for the National Institute of Health to distribute investigational agents to oncologists for the treatment of cancer under NCI protocols outside a controlled clinical trial. Most Group C drugs have undergone Phase III testing and have some preliminary evidence of efficacy in a specific tumor type.

Compassionate Use / Single Patient Use

In specific situations, a physician may be granted special permission to use an investigational product for treatment purposes. Compassionate use involves a single patient who is unresponsive to standard therapy or for whom no standard therapy is available and there is reasonable scientific evidence to support the use of the investigational product. (If the situation is a life-threatening emergency, emergency use guidelines apply.)

Compassionate Use is not defined by the FDA; it falls under Treatment IND or Humanitarian Device Exemption (HDE) regulations. However, an investigator must follow additional Penn procedures in order to obtain approval to use an investigational product for a single patient use (see procedures that follow).

Emergency Use

Emergency Use is defined as the use of an investigational product in a human subject with a life-threatening condition in which no standard acceptable treatment is available and in which there is insufficient time to obtain IRB approval.

All of the following conditions must be met to justify emergency use:

1. There is a high likelihood of death unless the course of the disease is interrupted
2. No alternative method or recognized therapy is available that provides an equal or greater likelihood of saving the subject's life
3. The subject is in a life-threatening situation requiring intervention before review at a convened meeting.

Data from emergency-use situations may not be utilized for investigational purposes. FDA regulations require that any subsequent use of the investigational product have prospective

To obtain approval for Compassionate or Emergency Use

- Contact the manufacturer of the investigational product and request permission to use the drug/device under the manufacturer's IND, IDE, or HDE.

IF.	THEN.
the sponsor requests acknowledgement that the IRB is aware and recognizes such emergency use	An acknowledgement letter can be obtained through contact with the Office of Regulatory Affairs
IND / IDE / HDE does not exist OR the manufacturer is unwilling to sponsor a physician under an existing IND / IDE / HDE	FDA may issue an IND / IDE / HDE directly to the physician. Contact the FDA at: Drugs (301) 827-4570 Devices (301) 594-1190 Blood products (301) 827-3518 Biological vaccines (301) 827-3070 Nights and weekends (301) 443-1240

A licensed physician must take responsibility for the study. This includes a commitment to the manufacturer to complete data collection forms, if applicable.
For a project involving an investigational drug, the investigator must submit an FDA-1572 and Curriculum Vitae.

- A consent form must be prepared. Most manufacturers should be able to provide a template; however, the consent must conform to Penn's standards.
- Submit the protocol/treatment plan to the IRB for approval. Or, in an emergency situation in which insufficient time is available, notify the IRB of the planned use and obtain an independent assessment by a physician uninvolved with the patient's care confirming the emergency status.
- Investigational devices may be sent to the investigator's office or clinic.
- Investigational drugs should be shipped to the following:
  - **HUP Inpatient:** Notify the Penn Investigational Drug Service (IDS) that the investigational drug has been requested and provide a copy of the protocol and approval letter. Send the drug directly to the PENN IDS.
  - **PMC Inpatient:** Send drug directly to the Penn Presbyterian Hospital Pharmacy. (Make certain that the Penn Presbyterian Hospital Pharmacy is notified in advance and provide a copy of the protocol and approval letter.)
  - **Outpatients/Ambulatory:** Send the drug either to Penn IDS, or to the investigator's office or clinic. In either case, contact the Penn IDS.
- Obtain written informed consent from the subject prior to administering the investigational product.

  Exception: subjects who are in need of emergency medical intervention but cannot give informed consent because of their life-threatening medical condition and who do not have a proxy to represent them. In such circumstances, the investigator and a second physician who is not otherwise participating in the investigation or care of the patient must document:

  - the criteria that the patient met for emergency use of investigative product
  - AND the lack of alternatives
  - AND the inability to obtain consent from the subject
  - AND the methods used to reach a legal representative and/or relatives
  - AND the lack sufficient time to obtain the aforementioned consent
- Place a copy of the protocol/treatment plan in the location where the subject is being treated.
- A written report must be sent to the IRB within 5 working days of the start of treatment. This letter must include 1-2 paragraphs about the situation that required treatment, the protocol, and a copy of the signed consent form.

Manufacturing of In-house Investigational Agents

The manufacture of investigational drugs in house or by the Principal Investigator must always follow the guidelines set by the FDA.

- The investigator must submit an IND form to the FDA for review.
- The investigator must follow current Good Manufacturing Practices (GMP).
- The FDA may require a pre-approval inspection.

Guidelines from the PENN Investigational Drug Services (IDS) must also be followed.

- The investigator must develop Standard Operating Procedures for the manufacturing process.
- IDS needs to review the protocol, regardless of whether or not IDS is being contracted for services.
- If IDS is to manufacture, mix, store or supply the agent IDS will develop a fee for services to be included in the budget.

Radioactive Agents

- IDS must be approved by the Environmental Health and Radiation Safety (EHRS) Radiation Safety Board.
- Non-stable radioactive agents Standard Operating Procedures must be approved by EHRS, Radiation Safety Board.

Research Involving Human Tissue Banks

Overview

Human Tissue Banks (repositories) collect, store, and distribute human tissue materials for research purposes. This section explains the components of a tissue bank and the management and oversight responsibilities. The requirements are taken from the Department of Health and Human Services/Office of Human Research Protections (DHHS/OHRP), with some modifications for Penn-specific requirements. While the OHRP requirements govern tissue banks created from or for projects supported by the DHHS, the University of Pennsylvania applies the same standards to any human tissue bank/repository at Penn regardless of the funding source.

Tissue bank/repository activities involve three components:

- **Collectors** of tissue samples
- **Repository** storage and data management center
- **Recipient** investigators

These three components are governed by certain regulatory requirements:

Any tissue bank created and maintained at Penn must be registered with the Penn IRB and is subject to oversight by the IRB and Office of Human Research. The IRB must review and approve a **tissue bank protocol** that specifies the conditions under which data and specimens may be accepted and shared, and ensures adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

The Tissue bank operators/owners must submit a **sample collection protocol** and **informed consent document** used for distribution to tissue collectors. If the tissue collectors are external to Penn, the collection protocol and consent form must be submitted to the collector's local IRB for review and approval. A **Certificate of Confidentiality** should be obtained to protect confidentiality of repository specimens and data (see Vulnerable Populations).

Summary of Tissue Bank requirements:

Tissue bank operations

- The Penn IRB sets the conditions under which data and specimens may be accepted and shared.
- Tissue bank specimens and data are subject to applicable HIPAA regulations.
- Collection and maintenance of data and specimens are subject to oversight by the Penn IRB and the Office of Human Research.

Tissue bank protocol

A tissue bank protocol is a document describing the following:

- Background summarizing the purpose and goals of the repository
- Eligibility to participate in the repository
- Description of sample collection process
- Description of sample processing and storage
- Duration of sample storage
- Access to samples and data associated with samples
- Use of repository samples for research studies and release to recipient investigators
- Means to protect patient and data confidentiality

A Tissue Bank Protocol Design Template is available at www.med.upenn.edu/ohr/docs/ProtocolTemp_TissueBank.doc.

Informed Consent

- For tissue samples collected specifically for research, written informed consent should be obtained from each donor-subject in accordance with HHS regulations noted in 45 CFR 46.116. Included among the basic elements of informed consent should be a clear description of the:
  - operation of the cell repository
  - length of time the specimen will be stored

- conditions under which data and specimens will be released to recipient-investigators
- procedures for protecting the privacy of subjects and maintaining the confidentiality of data

Informed consent information describing the nature and purposes of the research should be as specific as possible. Where human genetic research is anticipated, informed consent information should include information about the consequences of DNA typing (e.g. regarding possible paternity determinations).

- If the tissue is collected from specimens that were obtained for reasons other than research (e.g. tissue that would normally be discarded after a surgical procedure or pathology assessment), the surgical consent form can suffice as the necessary consent provided that there is an opt-out choice for the patient to donate any such tissue. Such an opt-out section should clarify that the tissue being donated is only that which would otherwise be discarded, that the tissue is being donated for research purposes, and that the patient's confidentiality will be protected in accordance to federal research and privacy regulations.
- Informed consent documents may not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights (see Special Language Requirements).

A Tissue Bank Informed Consent Template is available from the IRB Forms site (IRB Forms).

Specimen collection protocol

- Where applicable, a specimen collection protocol should be created for use by tissue collectors. The purpose of this document is to clearly define the procedures for proper specimen collection, processing, and transfer of sample to the tissue bank, for personnel involved in tissue collection.
- If the tissue collectors are external to Penn, the sample collection protocol and associated consent form must be reviewed an approved by the local IRB.

Release of tissue to recipient investigator or entity

- If the following conditions are both met, IRB submission and review is not required:
  1. the private information or specimens were not collected specifically for the currently proposed research project; and,
  2. the investigator cannot readily ascertain the identity of the individuals to whom the coded private information or specimens pertain because the key to decipher the code is destroyed before the research begins OR the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances
- If both conditions above are not met, then research plans for repository samples must be submitted to the Penn IRB for review.
  - When the tissues samples are sent to Penn investigators, the tissue repository personnel managing the exchange should remind the recipient investigator in writing that:
    - "Recipient acknowledges that the conditions for use of this research material are governed by the Penn IRB in accordance with Department of Health and Human Services regulations at 45 CFR 46. Recipient agrees to comply fully with all such conditions and to report promptly to the cell repository any proposed changes in the research project and any unanticipated problems involving risks to subjects or others. Recipient remains subject to applicable State or local laws or regulations and institutional policies which provide additional protections for human subjects. This research material may only be utilized in accordance with the conditions stipulated by the Penn IRB. Any additional use of this material requires prior review and approval by the IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an applicable OHRP-approved Assurance."
  - When repository samples are to be sent to parties external to Penn, a tissue transfer agreement is required. Please contact the Office of General Council for guidance and assistance in the construction of a proper tissue transfer agreement (215-746-5200). The tissue transfer agreement should include information similar to the above noted quote.
  - DHSS recommends that a Certificate of Confidentiality be obtained to protect confidentiality of human cell repository specimens and data. A Certificate of Confidentiality can be obtained regardless of whether any DHHS institute is funding the repository (see Vulnerable Populations).

The Cooperative Human Tissue Network (CHTN)

The following information is adapted from the Cooperative Human Tissue Network (CHTN) website (www-chtn.ims.nci.nih.gov/). The CHTN is a DHSS-funded national network of institutions that process and provides normal, benign, pre-cancerous and cancerous human tissue for biomedical research. Trained personnel coordinate the retrieval, preservation and delivery of specimens from surgical resection and autopsy. The CHTN began in 1987 with three member institutions and currently includes five member institutions that coordinate the collection and distribution of tissues in the US and Canada:

- Children's Hospital of Columbia, Pediatric Division
- Ohio State University (CHTN Midwestern Division)
- The University of Alabama at Birmingham (CHTN Southern Division)
- The University of Pennsylvania (CHTN Eastern Division)
- The University of Virginia (CHTN Mid-Atlantic Division)
- Vanderbilt University, Tissue Procurement program (CHTN Western Division)

There are three standard preservation methods used in the storage of specimens (*special requests may be accommodated*):

- **Fresh:** Specimens can be provided in media of choice, in saline, or dry, either at room temperature or on wet ice. Specimens can be shipped overnight on the day they are resected for delivery to the investigator's laboratory the following morning.

- **Frozen:** Specimens can be provided snap frozen in liquid nitrogen or frozen in cryoembedding media such as OCT and stored at liquid nitrogen or -70° C temperatures. Specimens can shipped on dry-ice overnight as they are collected or stored for batch shipment of multiple specimens once they are collected. Frozen sections are also available.
- **Fixed:** Specimens can be provided wet-fixed, as paraffin blocks, or as stained or unstained slides. Human tissue specimens are collected to meet an investigator's individual requirements. Researchers may specify preservation methods including fresh tissue (in any medium), fixed (in any fixative), and frozen (snap frozen or frozen in a tissue embedding media such as OCT). Histological specimens (blocks and slides) may also be available. Pathology data and histological characterization is routinely provided with the specimens. Additional information may be available if requested in advance. Since the most appropriate collection, storage and distribution methods depend on the research approach and tissue type, investigators should discuss their needs with the CHTN representative to assure access to the largest number and range of appropriate research specimens.

In order for the CHTN to collect and provide quality tissue specimens to meet specific user needs, each investigator is required to complete a detailed tissue form. This includes information about the type and amount of tissue required, tissue preparation, storage, and shipment requirements (e.g., media, snap frozen, sterile). The CHTN makes every effort to tailor collection, storage and shipment to the needs of the investigator. Tissue is provided according to the following priority order:

1. Funded, peer-reviewed investigators, including those from Federal and National laboratories
2. New investigators and academic investigators developing new research projects
3. Other investigators

A nominal processing fee is charged to cover some of the cost of collecting, preparing, and handling the tissue. In addition, the investigator must pay for the cost of shipping specimens to his/her laboratory.

The University of Pennsylvania is the CHTN Eastern Division institution responsible for supporting the northeast, the area bounded by the western border of Pennsylvania, and the southern border of Maryland, and also includes Alaska and Hawaii.

For additional information, contact:

Ms. Diane McGarvey
University of Pennsylvania Medical Center
566 Dulles Building
3400 Spruce Street
Philadelphia, PA 19104-4283
Telephone: (215) 662-4570
FAX: (215) 614-0251
Email: dfitzsim@mail.med.upenn.edu

Monitoring Plan Development

The monitoring of a clinical trial is an essential element of study processes designed to ensure the protection of the subject's rights, the safety of subjects enrolled in the trial and the integrity and quality of the resulting data. It is important to note that monitoring encompasses both data and safety oversight. Both activities complement one another to ensure that the study is safe and ethical. The degree of oversight will vary based upon the risk level, the size and complexity of the study, the nature of the investigation, the regulatory requirements, and the study sponsor.

A monitoring plan specifies a course of action to oversee the integrity of the study data. This plan typically details who will be responsible for monitoring (roles), what will be monitored (scope), and when monitoring will occur (timing).

The IRB has Guidelines for IRB Review of Data and Safety Monitoring Plans available on their website (http://www.upenn.edu/regulatoryaffairs//index.php?option=com_content&task=view&id=21).

Roles

The Principal Investigator is always responsible for ensuring that the protocol is followed, the data is accurate, and the research subjects at his or her site are safe. The Principal Investigator may designate some responsibilities to other study team members, but ultimately he or she will be held accountable for their activities.

Depending on the risk level of the study, the following individuals or groups may review the adverse events, safety data, and research activities and recommend a course of action to ensure the safety of research participants.

Study Monitor or Clinical Research Associate (CRA)
: The primary role of a study monitor is to verify data integrity and compliance to the protocol. A study monitor reviews source data/medical records, Case Report Forms, and regulatory documents for accuracy, completeness, and legibility in accordance with the study protocol. A monitor need not be a person qualified to diagnose and treat the disease or other condition under investigation.

Medical Monitor

The medical monitor is a licensed physician with clinical expertise in the area under investigation. Typically, the PI is the medical monitor, however when the PI is not an MD, a physician must be involved as the medical monitor. The medical monitor reviews and interprets adverse events, relevant animal and toxicology studies, and other safety data throughout the conduct of a research study and issues recommendations to maintain subject safety. The medical monitor's role and responsibilities within the research project should be clearly outlined prior to initiation.
NOTE: In cancer studies, the medical monitor must be independent from the study.

Safety Monitoring Committee

A Safety Monitoring Committee is a group of individuals responsible for the oversight of the study. The terms Safety Monitoring Committee may be used to refer to a less formal group than a Data and Safety Monitoring Board, though the terms are sometimes used interchangeably.

Data and Safety Monitoring Board (DSMB)

A Data and Safety Monitoring Board is an independent group of experts convened to protect the safety of research subjects and to ensure that the scientific goals of the project are being met. DSMBs are generally used in large multi-center studies, but may also be used in early-phase investigations of high risk medical interventions or studies with vulnerable populations.
Factors that suggest a DSMB is needed:
1. A large study population
2. Multiple study sites
3. Highly toxic therapies or dangerous procedures
4. High expected rates of morbidity or mortality in the study population
5. High chance of early termination of the study.

DSMBs should have a charter that outlines the structure and operation of the Board. A charter typically includes: the board's composition, operating procedures, frequency of ongoing monitoring, the data submitted to the DSMB, plans for statistical analysis and review, and the content of reports issues by the DSMB. The DSMB should have a broad multi-disciplinary representation including a biostatistician and a physician with relevant clinical expertise.
The DSMB's analysis plan describing what data will be reviewed, how the data set will be prepared for analysis, and the specific type of analysis used to assess safety. Generally, these analyses are performed on un-blinded data. After conducting the planned analysis (or analyses), the DSMB should issue a report either permitting the study to continue or recommending halting the study. Typically, the DSMB disseminates an 'open' report that contains aggregate data and administrative recommendations while also maintaining a 'closed' report that contains confidential data, un-blinded statistical reviews, and individual discussions.

Scope

Items typically monitored include study regulatory files, Case Report Forms, tracking logs (e.g. for enrollment, drug storage and dispensing, etc.), subject Informed Consent Forms, and study source documents. The monitoring plan should include a plan for collecting study data (Case Report Form). The plan should outline the procedures used to verify that the data collected on the CRF is correct and that the protocol has been followed.

The protocol defines procedures for reporting, reviewing, and analyzing safety data and plans for intervening (e.g. stopping rules or un-blinding procedures). The monitoring plan ensures that these procedures have been followed.

Timing

The occurrence of monitoring activities depends primarily upon the risk of the study. The higher the risk to subjects, the more frequently monitoring should be conducted. Monitoring frequency will also depend upon the size of the research study, the accrual rate, and the complexity of the Case Report Form. In general, there is a need for on-site monitoring before, during, and after the study.

Penn's Monitoring Templates

Office of Human Research: Study Monitoring Templates

Cancer Center: http://www.ctsrmc.org/forms.php

General Clinical Research Center: http://www.gcrc.upenn.edu/protocol/DSMP_Instructions.doc

Case Report Form Development

CRF Content, Organization and Format

Case Report Forms (CRFs) are documents used to systematically collect data that will be analyzed to fulfill the specific aims of the research project and monitor subject safety. Case report forms may be created in paper or electronic (eCRF) form.

The protocol defines all data to be documented and/or collected; therefore, the best time to construct the CRF is either during or shortly after protocol creation. Case Report Forms should be created by someone who is knowledgeable about form construction, data collection methods, and the aims of the research project. Before creating CRFs, researchers may find it helpful to review pre-existing CRFs from similar projects. It is advisable to seek the advice of an experienced data manager or biostatistician when constructing the study CRF.

Case Report Forms are typically tested in a piloting period to identify and eliminate problems. The piloting can be completed by having end-users enter historical data from medical records into the CRF. A study should never begin before the CRFs are finalized.

Content

The data collected on CRFs should be concise and driven by the objectives of the protocol. Therefore, extraneous information collected for patient care and not outlined in the study protocol should not be included in the CRFs. It is also important to carefully think through how much of the protocol-required activities should be collected in the CRF. For example, the protocol may require a full physical examination at regular intervals during the study, though it may not be efficient or useful to collect all data associated with the physical exam, rather only those changes from baseline or new abnormal findings. As the volume of data collection increases the quality of the information tends to decrease. Therefore, it is important to collect data on items which are truly necessary to answer the objectives of the project and limit the collection of data that 'might prove useful' in the future. If there are changes made to the protocol (amendments) after the study begins collecting data, all of the CRFs need to be carefully reviewed and updated if necessary.

CRFs can also be comprised of measurement tools that have been previously tested in subject populations with published results. Standardized, tested instruments allow for generalization between populations and illustrate consistency among other related research projects using the same instruments. When using a standardized form, it is important to maintain the validity of the instrument by not altering the format or content. If the forms are to be completed by the subject or will be verbally presented to the subject, IRB approval is required.

Organization

The data should be logically organized so that the respondent can follow the progression of the CRF. In other words, the CRF should progress chronologically with data collection activities. Usually, the CRF is divided by study visit. Further sub-divisions may be based upon where the data is collected and by whom. For example, during a visit, data may be collected by a research coordinator from the medical records and by a surgeon during an operative procedure. Some of the data collection activities may span several visits, and it may therefore make sense to capture this information in a separate section of the CRF (e.g. concomitant medications or adverse events). Extra forms should also be provided to accommodate unscheduled visits, additional findings, or early terminations.

Format

A well-designed CRF will be uncluttered and contain logical divisions between sections. It is not a good idea to minimize the number of forms by crowding as much information onto a page as possible. Ample space should be provided within and between each data field for ease of reading and data recording.

The header on each page of the CRF should include identifiers. At minimum the header will need to include the Study and Subject ID (initials and/or unique study number), but the Date of Visit and Site ID may also need to be included. In certain sections, it may also be necessary to include a space to identify each interviewer, data collector or CRF respondent. The last page of the CRF usually contains a line for the Principal Investigator to sign to attest to the accuracy of the CRF.

The footer on each page should contain identifiers as well. A unique form identifier (e.g. abbreviated form name: Adverse Events log = AE) and a version number. The date the form was created is also useful. The version number and date should be updated when changes are made to the form and older versions of the form should be archived.

See Tips for Creation for examples of well-written CRF items.

Tips for CRF Creation

The following guidelines are suggested when creating a CRF.

1. Have self-contained forms
   - Instructions should be brief, clear, and conveniently located
   - If algorithms, anatomical drawings, or charts are required for classification, they should be included in the CRF
2. Maintain a consistent design

- Page layouts should be similar across forms
- Coding conventions should be uniform, defined, and familiar to the respondent
- Terminology and phrasing should be consistent

3. Avoid blank items
   - Account for no opinion, not applicable, unknown, or missing information

4. Address one data element at a time
   - Avoid compound questions

5. Use forced responses
   - Questions should contain closed-system choices rather than open ones

6. Contain responses that are mutually exclusive and mutually exhaustive
   - If possible, all responses should fit into one and only one category
   - Choices should be inclusive by including all possible variations
   - If choices are not mutually exclusive, then indicate in the question instructions to "check all that apply" or " check only one response"

7. Capture raw data
   - Minimize the number of arithmetic calculations required to complete the form

8. Avoid leading questions or items
   - Questions should not lead the subject to a certain response
   - Capture occurrence of events, do not assume that the protocol is being followed

9. Use formatted boxes, lines, and/or checkboxes to keep data collection consistent
   - Identify the values or unit of measurement being used
   - Categorical values should have the correct number of spaces and proper punctuation inserted

10. Phrase questions in the positive
    - Multiple negatives are sometimes still negative and at the very least confusing

Electronic Data Capture

Electronic Data Capture (EDC) is the process of collecting clinical data for study analysis into a structured, computerized format which is permanent. The term permanent means that any changes made to the electronic data are recorded via an audit trail (see section 2.1). One type of EDC is an **electronic case report form (eCRF)**, wherein clinical data is entered directly into the database rather than being initially transcribed onto a paper CRF. Generally, an eCRF is accessed through a web browser and internet connection, and presents the users with a data collection form on screen similar to a paper CRF. Other forms of EDC include optical character recognition (OCR) forms, interactive voice recognition systems (IVRS), and automated (or direct) data acquisition (e.g. electronically transmitted ECG readings; laboratory data exported/imported directly into a study database).

Capabilities of an eCRF include:

- An interface that uses a directory and symbols to help the user quickly navigate through the required forms
- Edit checks that catch typical data errors as the form is completed
  - For example, if the protocol inclusion criteria require subjects of a specific age, when entering the subject's birth date, the system would calculate the age based on the birth date. If the subject's age falls outside the range of the inclusion criteria, the user could immediately be prompted that the age is out of range and permitted to correct the birth date, if it was simply a transcriptional error.
- Range checks applied to laboratory data fields
- Conditional questions that can remain hidden unless applicable
  - For example, the pregnancy testing results field would only show if the gender of the subject was female.
- Randomization of subject permitted only after pre-determined information has been collected

Trends in Electronic Data Capture

Currently, a number of EDC products are used in clinical research, some from third party vendors and others from pharmaceutical companies.

PROS
: EDC has the potential to conserve time and resources. The use of EDC can eliminate all or part of the data entry process, reduce errors due to legibility, provide immediate feedback via automated edit and range checks, and conserve paper.

CONS
: There are no standard interfaces; the look, feel, and navigation of each system vary enough that the researcher generally needs to go through a learning process for each EDC tool. Another impediment is that most EDC products rely on desktop/laptop computers for data collection - something that may not always part of the usual workflow at an investigative site. Also, certain edit or range checks can restrict the responses that can be entered in a way that may introduce bias into the study.

Informed Consent Form Development

The consent form is a document used to inform potential subjects about research participation. It is important to recognize that Informed Consent is an *ongoing* process that includes disclosure of information, comprehension, and voluntary choice. The consent form is used as a tool to help researchers fully disclose information.

The elements of the consent form are specifically regulated in 45 CFR 46 and 21 CFR 50, as well as outlined in the Good Clinical Practice (ICH) Guidelines. The IRB scrutinizes the consent form during its review to ensure that the proper elements are present, the form is written in lay language, and no coercive or misleading statements are included. The investigator cannot employ the informed consent form until it has received final IRB approval. The Penn IRB indicates this approval by stamping the consent form.

Penn has developed an informed consent template to assist researchers in developing an Informed Consent Form that is understandable, written in lay language, and includes all of the required elements of the consent form: Informed Consent Template

Industry-sponsored studies may provide investigators with a consent form template. This template should be integrated with the University of Pennsylvania's informed consent requirements. The revised consent should be forwarded to the sponsor for comments and approved prior to submitting to the IRB.

General ICF Writing Tips

Do's and Don'ts

- DO view the consent form as an instructional tool rather than a legal tool
- DO, if using published data that is not part of the FDA-approved label to discuss safety and/or efficacy, clarify that this is "research data" and not FDA-endorsed or FDA-approved as evidence of safety or efficacy of the study agent
- DON'T make claims that a study is FDA-approved. The FDA does not "approve" studies; it only approves medical treatments and devices for marketing.
- DON"T make statements that would suggest a subject is waiving his/her rights in any way.
- DON'T make statements that would suggest a subject the PI or study sponsor is relieved from liability for negligence (refer to Exculpatory Language in Special Language Requirements).
- DON'T make claims about safety/efficacy of the study agent that haven't been demonstrated (i.e. approved by the FDA), or are not applicable to the study population.

Content

- Be brief, but include complete information
  - sentences should be short, simple, and direct
  - paragraphs should convey one idea at a time
- Be comprehensible
  - written towards a reading age of 12-14 years
  - use lay language and avoid technical words or jargon
  - where use of technical terms are unavoidable, provide clear definitions
  - use the same words consistently when referring to a condition or treatment
  - use words that are concrete rather than abstract
  - use verbs that are active rather than passive
- Help people remember information
  - state ideas explicitly rather than implicitly

- Study purpose (repeat throughout and/or summarize critical study issues at the beginning or end
  - highlight important points by underlining, bolding, or boxing information

- Facilitate discussion
  - organize the form logically
  - use numbering or lists when presenting facts
  - use charts and visual aids

Lay Term Glossaries

A number of academic health centers have developed lay term glossaries, which may be helpful in defining and describing procedures and risks in informed consent forms. Please note that the IRB has not reviewed or approved any of these definitions, and so use of these does not guarantee IRB acceptance of the definitions.

- New York University: http://www.med.nyu.edu/irb/glossary/
- Stanford: http://humansubjects.stanford.edu/general/glossary.html
- University of California-Davis: http://www.research.ucdavis.edu/home.cfm?id=OVC,1,1081,1433,1064
- Partners Human Research Committee: http://healthcare.partners.org/phsirb/irbforms/Consent%20Form%20Instructions%20and%20Forms/Alternative_Lay_Language_for_Medical_Terms_in_Consent%20Forms.052307.pdf
- Northshore Long Island Jewish Health System: http://www.northshorelij.com/body.cfm?ID=1118
- University of Rochester Medical Center: http://www.urmc.rochester.edu/rsrb/pdf/layterms.pdf
- Winthrop University Hospital: http://www.winthrop.org/departments/research/irb/glossary
- University of Kentucky: http://www.research.uky.edu/ori/ORIForms/LAYTERM.pdf
- Lawrence Berkley National Laboratory: http://www.lbl.gov/ehs/health_services/harc/HSCforms/glossary.of.lay.terms.doc
- University of Pittsburgh: http://www.irb.pitt.edu/manual/apendi.pdf

Exculpatory Language

The consent form is not a legally binding contract. The researcher should view the consent form as an instructional tool rather than a legal document. Exculpatory language is not allowed, which means the consent form cannot waive *or appear to waive* legal rights or release the investigator, sponsor, or institution from liability for negligence.

Examples of Exculpatory Language:

In the following examples, subjects are being asked to agree with and accept these unfavorable conditions.

- By agreeing to this use, you should understand that you will give up all claims to personal benefit from commercial or other use of these substances.
- I voluntarily and freely donate any and all blood, urine, and tissue samples to the University and hereby relinquish all right, title, and interest to said items.
  By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
- I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

Examples of Acceptable Language

In the following examples, the intent and policies are set forth in a factual manner, but the subjects are not being asked to agree with or accept the conditions as part of their participation in the research.

- Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
- By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.
- This university is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.
- This university makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge.

* Examples adapted from Office for Protection from Research Risks (OPRR) Cooperative Oncology Group Chairpersons Meeting guidance document "'Exculpatory Language' in Informed Consent." http://www.hhs.gov/ohrp/humansubjects/guidance/exculp.htm

Format

- The second person pronoun (you and your) should be used throughout the document.
- Type should be easy to read.
  - Use sans serif fonts, legible size (e.g. Arial 12 pt, Verdana 12 pt).
- Use standard margins.

- Do not sacrifice font size or margin space for fewer numbers of pages.
- Indent the first line of a paragraph and leave paragraphs unjustified. Double-space between paragraphs.
  - This increases the speed and ease of reading.
- Avoid using sentences in all capital letters or italics.
  - This reduces the speed of comprehension and reading.
- Place the Study Title, Principal Investigator, and Institution in the header of each page.
  - Consider adding the IRB Protocol Number as an additional identifier.
- Place the Page # of # and the Consent Form Version in the footer of each page.

Formatting Examples

In the example on the top, narrow margins, no space between paragraphs, and use of a smaller serif font has made this document intimidating to look at and difficult to read. In the example on the bottom right, standard margins and double-spacing between paragraphs "chunks" the information into smaller segments. This facilitates reading and retention.

In addition, the use of all-caps for an entire sentence significantly slows reading. Use of all-caps is acceptable for one or two words that you want to stand out, but to emphasize an entire sentence, use of bold or underlining in preferred and will not affect readability.

Click on the images below to view full ICF documents (in Word)

Elements of Informed Consent

The elements of the Informed Consent Form required by Federal regulations and GCP guidelines are listed below. The Common Rule, FDA regulations and ICH guidelines have been harmonized to contain the same requirements (45 CFR 46.116, 21 CFR 50.25, ICH E6 4.8.10).

- A statement that the study involves research.
- An explanation of the purpose of the research.
- An explanation of the expected duration of the subject's participation.
- A description of the procedures to be followed.
- **If applicable, include*:
  - Aspects considered experimental
  - Procedures to be followed, including all invasive procedures and treatments
  - Probability for random assignment to each treatment.
  - Subject's responsibilities.
- A description of any reasonably foreseeable risks or discomforts.
- A description of any benefit to the subject or to others which may reasonably be expected from the research. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that may be advantageous.
- *If applicable, include*:
  - Important risks and benefits of alternatives.
  - The option of choosing "no treatment" or doing nothing.
- A statement describing the extent, if any, to which confidentiality of records will be maintained.
- *If applicable, include*:
  - The possibility that the government agencies (e.g. FDA, NIH, etc.) may inspect records.
  - Records will be kept confidential, and to the extent permitted by law and/or regulations, will not be made publicly available.
  - Published results will not identify the subject.
- For studies involving more than minimal risk, an explanation as to whether any treatment or compensation is available if injury occurs.

- An explanation of whom to contact for answers to pertinent questions about the research, the research subject's rights, and in the event of a research-related injury.
- A statement that participation is voluntary.
- Statement that refusal to participate will involve no penalty/loss of benefits. A statement that the subject may discontinue at any time without penalty/loss of benefits.

When relevant the informed consent must also include the following elements:

- Unforeseeable risks to embryo, fetus, or nursing subject.
- Anticipated circumstances under which a subject's participation may be terminated without regard to the subject's consent.
- Any additional expenses that may result from participation in research.
- **If applicable, include:*
  - The anticipated prorated payment, if any, to the subject.
- The consequences of a subject's decision to withdraw. A description of the procedures for termination.
- A statement that the subject will be told of significant new findings or information that may be relevant to the subject's continued willingness to participate.
- Approximate number of subjects involved in the study.

** These elements are specific to ICH E6 Guidelines*

Informed Consent Template

Penn has developed a template to aid in the construction of a research subject informed consent form. This standard form flows logically from a research subject perspective, and is designed to ensure all required elements of informed consent are captured as well as to improve the ease of IRB review. The available downloads are:

- Informed Consent Template with Annotated Guidelines (Word)
- The IRB Forms website has additional templates available for Social and Behavioral Sciences Research, Venipuncture, Cancer Studies, Tissue Research, Assent, and Humanitarian Use Device.

  HINT: It is recommended to Right-Click on the link above, select Save Target As..., and choose a location to save the document on your computer. Then, open the file from that location or from within Microsoft Word.

Why am I being asked to volunteer?

- The subject is being invited to participate in a research study and why are being asked to volunteer.
- Participation is voluntary
- The subject will get a copy of the consent form and should ask questions
- The subject will be asked to sign this form if consent is given to participate
- OPTIONAL: Can include some information about the study such as "a study of "X" (drug or device, etc.) in patients with "Y" disease

  You are being invited to participate in a research study. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

- A concise explanation of the purpose of the research, incorporating any intent to assess safety +/- efficacy
- A Clarification that the drug/device is investigational. Can note that the drug/device is approved for another indication if applicable, but must clarify that the use of the drug/device in this study is experimental

How long will I be in the study? How many other people will be in the study?

- Expected duration of a subject's involvement with the study
- Expected total duration of study
- Total number of subjects in study
- OPTIONAL: Include number of subjects at Penn

What am I being asked to do?

- A high level overview of the major elements of the study and what is expected of the subject (i.e. note here only the major procedures and milestones)
- Following the overview, provide a full list of procedures/tests by lay-term names; Consider including number of times each test will occur, amount, exposure if appropriate, etc. in easy lay terms
- Describe each test/procedure in lay terms
- Clearly identify which procedures are experimental
- OPTIONAL: May be complimented by a simple table or chart and/or other additional materials may be inserted here or given as a handout; any such materials require IRB approval

What are the possible risks or discomforts?

- Known risks from the study agent. May also be detailed in chart format and additional material inserted here or given as a handout. Any such materials require IRB approval.
- Risks, discomforts/inconveniences of study-related procedures noted in the section “What am I being asked to do?”. If standard of care is testing is being changed, describe any resultant risk, if applicable. May also be detailed in chart format and additional material inserted here or given as a hand out. Any such materials require IRB approval.
- Clarify that if the subject is injured, they should inform treating physician that they are in a research study.
- Include information on reproductive issues, if appropriate. NOTE: If male contraception methods or warnings are warranted, the appropriate information must be provided in this section as well.
- Do not make statements of proven safety unless that safety data is part of FDA-approved labeling. If the labeling safety data does not include data in the proposed study population for this study, make clear that there is no safety data in the population under study.
- Include a statement that the research may involve risks that are currently unforeseeable.

Reproductive Risks
Reproductive risks: Because of the effects of this drug/device, there could be serious harm to unborn children or children who are breast-feeding. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant, it is important that you inform the investigator because you will not be able participate in the study. If you are able to become pregnant, you will be given a serum pregnancy test before entry into the study. You are asked to use a medically accepted method of birth control (such as...) while you participate in the study. You should not become pregnant while you are taking this drug/device. If you do become pregnant, you must discontinue the drug/device, tell the investigator and consult an obstetrician or maternal-fetal specialist.

- **Reproductive Risks for Studies Involving MRIs**
- Gadolinium-based IV contrast agents are not approved in pregnant women and they are to be excluded from trials using such. A negative urine pregnancy test will be mandated before house stock agents can be administered to any woman of child bearing potential.
- The 4T Scanner is not approved in pregnant women and they are to be excluded from trials utilizing the 4T Magnet. A negative urine pregnancy test will be mandated before a woman of child bearing potential can be scanned on a 4T Magnet.
- There are no known risks of MRI on pregnant women or a fetus. Therefore routine, non-contrast, imaging protocols at 1.5T and 3T scanners need not exclude pregnant women if there is any possibility that they may benefit from this research. However, these women should be informed that there is a possibility of a yet undiscovered pregnancy related risk and a urine pregnancy test could be made available to them to help them make an informed decision whether or not to participate

Reproductive Risks for Studies Involving MRIs
Although there are no known risks of MRI on pregnant women or a fetus, there is a possibility of yet undiscovered pregnancy related risks. Since there is no direct benefit from participating in this protocol for a pregnant woman, we will exclude pregnant women. A negative urine pregnancy test will be mandated before a woman of child-bearing potential can participate in this study.

What if new information becomes available about the study?

- A statement that if information about the safety of the study drug/device/study is discovered during the study, which may affect one's willingness to participate, the subject will be notified

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

- If direct subject benefits can reasonably be anticipated as a result of participating in the protocol (section II.16 of application), then describe these possible benefits. Conclude with the following standard clause:

You may not get any benefit from being in this research study.

- If direct subject benefits are NOT anticipated, then use the following standard clause

  You are not expected to get any benefit from being in this research study.

- Anticipated benefits to society

What other choices do I have if I do not participate?

- Information on other treatments available.
- Alternatives to entering the study including, when appropriate, supportive care with no additional disease-directed therapy
- A statement that they may discuss alternatives with their personal physician

Will I be paid for being in this study?

- Description of any monetary compensation (*payments/stipend), if subjects are being compensated for their time and travel
- (optional) A break down of the total compensation (i.e. clarify if paid after each visit/procedure or upon completion of the study, etc.)
- If there is no compensation for participation in this study, state that here
- Refer to Considerations for Subject Payment for guidance on this topic

"No Cost" Language
You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay.

Will I have to pay for anything?

- Procedures or tests that will be covered by the study
- Procedures or tests that are not covered by the study, stating how they will be paid for (i.e., third party payer (payor), etc.)

What happens if I am injured or hurt during the study?

- Provide contact information for research-related injury (i.e. can refer to the contact information noted in Consent header, if appropriate)
- Describe what treatment will be provided for research related injuries
- Explain how treatment for research related injuries would be paid
- Describe procedure for emergency care
- OPTIONAL: Subject's responsibilities relating to research related injuries

If you have a medical emergency during the study you should go to the nearest emergency room. You may contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise offered from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

When is the Study over? Can I leave the Study before it ends?

- Define when the overall study is to end
- Explain what events could lead to early study closure
- Note that the subject can elect to leave the study at any time
- If early withdrawal could expose the subject to medical risks, describe and how those risks will be minimized or prevented (e.g. in a hypertensive study, it may be necessary to wean a subject off of the study medication or to transition them to alternate therapy)

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide not to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

The investigator and staff involved with the study will keep your personal health information collected for the study strictly confidential. Please refer to the separate "HIPAA Privacy Authorization" document that explains more specifically how your personal information will be protected.

Who can I call about my rights as a research subject?

- Indicate who to contact for questions relating to the participant's rights as a research subject; generally, this is the Office of Regulatory Affairs at the University of Pennsylvania, (215) 898-2614

If you have questions regarding your participation in this research study or if you have any questions about your rights as a research subject don't hesitate to speak with the Principal Investigator listed on page one of this form. Concerning your rights as a research subject, you may also contact the Office of Regulatory Affairs at the University of Pennsylvania by calling (215) 898-2614.

Closing and Signature Section

Include the Authorized Subject Representative signature line only in studies which are approved by the IRB to use representatives to authorize a subject's participation in research. Delete if not applicable.

- Provide a brief description of above person authority to serve as the subject's authorized representative.

Every informed consent should have a signature and date line for the subject and the person obtaining informed consent

- A witness is required when a subject cannot verify the accuracy and completeness of the information by reading the consent form (e.g. blind or illiterate subjects)
- A legally authorized representative is required when subjects are unable to give consent for themselves (because of their age, medical condition, or cognitive state). The IRB must approve the study to use representatives to authorize a subject's participation in research.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

Special ICF Language Requirements

Assent Forms

Generally, minors and adults with limited decision-making capacity do not have the legal authority to provide consent for their own participation in a research study. However, an investigator should still seek affirmative agreement (assent) from such research subjects. An assent form is a simplified version of the consent form and should be written to the subject's level of understanding. A typical assent form explains a study's purpose, procedures, risks, benefits, confidentiality, and voluntary nature in simple terms.

Refer to Research Involving Special Populations for more information about Consenting Minors.

Human Immunodeficiency Virus (HIV) Testing

Pennsylvania state law requires HIV testing to be reported to the Pennsylvania Health Department. If HIV testing is completed as part of the research procedures, prospective subjects must be informed of the reporting requirements.

Sample consent form language for HIV testing :

> Pennsylvania state law, like laws in most states, requires health care workers to report the names of people who test positive for HIV to the Pennsylvania Health Department. The reason for this is to keep track of how many people in the U.S. have HIV infection, and to make sure that the U.S. government provides enough money to each state to support the medical care of people living with HIV. The Pennsylvania Health Department does not share the names of HIV infected individuals with any other governmental or nongovernmental agency. This maintains the privacy of HIV infected individuals whose names are reported.

Magnetic Resonance Imaging

Studies involving MRIs must include a risk statement similar to the following:

> The known risks associated with this MRI study are minimal. The greatest risk is a metallic object flying through the air toward the magnet and hitting you. To reduce this risk we require that all people involved with the study remove all metal from their clothing and all metal objects from their pockets. No metal objects are allowed to be brought into the magnet room at any time. In addition, once you are in the magnet, the door to the room will be closed so that no one inadvertently walks into the magnet.
>
> Although there are no known risks of MRI on pregnant women or the fetus, there is a possibility of yet undiscovered pregnancy related risks. If you are a woman of child-bearing age and it is possible that you are pregnant, then a pregnancy test can be made available to you in order to help you make an informed decision about your participation in the study. In the event you elect to have a pregnancy test, several tablespoons of urine would be collected on a day prior to your participation in the MRI study. If you are found to be pregnant, the MRI session would be scheduled for a later date. You would practice a medically accepted form of birth control, such as _____, during the time between pregnancy testing and your MRI session.

In addition, there are specific consent form requirements for studies involving the 4T magnet, new pulses or coils, and gadolinium. For more information, visit http://www.mmrrcc.upenn.edu/CAMRIS.

Radiation

The Environmental Health and Radiation Safety (EHRS) requires standard statements of risk for consent forms involving diagnostic uses of radiation and radioactive material.

> Language for protocols involving exposures below 10,000 mrem effective dose:
> This research study involves exposure to radiation from a [name procedure(s)] and therefore you will receive a radiation dose. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.
>
> For protocols involving exposures above 10,000 mrem effective dose:
> Statements of risk from diagnostic uses resulting in greater than 10,000 will be approved on a case-by-case basis.

Note: If biological effects are anticipated from the radiation, regardless of the effective dose, then a statement about the biological effect must be included in the radiation risk statement

Tissue or Blood Banking

If a secondary aim of the research study is to bank tissue or blood for future genetic analyses, subjects should have the ability to refuse without jeopardizing overall study participation. To do this, the consent form can include an opt-in/opt-out section or a separate consent form can be used for blood and tissue banking.

Variations in Informed Consent

Deception in Research

Certain research studies are designed to test responses when the research subjects are intentionally misinformed or have had certain information withheld from them. This type of research is categorized as deception.

To request approval from the IRB for the use of deception, the investigator should demonstrate that:

- the use of deceptive techniques is unavoidable (alternatives are not feasible)

- debriefing does not diminish significant risk
- subjects are not deceived about aspects of the study that would affect their willingness to participate
- data collection will be followed by a sensitive debriefing session (explanation of the deception) that protects the rights and dignity of research subjects

Writing an informed consent form for a study that involves deception

- the consent form cannot include anything that is untrue
- the consent form should reveal as much information as possible without compromising the study aims
- this may include a statement that the subject may not be told complete information due to the study design, but will be informed at the completion of the study
- a separate post-debriefing consent form is recommended to give subjects the opportunity to opt-out of having their data included in the research

Waiver of the informed consent process

In specific circumstances, the IRB may waive part or all of the informed consent process. For example, an investigator may want to conduct a retrospective study of existing, anonymous laboratory specimens without obtaining informed consent.

To request a waiver of informed consent, the investigator must demonstrate in a letter to the IRB that all of the following conditions are met:

- The research involves no more than minimal risk
- The waiver will not adversely affect the rights or welfare of subject
- The research could not practicably be carried out without a waiver
- When appropriate, the subjects will be provided with additional, pertinent information after participation

Note: The investigator will also be responsible for requesting an exemption or waiver of the HIPAA authorization (refer to HIPAA Authorization).

Translated Consent Forms

The consent form must be written in a language understandable to the subject or the subject's representative. If non-English speaking subjects are anticipated to be enrolled into the study, or if it is found that more than a few subjects are enrolled who speak the same non-English language, the consent form must be translated. The IRB must approve the translated form(s) or short form.

Translated consent forms must be certified as correct. This can be done by having a translated consent re-translated back into English to see if it results in language consistent with the original consent. Or, the translation service can provide a letter certifying that the translation is a true and accurate translation of the original Enlish version. Following are a few of the translation service available:

TransPerfect Translations
Tel: 215-854-6388
www.transperfect.com

Translators, Inc.
1-866-372-7373
www.translators.com

Verbal informed consent with a Short Form

If a non-English speaking subject is unexpectedly encountered, it is possible to obtain informed consent through an oral presentation of a study summary, presented in the subject's native language, accompanied by a translated short form consent document (Common Rule 45 CFR 46.117, FDA regulations 21 CFR 50.27). The short form consent is a means of permitting equal access to the study. This approach and associated documents must be approved by the IRB.

The use of the short form consent process requires IRB approval and involves the following:

- *Short form consent document* - translated into the subject's native language. overviews the required elements of informed consent and notes that these elements, as they pertain to the study, will be presented orally to the subject or legally authorized representative.

  The Office of Human Research and Institutional Review Board have developed a Short Form Consent form and have had it translated into 9 languages. These consent forms are available from the IRB website at IRB Forms

- *Summary document* - an orally presented summary of the study and study requirements in the subject's native language . A written English version of the oral summary must be submitted to the IRB for review and approval . The IRB-approved standard informed consent form can be used as the summary document.
- *Interpreter* - a person to orally present the summary document to the subject and translate the consent conversations. This can be the person obtaining consent.
- *Witness* - who understands English and the subject's native language and is not part of the study team or otherwise involved with the study , and witnesses the consent process.

This form may also be used by a person obtaining consent.
- *Signatures*: Signatures and date of signature are required for both the short form and the summary document as follows:
  - *Short form written consent*: subject and witness
  - *Summary document*: witness and person obtaining consent

The subject must receive a copy of the short form document and the study summary.

Note: The short form written consent is intended for the special circumstances noted above. If subjects not fluent in English are expected to be enrolled, then a fully translated consent form must be used rather than the use of a short form consent document.

An example English version of the short form consent document appears on the facing page. This document has been translated into 9 languages and can be downloaded from the IRB website and used when a non-English speaking subject is unexpectedly encountered.

HIPAA Authorization

The Health Insurance Portability and Accountability Act (HIPAA) are privacy regulations that limit the collection and disclosure (defined below) of protected health information. Protected health information (PHI) is *individually identifiable* health information. PHI includes any of the following *individually identifiable* elements:

- Names
- Street address
- Postal or street address information (some exclusions apply here)
- All elements of dates (except year) related to an individual (including hospital admission and discharge dates)
- Ages of individuals over 89
- Telephone and fax numbers
- Email addresses
- Social security numbers
- Medical record, health plan, or other account numbers
- Certificate/license numbers
- Vehicle identifiers
- Device identifiers
- Web (URLs) and Internet (IP) addresses
- Biometric identifiers
- Full face photos
- And any other unique identifying number

Investigators must obtain a signed HIPAA Authorization form or IRB Waiver of HIPAA Authorization from the subject to collect, use, or disclose protected health information for research.

Disclosure refers to the release of PHI outside of the "covered entity." At Penn, the covered entity consists of the following institutions/groups:

- Hospital of the Univ of Penn
- School of Medicine
- Clinical Practices of the Univ. of Penn
- Penn Presbyterian Medical Center
- Pennsylvania Hospital
- Penn Center for Rehabilitation and Care
- Penn Presbyterian Anesthesiology Foundation
- Clinical Care Associates
- Wissahickon Hospice
- Clinical Health Care Associates of NJ
- Penn Presbyterian Personal Care Residence, Inc.
- Penn Presbyterian Multi-Specialty Group Practice Foundation

Accounting of Disclosures under HIPAA

The Health Insurance Portability and Accountability Act (HIPAA) are privacy regulations that limit the collection and disclosure of protected health information (PHI). However, the privacy regulations also require the protection of data through an ongoing mechanism known as accounting disclosures, an institutional method of tracking whenever data is disclosed outside of the Covered Entity (the health system holding the PHI).

Subjects have the right to receive an accounting of disclosures made of their protected health information (PHI). In order to provide subjects with an accounting of their PHI, investigators and their research staff must record all applicable disclosures, EXCEPT in two cases:

- When a research subject has signed a study HIPAA authorization form (a form documenting the subject's authorization to use and disclose personally identifiable data)

- When PHI is disclosed to a Business Associate. A Business Associate is an entity that has been contracted on behalf of the Covered Entity to assist with the business processes associated with healthcare or clinical research.

This accounting must include:

- Date (or range of dates) of disclosures
- Name of subject whose data was disclosed
- Address of the entity or person to whom the information was disclosed
- Brief description of information of the PHI disclosed
- Brief statement explaining the purpose for the disclosure or a copy of the written request for the disclosure
- The UPHS has implemented a web-based system for reporting a research disclosure at https://secure.pennhealth.com/HIPAADISCLOSURE/MustLogIn.htm . This system only enables reporting for one patient at a time. For larger data sets, the researcher may want to coordinate to transmit disclosures electronically by contacting UPHS Information Technology: 215-662-7474 http://uphsxnet.uphs.upenn.edu/helpdesk

HIPAA Authorization Form

The content of the HIPAA form is regulated in the Code of Federal Regulations in 45 CFR 160 and 164.

A HIPAA authorization must include the following core elements:

- Description of the protected health information (PHI) in a specific and meaningful way
- Who may use or disclose the information
- Who may receive the information
- Purpose of the use or disclosure
- An expiration date or event
- Individual signature and date
- Right to revoke the authorization including exceptions
- Reference to the Notice of Policy Practices
- Right to inspect or copy PHI disclosed
- Right to signed copy of HIPAA
- Covered entity may continue to use PHI pursuant to authorization
- Covered entity may continue to use data to protect the integrity of the research
- Re-disclosure of health information are no longer protected by HIPAA

Penn has a template available that will ensure investigators include the required elements of a HIPAA Authorization. This template is available at www.med.upenn.edu/ohr/hipaa/attach1.html.

The HIPAA authorization may be incorporated into the research consent form or it may be kept as a separate document. The IRB encourages investigators to keep the authorization as a stand-alone form.

A sponsor-supplied HIPAA Authorization form cannot be used in place of the University-approved HIPAA Authorization form. HIPAA regulations apply to the healthcare institution, not the industry sponsor. The Office of Research Integrity and Compliance (School of Medicine) or the Chief Privacy Officer (UPHS) can assist researchers in communicating this to the sponsor, if necessary.

IRB Exemption / Waiver of HIPAA Authorization

Research Using De-identified Information

De-identified information is health information that has been stripped of all identifiers (refer to the HIPAA Overview) and is no longer protected under HIPAA. A research study may use or disclose de-identified data for research purposes *if* it is an IRB-approved protocol that received an exemption from IRB review. For exempt studies, the IRB Waiver of HIPAA Authorization form should be completed and submitted with the Request for Exemption form sent to the IRB.

IRB Waiver of HIPAA authorization

In certain instances, an investigator may access protected health information for research without obtaining a HIPAA authorization from subjects. In these situations, the IRB may waive part or all of the HIPAA authorization. For example, an investigator may request a HIPAA waiver to conduct a retrospective chart review.

To request an IRB waiver, the investigator must complete the IRB Waiver of Authorization form and submit it to the IRB: http://www.upenn.edu/regulatoryaffairs/human/forms/hipaawaiver.doc. The Waiver of Authorization form requires the signatures of the Principal Investigator and of the departmental head or dean.

To be granted a waiver of HIPAA authorization, the investigator must demonstrate that:

- The disclosure involves no more than minimal risk and has in place the following:
  - Protection Plan: plan to protect identifiers from disclosure
  - Destruction Plan: plan to destroy identifiers at earliest opportunity
  - Assurances against Re-disclosure: information will not be reused or disclosed except as required by law
- The research could not practicably be carried out without a waiver
- The research could not be carried out without access to protected health information

Exception from HIPAA Requirements

Research Using a Limited Data Set

Investigators can use a “limited data set” without obtaining a HIPAA authorization, provided that the following identifiers have been removed:

- names
- street addresses (other than town, city, state and zip code)
- telephone numbers
- fax numbers
- e-mail addresses
- Social Security numbers
- medical records numbers
- health plan beneficiary numbers
- account numbers
- certificate license numbers
- vehicle identifiers and serial numbers, including license plates
- device identifiers and serial numbers
- URLs
- IP address numbers
- biometric identifiers (including finger and voice prints)
- full face photos (or comparable images)

A limited data set may include the following indirect identifiers:

- dates such as admission, discharge, service, date of birth, date of death;
- city, state, five digit or more zip code; and
- ages in years, months or days or hours

When conducting research using a Limited Data Set, an application must be submitted to the IRB for this purpose. The application can be found at www.upenn.edu/regulatoryaffairs/human/forms/limiteddatasetapplication.doc.

A Data Use Agreement is required in these circumstances to specify the terms for using the data. The Data Use Agreement must be enacted by the Office of Research Services. To download a template, go to: www.med.upenn.edu/ohr/docs/DataUseAgreement.doc.

Activities Preparatory for Research to Prepare a Protocol

An investigator can obtain PHI for data collected "preparatory for research" without a HIPAA authorization provided that all of the following conditions are met:

- The data is sought solely to review PHI as necessary for activities preparatory for research.
- No PHI will be removed from UPHS/SOM by the researcher in the course of review.
- The PHI is necessary for the research purposes.

"Preparatory for research" includes developing research questions, determining study feasibility, and determining study eligibility. Please note, that although HIPAA regulations consider determining study eligibility an activity preparatory to research, the actual process used to recruit subjects remains a research activity that requires IRB approval.

Research Using Decedent Information

An investigator may use or disclose the protected health information of individuals who have died without a HIPAA Authorization or a Waiver of Authorization provided that the researcher can demonstrate in a letter to the IRB that:

- The use is solely for research on the protected health information
- The research could not be carried out without access to protected health information
- Individuals are deceased

Subject Recruitment Plan

Successfully recruiting the desired number of subjects for a study is critical to its success. Subject recruitment can often be challenging. There are several methods that can be developed in a comprehensive subject recruitment plan to help meet this challenge.

Recruitment Strategies

Clinical Care Settings and Resources

- Screening incoming patients in healthcare setting
- Medical record reviews
- PICARD database query (see below)
- Departmental databases and registries

Physician Referral

- Networking with other practices and clinics
- Educational forums for physicians, nurses and hospital staff
- Mailings, referral packets

NOTE: The Penn IRB strictly disallows the use of “finder’s fees”, a payment or gift to an individual who identifies or assists in the recruitment of prospective subjects. See the IRB Guidelines for Payment for Recruitment of Subjects in Human Research available at IRB Guides

Community Awareness

- Advertising through news, magazine, and journal ads
- Advertising through direct mail, posters, flyers, and brochures
- Advertising to the general public through media such as radio, TV and the Internet
- Participating in community health events and forums
- Educational forums to patient advocacy groups and community
- Use of a public relations firm
- Press releases and media events

Recruitment of Veterans

Veterans Administration (VA) patients who receive care at the Philadelphia Veterans Administration Medical Center (PVAMC) are sometimes sent or transferred to the Hospital at the University of Pennsylvania for certain procedures. These patients are not eligible to be recruited for any Penn research protocol unless that protocol has been previously reviewed and approved by the VA Institutional Review Board. These patients are still under the care and jurisdiction of the VA as the primary provider. As such, the Philadelphia VAMC IRB must remain the primary advocate protecting the rights and welfare of all Philadelphia VAMC patients in research protocols. If you have any questions, call the PVAMC Research & Development office at 215-823-7847.

Recruitment Support Using the PICARD Database

As mentioned in Recruitment Potential, PICARD is a comprehensive database containing inpatient and outpatient records of all UPHS patients. A query of this database, with specific diagnostic and/or time-limited search criteria can produce a list of patients with contact information. This list can also be grouped by the physicians who care for the patients.

In order to obtain a list of prospective patients, the study will first require IRB approval. The protocol should include specific methods for obtaining the recruitment list, as well as the methods by which the subjects will be contacted. Below is sample language that could be included in the protocol to specify use of the PICARD database for recruitment purposes - replace the query details with study-specific query criteria:

> "Subject recruitment will be facilitated through assistance from the Office of Human Research (OHR) using the Pennsylvania Integrated Clinical and Administrative Research Database (PICARD). OHR will provide a list of patients, *(specify search criteria here, e.g. aged 35 to 60, who have sought treatment within the UPHS, with a diagnosis of Type II Diabetes and a diagnosis of Above Knee Amputation made within the past 2 years)*. Preliminary query data has identified a potential pool of xxx patients.

A list of patients meeting the criteria will be provided to the study team, including the treating UPHS physician name, patient name, contact information, diagnoses, visit dates, and medical record numbers. The physicians for patients who will be sought for recruitment will be contacted and asked for their written permission for the research team to approach the patient for recruitment into the study. The treating physician will be asked to indicate their approval by signing a cover letter that will be mailed to the patient."

Considerations for Subject Payments

Subjects are often offered monetary payments for their participation in research studies. While many differing perceptions exist on the ethics and effectiveness of this practice, the decision to provide payment to research subjects is generally made by the PI in order to facilitate timely recruitment of subjects for the study. The justification for payment to research subjects include the provision of an incentive to participate, reimbursement for expenses that the subject may incur to participate, or payment for the subject's time and inconvenience. It is never acceptable to use payment as a benefit to offset the risks of a study.

Several important ethical considerations should be weighed when considering whether or not to pay subjects, how much, and on what schedule. One important concern is that the payment may cause undue influence on the subject's decision to participate in the study. That is, the financial incentive may render potential subjects less likely to fully weigh the potential risks. While there is no concrete guidance on what size payment may induce undue influence on a subject, it is essential to evaluate the nature of the study, the contributions and sacrifices made on the part of the research subject, vulnerabilities that may be inherent in the study population, and local and societal norms.

Subject payments typically are classified as either reimbursement or renumeration.

- *Reimbursement* refers to payment, monetary or other form, paid to a subject for out-of-pocket expenses such as study-related travel, lodging, meals or lost wages.
- *Renumeration* refers to monies paid to subjects as repayment for their personal time and effort committed to study participation.

NOTE: The term "compensation" should be used only to refer to payment or medical care provided to subjects injured in research.

All subject payments should be described in the study protocol and informed consent form, which must be approved by the IRB prior to project initiation.

Determining the Amount of Payment

Payments vary based upon the complexity of the study, the type and number of procedures, the time involved, and the anticipated inconveniences. Investigators may calculate payments by estimating the number of biological samples collected, the amount of time spent on the project, the subject's anticipated out-of-pocket expenses, or a variety of other factors. Some investigators utilize predetermined formulas to calculate subject payments, (e.g. TIME (hours of commitment) X HOURLY RATE ($4 - $10/hr), or a FLAT RATE for INPATIENT ($125/day) vs. OUTPATIENT ($25/day)). Monetary inducements are not allowed solely for the purpose of attracting subjects for studies involving significant risk or excessive pain or discomfort, such as a bone marrow biopsy.

A number of models exist to guide this process (reference Grady 2005):

Market Model
: In this model, the laws of supply and demand determine how much a subject should be paid for participating in a research trial. Payment is viewed as a "benefit" to offset risks associated with a particular trial. Studies that involve greater risk or have no other benefit for participation, such as a healthy volunteer trial, would likely have the highest rate of payment. Studies in which the subjects stand to gain a significant health benefit as in therapeutic trials would likely have minimal or no monetary payment. This model allows for higher payment to speed recruitment, and bonuses to ensure that subjects complete the study. Use of this model has the potential to create undue influence where the payments are set high to overcome risks or inconveniences. (Amdur, 2003)

Wage-Payment Model
: The wage-payment model determines the payment amount on the amount of time and effort the subject contributes to the study, using a standardized hourly wage. Additional payment is often added to this amount for inconvenience. In general, the hourly wage is often commensurate with wages for unskilled, but essential jobs. Using a standardized wage may provide incentive for lower income subjects, but may be a disincentive for subjects with higher incomes.

Reimbursement Model
: The reimbursement model focuses strictly on reducing or eliminating the financial burden on an individual to participate in a research study. Reimbursement generally refers to payment to the subject for out-of-pocket expenses such as study-related travel, lodging, or meals. Reimbursement could also include payment for lost wages, however, this may result in uneven payments to subjects with differing salaries. This model generally makes research participation a financially-neutral endeavor for the subject, and may have little impact on recruitment efforts.

Appreciation Model
: The appreciation model uses payment as a reward or token of appreciation for the subject's participation. It is often provided at the end of the study, and the amount is not based on market, time, or reimbursement.

Fair Share Model

In this model, subjects are treated as a partner in the research enterprise rather than a commodity or a wage laborer. Investigators are typically reimbursed a certain amount of money per subject. This is then used by the investigator to pay the direct (e.g. lab fees, IV tubing) and indirect (e.g. salaries, overhead) costs associated with running the trial. Utilizing this model, subjects would be compensated a fixed proportion of the per-subject reimbursement. Since investigator reimbursement per patient is based in part on whether a subject completes the trial, subjects' payment would thus be prorated depending on the duration of their participation.

Payment Schedule

Payment should be accrued or prorated as the study progresses and not be contingent upon the subject completing the entire study. Subjects who withdraw early from the study may be paid at the time they would have completed the study had they not withdrawn (unless it creates undue inconvenience or appears coercive). All information concerning the payment, including the amount and schedule of payment(s), should be described in the informed consent form.

The investigator may include a small extra payment at the end of the study (bonus) as an incentive for completion, providing that it is not coercive. If a bonus is awarded it should be provided to all completed subjects, not just "favorite" or compliant subjects. The bonus should not be offered as an alternative to withdrawal if the subject wishes to discontinue participation in the study. In general, the IRB recommends that the final payment be no more than 25% of the total payment.

For more information, the IRB had developed a guidance document on Payment to Human Subjects Participating in Research found at www.upenn.edu/regulatoryaffairs/human/guidance/paymentguidance.pdf.

References:

- Amdur, R. (2003). Institutional Review Board Member Handbook. Chapter 3-5. Jones and Bartlett Publishers, Inc. Sudbury, MA.
- Grady, C. (2005, July). Payment of Clinical Research Subjects. *The Journal of Clinical Investigation*, 115,:7, 1681-1687.

Privacy Rules Regarding Subject Recruitment

Under the provisions of HIPAA's Privacy Rule in April of 2003, Penn's Notice of Privacy Practices informs every patient that their health information may be used to support research, which means the institution can contact patients to assess their interest in participating in research. However, University policy mandates the methods by which patients can be contacted.

Acceptable Methods of Contacting the Subject (in order of priority)

1. The preferred method is to have the physician or other health care provider who has taken care of the patient in the past to contact the patient directly. Or the research staff can be authorized by the physician to contact the patient on the physician's behalf.

2. If this is impractical, the Penn researcher may develop a letter to be used to contact the patient. The letter must be approved and signed by a physician or other health care provider who has cared for the patient. Alternatively the physician may authorize the research staff to send a letter on the physician's behalf and signed by the research staff. The language of the letter must also be approved by the IRB.

3. If the first two methods are impractical, the Penn researcher may contact the potential subject directly. This method of recruitment will require specific IRB approval, and approval will only be granted if the impracticality of the first two methods is well-substantiated.

Advertisement Development

Direct advertisements (radio, television, print, internet, telephone, brochures, websites, etc.) are used to recruit subjects for research in general and/or for specific studies. Direct recruiting advertisements are considered a part of the informed consent and subject selection process and, therefore, governable by federal regulations. Several federal regulations govern the use of advertisements (21 CFR 50, 21 CFR 56 and 21 CFR 812). These regulations stipulate that advertisements must not present any coercive or misleading information by implying a certainty of favorable outcome, claiming the safety or efficacy of an investigational product, implying the study is a medical treatment, promising free medical care, or overemphasizing payments.

The IRB provides guidance on recruitment materials which can be found at IRB Guides.

Advertisements are not limited to the printed word, such as appears in newspapers or brochures. Radio advertisement and videos (such as are used for television) also fall within this purview and are subject to the same guidelines and submission requirements.

To recruit subjects, advertisements may include the following information:

- Name and address of the investigator and/or research facility
- Condition under study and/or the purpose of the research
    - Include the word research, investigational, or experimental

- Abbreviated description of criteria that will be used to determine eligibility
- A brief list of participation benefits, if any
- Time and/or expected commitment required of the subject
- The person to contact for further information

Well-designed advertisements are clear in phrasing and simply worded, using non-medical terminology where possible. An appropriately worded advertisement may include the expected payment as long as it is not overemphasized so that it can be perceived as a benefit.

What's wrong with this advertisement?

1. Coercion
   - Uses misleading words like *cutting edge*
   - Treatment is implied
   - Investigational medication is called *new medication*
   - Research or investigation is not mentioned
   - $$ money is over-emphasized
2. Contact Name is not provided
3. Facility is not provided
4. Time commitments/procedures not mentioned

Rewriting the example into a good advertisement

Recruitment Brochures

Brochures are a type of advertisement tool used to help with the recruitment of subjects. Brochures are often created in the start-up phase of research. However, recruitment brochures are usually not subject to the space limitations of other written advertisements and, as such, their formatting may vary slightly.

Recruitment brochures generally incorporate the elements of an advertisement in several distinct sections:

Call to action
: This section notifies the potential subjects of the focus of the project. Typically this call to action is worded in question format asking the reader if they have experienced a given situation.
e.g. Have you ever..?, Are you planning..? Do you have..? Have you and your provider discussed..?

Study Significance
: This section explains the importance of the research project and the significance of the intended research. Typically this section is worded as a question drawing attention to the study importance.
e.g. Why is this study important?

Inclusion/Exclusion Criteria
: This section outlines the protocol-defined parameters for study eligibility. This section helps the targeted audience understand the likelihood of participation. Typically inclusion/exclusion criteria are worded as a directive guiding participation eligibility.
e.g. You may participate if you: .. You may not participate if you.

Study Procedures
: This section explains the study-related procedures and clearly discusses the activities as part of research participation. Typically this section outlines the activities in chronological order and directly correlates with the study protocol and informed consent form.

Principal Investigator
: This section includes the name, title and affiliation of the Principal Investigator. Typically this section is located on the back of the brochure.
e.g. Name of Principal Investigator
Title of Principal Investigator
Affiliation

Institutional Review Board (IRB) Submission

Research advertisements must be approved by the IRB prior to implementation. The IRB must ensure that advertisements do not contain information that is misleading to potential research subjects. Most advertisements are reviewed in an expedited fashion.

The IRB prefers that radio and video advertisements be submitted as transcripts rather than audio or video presentations. If an advertisement is translated, the translation must be submitted with a copy of the original English version for review and approval. Copies of recruitment letters to subjects and intermediaries ("Dear Doctor" letters) must also be submitted to the IRB.

The IRB does not need to review patient education materials which do not detail specific studies nor mention research. The IRB also does not need to review study lists of basic information posted on the internet. These database listings are strictly limited to the study title, the eligibility criteria and contact information. Examples include the National Institute of Health (NIH) registry of clinical trials, the National Cancer Institute's (NCI) cancer clinical trial listing (PDQ) and the AIDS-Clinical Trial Information Services (ACTIS). To clarify whether an internet listing qualifies as exempt from IRB review, contact the Office of Regulatory Affairs.

Advertising Venues

This section provides a number of advertising venues to consider for reaching potential subjects in the Delaware Valley. It is also advised to consider nationwide advertising venues specific to the target population (for example, AARP, Diabetes Digest, etc.).

Most newspapers, catalogs, radio and TV stations offer statistics about the audience they reach. It is advisable to ascertain which media would best reach the target population in terms of age, gender, ethnicity and other demographics. Another consideration is that university-operated stations offer public service announcements and may offer less expensive advertising.

Listing these sources does not imply endorsement.

Print Media

Penn Bulletin Boards

The hospital has provided designated space for all Penn Research Studies being conducted. All postings should be dated in a visible area, so they are not mistakenly taken down by those helping to maintain the board.

The following locations have been approved for posting recruitment advertisements:

- **Maloney Lobby**
  (36” x 48”) - On wall to the left side of the Safety Office across from the Passenger Elevator.
- **Founders 1st Floor**
  On the wall across from the Stair Tower next to the Passenger Elevator Lobby (24" X 35").
- **Founders 2nd Floor**
  Two (36” x 48”) - One on the wall to the right side of the ATM machine and the other to the right of the House Phone next to “Starbuck Coffee” about 6 to 8 feet down – centered with the 1' x 2' light fixture.
- **Rhoads 1st Floor Link**
  On the wall across from the Pay Phones above the bench (36” x 48”) and one (36” x 48”) on the wall across from the Fire Command Center.
- **Silverstein 1st Floor**
  One (24” x 36”) to the left of the ATM machine – centered on the Column and one (36” x 48”) to the left of the fire tower door starting about 6” from door frame on the Patient Education office wall.
- **Ravdin 1st Floor**
  One the wall to the right of Visitor Elevator #4 – centered on the soffitt (36”x 48”).
- **Ravdin Ground**
  On the wall to the left of Visitor Elevator #3 above the mailbox (24” x 36”).
- **Silverstein Ground**
  On the wall opposite from the Vending Machines centered in between the strobe lights (36” x 48”).
- **Ravdin Ground**
  On angle wall opposite from the Entrance door to the PEEC (36 x 48).
- **Dulles Ground**
  On wall across from Passenger Elevator Car #2 next to the directional sign (35” x 48”).
- **Dulles 2nd Floor**
  On wall across from Freight Elevator Car #1 (36” x 48”).
- **Gates Lobby**
  On the wall to the left of the Fire Panel and right of the Electrical Closet (24” x36”).
- **Rhoads Link 1st Floor**
  On the wall across from the Fire Command Center (36” x48”).

Newspapers

- Philadelphia Inquirer (philly.com)
- Philadelphia Daily News (philly.com)
- Philadelphia City Paper (citypaper.net)
- Philadelphia Business Journal (http://philadelphia.bizjournals.com/philadelphia/)
- Philadelphia Gay News (http://www.epgn.com/paper.asp?paper=1)
- Al Dia (http://news.aldiainc.com/) - Spanish language weekly newspaper
- Philadelphia Tribune (http://www.phila-tribune.com/)
- Philadelphia Weekly (http://www.phillyweekly.com/)
- Philadelphia Metro (www.metropoint.com)

Local Magazines

- Philadelphia (phillymag.com)
- Main Line Today (http://www.mainlinetoday.com/)
- Philadelphia Style (www.phillystylemag.com)
- Neighborhood papers

Penn Publications

- Check your department's publication or newsletter
- The Pennsylvania Gazette (www.upenn.edu/gazette) - for alumni
- Daily Pennsylvanian (www.dailypennsylvanian.com) - for students
- 34 th Street Magazine (www.dailypennsylvanian.com)
- The Almanac (www.upenn.edu/almanac)
- Health System Periodicals (www.uphs.upenn.edu/prnews/publications)
    - Includes HUPDate, Penn Medicine, Penn Pulse, Quill, and Presby Bulletin

Radio Stations

FM Radio

- WXPN 88.5 (www.xpn.org) - University of Penn station
- WRTI 90.1 (www.wrti.org) - Temple University's station
- WHYY 90.9 (www.whyy.org) - PBS television and NPR radio affiliate
- WXTU 92.5 (www.wxtu.com) - country station
- WMMR 93.3 (www.wmmr.com) - rock 'n roll
- WSTW 93.7 (www.wstw.com) - Delaware station for hit music
- WYSP 94.1 (www.94wysp.com) - rock station
- WBEN 95.7(www.957benfm.com) - hit music
- WRDW 96.5 (www.wired965.com) - hip hop and rap
- WKDU 97.1 (www.wkdu.org) - Drexel University station
- WPST 97.5 (www.wpst.com) - hit music
- WUSL 99 (www.power99.com) - urban contemporary music
- WPLY 100.3 (www.y100.com) - alternative rock
- WBEB 101.1 (www.b101radio.com) - soft rock
- WILQ 102.1 (www.q102philly.com) - hip/hop, dance
- WMGK 102.9 (www.wmgk.com) - classic rock
- WSNI 104.5 (www.alice1045.com) - hit music
- WDAS 105.3 (www.wdasfm.com) - classic soul and R&B
- WJJZ 106.1(www.wjjz.com) - smooth jazz

AM Radio

- WFIL (www.wfil.com) - Christian talk radio
- WIP 610 (www.610wip.com) - sports radio. Home of the Sixers and Flyers
- WEEU 830 (www.weeu.com) - Berks County talk radio
- ESPN 920 (www.920espn.com) - ESPN Philadelphia sports station
- WPEN 950 (www.wpen.com) - American standards, Phillies
- KYW 1060 (www.kyw1060.com) - all news station

WDEL 1150 (www.wdel.com) - Delaware talk radio
- WPHT 1210 (www.thebigtalker1210.com) - Local and national talk show hosts
- WNJC 1360 (www.wnjc1360.com) - variety, news, talk, oldies
- WCOJ 1420 (www.wcoj.com) - Chester County variety
- WILM 1450 (www.wilm.com) - Delaware all news station
- WDAS 1480 (www.wdasam.com) - gospel music
- WBCB 1490 (www.wbcb1490.com) - Bucks county talk and music
- WNWR 1540 (www.wnwr.com) - multicultural programming

Television Stations

- Comcast SportsNet Philadelphia (philadelphia.comcastsportsnet.com) - cable sports network for the mid-Atlantic states
- KYW 3 (www.kyw.com) - CBS affiliate
- WCAU 10 (www.nbc10.com) - NBC affiliate
- WHYY (www.whyy.org) - PBS television and NPR radio affiliate
- WPHL 17 (www.wb17.com) - WB affiliate
- WPSG 57 (www.upn57.com) - UPN affiliate
- WPVI 6 (abclocal.go.com/wpvi) - ABC affiliate
- WTFX 29 (www.foxphiladelphia.com) - Fox affiliate
- WTVE 51 (www.wtve.com) - Christian programming

Web Sites

- CenterWatch (centerwatch.com) - includes local classified ads
- Philly.com (philly.com) - includes local classified ads
- Craigslist.org (philadelphia.craigslist.org) - free posting of classified ads

Direct Mailing

City List Co.

City List Company provides direct mail services focusing specifically on recruitment for clinical trials. The mailing addresses are acquired through survey data that the respondents voluntarily provide, and can be queried for specific areas, disease conditions, and treatments. This services is HIPAA-compliant as the researcher never receives the names or addresses of the individuals. City List develops and prints the flyer, then addresses and mails directly to the consumers.

For more information, contact Dawn Peltier at 1-888-299-1202 or visit www.citylistco.com.

Advertisement Examples

To see the full-size examples of each ad, click on the image.

Standard Newspaper Ad - short, catchy wording, no graphic

DOES IT HURT TO MOVE? Are your joints painful and swollen?
Do you have Rheumatoid Arthritis? If you answered YES to these questions....
Come join a rheumatoid arthritis research study at the University of Pennsylvania.
For more information call Susan at 215-662-XXXX
Compensation will be provided.

2- Column Ad

This ad, a 2-column x 5" ad was developed by Penn Publication Services (formerly Creative Communications). Penn Publication Services can help design ads and also have already negotiated prices with local papers for advertising.

www.hrposervices.upenn.edu/publications/forms

Click on image for ad download as PDF file

CenterWatch Ad

CenterWatch, a clinical trials listing service, requires more information than a typical ad, and also requires a copy of the IRB approval letter for the ad.

www.centerwatch.com

Click on image for ad download as MS Word document

Flyer/Flyer with Tabbed Tear-Offs

Click on image for flyer download as PDF file

Click on image for flyer download as PDF file

Brochure

Click on image for brochure download as MS Word document

Clinical Trials Web Posting

All U.S. drug or device clinical trials must be registered on the ClinicalTrials.gov website in accordance with requirements published by the International Committee of Medical Journal Editors (ICMJE) and the FDA Amendment Act of 2007. The following clarifies who is responsible for registering your clinical trial:

1. Faculty holding IND or IDE applications with the FDA: the Penn faculty IND/IDE holder is required to register the clinical trials conducted under the IND/IDE application
2. Investigator-initiated, government-sponsored clinical trials: Generally the sponsoring federal or state agency is required to register the clinical trial
3. Industry-sponsored clinical trials: the industry sponsor is required to register the clinical trial

Note: A Penn investigator may receive permission from the industry sponsor or the government funding sponsor to register a study on the ClinicalTrials.gov website. For **cancer clinical trials, the Abramson Cancer Center** may assist you in registering your trial through an NCI-sponsored system that interfaces with the ClinicalTrial.gov system.

In order to register your trials directly to ClinicalTrials.gov, you will need to designate a person who will be responsible for posting your clinical trials, and request an account from the ORA Clinical Trials administrator for that individual. That individual can then submit the required information for your clinical trials to be approved by an ORA Clinical Trials administrator

The ORA Clinical Trials administrators are responsible for all clinical trial information that is released to ClinicalTrials.gov from the University of Pennsylvania. Prior to releasing the trial information for public access, the ORA Clinical Trials administrators must ensure the following for each submission:

1. There are no system-generated red error warnings in the submission;
2. The study is IRB approved; and
3. If the listed collaborator is an industry sponsor, that written authorization for posting has been provided by the industry sponsor

When entering your registration information into the ClinicalTrials.gov web form, please ensure that all red error warnings have been resolved prior to clicking the "Complete" button. The red error warnings indicate missing or discrepant information, and the ORA administrator cannot release the trial for posting with unresolved errors.

To request a ClinicalTrials.gov account, please contact Ms. Kituria Gaines or Mr. Patrick Stanko at irbct@exchange.upenn.edu.

For more information, visit ClinicalTrials.gov at http://www.clinicaltrials.gov/.

If your study is already registered please visit Clinical Trials Login at https://register.clinicaltrials.gov/.

IRB Submission

The Institutional Review Board (IRB) is an independent committee that oversees the protection of human subjects. This committee reviews research studies and the ongoing activities of approved research.

In compliance with federal regulations, the IRB must include at least 5 people including men and women and representing various professions and affiliations. At least one member may not be affiliated with the institution. Minimal attendance at a meeting, called a quorum, is defined as a convened meeting with a majority of members present including one member whose primary concerns are nonscientific. The regulations require that a quorum be present in order for the full board to review full board actions, including new studies, amendments, continuing review of previously reviewed research, reports of unanticipated problems posing risk to subjects or others, and reports of serious or continuing noncompliance with the regulations.

Penn IRB Review

The term IRB is often used synonymously with the Office of Regulatory Affairs; however, the Office of Regulatory Affairs is the administrative office supporting the IRBs. The Office of Regulatory Affairs includes both the IRB and Institutional Animal Care and Use Committee (IACUC). Penn has several different IRB committees with periodic changes in membership; whereas, the Office of Regulatory Affairs has a constant staff that help to manage IRB activities.

Office of Regulatory Affairs
3624 Market Street, Suite 301 S
Philadelphia, PA 19104-6006
Mail Code 6006
Phone: 215-898-2614
Fax: 215-573-9438

The University of Pennsylvania IRB Meeting Schedule

The University of Pennsylvania has eight IRBs that review research protocols.

- Four general medical boards
- Three specialty boards
- One board that reviews social and behavioral research

In general, there are two IRB meetings each week of the month.

Researchers can call the Office of Regulatory Affairs to find out which board has been assigned the protocol, whether it has been assigned an IRB protocol number, and when it will be reviewed. Faculty are able to track the status of a submitted protocol through Ben Reports, an administrative system developed to track and report protocol review status (http://benapps.isc-seo.upenn.edu/).

A protocol will normally be reviewed approximately two to four weeks after submission, depending on the level of review, the completeness of the submission and the board assignment. The time from submission to a board will vary as a function of the meeting schedule of the IRB appropriate to a specific protocol. A General Medical board meets weekly, specialty boards meet twice per month and the social and behavioral board meets once per month. The schedule can be found online at www.upenn.edu/regulatoryaffairs/human/meet2.html.

Determining IRB Review Type

These are general guidelines to determine the level of risk and corresponding IRB review mechanism and submission requirements for research protocols involving human subjects. Other factors that may impact review type include: the involvement of vulnerable populations, the use of protected health information (PHI), privacy/confidentiality issues, psychological effects, conflicts of interest, experience of research team, etc. Assessing the review type for a study will determine the requirements for submitting the study to the IRB for review. Please note that the IRB makes the final determination of level of review.

The first question one should consider when assessing the requirement for IRB review is whether the activity meets the regulatory definition of human research (see Human Subject Research).Anyone unsure of about IRB review requirements and whether their proposed activity constitutes “human research” requiring IRB review should contact the Office of Regulatory Affairs. The IRB staff will determine if the activity is human research. If an activity does not meet the regulatory definition of human research, the IRB will, upon request, issue a letter stating that the project does not require IRB review or approval.

The IRB provides a helpful guidance document and research determination worksheet to assist with this determination: “Is IRB Review Required?”, available from www.upenn.edu/regulatoryaffairs/human/IRBGuides.html.

Once it is determined that the project meets the definition of human research, the level of review must then be determined. The initial criteria used in determining the review level is ascertaining if a study meets the criteria for minimal risk. Minimal risk research may be eligible for either expedited or full board review.

Minimal risk means that the risk of harm anticipated in the proposed research that is not greater, considering the probability and magnitude, than those ordinarily encountered in daily life of a healthy individual or during the performance of routine physical or psychological examinations or tests."

Below are general guidelines for determining the review level. All research-related activities within a study must fall in their entirety within the exempt categories in order to qualify for exempt status. This is also true for expedited review.

Exempt From Review

DHHS and FDA regulations allow specific categories of research to be exempt from human subject review. Research that is considered exempt from Committee review must still be filed with the IRB and screened for exempt status. Protocols qualifying for exempt status receive a three year approval period and do not require annual continuing review. Investigators are required to notify the IRB if any changes are proposed that could alter the exempt status of the protocol.

Categories of Exempt Research

Following is a list of categories that are typically eligible for Exemption from IRB Review. Additional conditions and limitations exist for each category as specified in the IRB's Claim of Exemption Instructions. For more detailed guidance on research that may qualify for exemption and instructions for filing a Claim of Exemption visit www.upenn.edu/regulatoryaffairs/human/ApplicationProcedures.html.

NOTE: The FDA only allows research to qualify for Exempt from Review that falls under Category 6 below. All other categories of research that is subject to FDA regulations require Expedited or Full Board Review.

Category 1
Research conducted in established educational settings that involve normal educational practices

Category 2
Research that involves the use of educational tests ONLY (cognitive, diagnostic, aptitude, achievement),or research that involves ONLY observation of public behavior of adults.

Category 3
Research that involves the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or the observation of public behavior.

Category 4
Research that involves the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens if these sources are publicly available.

Category 5
Research and demonstration projects that are conducted by or subject to the approval of federal department or agency heads, and are designed to study or evaluate public benefit or service programs; procedures for obtaining benefits or services under those programs; Possible changes in or alternatives to those programs or procedures; or Possible changes in methods or levels of payment for benefits under those programs.

Category 6
Taste and food quality evaluation that involves wholesome/safe foods

Expedited Review

To qualify for expedited review the following must apply:

a) Research activities must:

- Present no more than minimal risk to human subjects AND
- Involve only procedures listed on **www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm**.

b) Reasonable and appropriate protections must be implemented by the investigator so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability, or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing.

c) The expedited review procedure may not be used for classified (e.g., military) research with human subjects.

d) The standard requirements for informed consent (or its waiver, alteration, or exception) apply.

Protocols qualifying for expedited review are not reviewed by the fully convened meeting, but do require continuing review at least once annually and informed consent (or waiver of informed consent).

Examples of research eligible for expedited review:

- Non-invasive medical procedures that do not involve x-rays or sedation (e.g. MRI, EKG, EEG)
- Minimal blood draw amounts in healthy nonpregnant subjects
- Prospective collection of biological specimens by noninvasive means (e.g. buccal scrapins, saliva, excreta, sputum)
- Voice recordings; research on individual or group behavior such as interviews or focus groups.
- Moderate exercise by healthy volunteers

Note: HIPAA waiver applies to the extent that identifiable data sources are accessed & used. All protocols including medical chart reviews are reviewed with an expedited mechanism and require a HIPAA Waiver of Authorization

Full Board Review

Studies that do not qualify for expedited review require approval by an IRB panel composed of members trained to review research in that field (full board review).

Examples of *minimal risk* research requiring full board review include:

- DEXA scan for bone density
- Any protocol involving X-Rays occurring for the purposes of the research

Examples of *greater than minimal risk* research requiring full board review include:

- Any survey or interview that is likely to be stressful for the subjects
- Research that involves experimental drugs or devices, invasive procedures
- Involve increased risk due to the nature of the research or the population being evaluated.
- Involve a washout period or placebo use in an otherwise treatable disease.
- Involve "greater than minimal risk and no prospect of direct benefit to the individual subjects but likely to yield generalized knowledge about the subject's disorder or condition" (CFR 45 Part 46.406}).

IRB Submission Requirements

For a detailed listing of application procedures and required documents, refer to the IRB Application Procedures at Application Procedures.

Tips for IRB Submission

- Include complete and current mailing address and fax number for Principal Investigator (PI) and study coordinator in the submission.
- Include page numbers, version number & date on all study documents: protocol, protocol summary, informed consent, HIPAA Authorization, etc.

Submission Process

Effective June 2, 2008, IRB submissions may be submitted through the online **HS-ERA System**, as an alternative to the paper submission process. Later in 2008, all submissions will be required to go through the online HS-ERA System.

Online Submission

The Human Subjects Electronic Research Application (HS-ERA) is now available to researchers at Penn. HS-ERA is a new secure, web-based protocol application. HS-ERA may be used by members of the research community to create and submit IRB initial IRB Biomedical or Social and Behavioral Applications.

NOTE: The system may be used to create and submit NEW applications/protocols. Existing applications will not be viewed, edited, or submitted via HS-ERA.

To access the application:

1. With a web browser, go to **https://medley.isc-seo.upenn.edu/hsProtocol/jsp/fast.do**.
2. Authenticate with your PennKey and PennKey password.

Paper Submission

The IRB Biomedical Sciences Application for Review of Human Research consists of 3 sections:

1. IRB Facesheet

- The IRB Facesheet provides a brief overview of the study and identifies which University departments will be involved with the research study.
  - The IRB Facesheet must be signed by the Principal Investigator and the department chair, or if the PI is the department chair, the Dean.
  - In the School of Medicine , the department chair signature can be obtained by submitting the completed IRB Facesheet and a non-returnable copy of the protocol summary to HUP, 1 Gibson in the Research Administration Office.
2. Protocol Summary
3. IRB Required Documents (a checklist of documents to include in the submission along with instructions regarding how many copies to make of each packet)

Submission packets should be dropped off at the Office of Regulatory Affairs:

3624 Market Street, Suite 301 S
Philadelphia, PA 19104-6006
Mail Code 6006
Phone: 215-898-2614
Fax: 215-573-9438

IRB Post-Review Actions

Following the IRB review of the study, one of the following outcomes will result. The follow-up actions taken by the investigator depend upon the outcome of the IRB review.

Outcomes

Approval
No action is needed. The study can begin provided that approval has been received from all other applicable penn reviewing entities (see Other Penn Reviewing Entities).

Withheld approval pending clarification
The IRB will provide the investigator with specific modifications that are necessary for approval. Revise the study documents and provide clarifications as recommended. Return one copy with the revisions highlighted for expedited review. Response is reviewed by an expedited mechanism and does not need to return to the full board for initial approval.
The study cannot begin until the revised submission has been approved.

Tabled
The IRB will provide the investigator with specific questions that need to be addressed before approval will be considered. Revise the study documents as recommended. Return 15 copies of the revised documents as would be done for a full review submission. Tabled studies are re-reviewed by the full IRB. Investigators are encouraged to attend the IRB meeting following a tabled decision.
The study cannot begin until the revised submission has been approved.

Disapproval
The investigator may discuss the review with the IRB Chairperson. The protocol must be resubmitted in its entirety as per the Submission Requirements.
The study cannot begin until the new submission has been approved.

Investigators whose studies are not approved can benefit from a consultation with the Office of Human Research on issues such as protocol design, informed consent and other human subject protection issues.

External Institutional Review

When conducting a multi-center study (the protocol will be conducted at other institutions), the study must be submitted to all the respective IRBs. For example, the Philadelphia Veteran's Affairs (VA) hospital and the Children's Hospital of Philadelphia (CHOP) function under their own IRBs.

Penn-CHOP Cooperative Agreement

Effective December 2005, the IRBs of Penn and CHOP established a cooperative agreement under which collaborative research can undergo a single IRB review in certain situations. This agreement significantly reduces the need for dual IRB review. Depending on the nature of the collaboration, the research may be reviewed by either the Penn IRB or CHOP's IRB. To review the specific scenarios and procedures, refer to the memo from the Office of the Vice Provost for Research that defines this agreement (http://www.med.upenn.edu/ohrobjects/PM/2_pennchopdetermination.doc).

Other Penn Reviewing Entities

Abramson Cancer Center (ACC)

The Abramson Cancer Center (ACC) is responsible for overseeing all cancer research being conducted at the UPHS, whether or not the research is funded by the National Cancer Institute (NCI). The Cancer Center has a scientific peer review committee, known as the *Clinical Trials Scientific Review and Monitoring Committee* (CTSRMC), which is responsible for reviewing cancer-related protocols.

Required Protocol Submission to the Cancer Center

The CTSRMC reviews *protocols involving cancer subjects*. This requirement is mandated by NCI 's policy for Comprehensive Cancer Centers. Cancer-related protocols that must be submitted for approval include all investigator-initiated studies, industry-sponsored studies, and any protocol that is not part of a national cooperative group. National cooperative group protocols must be sent to the CTSRMC for tracking but not approval.

Protocol Submission Process

The CTSRMC meets on the second Monday of every month to review protocols. Information required for submission to the CTSRMC include:

- IRB Facesheet
- Study protocol
- IRB protocol summary
- Informed Consent Form
- Investigational drug/device brochure (if applicable)
- Monitoring plan.

For more information about the CTSRMC and detailed instructions about the application process, please see the following ACC weblink: www.ctsrmc.org/submitting_a_protocol.php.

ACC Contact Information

Abramson Cancer Center of the University of Pennsylvania
3400 Spruce Street, 2017 Penn Tower
Phone: 215-349-5238
Fax: 215-662-2139

Timing ACC and IRB Submission

Protocol submission to the ACC should be done before the IRB submission.
Note: No cancer-related protocol may initiate subject enrollment at Penn without both IRB and CTSRMC approval.

Center for Advanced Computer Tomography Imaging Services (CACTIS)

CACTIS works to establish policies and procedures for the research use of Computed Tomography (CT) scanners within the Department of Radiology. The mission of CACTIS is to oversee proposed research protocols involving human or animal studies to ensure all research performed within the CT facilities complies with CACTIS policy, University policy and federal regulations.

Required Protocol Submission to CACTIS

Authorization from CACTIS is required for all studies using CT scanners that fit into one of the following categories:

- Studies conducted on normal volunteers for the purposes of a final modification of protocols and/or acquisition of preliminary data (pilot studies). Investigators must provide their own “normal subjects” consent form.
- Research studies carried out on patients and/or control groups. However, the study design does not include the use of the ct data to guide clinical decisions and there is no treatment component of the protocol. Investigators must provide their own consent forms
- Clinical trials: studies are carried out on patients and/or control groups. The study results are used to guide clinical decisions and/or treatment as part of the study protocol. Investigators must provide their own consent forms

Protocol Submission Process

CACTIS is a review committee that meets every two weeks to review protocols.

Submission materials include: CACTIS application, copy of IRB approval letter, IRB approved consent form, IRB face sheet, CT protocol, protocol summary, fullprotocol, copy of radiography/flouroscopy operators certification, copy of the radiation safety approval letter, drug brochure/package insert for outside contrast agents, and for studies involving cancer patients a copy of the approval letter from CTSRMMC.
- The instructions and application can be found online at **www.uphs.upenn.edu/radiology/depa/CACTIS**

CACTIS Contact Information

Department of Radiology
Melissa Myers, BS, RT(R), RDMS
Hospital of University of Pennsylvania, Silverstein 1
Phone: 215-349-5891
melissa.myers@uphs.upenn.edu

Timing CACTIS and IRB Submission

Protocol submission to CACTIS should be done before the IRB and Radiation Safety submissions.
Note: CACTIS will not set up a billing account until they have received a copy of the IRB approval letter and stamped consent form.

Center for Advanced Magnetic Resonance Imaging & Spectroscopy (CAMRIS)

The Center for Advanced Magnetic Resonance Imaging and Spectroscopy (CAMRIS) oversees the research use of magnetic resonance imaging (MRI) and spectroscopy equipment in the Department of Radiology.

Required Protocol Submission to CAMRIS

Research protocols that involve MRIs or spectroscopy specifically for research purposes must obtain CAMRIS approval. If an MRI/spectroscopy is performed as part of standard of care, the study is not subject to CAMRIS review. CAMRIS ensures that research involving MRI facilities complies with University policies and federal regulations and determines whether resources are available to carry out the research protocol.

Protocol Submission Process

CAMRIS is a review committee that meets every two weeks to review protocols.

- Submission materials include: CAMRIS application, protocol (including data analysis plan), informed consent, copy of IRB facesheet, copy of approval of experimental coils/ sequences/software (if applicable), copy of study plan from study grant (if applicable).
- The instructions and application can be found online at **www.mmrrcc.upenn.edu/CAMRIS**

CAMRIS Contact Information

Center for Advanced Magnetic Resonance Imaging and Spectroscopy
Hospital of University of Pennsylvania, 1 Founders
Phone: 215-349-5470

Timing CAMRIS and IRB Submission

Protocol submission to CAMRIS should be done before the IRB submission.
Note: CAMRIS will not set up an MRI billing account until they have received a copy of the IRB approval letter and stamped consent form.

Clinical and Translational Research Center (CTRC)

The Clinical and Translational Research Center (CTRC) is a special research unit funded by the National Institutes of Health (NIH) to provide facilities and nursing care for research subjects. The CTRC has inpatient and outpatient nursing beds, a core laboratory, nutritionists, bioinformatics and a statistical consultant that provide research services to investigators.

Required Protocol Submission to the CTRC

Submission to the CTRC is not required. It is a voluntary decision made by investigators who wish to utilize CTRC resources. Investigators may want to employ the specialized services available through the CTRC. NIH-funded projects and those that are investigator-initiated may qualify to use CTRC facilities without cost. Industry-sponsored studies must pay for the use of these services, but may want to use the CTRC to help execute research procedures in a controlled setting. See Resources for Researchers for more information.

Protocol Submission Process

The CTRC's Scientific Advisory Committee is a scientific peer review committee that meets on the last Monday of every month to review protocols. This review determines priority of funding for eligible studies. The Principal Investigator is present during the review.

- Submission materials include: CTRC application, protocol, protocol summary, informed consent, investigational drug/device brochure (if applicable), biographical sketch in NIH format, Patient Oriented Research Certificates, and other grant support (if applicable).
- The instructions and application can be found online at **http://www.itmat.upenn.edu/ctrc.shtml**

CTRC Contact Information

Clinical Translational and Research Center
Hospital of University of Pennsylvania , 1 Dulles
Phone: 215-662-2641
Fax: 215-662-2643

Satellite:
Penn Presbyterian Medical Center
3 PHI, Room 379
Phone: 215-662-9026
Fax: 215-243-3424

Timing CTRC and IRB Submission

Protocol submission to the CTRC should be done before the IRB submission.
Exception: Cancer protocols should submit after approval is obtained from the IRB and CTSMRC.
Note: The CTRC will not send out a final approval letter until they have received a copy of the IRB approval letter and stamped consent form.

Conflict of Interest Standing Committee (CISC)

The Conflict of Interest Standing Committee (CISC) reviews potential conflicts of interest held by investigators and their research staffs, and recommends management strategies to the Vice Provost for Research. The CISC consists of approximately 10 members of the standing faculty appointed by the Vice Provost for Research.

Requires Submission to CISC

If the investigator or any member of the research team has any equity/financial interest in the research or if any payments are received from the study sponsor other than the usual and customary fees for conducting the research study, the individual must disclose this to the IRB. The IRB will determine whether the financial interest meets the institutional definition of a significant financial interest constituting a conflict of interest that must be reviewed by the CISC. Additional information, including the policies on conflict of interest can be found online at www.upenn.edu/research/rcr/conflict.htm.

In other words, if the answer to the question noted in the IRB submission system section on Disclosure of Financial Interests is " *yes"*, the investigator must disclose the interest to the IRB:

"Does any person who is responsible for the design, conduct, or reporting of this research protocol have a FINANCIAL INTEREST, ... including:

- *You and your spouse, parents and any children*
- *The spouses, parents and any children of any person responsible for the deign, conduct or reporting of this research; and*
- *Any corporation, foundation, trust or other entity controlled or directed by any of the above individuals?"*

Submission Process

The CISC meets every 2-4 weeks as needed to review conflict of interests.

- Submission materials include : Confidential Financial Disclosure Statement with a copy of the protocol or grant application (Additional materials may be requested as needed).
- The Confidential Disclosure Statement can be accessed at **www.upenn.edu/researchservices/pdfs/findisc.pdf**. The Confidential Financial Disclosure Statement should be submitted in a sealed envelope.

CISC Contact Information

Office of the Vice Provost for Research
118 College Hall, University of Pennsylvania
Phone: 215-898-3602
Fax: 215-573-2108

Environmental Health and Radiation Safety (EHRS)

The Environmental Health and Radiation Safety (EHRS) is a section of the Office of the Vice Provost for Research that is responsible for education and compliance involving environmental hazards such as chemicals, human blood, blood products, fluids, and human tissue specimens.

Required Protocol Submission to EHRS

- *Human Gene Transfer and Human Vaccine protocols* must be approved by the Institutional Biosafety Committee (IBC) prior to initiation.
- *Radioactive material and/or x-rays* administered to subjects solely for research purposes must be approved by the Radioactive Drug Research Committee (RDRC) prior to their initiation.
- *"Select Biologic Agents or Toxins* ". Use of these agents or toxins must be approved by EHRS and registered with the USDA. A list of these agents can be found at: **www.ehrs.upenn.edu/protocols/slctagnts_list.html**.

Protocol Submission Process

1. Human gene transfer and vaccine studies must be submitted to the Institutional Biosafety Committee (IBC). The IBC meets every other month to review protocols.
   - Submission materials include: Registration Document for Recombinant DNA Research, protocol, investigator's brochure, and Appendix M/Points to Consider (for gene transfer research).
   - Instructions and forms can be found at: **www.ehrs.upenn.edu/protocols/bio_humans.html**

2. Protocols administering radioactive materials and/or x-rays must be submitted to the Radioactive Drug Research Committee (RDRC). The RDRC meets the third Friday of the month to review protocols.
   - Submission materials include: protocol, protocol summary, consent, IRB facesheet, and investigational brochure.
   - Instructions can be found at: **www.ehrs.upenn.edu/protocols/radiohuman.html**

3. Studies involving one of the "Select Biologic Agents or Toxins" must be submitted to the IBC . Additionally, the procedure for registering with EHRS and the appropriate federal agencies can be found at: **www.ehrs.upenn.edu/protocols/sa_registration.html**

EHRS Contact Information

Environmental Health&Radiation Safety
3160 Chestnut Street, Suite 400
Phone: 215-898-4453
Fax: 215-898-0140

Timing EHRS and IRB Submission

Protocol submission to the EHRS should be done before the IRB submission.
Note: The IRB will not approve the protocol until it receives documentation of EHRS approval.

Hospital Perioperative Services

Hospital Perioperative Services is responsible for operational oversight within the UPHS Operating Rooms. The group is comprised of key clinical and administrative personnel within each hospital. Researchers must obtain permission from Perioperative Services in order to conduct research involving investigational devices in any UPHS Operating Room.

Required Protocol Submission to Perioperative Services

Research protocols that involve investigational devices that will be used, deployed, or evaluated in UPHS Operating Rooms must be authorized by the Hospital's Perioperative Services. The group requires that research projects have specific systems in place in order to ensure device costs, accountability, correct billing procedures, and staff training.

Protocol Submission Process

The Perioperative Services group at each hospital meets every week and will review protocols as needed on an ongoing basis.

- Submission materials include: protocol, protocol summary, device brochure, copy of contract or clinical trial agreement, and device catalog #'s.

Contact Information

Hospital of the University of Pennsylvania
Senior Project Manager of Perioperative Services and Materials
1214 Penn Tower
Phone: 215-615-4493

Pennsylvania Hospital
Director of Perioperative Services
PAH, 9 Schiedt
800 Spruce St .
Phone: 215-829-5975
Fax: 215-829-5310

Penn Presbyterian Medical Center
Director of Perioperative Services
PMC , 107 Wright-Saunders
51 N. 39 th Street
Phone: 215-662-9376
Fax: 215-243-3298

Timing Hospital Perioperative Services Submission and IRB Submission

Submission to Perioperative Services can be done concurrently or after the IRB submission.
Note: The project cannot be initiated in the operating room until it has received authorization from the Hospital's Perioperative Services and has a fully executed contract/clinical trial agreement in place.

Investigational Drug Service

The Investigational Drug Service (IDS) is a research pharmacy charged with overseeing pharmaceutical products (and some devices) used in clinical research throughout the UPHS. The IDS ensures that the medication dispensed meets FDA regulations, JCAHO guidelines, and state regulations.

Required Protocol Submission to the IDS

All research protocols involving pharmaceutical products (including medications, over-the counter-drugs, vaccines, gene therapy, supplements, etc.) are required to register with the IDS , whether or not the services of the research pharmacy are utilized.

Protocol Submission Process

The IDS pharmacist will review the protocol and, if applicable, provide the investigator with a budget for the estimated pharmacy expenses.

- Submission materials include:

- The study drug and/or investigational devices of the research pharmacy are being requested - registration form and protocol
  - If the study involves outpatients and the study drug supply is being managed at the study site or through use of a different pharmacy- registration form and protocol summary
- The Instructions and registration can be found online at **www.itmat.upenn.edu/ids/ids_forms.shtml**.

IDS Contact Information

Penn Investigational Drug Service
3400 Spruce Street , Maloney Bldg, Ground Floor
Phone: 215-349-8817
Fax: 215-349-5132

Timing of IDS and IRB Submission

Registration of the protocol with the IDS should occur before the IRB submission. The IDS will provide a registration number that is needed for the IRB submission system.

Contracts and Study Finances

Study Budget Development

When requesting funding for a study, all study-related costs should be noted in the budget including personnel, consultants, equipment, supplies, travel, and other expenses. NIH applications have special Budget and Justification forms that contain detailed instructions. Penn investigators must have their grant budgets approved by the Office of Research Support Services (ORSS). The proposal should be submitted to ORSS at least eight working days prior to the planned date for grant submission.

Penn sponsor-investigators should develop a budget based upon the expected expenses **at each site**. Billing rates for the same procedure will vary from place to place.

When considering an industry sponsored-study all study related expenses should be determined and compared to the overall reimbursement offered by the sponsor to ensure the study is financially feasible.

Depending on the funding source, items may or may not be included in the budget and expenses may or may not have an associated overhead charge. Information on specific allowable expenses and overhead charges for federal grants can be found in the Chart of Allowable Expenses. The Chart of Allowable Expenses lists expenses that may be included in a budget for industry-sponsored studies versus federally-funded studies, along with applicable overhead rules.

The following is a list of potential expenses involved in the conduct of a study:

Personnel

Estimate the amount of time for the PI, the coordinator(s), and any other staff that would be paid out of the study budget (i.e. research assistants, administrative staff, statisticians). This estimate should include not only salary, but also fringe benefit costs.

Labs, Tests, and Procedures

Technical Fees - A technical fee is the cost incurred for use of the mechanical equipment and processing. Tests/procedures that are study related and are not "standard of care" must be charged to the research budget. All costs should be based on the currently approved technical "research rate".

Professional Fees - The professional fee is the physician's charge for interpretation of diagnostic procedures/tests. It is important to note that if there is a professional fee associated with a test/procedure you must include that charge in your expenses. A limited number of laboratory tests have professional fees associated with them. All radiology and cardiology procedures have a professional fee, as do various other procedures. All costs should be based on the currently approved professional "research rate".

Subject Reimbursement

These charges may be incurred per visit or per subject. Examples include monetary compensation, meals and parking/transportation costs.

Additional Study Expenses

Other potential study expenses to consider:

Training Seminars/Conferences (directly related to the research projects)
  - Travel expenses
- Institutional Review Board (IRB) fees
- Investigational Drug Service (IDS) fees
- Advertising/Recruitment
- Sub-contracts
  - Clinical Research Computing Unit (CRCU) fees
  - Biostatistics and Epidemiology Consulting Center (BECC) fees
  - External Monitor or Contract Research Organization (CRO)
- Monitoring
  - Travel Expenses
- Non-refundable start-up costs
- Screen failures
- Supplies
  - E.g. blood collection tubes, chemicals, dry ice)
  - E.g. centrifuges, mass spectrometers, liquid simulation counters)
  - Technology (e.g. telephone, computer)
  - Shipping/Packaging Supplies (e.g. dry ice)
- Service Contracts (e.g. instrument maintenance)
- Medical Record Pulls
- Archival fees
- Site Visit&Site Initiation Costs
  - Travel Expenses

Facilities and Administrative Cost

Facilities and Administrative (F&A) cost is the indirect cost associated with the project or study; e.g. space, research administration, facilities, maintenance, human resources, etc. The Penn standard approved F&A rates are as follows:

- 26% for industry-sponsored studies
- 57% for federally-funded studies.

F&A can only be assessed on certain activities and items depending on whether or not the study is federally-funded (see the specific grant guidelines). For industry-sponsored studies, the contract may specify which items can include F&A, though typically F&A is applied to all costs for industry-sponsored studies. If you cannot locate the F&A rule on the Chart of Allowable Expenses, you can consult with the Office of Research Support Services.

Available on the Office of Human Research (OHR) website is a Chart of Allowable Expenses to include in a budget for industry-sponsored studies versus federally-funded studies, along with applicable overhead rules.

CostFinder application

Penn Medicine provides standardized research rates for all Health System tests/procedures. Penn Medicine researchers can access this institutionally maintained costing information through the CostFinder application at this web address: www.med.upenn.edu/apps/my/costfinder.

The CostFinder tool supports searches for specific clinical services, tests, or procedure by name, CPT code, or hospital Service Code. The costs displayed are the institutional standard research rates, to be used for budget development for all clinical research studies utilizing Penn Medicine clinical tests/procedures. The costing information is applicable to all studies regardless of funding source (e.g. Federal Government, Industry , Foundations, etc.). This tool displays both the technical fee and the professional fee (if applicable) components of a given procedure. Users can even create a customizable "My Lists" to store commonly used tests/procedures important to the user. Any such customized lists in the tool always display the current institutional rate, regardless of how long the "My List" is maintained by the user.

Contract Submissions

Contract Submission for Sponsored Research

Contracts should be submitted with an appropriately developed budget (See Study Budget Development**)** to your Department Business Office as soon as possible to ensure that negotiations with the sponsor are resolved and project initiation is not delayed.

The following documents should be included in a contract submission packet, which is submitted to the Department Business Office (Business Administrator):

- Copy of ORS (Office of Research Services) Proposal Transmittal Form (4 copies)
- Clinical Trial Agreement (CTA) with Grant/Budget and Indemnification (2 originals, 2 copies)

- Protocol (1 copy)
- Protocol Summary (4 copies)
- Informed Consent (4 copies)
- IRB facesheet (4 copies)

Document Submission for Investigator-initiated Research

Documents should be submitted with an appropriately developed budget (See Study Budget Development) to the Department Business Office as soon as possible to ensure that the project initiation is not delayed. The following documents should be submitted to the Department Business Office (Business Administrator):

- Copy of ORS Proposal Transmittal Form (4 copies)
- Contract (negotiated with the funding agency) with Grant/Budget and Indemnification (2 originals, 2 copies)
- Protocol (1 copy)
- Protocol Summary (3 copies)
- Budget for grant or sponsorship
- A letter that describes the limitations and conditions or intention for use and the dates of administration (include a copy of the award letter from the sponsor)

The contract submission packet, for either Investigator-Initiated or Sponsored Clinical Trials follows the process below:

Office of Research Services (ORS) Proposal Transmittal Form

- The *Proposal Transmittal Form* is similar to the IRB Facesheet in that it provides contact and background information for the study and notifies the responsible Penn business offices of the potential project.
- Before submitting to the ORS, the Investigator, and the Department Chair must sign the Proposal Transmittal Form. Once the appropriate signatures are obtained, the entire contract packet is reviewed by the Office of Research Support Services (ORSS) for budgetary and School of Medicine Requirements. The documents will then be forwarded to the Office of Research Services (ORS) for processing.
- Penn's Proposal Transmittal Form, along with instructions for completion, can be found online under 'forms and agreements' at www.upenn.edu/researchservices.
- **Note**: For *Letter of Responsibility* requirement, all research and training proposals must carry as Principal Investigator or Co-Principal Investigator at least one person holding academic rank of professor, associate professor, or assistant professor. Otherwise, the proposal must include a letter of responsibility for study activities.

Clinical Trial Agreement (CTA)

The Clinical Trial Agreement is a contract between Penn and the industry research sponsor that includes provisions to define the scope of work, performance period and enrollment of subjects, cost and payment, proprietary rights, and publications.

- The CTA represents the legal agreement between the Sponsor and the Trustees of the University of Pennsylvania and an acceptance of such by the Investigator.
- There is a standard contract that Penn uses as a template for clinical trials. Penn's contract template can be downloaded from: www.upenn.edu/researchservices/pdfs/ClinicalTrial.pdf

- The elements of a research contract may include: (1) Scope of work, (2) Responsible investigator (Principal Investigator), (3) Performance period, (4) Record-keeping obligations, (5) Reimbursement, (6) Confidentiality of Information, (7) Patents and Inventions, (8) Advertising (mutual agreement covering use of institution or sponsor's name), (9) Indemnification (see below), (10) Termination of the Contract, (11) Publication Rights/Intellectual Property.

Penn has instituted Master Clinical Trial Agreements (CTA) with a number of companies. These agreements are available from Clinical Trial Agreements (CTA) Master/Standard Agreements

The companies for which there is an existing Master CTA include:

• Alexion Pharmaceuticals Inc. • Amgen • Bayer Corporation • Berlex • Bristol-Myers Squibb • Pharmaceutical Research Institute • Cephalon • Cook	• Eli Lilly&Co. • Gambro • Genetics Institute, Inc. • GlaxoSmithKline • Merck & Co., Inc. • Millenium • Novartis Pharmaceuticals Corporation • Ortho Biotech	• Pfizer-Groton • Pfizer-NY • Purdue • Schering-Plough Research Institute • Scripps Clinic Liver Research Consortium • TAP Pharmaceuticals • Wyeth-Ayerst Research

A Clinical Trial Agreement may be submitted along with a Request for Early Review (www.upenn.edu/researchservices/pdfs/clintrlreq.pdf) to the Office of Research Services. Typically the

ORS requests only a budget and consent form, though otherwise does not require any other additional information, which allows the ORS to begin negotiation before the protocol is submitted to the IRB.

Budget Agreement

- The budget agreement is a part of the Clinical Trial Agreement and specifies the reimbursement to be paid per enrolled subject, the miscellaneous and non-subject expenses, and the reimbursement schedule. Refer to **Study Budget Development** for more details.

- The budget should be evaluated and negotiated during the review of the protocol or grant/proposal submission and should realistically capture all costs associated with conducting the research, including faculty time commitment.
- Payment is usually received in the Office of Research Services where an account is set up to receive funds (26-digit BEN Financial account). The appropriate business administrative office will be notified when the account is active and expenses can be charged to the study account.

Indemnification Agreement

- The indemnification language of the Clinical Trial Agreement protects the investigator and institution from liability for damage incurred by a research subject as a result of study participation. This protection is contingent upon the investigator practicing standard of care medicine and complying with the protocol and regulatory requirements and GCP standards.
- The sponsor is held accountable for medical expenses incurred by research subjects as a result of study participation. It does not obligate the sponsor to reimburse for "standard medical care" or care that would have occurred irrespective of study participation.
- In certain types of research, the sponsor may not be accountable for all expenses incurred by a subject's participation in a study. One example is cancer research where expenses for certain procedures and drug regimens are often borne by the subject's insurance carrier

Site Implementation

Site Selection for Multi-Center Studies

For multi-center studies, it is the responsibility of the sponsor to choose sites to participate in the research study. The sponsor may be an investigator collaborating with other institutions or a pharmaceutical company conducting a multi-center trial. Regardless, sponsors and sponsor-investigators should follow the criteria set forth in Good Clinical Practice Guidelines 5.6.1. The selection process identifies investigators who are qualified and have adequate resources to implement the protocol.

The following items are evaluated during the site selection process:

Suitability of the investigator

- Does the investigator have expertise in the area being studied?
- Does the investigator have experience with this type of research?
- Is the investigator accessible?
- Does the investigator have appropriate training and qualifications in clinical research?
- Has the investigator ever been sanctioned for research misconduct?

Presence and experience of staff

- Are research-designated staff members involved and are they qualified?
- Are the potential sub-investigators qualified for the protocol?
- Is there an affiliated IRB to review the protocol?
- Will there be a qualified pharmacist or research pharmacist?

Adequacy of facilities/resources

- Is there a research office? A location for monitoring? An examination office?
- Is there a secured location for storing study files and/or investigational products?
- Does the investigator have access to the technology and equipment needed for the study (e.g. centrifuge, freezers, computers, ultrasounds, etc.)?

Access to subjects

- How many patients with the appropriate diagnosis are accessible?
- Are there any studies that may be competing for the same population?
- What is the investigator's enrollment history in previous studies?

If the site fulfills the needed requirements for the study, the sponsor will notify the site of acceptability as an investigative site. The sponsor will begin the site initiation process (refer to Site Orientation/Initiation).

Sponsor-investigators often choose sites based upon their interactions with fellow researchers at other institutions. Whether sites are evaluated through a telephone interview, documented correspondence, or on-site visits, the Sponsor-Investigator must take the appropriate measures to select and evaluate investigative sites.

Generally, site selection is accomplished initially via questionnaires or surveys, and further evaluated during the site qualification visit by the monitor (CRA). The site qualification visit may include:

- Tour of facilities including: patient care areas, screening areas, lab processing area, research office, pharmacy (if applicable) and location for monitoring of study data
- Introduction to study personnel including: Principal Investigator, research coordinator(s), sub-investigators, and pharmacists
- Confirmation of secured location for storage of investigational materials: separate area/office for Case Report Forms (CRF) and an area for study drugs and/or devices (if the pharmacist is responsible for investigational drugs, there must be a separate locked area for storage within the pharmacy)
- Discussion of the investigator's responsibilities, monitoring plans, and review of the protocol.

Note: A full description of the site selection and qualification process, along with templates to document qualifications can be found in the Penn Sponsor-Investigator Standard Operating Procedures (Sponsor-Investigator SOP 401: Investigator Selection at www.med.upenn.edu/penn/ohr/sop/400/401.html).

Site Orientation

Prior to study initiation, the research team should be versed in the proper techniques to conduct the study in accordance with the protocol, federal regulations, and GCP. This is true regardless of whether a study involves one department or institutions from around the world. Study orientation may be accomplished through an investigator meeting, onsite training, online training, conference calls, or a combination of these methods.

Site orientation may include:

Site Initiation

Prior to study initiation, the research team should be versed in the proper techniques to conduct the study in accordance with the protocol, federal regulations, and GCP. This is true regardless of whether a study involves one department or institutions from around the world. Study orientation may be accomplished through an investigator meeting, onsite training, online training, conference calls, or a combination of these methods.

Site orientation may include:

Site Initiation

During the site initiation visit, the study monitor (CRA) will have a list of criteria to evaluate and review. The monitor will also provide one-on-one instruction and reinforce protocol training/orientation with the research team.

Sponsor-Investigators are similarly responsible for evaluating and initiating sites. For the monitor's Site Initiation Checklist, see the applicable forms in the Sponsor-Investigator SOPs (refer to SOP 402: Initiation Visit at www.med.upenn.edu/penn/ohr/sop/400/402.html).

A monitor's site initiation checklist may include:

- Confirmation of regulatory documentation
- Collection of outstanding regulatory documentation
- Review of protocol procedures, amendments, case report form completion, etc.
- Review study monitor expectations
- Review consent form and consent process
- Inspect and inventory study supplies
- Inspect storage site and dispensation records of study drug and/or device

HANDBOOK FOR FACULTY AND ACADEMIC ADMINISTRATORS
Revised 2009

A SELECTION OF POLICIES AND PROCEDURES OF THE UNIVERSITY OF PENNSYLVANIA

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1. As in all research involving human subjects, undertaken under University auspices, research in the community must be approved by the Institutional review Board, and meet all of the required protections of human subjects.

2. Whenever possible, researchers investigating community issues should work with community-based organizations to discuss all aspects of the research process, including problem definition, hypothesis generation, study design, data analysis, and dissemination.

3. Whenever possible, researchers should have a dissemination plan that includes distribution or presentation of results to community members and organizations, particularly those who participated in the research.

4. Researchers should determine if other projects are underway in a community, and whenever possible, coordinate efforts with other research projects to minimize disruption and maximize positive impacts on community members and organizations.

5. In the spirit of mutual learning and benefit, researchers should consider how study results could be used to the benefit of the community whenever possible, and should make extra efforts to communicate those recommendations to appropriate community members.

III.K. Human Research Protection Program

(Source: Office of the Provost, Almanac, July 11, 2006)

The University of Pennsylvania is committed to maintaining a comprehensive program to protect human subjects engaged in research conducted or supported by the University and the University of Pennsylvania Health System.

The institution adheres to the ethical principles and guidelines for the protection of human subjects in research enumerated in the Belmont Report, produced by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 1979). The University has provided the Department of Health and Human Services' Office for Human Research Protections (OHRP) a Federal-wide Assurance of compliance with the ethical principles and regulations governing research with human subjects. This Federal-wide Assurance is written documentation of Penn's commitment to comply with local and federal laws and regulations governing human research.

The Vice Provost for Research is empowered by the Board of Trustees through the Provost to coordinate the overall human research protection program and has direct authority over the key components of that program. The responsibilities of the Vice Provost for Research include:

- Ensuring protection of human research subjects.
- Ensuring compliance with local, state and federal laws and regulations.
- Ensuring the independence of the Institutional Review Boards (IRBs).
- Ensuring the number of IRBs is appropriate for the volume and types of human research reviewed, and that reviews are accomplished in a thorough and timely manner.
- Responding to allegations of scientific misconduct.

The Vice Provost for Research has the authority to:

- Create and approve policies and procedures governing the human research protection program.
- Create an annual budget for the human research protection program.
- Allocate resources within the program.
- Suspend or terminate research.
- Place administrative sanctions on investigators for noncompliance, such as suspension or termination of research privileges; requiring investigators or research staff to undergo additional training as a condition of continuing research; and mandating independent monitors for ongoing research

The Vice Provost for Research may not approve a study that has been disapproved by one of the IRBs.

The Vice Provost for Research has established an oversight committee known as the Human Research Advisory Committee (HRAC). The HRAC represents all the offices of the University with interest in the conduct of human research including the Office of Regulatory Affairs; the Office of Research Services; the Office of General Counsel; the Office of Audit, Compliance and Privacy; representatives of the schools conducting research as well as faculty members. This committee advises the Vice Provost for Research on the need for and implementation of policies and procedures governing human subject research. Upon the recommendation of the HRAC, the University shall conduct periodic reviews of the human research protection program and budget support for the various components of the program, either through independent mechanisms or as part of a scheduled accreditation process.

Prior to initiating any research on human subjects, investigators at the University of Pennsylvania must first obtain the approval of one of the University IRBs through their established policies and procedures. The University supports eight IRBs through

the Office of Regulatory Affairs (ORA). IRB is composed of scientists, non-scientists and members who are unaffiliated with the University of Pennsylvania. The Director of the ORA reports directly to the Vice Provost and informs the Vice Provost for Research of the IRB actions to approve, withhold approval, disapprove, terminate or suspend human subject research.

All personnel—faculty, research fellows, students and staff—engaging in human research must have documented education regarding human subject protection, in accordance with certification standards defined by the Vice Provost for Research. Training for investigators engaged in biomedical research is available through a web-based program developed by the School of Medicine's Office for Human Research. Researchers engaged in social and behavioral research are offered web-based training through the Office of the Vice Provost, in cooperation with the IRB.

In addition, the School of Medicine Office for Human Research (OHR) maintains high level support for medical researchers conducting trials including those where the faculty member has a role as sponsor-investigator. The OHR also provides monitoring of investigator compliance for the University.

Any individual with questions concerning human research or noncompliance with regulations may contact the Office of Regulatory Affairs at (215) 898-2614. Allegations of noncompliance may also be reported to the Office of Audit, Compliance and Privacy using 1-888-BEN-TIPS. All allegations are investigated with appropriate protections of the rights of the complainant.

This notice shall be published periodically as a reminder to the University community or when the various components of the human research program are materially changed.

III.L. Policy Regarding Human Subject Research in the Sociobehavioral Sciences

(Source: Office of the Provost, Almanac, October 3, 2006)

Scope

This policy is applicable to all employees, students, trainees, faculty, and other persons working for or in facilities owned and operated by the University of Pennsylvania and conducting sociobehavioral research. This policy is meant to apply University-wide to all research involving human subject data, and inclusive of biomedical research protocols applying sociobehavioral techniques (e.g., survey research). Depending on the type of research, other policies (e.g., those pertaining to biomedical research) may apply as well. Relevance is determined by the involvement of living human subjects in observational or experimental research, or in the use of records or specimens that may conceivably place the subjects of these records at risk, as per the Common Rule.

The term "sociobehavioral sciences" (or the term "social and behavioral sciences") must be understood as a shorthand term for the set of inquiries involving human subjects not otherwise subsumed under the biomedical sciences. It includes fields of research specifically defined as behavioral and social sciences in federal manpower reports; that is, "anthropology, demography, the non-clinical fields of psychology, sociology, and the speech and hearing sciences." It also includes human subject research in economics, business, education, and history, among others (see the Common Rule. Thus, the proposed policy applies to all sociobehavioral research irrespective of its institutional setting within the University or its source of funding. Note that disciplinary predilections—for example, rejection of the rubric "science"—are insufficient warrant for self-abstention from the policy promulgated here.

Regulatory Background

In the context of Institutional Review Board (IRB) oversight of human subject research, the Common Rule specifies three levels of review of proposed research, which can be summarized as follows:

1) *full board review*—a convened IRB committee must approve the proposed research, applying criteria set forth in the Common Rule, before the research can be conducted;

2) *expedited review*—certain kinds of research involving no more than minimal risk, as well as minor changes in approved research, can be approved by an administrative mechanism not requiring a convened IRB committee;

3) *exempt from review*—minimal risk research activities in a number of specified categories, involving human subjects not from vulnerable populations, are exempt from full review as per the Common Rule.

These three levels of review require submission of a research protocol to the IRB. Specific submission requirements for each category can be found at the IRB website, as can a definition of research activities in a number of specified categories and vulnerable populations. The website is:
www.upenn.edu/regulatoryaffairs/human/forms.html.

At the University of Pennsylvania, "expedited review" is typically performed by Office of Regulatory Affairs personnel. The University is also required to have a mechanism in place for determining whether a proposed research protocol is "exempt from review." As per the federal-wide assurance (FWA) that the University has in place, this determination is made by an administrative mechanism similar to that for "expedited review." In addition, there are certain kinds of research not covered by the Common Rule. Such research does not require any involvement of the IRB, even at the level of "exempt from review."

This policy clarifies that specific activities in the social behavioral sciences do not require IRB involvement. As a category distinct from "exempt from review," it is referred to as "*not under the purview of the IRB.*"

Implementation

Implementation of the policy outlined below will be the responsibility of the Office of the Vice Provost for Research. In consultation with the schools and their faculty, the Vice Provost will create a training program, and a certification process documenting successful completion of the training program. Any sociobehavioral research activities involving human subjects or human subject data will require prior official certification once this policy becomes effective.

Policy

All Personnel—faculty, research fellows, students and staff—engaging in Sociobehavioral research must have documented disciplined-appropriate education regarding human subject protection, in accordance with certification standards defined by the Vice Provost for Research.

The training program and certification process are to be kept current under the auspices of the Vice Provost for Research and in consultation with the schools and their faculty. This policy in its entirety may be found at:

www.upenn.edu/almanac/volumes/v53/no6/or-hsresearch.html.

III.M. Standard Operating Procedures and Policies of the University of Pennsylvania Institutional Animal Care and Use Committee (IACUC)

(Source: Office of the Vice Provost for Research, March 9, 2000; revised, May 2002; revised, June 2003; revised, July 2004)

The University of Pennsylvania recognizes the scientific and ethical responsibility for the humane care and use of animals involved in research and education and enjoins all individuals involved to maintain the highest standards of animal care and consideration. This concern extends to investigators to protect the animals as well as comply with the specific requirements established and regulated by the sponsors of their research, University Policies and/or federal regulations.

The University of Pennsylvania recognizes and supports fully The Institutional Animal Care and Use Committee (IACUC), as the agent for The University of Pennsylvania in its obligations for the humane care and use of animals.

The University of Pennsylvania and the IACUC shall:

1. Assure all activities (involving animals) meet the ethical and legal

Institutional Review Board

Standard Operating Policies

Version 7.0
April 16, 2009
Version 7.1
August 25, 2009

Standard Operating Policies, versions 7.0 & 7.1 were reviewed and approved by the Executive IRB Chair and by the IRB Executive Director.

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GA 101 COMPOSITION OF THE BOARD

1. PURPOSE

The purpose of this SOP is to:

- State the institutional authority under which the IRBs are established and empowered.
- Define the purpose of the IRBs.
- State the principles governing the IRBs to assure that the rights and welfare of subjects are protected.
- State the authority of the IRBs.
- Define the scope of the IRB
- Define the relationship of the IRBs to other committees and to officials within the University system.

2. POLICY STATEMENT

2.1 Statement of Institutional Authority

The University of Pennsylvania's Institutional Review Boards (IRBs) are established and empowered under the authority of the Trustees of the University of Pennsylvania. The University of Pennsylvania requires that all research projects involving humans as subjects be reviewed and approved by one of the University of Pennsylvania's IRBs prior to initiation of any research related activities, including recruitment and screening activities.

2.2 Purpose of the IRBs

The IRBs purpose is to protect the rights and welfare of human subjects participating in biomedical and behavioral research conducted at the University of Pennsylvania. The IRBs review and oversee such research to assure that it meets ethical principles and that it complies with federal regulations that pertain to human subject protection at 45 CFR 46 and 21 CFR 50 and 56, and other pertinent regulations and guidance.

2.3 Governing Principles

The IRBs are guided by the ethical principles regarding all research involving humans as subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, entitled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). These principles are defined in the Belmont Report as follows:

- Respect for Persons – Individuals should be treated as autonomous agents; and persons with diminished autonomy are entitled to protection.

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- Beneficence – Maximize the benefits and minimize the possible harms.

- Justice -- The burdens and benefits of research should be justly distributed.

2.4 IRB Authority

2.4.1 The IRBs are established to review biomedical and behavioral research involving human subjects that is conducted by faculty, staff and students of the University regardless of the source of funding and location of the study if :

- The research is sponsored by the Trustees of the University of Pennsylvania;
- The research is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania in connection with his or her institutional responsibilities;
- The research is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania using any property or facility of the University of Pennsylvania;
- The research involves the use of the University of Pennsylvania's nonpublic information to identify or contact human research subjects; or,
- The research involves the use or disclosure of protected health information.

2.4.2 Each IRB has the authority to ensure that research is designed and conducted in such a manner that protects the rights and welfare and privacy of research subjects. Specifically, each IRB may disapprove, modify or approve or suspend studies based upon consideration of human subject protection aspects.

3.0 SPECIFIC POLICIES

3.1 Federally Funded Research

If the study is part of an application to a sponsoring agency, the human research protocol must be reviewed by the IRB before, or when the application is processed in the Office of Research Services and prior to expenditure of any grant funds.

3.2 Pennsylvania State Law

The IRBs recognize that Pennsylvania laws impose additional requirements. To ensure that the applicable requirements are met, the IRB members or administrative staff will consult with the General Counsel’s Office for guidance on additional legal requirements under Pennsylvania state law.

3.3 Relationship of the IRBs to University Officials and Other Committees

3.3.1 Review of research by officials and other committees: Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials or other committees of the University of Pennsylvania. However, those officials or committees may not approve research if it has been disapproved by an IRB.

3.3.2 IRB relationship to university officials and other committees: The IRB functions independently of, but in coordination with University officials and other committees.

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3.3.3 For funded research, reseach may not begin until the contract is finalized.

3.3.4 When review is required by other University committees, research may not begin until the required committee reviews are complete.

3.4 Use of Policies and Procedures

Each IRB must maintain and follow all written policies and procedures consistent with federal regulations, good clinical practice, and research ethics when reviewing proposed research.

3.5 Number and Scope of IRBs

The Board of Trustees has authorized 8 IRBs to review research involving human subjects conducted by faculty, staff and students of the University. The University consists of the undergraduate and graduate schools of the University of Pennsylvania, and the University of Pennsylvania Health System.

In general, IRB applications involving biomedical research or clinical trials are assigned to IRBs 1-7. Research involving social or behavioral sciences is reviewed by IRB 8. Research that is conducted in the Clinical Research Translational Center is assigned to IRB 3. IRB 6 reviews research conducted by Pennsylvania Hospital.

4. REFERENCES

Provost HRPP Statement; Belmont Report; 21 CFR 56.108; 21 CFR 56.109; 45 CFR 46.103(b)(4), 45 CFR 46.113

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GA 102 ACTIVITIES REQUIRING IRB REVIEW

1. PURPOSE

The purpose of this policy is to describe specific activities that require IRB review and, conversely, those activities that do not require IRB review.

2. POLICY STATEMENT

The University conducts biomedical and social science and behavioral research. No intervention or interaction with human subjects in research, including recruitment, may begin until the IRB has reviewed and approved the research protocol. “Human subjects research” is any activity that either: 1) meets the HHS definition of “research” involving “human subjects” as defined in the HHS regulations or 2) meets the FDA definition of “clinical investigation” that involves “human subjects as defined in the FDA regulations.

All research involving human subjects (as defined above), and all other activities which even in part, involve such research, regardless of sponsorship, must be reviewed and approved by a University of Pennsylvania IRB.

Under certain conditions, the University may rely on another organization’s IRB. The reliance on another IRB will be outlined in an approved IRB Authorization agreement or under the conditions of an approved cooperative agreement. The criteria used to evaluate the appropriateness of relying on another IRB are outlined in the Guide to Daily Operations.

3.1 Activities that Require IRB Review

Specific activities that require IRB Review include, but are not necessarily limited to:

3.1.1 Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

3.1.2 Collection and use of data about a series of standard procedures or treatments for dissemination or generalization if the activity meets the definition of “human research”.

3.1.3 Patient care or the assignment of normal participants to any intervention is altered for research purposes in any way.

3.1.4 A diagnostic procedure for research purposes that is added to a standard treatment.

3.1.5 “Systematic investigations” involving innovative procedures or treatments. For example, if an investigator plans to collect information about an innovative procedure

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for scientific purposes or will repeat the innovation with other participants in order to compare it to the accepted standard.

3.1.6 Emergency Use of an Investigational Drug or Device. One time emergency uses of an investigational drug or device may proceed without prospective IRB review. When emergency medical care involving an investigational article, the research does not require prospective IRB review and approval, the patient is a research subject as defined by FDA regulations, but may not be considered a research subject as defined by HHS regulations, and data generated from such care *cannot be included in any prospectively conceived report of an HHS regulated research activity*.

3.1.7 Emergency Medicine Research. Prospectively planned emergency medicine research with investigational drugs, devices, or biologics requires IRB approval. If the researcher intends to waive the requirement for informed consent, additional requirements must be met including community consultation and pubic disclosure.

3.1.8 Data, Human Cell or Tissue Repository. Human cell or tissue (genetic tissue) research typically involves repositories that collect, store, and distribute human tissue materials for research purposes.

3.1.9 Investigator Research. A University of Pennsylvania investigator who both initiates and conducts, alone or with others, a research project or clinical trial regardless of source of funding or support.

3.1.10 Student Research. Directed or independent human research projects which employ systematic data collection with the intent to contribute to generalizable knowledge.

These activities include: (i) All master's theses and doctoral dissertations that involve research with human subjects; and (ii) All projects that involve research human subjects and for which findings may be published or otherwise disseminated.

3.1.10 Access to protected health information. Investigators conducting research with protected health information maintained within any of the covered entities of the University of Pennsylvania must provide the IRB with appropriate information to obtain approval of the activity prior to access of the protected health information.

3.1.11 Collaborative Research. Collaborative research requires IRB review by each performance site unless an IRB authorization or Independent Investigator Agreement is in place or carried out under the terms of a cooperative agreement.

3.2 Activities Not Subject to IRB Review

3.2.1 Proposals that lack definite plans for involvement of human subjects will not require IRB review. Additionally, activities such as quality assurance or quality control, program and fiscal audits, and certain disease monitoring as prescribed by the Public Health Department generally do not qualify as research.

3.2.2 Case Studies. A single retrospective case report is a medical/educational activity and does not meet the Federal Policy for the Protection of Human Subjects

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definition of "research" which is “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”

In general, the review of medical records for publication of case reports of three or fewer patients is not considered human research and does not require IRB review and approval.

Under HIPAA, a single case report is an activity to develop information to be shared for medical/educational purposes. Therefore, the use of protected health information to prepare a paper for publication of a single case report does not require IRB review for HIPAA purposes. If the data are de-identified, no waiver or authorization is required. If, however the investigator wishes to publish data with HIPAA identifiers anauthorization signed by the patient is required.

Investigators are encouraged to obtain from the IRB documentation that the activity is not subject to IRB review. Research that does not meet the regulatory definition of human research or clinical investigations does not require IRB approval.

3.2 Collaborative Research with the Veterans Affairs Medical Center - Philadelphia

When all work is to be done at the VAMC and the only association with the research at Penn is the investigator’s dual appointment, there is no requirement for submission or review by Penn’s IRB.

When research is conducted at both the VAMC and at Penn, the research must be reviewed and approved by both IRBs.

3.3 Failure to Submit Project for IRB Review

The implications of engaging in activities that qualify as research that is subject to IRB review without obtaining such review are significant. If an investigator begins a project without prospective IRB review and approval and later learns of the review requirement, the investigator should promptly notify the IRB. The IRBmay allow or deny use of the data.

If an investigator begins a project and later finds that the data gathered could contribute to generalizable knowledge, has changed in some fashion as to now require IRB review, or that he or she may wish to publish the results, the investigator should submit a proposal to the IRB for review as soon as possible. If the IRB does not approve the research, the IRB may determine that the research cannot be used as part of a study, thesis or dissertation nor may the results of the research be published.

4.0 REFERENCES

Federalwide Assurance; 45 CFR 46.102(d)(f); 21 CFR 50.3(d)(g); 21 CFR 56.108(b)(1); 45 CFR 46.103(b)(4); 21 CFR 50.24; OPRR Reports, Emergency Medical Care, May 15, 1991; OPRR Reports: Informed Consent Requirements in Emergency Research, October 31, 1996; OHRP Guidance Research Involving Coded Private Information or

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Biological Specimens, Oct. 16, 2008; OHRP Issues to consider in the research use of stored data or tissues, Nov. 7, 1997; OHRP Guidance; Engagement of Institutions in Research, Oct. 16, 2008

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GA 103 POLICIES AND PROCEDURES MAINTENANCE

1. PURPOSE

The purpose of this section is to state the IRBs' commitment to maintain, and follow up-to-date policies and procedures that adhere to regulatory mandates and ethical principles.

2. POLICY STATEMENT

Following federal regulations and guidance supported by institutional policies assures that the rights and welfare of the human subjects of such research will be overseen and protected in a uniform manner, regardless of changes in personnel. Written procedures must be in place to insure the highest quality and integrity of the review and oversight of research involving human subjects and for the adequate documentation of such oversight.

Standard operating policies (SOPs or Policies) and procedures provide the framework for the ethical and scientifically sound conduct of human research.

3. SPECIFIC POLICIES

3.1 Review and Revision of Policies & Procedures

3.1.1 Changes to regulations, federal guidelines, or research practice as well as the policies and procedures of the University of Pennsylvania may require a new policy or a revision to a previously issued policy.

3.1.2 Policies will be reviewed at least annually by the IRB Executive Director and IRB administrative staff.

3.2 Policy Dissemination and Training

3.2.1 New or revised policies are approved by the IRB Executive Director and will be disseminated to the appropriate individuals and departments.

3.2.2 Training will be provided to all members of the IRB and IRB staff on any new or revised policy and or relevant procedure.

3.2.3 Each new IRB member or staff employee must review all applicable policies prior to undertaking any responsibilities at the IRB. Evidence of training must be documented and filed with the Executive Director.

3.3 Forms

Forms including checklists and worksheets are used to ensure that policies are integrated into the daily operations of research and review throughout the University, and to enable IRB staff to manage review, tracking, and notification functions consistently. Forms are either controlled or non-controlled.

3.3.1 Controlled Forms are regulatory documents that become part of the permanent record of IRB review.

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3.3.2 Non-controlled forms are management tools that are not subject to the standards of control cited in GDO FO 304, Section 5.

4.0 REFERENCES

45 CFR 46.103(b)(4)(5); 21 CFR 56.108; 21 CFR 56.115(6)

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GA 104 TRAINING AND EDUCATION

1. PURPOSE

This policy describes the training and educational requirements and options for IRB members and staff.

2. POLICY STATEMENT

Training of IRB staff and members is critical if the IRB is to fulfill its mandate to protect the rights and welfare of research subjects in a consistent manner throughout the University of Pennsylvania research community.

IRB members, staff and others charged with responsibility for reviewing, approving, and overseeing human subject research should receive detailed training in the regulations, guidelines, ethics and policies applicable to human research.

The University of Pennsylvania has written policies and procedures requiring all individuals involved with the Human Research Protection Program to understand and apply their obligation to protect the rights and welfare of research participants. The University requires all researchers and other personnel involved in the design or conduct of a project to provide evidence of training and qualifications by submitting relevant documentation to the IRB, sponsor, or regulatory authorities.

3. SPECIFIC POLICIES

3.1 Training

3.1.2 Management level staff and members of any IRB who are overseeing research on human subjects (human subjects as defined in 46.102(f) and/or 56.102(e) that is managed, funded, or taking place in an entity under the jurisdiction of the Trustees of the University of Pennsylvania will receive initial and ongoing training regarding the responsible review and oversight of research and these policies and accompanying procedures.

3.1.3 The IRB Executive Director establishes the educational and training requirements for IRB members and staff who review biomedical and behavioral research at this institution and who perform related administrative duties. Initial and ongoing training is documented by the IRB Associate Director.

3.1.4 Members of the IRB will participate in initial and continuing training in areas germane to their responsibilities.

3.1.5 Chairpersons will receive additional training in areas germane to their additional responsibilities.

3.1.6 IRB staff will receive initial and continuing training in the areas germane to their responsibilities.

3.1.7 IRB members and staff will be encouraged to attend workshops and other educational opportunities focused on IRB functions. The University will support such activities to the extent possible and as appropriate to the responsibilities of members and staff..

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3.2 Evaluation of IRB Member Performance

The Executive IRB Chair is responsible for periodic evaluation of the performance of IRB members and Chairs and for the periodic evaluation of the composition of the IRBs to meet regulatory and organizational requirements.

4. REFERENCE

Terms of the HHS Federalwide Assurance; 45 CFR 46.107(a); 21 CRF 56.107(a)

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GA 105 MANAGEMENT OF IRB PERSONNEL

1. PURPOSE

This section describes management policies and procedures to promote the long-term commitment of IRB administrative staff employees and ensure the efficient and effective administration and enforcement of IRB decisions.

2. POLICY STATEMENT

The IRB administrative staff provides consistency, expertise, and administrative support to the IRBs, and serves as a daily link between the IRB and the research community. Therefore, the highest level of professionalism and integrity on part of IRB staff is expected.

3. SPECIFIC POLICIES

3.1 Job Descriptions and Performance Evaluations

Members of the IRB staff should have a description of the responsibilities expected of their positions. The performance of IRB staff will be reviewed according to current university policy.

3.2 Staff Positions

Staffing levels and function allocation will be determined according to university policy, management assessment of support requirements and budget constraints. The Vice Provost for Research reviews the IRB budget with the IRB Executive Director periodically and no less then annually to ensure adequate allocation of resources to IRB administration.

3.3 Hiring and Terminating IRB staff

The human resource policies of the University of Pennsylvania determine the policies for recruiting and hiring staff.

3.4 Delegation of Authority or Responsibility

Delegation of specific functions, authorities, or responsibilities by the Executive Chair or IRB Executive Director to a staff member must be documented in writing.

3.5 Documentation

The HR policies of the University of Pennsylvania determine the policies for identifying, documenting and retaining formal staff interactions (such as performance reviews, termination procedures).

4. REFERENCE

None

Title	GA 105 Management of IRB Personnel
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GA 106 A MANAGING CONFLICTS OF INTEREST: IRB MEMBERS, CONSULTANTS, AND STAFF

1. PURPOSE

This policy requires any IRB member or consultant with a conflicting interest in a research protocol to disclose that information to the IRB Chair or IRB administrative staff.

2. POLICY STATEMENT

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

This policy applies to all research protocols reviewed by the IRB, regardless of whether the project is exempt or considered during expedited or continuing review or during a review by the convened IRB.

The standard that should guide decisions about conflicting interests whether an independent observer could reasonably question whether the individual's actions or decisions would be based on factors other than the rights, welfare, and safety of the subjects.

The Vice Provost for Research has the authority to determine when conflicts of interest (COI) exist as defined by institutional policy and to impose and enforce disciplinary action in the event that COI is not disclosed.

3. SPECIFIC POLICIES

3.1 Definitions

Financial Interest Related to Research: Financial interest in the sponsor, product or service being tested.

Certain other types of interests may also be conflicting interests, as explained below. A conflicting interest may arise because of an interest that the IRB member or consultant, or his/her immediate family, has; the aggregate interest of the IRB member or consultant, and his/her immediate family, is considered.

3.1.1 "Immediate family" means the IRB member's or consultant's spouse or domestic partner and dependent children as defined by IRS.

3.1.2 "Participation in a project" means the IRB member or consultant is listed as an investigator on the protocol or is a member of the research team.

3.1.3 "Supervision of a project" means the IRB member or consultant or their immediate family member is a faculty sponsor of researcher or a situation in which any investigator must report to or is under the professional supervision of the IRB member or consultant or their immediate family member, or where the IRB member or consultant, or their

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immediate family member is involved in the design, conduct, or reporting of the research.

3.1.4 A “financial interest” is a conflicting interest under this policy if it is one of the following situations:

Receiving more than $10,000 annually as salary, consulting income, or other compensation from the sponsor of the project;

Having an equity interest (including stock or stock options) unless the interest meets all four of the following tests:

The value of the equity is less than $10,000.

The equity represents less than 5% interest in any one entity.

The equity is in a publicly traded company whose share value can be assessed by reference to publicly available prices. (e.g., listed on a major stock exchange.)

The value of the equity will not be affected by the outcome of the research.

Having an ownership interest (including patent, trademark, or copyright interest) in the drug/product/technology that is the subject of the research project; or

Receiving or expecting to receive compensation with a value that may be affected by the outcome of the study.

3.1.5 “Personal relationship” means having an immediate family relationship or other close personal relationship with the investigator.

3.1.6 “Fiduciary relationship” means serving as an executive to a company sponsoring the research or serving on the company’s board of directors.

3.1.7 Other examples of conflicting interests include but are not limited to the following:

An IRB member or consultant has an interest the IRB member or consultant believes conflicts with the ability to review a project objectively; or,

An IRB member or consultant is in direct competition with the investigators for limited resources, funding, sponsorship, or research subjects, or the IRB member or consultant is considered a personal or professional adversary of the investigators.

Any other reason for which the IRB member believes he or she has a conflicting interest with the research.

The definition of conflicting interests included in this section of the SOPs only applies to the conflicting interests of IRB Members, Consultants and Staff. Investigator conflicts of interest are defined by institutional policies.

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3.2 Disclosing, Managing, and Documenting Conflicts of Interest

No regular, alternate IRB member or consultant may participate in the initial or continuing review of any research project or protocol, in which the member has a conflict of interest, except to provide information as requested.

IRB members are expected to self-identify their conflicting interests for all reviews, including reviews by the convened IRB and reviews using the expedited procedure. For protocols reviewed by the convened IRB, the IRB will document the name of the IRB member with the conflict and will document that the IRB member left the room during the discussion of the protocol. IRB members with conflicting interests do not count towards quorum.

3.3 IRB Staff

Institutional staff whose job status or compensation is impacted by research that is reviewed by the IRB must be absent from IRB deliberations and voting. The Executive Director and Administrators are required to provide yearly confirmation of their possible financial interest and the requirement to be absent from IRB deliberations and voting on a particular research protocol. Any case of disclosure of conflict of interest by staff shall be referred to the Executive Director for development of a management plan.

3.4 Education and Training in COI

IRB members and staff are required to participate in education and training activities related to conflict of interest issues.

4. REFERENCE

45 CFR 46.107(e); 21 CRF 56.107(e); FDA Information Sheets, FAQ, Section II, Question 12

Title	GA 106 A Managing Conflicts of Interest: IRB Members, Consultants, and Staff
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GA 106 B IRB INTERACTIONS WITH THE CONFLICTS OF INTEREST STANDING COMMITTEE

1. PURPOSE

This policy is concerned with the processing of disclosures of conflicts of interest by investigators engaged in human research and their review by the IRB to ensure adequate protection of subjects.

2. POLICY STATEMENT

The protection of human subjects in research requires that conflicts of interest involving investigators be eliminated or managed so that the results of the research are free from bias. The management of conflicts of interest is the responsibility of the Vice Provost for Research as advised through the Conflicts of Interest Standing Committee (CISC). It is the policy of the IRB that review of the management, minimization or elimination of conflicts of interest involving investigators is an integral part of the review of human research.

In the interests of protecting human subjects, the Institutional Review Board requires the following steps be taken to address such potential conflicts of interest in the conduct of human research.

3. SPECIFIC POLICIES

3.1 Submission of Confidential Financial Disclosure Statements

Principal Investigators submitting research applications to the IRB are required to certify:

3.1.1 They have reviewed the University policies on conflicts of interest with all investigators (including staff and family members as defined in the COI policies) and,

3.1.2 As part of the current protocol application, an investigator and others engaged in research must indicate if conflicts of interest exist. If so, the individual with the conflict must submit a financial conflict of interest disclosure form if they have any financial interests in the project as defined by institutional policies. The Disclosure Form and a copy of the IRB Application and informed consent documents will be forwarded to the Conflicts of Interest Standing Committee for review.

3.2 IRB Review

It is not the purview of the IRB to reinterpret institutional conflict of interest policies or their implementation. Rather its function is to ensure that subject protection, the integrity of IRB review, and the conduct of a research are not jeopardized by an unidentified and unmanaged conflict of interest. When human research requires review by the CISC, the IRB will not approve the research until the CISC management plan is complete and agreed to by the Investigator(s).

The IRB review shall concentrate on those aspects of any conflict of interest that may reasonably affect human subject protection and may require changes to the protocol or consent form that may include, but are not limited to the following:

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3.2.1 The IRB may require an independent data safety monitoring process or enhanced data safety monitoring plan.

3.2.2 Where applicable, the informed consent will disclose the nature of an investigator's conflict including but not limited to such conflicts as; consulting or educational activities supported by the sponsor; disclosure that the investigator is the inventor; has an interest in a related patent or technology; or that the investigator or the University may receive financial benefits from development of the technology, and that these financial benefit(s) may depend on the outcome of the research.

3.2.3 The IRB may require consent monitoring, or request additional information from the conflicted investigator about how sponsors or their agents will mitigate or monitor for risks presented.

4. REFERENCE

Principles of Responsible Conduct, *Almanac, Volume 54, No, 27, April 1, 2008*,
Financial Disclosure Policy for Research and Sponsored Projects, *Almanac, Vol.54, No. 1, July 17, 2007,* Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials, *Almanac, Vol. 49, No. 32, May 6, 2003*

Title	GA 106 B IRB Interactions with the Conflicts of Interest Standing Committee
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GA 107 SIGNATORY AUTHORITY

1. PURPOSE

This policy describes signature authority for IRB related activities.

2. POLICY STATEMENT

The Vice Provost for Research, IRB Executive Chair, IRB Executive Director, and IRB Associate Director are authorized to sign all documents in connection with the review and approval of research projects involving the use of humans as subjects, which have been reviewed and approved pursuant to University policies and procedures and upon decision of the IRB.

This policy applies to all IRB administrative staff. Implementation shall be the responsibility of the IRB Director. In all cases individuals must sign their own name and no other and indicate their title under their signature.

3. SPECIFIC POLICIES

3.1 Authorization for Signatory Authority

Authorization to sign documents not described in this policy may be made in writing by the IRB Director or Executive Chair.

3.2 Results of Reviews, Actions and Decisions

The results of reviews and actions taken by the IRB, either by the full Board or expedited review that grant Investigators with initial or continuing approval of research, may be signed by the IRB Executive Director, the IRB Associate Director, or IRB Administrators as designated in writing by the IRB Executive Chair.

3.3 Routine Internal Correspondence

Any action, letter, memo or e-mail between the IRB or administrative staff and the faculty or staff of the University that provides information concerning the review of research protocols by the IRB or staff and which do not imply or appear to imply approval of this activity may be signed by the staff member.

3.4 Correspondence with External Agencies

Official letters or memos sent to agencies of the federal government, funding agencies (whether private or public) or their agents will be signed by the Vice Provost for Research.

3.5 Decisions Made by the Chair

Any letters, memos or email sent representing the decision or opinions of the Executive Chair of the IRB, other Chairs of the IRBs or their respective designees, as long as such correspondence does not imply review and approval of research subjects, may be

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signed by designated IRB staff if so designated by the Executive Chair, IRB Chair, or IRB majority in a convened meeting.

4. REFERENCE

45 CFR 46.103(b)(5); 45 CFR 46.115(a)(6); 21 CFR 56.108(b), 21 CFR 56.115(a)(6)

Title	GA 107 Signatory Authority
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OP 200	IRB ORGANIZATION
201	COMPOSITION OF THE BOARD
202	MANAGEMENT OF THE BOARD
203	DUTIES OF IRB MEMBERS

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OP 201 COMPOSITION OF THE BOARD

1. PURPOSE

This section states the requirements for the composition of the IRBs responsible for reviewing research conducted in the University of Pennsylvania system.

2. POLICY STATEMENT

The role of the IRB is to assess the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards or professional conduct and practice.

Therefore, each IRB will consist of at least five regular, voting members. Qualified persons from multiple professions will be considered for membership. IRB membership will not consist entirely of men or of women.

The institution will make every effort to have a diverse membership appointed to the IRB, within the scope of available expertise needed to conduct its functions.

3. SPECIFIC POLICIES

3.1 IRB Member Selection Criteria

The members of the IRB will be sufficiently qualified through experience and expertise, of reviewing research proposals in terms of regulations, applicable law and standards of professional conduct and practice and institutional commitments, therefore the IRB will include persons knowledgeable in these areas.

The membership will be diverse, so selection will include consideration of race, gender, cultural backgrounds, research, healthcare or professional experience and sensitivity to such issues as community attitudes to assess the research submitted for review.

There will be at least 1 member whose primary concerns are in scientific areas and at least 1 member whose primary concerns are in nonscientific areas.

There will be at least 1 member who has no affiliation with this institution.

3.2 Composition of the Board

3.2.1 Knowledge, Skills and Abilities

Regular Members: The backgrounds of the regular members will be varied in order to promote complete and adequate reviews of the types of research activities commonly reviewed by the IRB. Regular members must include:

Nonaffiliated member(s): The nonaffiliated member(s), who can be either scientific or nonscientific reviewers, should be knowledgeable about the local community and be willing to discuss issues and research from that perspective. Consideration should be given to recruiting individuals who speak for the communities from which the University will draw its research subjects. The nonaffiliated member(s) should not be vulnerable to intimidation by the professionals on the IRB.

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Scientific members: IRBs will include members whose primary interests are scientific. Such members satisfy the requirement for at least one scientist.

When an IRB encounters studies involving science beyond the expertise of the members, the IRB may use a consultant to assist in the review, as provided by 21 CFR 56.107(f) and 45 CFR 46.107(f). At least 1 member of each board must be a physician licensed to practice medicine in the Commonwealth of Pennsylvania.

Nonscientific member: The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, nonscientific members are individuals whose education, work, or interests are not solely in medical, behavioral or social science areas.

Representatives of special groups of subjects. When certain types of research are reviewed, members or consultants who are knowledgeable about the concerns of certain groups or local context may be required. For example, if an IRB reviews research involving prisoners, a member who can represent this group, either an ex-prisoner or an individual with specialized knowledge about this group must be included on the IRB.

Chairs: Chairs will be standing or associate faculty members who are proficient in human research and of sound and ethical character and reputation, without conflicts of interest that would curtail their ability to serve objectively and according to the mission of the IRB as defined in applicable laws, regulations, and policies. Highly qualified and experienced IRB members who do not have faculty appointments but who demonstrate the necessary qualities, may also serve as Chair.

IRB Executive Chair: The Executive Chair will be a senior, tenured faculty member of the University with demonstrated knowledge, skills, and abilities in the conduct of human research and in applicable laws, regulations, and policies regarding human research protections.

4. REFERENCES

45 CFR 46.107; 21 CFR 56.107; FDA Information Sheets, FAQ Section II, Questions 14 & 15

Title	OP 201 Composition of the Board
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OP 202 MANAGEMENT OF THE IRB

1. PURPOSE

To describe staff administration and oversight of the IRBs to ensure continuity of membership that has the expertise and commitment to meet its regulatory and institutional mandates.

2. POLICY STATEMENT

The management of the membership of the IRBs and oversight of member appointments, IRB related activities, communications, and other administrative details are the responsibility of the IRB Director.

3. SPECIFIC POLICIES

3.1 Term of Appointment

The initial term of appointment is one to three years. Reappointment for additional terms may occur, by mutual agreement of the IRB member, IRB Executive Chairperson, IRB Executive Director, and the Vice-Provost for Research.

3.2 Appointments

The Vice-Provost for Research in consultation with the IRB Executive Chairperson and IRB Senior Administrative staff has the authority to appoint members to the IRB.
Members will be solicited from the university and the greater Philadelphia communities.

3.2.1 IRB Members Including Alternates

IRB members are nominated from a variety of sources, including previous and current IRB members, division chiefs, department chairs, compliance administrators, and various public groups.

When an individual is nominated or when an individual expresses interest in serving on the IRB a copy of the individual's *curriculum vitae* (CV) will be requested. The nominee's CV and any relevant correspondence are reviewed by the IRB Executive Chair and Senior IRB Administrative staff. Nominees appointed to serve on the IRB receive a letter of appointment signed by the Vice Provost for Research. Terms of appointments may be for one, two, or three years.

3.2.2 IRB Chairs

During any period of temporary vacancy, the IRB Executive may appoint an interim or acting Chair.

Other than to make a temporary or interim appointment, the IRB Executive Chair will convene an advisory committee to solicit and review nominations from qualified candidates.

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The advisory committee will include at least one member of the faculty, one member of the IRB, and at least one member of the IRB Administrative staff.

The advisory committee will recommend to the Vice Provost for Research one or more candidates in the order of desirability. The Vice Provost for Research will select from among the candidates recommended, or request additional candidates.

3.2.3 Consultants

The determination that a consultant is required may be made under certain circumstances during the review process. Such circumstances are as follows: senior IRB administrative staff, the IRB Executive Chair, or IRB Chair determines, upon pre-review, that a consultant is required; or, members of the IRB may request at any time during the review process to request a consultant's review.

This determination will be based on the topic of the protocol and the expertise of the voting members.

The consultant will be selected by the Executive Chair or the Chair. The Chair may consult with the principal investigator, Department Chair, Division Chief, or any other individual deemed appropriate to determine a suitable consultant. A consultant may be an individual who is either internal or external to Penn. A consultant may be asked to review a protocol or provide education on a topic of specific concern to the IRB; to provide information to the IRB by written report, attending a meeting(s), or both. A consultant may participate in all discussions, however, is not authorized to participate in the deliberations and may not vote.

All individuals who are asked to serve as consultants will be provided with the Conflicts of Interest Agreement and SOP to determine whether any conflict of interest exists prior to their work with the IRB. If there is any conflict of interest they will not be allowed to consult, and another consultant will be selected.

The IRB administrative staff, Executive Chair or designee will contact the consultant and will determine how the information will be conveyed to the IRB: i.e., attendance at the meeting or written report.

Key information provided by consultant will be documented in the minutes. All written reports or other documentation of consultant reviews will be maintained in the protocol file.

Use of consultants will be documented in the protocol file and minutes.

3.2.4 IRB Executive Chair.

The IRB Executive Chair is appointed by the Vice Provost for Research.

3.3 Resignations and Removals

A member may resign before the conclusion of his/her term. The vacancy will be filled as quickly as possible. The Vice-Provost for Research may remove a member at any time.

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3.4 Compensation

Participation by University faculty or staff as an IRB member is considered a component of their job responsibilities as established by their supervisors. Regular members who are not affiliated with the University shall receive reimbursement for parking and other miscellaneous expenses IRB Chairs and Executive Chair receives compensation as permitted by the Vice Provost for Research in consultation with the Chair or Executive Chair's academic chairman.

3.5 Liability Insurance

Regular and alternate members have liability insurance coverage as part of their IRB membership in their capacity as agents of the University.

3.6 IRB Rosters

IRB rosters will be maintained by the ORA IRB Administrators and will include:

- Names of IRB members
- Earned degrees
- The representative capacity of IRB members
  - Scientist and nonscientist
  - Affiliated or nonaffiliated member including employment or other relationships between the IRB member and the organization.
  - Knowledge of vulnerable populations
  - Indications of IRB members' experience sufficient to describe each IRB member's chief contribution.
- Alternate members
- The regular members or class of regular members form whom each alternate may substitute.

4. REFERENCES

45 CFR 46.103(b)(3); 21 CFR 56.115(a)(5)

Title	OP 202 Management of the Board
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OP 203 DUTIES OF IRB MEMBERS

1. PURPOSE

This policy defines the duties required of IRB members.

2. POLICY STATEMENT

Each IRB member's primary duty is the protection of the rights and welfare of the individual human beings that are serving as the subjects of that research. The reviewer must understand that he or she is not serving on the Board to expedite the approval of research, but to serve as a link between the investigator and the research subjects. In order to fulfill his or her duties, IRB members are expected to be knowledgeable of the regulations governing human subject protection, biomedical and behavioral research ethics, and the policies of the University of Pennsylvania germane to human subject protection. The IRB must be and must be perceived to be fair and impartial, immune from pressure either by the institution's administration, the investigators whose protocols are brought before it, or other professional and nonprofessional sources.

3. SPECIFIC POLICIES

The IRBs are appointed as University Committees. As such, the IRB members serve the University of Pennsylvania as a whole, rather than a particular school or department. Therefore, members must not allow their own interests or that of their departments or schools to supersede their duty to protect the rights and welfare of research subjects.

Term of Duty

Regular IRB members and chairpersons are expected to commit to at least a 1-year term and during that time, fulfill certain duties. These duties will be described prior to appointment and each IRB member is expected to fully understand the duties of IRB members prior to accepting appointment as an IRB member.

3.3 Specific Duties

3.3.1 Regular Members: All members are expected to review all material, to be familiar with them, and prepared to discuss the materials at the convened IRB meeting.

Nonaffiliated member(s): Nonaffiliated members are expected to provide input regarding their knowledge about the local community and be willing to discuss issues and research from that perspective.

Non-scientific members: Nonscientific members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and other wise. For example, members who are lawyers should present the legal views of specific areas that may be discussed, such as exculpatory language or state requirements regarding consent. Non-scientific members should advise the Board if additional expertise in a non-scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects and to comment on the comprehension of the consent document.

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Scientific members: Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of practice. These members should also be able to advise the Board if additional expertise in a scientific or non-scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects.

Chair: In addition to the above responsibilities (germane to the member's capacity) the chair leads convened meetings of the IRB. The Chair is empowered to suspend the conduct of a research project or clinical trial deemed to place individuals at unacceptable risk pending IRB review.

The Chair may recommend to the Vice Provost for Research the appointment of a Co-chair to assist or act on behalf of the chair in particular IRB matters and at IRB meetings, either as a general procedure, or on a case-by-case basis. The Chair also may delegate any of his/her responsibilities, as appropriate, to other qualified individual(s). Such documentation must be in writing.

3.3.2 Primary Reviewers: In addition to the duties described in section 3.3.1 each regular member will be expected to act as a primary reviewer for assigned studies at convened meetings. The primary reviewer presents his or her findings resulting from review of the application materials and provides an assessment of the regulatory criteria and recommends specific actions to the Board. He or she leads the discussion of the study by the convened IRB. The primary reviewer is required to read the entire submission, be familiar with it, and be prepared to conduct an in-depth review of all materials. The primary reviewer is expected to contact the investigator, IRB Executive Chair, IRB Chair, or Administrator in advance of the convened meeting for clarification of unresolved issues related to the submission.

3.3.3 The Executive Chairperson: Is expected to provide oversight of all IRBs, determine eligibility for and, where appropriate, conduct expedited reviews. The Executive Chairperson may also designate one or more experienced IRB members to carry out expedited review.

3.3.4 Alternate members. The appointment and function of alternate members is the same as that for regular IRB members, and the alternate's expertise and perspective are comparable to those of the Principal member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a regular member, the alternate member will receive and review the same materials prior to the IRB meeting that the Principal member received or would have received.

The IRB roster identifies the regular member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the regular member is absent. The IRB minutes will document when an alternate member replaces a regular member.

3.4 Evaluation of IRB Members and Chairs Performance

3.4.1 IRB members and Chairs will be asked to complete Self Evaluation Forms on an annual basis and submit the forms to the IRB Executive Director.

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3.4.2. The IRB Executive Chair and IRB Executive Director will be review the IRB Member and Chair self assessments on an annual basis to determine education and training needs and to make recommendations to the Vice Provost for Research regarding continuation of IRB membership.

3.5 Periodic Review and Adjustment of the Membership and Composition of the IRBs

A least annually the IRB Executive Chair will review and adjust membership and composition of the IRB to meet regulatory and organizational requirements.

The process is outlined in the Guide to Daily Operations OP 203.

3.6 Allegations of Undue Influence

The Provost and the Vice Provost for Research prohibit attempts by investigators, employees, and sponsors contracting with institutional officials to use or using undue influence with the IRB, any of its members or staff, a investigator or any other member of the research team to obtain a particular result, decision or action.

“Undue influence” means attempting to interfere with the normal functioning and decision-making of the IRB or to influence an IRB member or staff, a investigator or any other member of the research team outside of established processes or normal and accepted methods, in order to obtain a particular result, decision or action by the IRB or one of its members or staff.

IRB members and IRB staff report undue influence to the HRPP Executive Director. The Executive Director is responsible for the initial investigation. The following institutional officials will be notified, as appropriate, of allegations of undue influence and may be asked to review and endorse a corrective action plan. Institutional officials may include the following:

- Provost
- Vice Provost for Research
- Dean of applicable School
- Department Chair
- Office of General Counsel
- Other compliance offices

4. REFERENCES

45 CFR 46.107; 21 CRF 56.107; 45 CFR 46.110(b)(2); 21 CFR 56.110(b)(2); OHRP: IRB Guidebook; FDA Information Sheets: FAQ, Section II, Question 17

Title	OP 203 Duties of IRB Members
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F0 300	FUNCTIONS AND OPERATIONS
301	RESEARCH SUBMISSION REQUIREMENTS
302	IRB MEETING ADMINISTRATION
303	ADMINISTRATIVE REVIEW AND DISTRIBUTION OF MATERIALS
304	DOCUMENT MANAGEMENT

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FO 301 RESEARCH SUBMISSION PROCEDURES

1. PURPOSE

This policy outlines the required documents and supporting information required from investigators for IRB assessment.

2. POLICY STATEMENT

IRB members often rely solely on the documentation submitted by investigators, or other parties for initial and continuing review. Therefore this material must provide IRB members with enough information about a study to assess if it adequately meets the IRB's criteria for approval. A submitted protocol will be scheduled for IRB review only when the IRB staff determines that the information and materials submitted present an adequate description of the proposed research.

3. SPECIFIC POLICIES

3.1 Submission Requirements for Initial Review

3.1.1 Submission requirements for initial review are outlined in the IRB Application. Investigators applying for initial approval of proposed research must follow the guidance.

3.2 Submission Requirements for Continuing Review

3.1.2 During the approval period, investigators must submit documentation to inform the IRB about changes in the status of the study. Submission requirements are outlined on the Modification Submission Form.

3.2.2 Progress Reports and/or Request to Renew IRB Approval

Sixty (60) days prior to IRB approval expiration date, investigators requesting renewal of an approved research project must submit a completed Continuing Review Request. All the required materials that are indicated on the form are also required prior to review.

3.3 Action Taken If Documentation is not adequate or Additional Information is Required

If the IRB or IRB staff determines that the submitted documents are not adequate, investigators may be required to submit additional information, or their presence may be required to answer questions or explain the details of the study. No incomplete submission will be reviewed by the IRB.

4. REFERENCES

45 CFR 46.115; 21 CFR 56.108(a)(4); OHRP Guidance on Continuing Review, January 15, 2007

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Title	FO 301 Research Submission Procedures
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FO 302 IRB MEETING ADMINISTRATION

1. PURPOSE

The policies in this section provide the framework to ensure that IRB meetings are conducted and documented in a consistent manner in order to meet federal and institutional requirements.

2. POLICY STATEMENT

Except when an expedited review procedure is used, the IRB will review proposed research at convened meetings at which a quorum in present. Each IRB will meet monthly, or at some other frequency determined by the Chairperson and the IRB Executive Director.

3. SPECIFIC POLICIES

3.1 Quorum

3.1.1 A majority of members must be present. Majority is defined as first whole number that exceeds 50%.

3.1.2 A quorum consists of regular and/or alternate members and includes at least one member whose primary concerns are in scientific areas, and one member whose primary concerns is in a nonscientific areas.

3.1.3 An alternate member may attend in the place of a regular member in order to meet the quorum requirements outlined above.

3.1.4 Special consultant(s) will not be used to establish a quorum.

3.2 Primary Reviewers

Prior to the meeting, the chairperson or IRB administrator will designate primary and secondary reviewers for each research protocol. For protocols requiring review by a convened meeting of the IRB, the primary reviewer will conduct an in-depth review of all materials and will be prepared to lead the discussion at the convened meeting of the IRB. All other members will review materials provided prior to the meeting and will be prepared to participate in the discussion at the convened meeting.

3.3 Meeting Materials Sent Prior to IRB Meetings

All IRB members will be sent study documentation required for review in sufficient time prior to the meeting to allow for adequate review. These include:

3.3.1 Agenda: A meeting agenda will be prepared by the IRB administrator or designee and distributed to IRB members prior to each meeting. A copy of the agenda and attached materials will be maintained on file with the meeting minutes.

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The meeting agenda will remind members to contact the IRB Administrator or Chair as soon as possible to declare any potential COI they may have with research that will be reviewed by the convened IRB.

3.3.2 Reviewer materials: Materials distributed to IRB members are outlined in the Guide to Daily Operations, FO 302. The read-ahead packets will include copies of the completed Pre-Review Forms and all appropriate IRB Reviewer Checklists.

3.4 Minutes

3.4.1 Recording: The IRB administrator or designee will prepare IRB minutes according to the Minutes Template.

3.4.2 Draft minutes will be distributed to members at the next IRB meeting following completion by staff for review. Any corrections requested by the IRB will be made by the administrator or designee and the minutes will be included on the agenda of the next IRB meeting.

IRB administrators will maintain copies of the agendas and minutes.

3.5 Telephone Use

3.5.1 Convened Meeting Using a Speaker Phone

Should a member not be able to be physically present during a convened meeting, but is available by telephone, the meeting can be convened using a speakerphone. The member who is not physically present will be connected to the rest of the members via speakerphone. In this manner, all members will be able to discuss the protocol even though one member is not physically present. Members participating by such speakerphone call may vote provided they have had an opportunity to review all the material the other members have reviewed.

3.5.2 Meetings Conducted Via Telephone Conference Calls

On occasion, meetings may be convened via a telephone conference call. A quorum (as defined above) must participate for the conference call meeting to be convened.

To allow for appropriate discussion to take place, all members must be connected simultaneously for a conference call to take place -- "telephone polling" (where members are contacted individually) will not be accepted as a conference call.
Members not present at the convened meeting, or participating in the conference call may not vote on an issue discussed during such a telephone conference convened meeting (no voting by proxy).

3.6 Voting

Members of the IRB vote upon the recommendations made by the primary reviewers according to the criteria for approval (See. SOP RR 403 and RR 405). If quorum is lost during a meeting, the IRB cannot take votes until it is restored.

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The IRB may take the range of activities described in RR 407. Members also will determine level of risk, the frequency of review for each protocol and monitoring of the investigative site and whether third party assessment and follow-up will be needed (Section 404 and 405 respectively).

If an IRB staff member is serving on the Board as a regular or alternate member that staff member will not be responsible for any administrative functions during that meeting, specifically, he or she will not take minutes and is expected to contribute to the discussion as a substantive participant.

4. REFERENCES

45 CFR 46.103(b)(4); 45 CFR 46.107(f); 21 CFR 56.107(f); 45 CFR 46.108; 21 CFR 56.108(c); 45 CFR 46.109(a); 21 CFR 56.109(a); 45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2); FDA Information Sheets

Title	FO 302 IRB Meeting Administration
Date Last Reviewed	16 April 2009
Version	7.0, 16 April 2009
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FO 303 ADMINISTRATIVE DISTRIBUTIONS OF MATERIALS

1. PURPOSE

The policies in this section describe the requirements to document pre-review and distribution prior to IRB review.

2. POLICY STATEMENT

The efficiency and effectiveness of the IRBs are supported by administrative procedures that assure that IRB members not only have adequate time for thorough assessment of each proposed study, but that the documentation they receive is complete and clear enough to allow for an adequate assessment of study design, procedures, and conditions.

3. SPECIFIC POLICIES

3.1 Incomplete Submissions

Incomplete applications will be logged into the database and assigned to an IRB. The IRB Administrative staff will contact the investigator and request all necessary material.

3.2 Scheduling for Review

If a complete submission meets expedited review requirements, the review will be performed as described in SOP 402. All other applications requiring review by a convened IRB will be placed on the agenda for the earliest meeting possible for review by the appropriately constituted IRB.

3.3 Distribution Prior to IRB Meetings

Primary reviewers, regular members and alternates receive and review the materials listed on the IRB Application Forms. Alternates are required to receive and review the same materials as any other IRB member. Consultants will only receive copies of material that pertain to their requested input as determined by the IRB Executive Director, Associate Director, or Chair.

Copies of application materials described in Policy 301 will be distributed to all IRB members within 7 - 14 days and no fewer that 7 days prior to the IRB meeting prior to the meeting. Late submission add-ons (e.g., a report of an unanticipated problem) will be submitted to members via e-mail within 2 days of the IRB meeting.

Original submission materials will be retained in the Office of Regulatory Affairs and available for the IRB meeting.

3.4 Confidentiality

All material received by the IRB will be considered confidential and will be distributed only to meeting participants (regular members, alternate members and special consultants) for the purpose of review. All application materials will be stored in an IRB study file with access limited to the IRB Executive Director, IRB Administrative staff, Executive Chair, IRB Chairs, and their designees.

3.5 Destruction of Copies

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All material received by the IRB considered confidential and in excess of the required original documentation and appropriate uncontrolled Forms will be collected at the end of the meeting and destroyed by a method deemed appropriate by the Executive Director.

4. REFERENCES

45 CFR 45.108(a); 21 CFR 56.108(a)

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FO 304 DOCUMENTATION AND DOCUMENT MANAGEMENT

1. PURPOSE

The policies in this section describe the requirements for document management, including

Document Retention;
Administrative Documents; and
Archiving.

2. POLICY

Institutional Review Board files must be maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including scientific reviews, if any, continuing reviews, modifications, reports of unanticipated problem increasing risks to subjects or others, subject complaints, and reports of serious or continuing noncompliance. All records regarding a submitted study (regardless of whether it is approved) must be retained in an appropriate manner as required by regulatory requirements and/or institutional policy.

Records must be accessible for inspection and copying by authorized representatives of the sponsor, funding department or agency and institutional auditors at reasonable times and in a reasonable manner.

Required documents must be submitted to the appropriate funding entity as required.

3. SPECIFIC POLICIES

3.1 Document Retention.

The IRB must retain all records regarding a project or protocol application (regardless of whether it is approved) for at least three (3) years. For all applications that are approved and the research initiated, the IRB must retain all records regarding that research for at least three (3) years after completion of the research or termination of IRB approval.

3.1.1 Adequate documentation of each IRB's activities will be prepared, maintained and retained, including:

Submissions: Copies of all original research protocols or project descriptions reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, progress reports submitted by investigators, and reports of unanticipated problems occurring to subjects and reported protocol deviations as submitted.

Regulatory Documents/documentation:
- Correspondence between the IRB and investigator
- Statements of significant new findings provided to participants
- For the initial & continuing review of research by expedited procedure
    - The specific permissible category
    - Descripton of action taken by reviewer
    - Any findings under the regulations

- For exemption determinations, the specific category of exemption
- Unless documented in the minutes, determinations requqired by the regulations and protocol specific findings for:
    - Waiver or alteration of the consent process
    - Research involving pregnant women, fetuses, and neonates
    - Research involving prisoners
    - Research involving children
- For each protocol's initial and continuing review, the frequency for the next continuing review.

Copies of all submitted monitoring reports, site visit reports and other continuing review activities.

Reports of any complaints received from participants, regulatory agencies and their resolution.

Agendas and Minutes of all IRB meetings.

3.2 IRB Administration Documents

The IRB must maintain and retain all records regarding IRB administrative activities that affect review activities for at least three (3) years. The IRB must retain all records regarding protocols that are approved and the research initiated for at least three (3) years after completion of the research or termination of IRB approval.

3.2.1 Rosters of regular and alternate IRB members identified by name, earned degrees, representative capacity, and indications of experience sufficient to describe each regular and alternate member's chief anticipated contribution to the IRB's deliberations; and any employment or other relationship between each member and the IRB and/or the University (e.g., full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant).

Alternate members will be included on the roster. In addition to the above information, the roster shall indicate the regular member for whom the alternate may substitute

Current and obsolete membership rosters will remain in the Office of Regulatory Affairs and then archived according to University policy.

The roster of IRB members must be submitted to Office for Human Research Protections (OHRP). Any changes in IRB membership must be reported to the head of the department or agency supporting or conducting the research, unless the department or agency has accepted the existence of an FWA. In the latter case, changes in membership are to be reported to OHRP.

3.2.2 Current and obsolete copies of the Standard Operating Policies.

3.2.3 Delegation of specific functions, authorities, or responsibilities by the Executive Chairperson or an IRB Chairperson must be documented in writing and maintained in the Office of Regulatory Affairs.

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3.3 Archiving

All documents and materials germane to IRB determinations will be archived according to institutional policy.

4. REFERENCES

45 CFR 46.103; 45 CFR 46.115; 21 CFR 56.115

Title	FO 304 Documents and Document Management
Date Last Reviewed	25 August 2009
Version	7.1, 25 August 2009
Supersedes	7.0, 16 April 2009

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RR 400	REVIEW OF RESEARCH
401 A	HUMAN RESEARCH
401 B	EXEMPT RESEARCH
402	EXPEDITED REVIEW
403	INITIAL REVIEW - CRITERIA FOR IRB APPROVAL
404	CONTINUING REVIEW
405	CONTINUING REVIEW - CRITERIA FOR RENEWAL
406	STUDY COMPLETION
407	CATEGORIES OF ACTION
408	RESPONDING TO REPORTS OF NONCOMPLIANCE
409	ADMINISTRATIVE HOLDS AND SUSPENSIONS, TERMINATION OF IRB APPROVAL
503	LEGAL COUNSEL

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RR 401 A HUMAN RESEARCH

1. PURPOSE

This policy describes the research that does not require IRB review because the activity does not involve human research.

2. POLICY STATEMENT

Human research is any activity that either 1) meets the HHS definition of "research" and involves "human subjects" as defined by the HHS regulations or 2) meets the FDA definition of "clinical investigation" and involves "human subjects as defined by the FDA regulation.

Unless otherwise required pursuant institutional policy, activities that do not meet the definition of human research do not require submission to the IRB.

The IRB Guidance: Is IRB Review Required? provides direction on making human research determinations.

3. SPECIFIC POLICIES

3.1 Activities that do not require IRB Review

In addition to the Executive Chair, IRB Chairs and delegated IRB members, the IRB Executive Director, IRB Associate Directors and IRB administrators (collectively referred to as "staff") may determine that an activity does not meet the regulatory definition of human research. Investigators who elect to an official determination may submit the Research Determination Worksheet for review.

Staff will review Research Determination Form and supporting documents. Formal submissions will be logged into the database and filed. Investigators will be notified in writing if proposed activities do not meet the regulatory definition of human research.

4. REFERENCES

21 CFR 50.3; 45 CFR 46.102; 21 CFR 812.3(p)

Title	RR 401 A Human Research
Date Last Reviewed	16 April 2009
Version	7.0, 16 April 2009
Supersedes	6.0, 18 April 2008

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RR 401B EXEMPT RESEARCH

1. PURPOSE

This policy describes the process for determining that human research is exempt from further review by the IRB.

2. POLICY

Research activities in which the only involvement of human subjects will be in one or more specific categories may be exempt from IRB review. Determination of exemption must be based on regulatory and institutional criteria and documented. Exempt status may be determined by the IRB Executive Chair, IRB Chairs, delegated IRB members, IRB Executive Director, Associate Directors, or IRB Administrators.

3. SPECIFIC POLICIES

3.1 Exempt Research Activities

The IRB will exempt from further human research review only those research activities that involve human subjects that, fall within one or more of the specified exempt categories which are listed within instructions for completion of the Claim of Exemption Form.

3.2 Ethical Standards for Exempt Research

When approving exempt research, the IRB will determine that the following criteria are met where applicable:

- The research presents no more than minimal risk to participants.
- Selection of participants is equitable.
- If the research involves interactions with participants, the circumstances of consent minimize coercion and undue influence.
- Participants will be informed that the study involves research, will be provided with information about the study procedures that the research is voluntary, and will be provided with information about whom to contact with questions.
- Provisions for protecting the privacy interests of participants are adequate.
- If private identifying data are recorded, provisions for maintaining the confidentiality of data are adequate.

3.3 Approval Period for Exempt Research

Annual continuing review is not required for research determined exempt. Investigators must submit request to close the research protocol when research is completed. Otherwise, the research protocol is approved for three years and expires at the end of the three year period. The PI may request an extension of the approval period.

Investigators are required to report modifications that may change the eligibility of the protocol's exempt status.

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It is the investigator's responsibility to notify the IRB of any changes or modifications that are made to the study's design, procedures, and so on, that do not fall within one of the categories exempted from the regulations.

4. REFERENCES

45 CFR 46.101(b); 21 CFR 46.102; 21 CFR 56.104

Title	RR 401B Exempt Research
Date Last Reviewed	16 April 2009
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RR 402 EXPEDITED REVIEW

1. PURPOSE

This policy describes the research that can be reviewed by the IRB chair or designee and outlines the process to determination if the research meets criteria for expedited review.

2. POLICY

An expedited review procedure consists of a review of research involving human subjects by the Executive Chair or Chair of the IRB or by one or more experienced reviewers designated by the Executive Chair from among members of the IRB.

The categories of research that may be reviewed by the IRB through an expedited review procedure include research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the specific categories listed in the regulations at 45 CFR 46.110 and 21 CFR 56.110.

This policy pertains to both initial and continuing IRB review of the items included in this policy.

The expedited review process may not be used for classified research involving human subjects. Expedited review may not be used for research involving prisoners.

3. SPECIFIC POLICIES

3.1 Authority of the Expedited Reviewer

The Executive Chairperson, Chair, Co-Chair or other experienced IRB member reviewers, designated in writing, by the Executive Chair or Chair, or by the IRB members voting in a convened meeting may exercise all of the authorities of the IRB, except that he/she may not disapprove the research. A research proposal may be disapproved only after review by the convened IRB.

Consultants may assist the IRB in the review of issues that require expertise beyond that available on the committee; but may not carry out the expedited review. Individuals conducting expedited review will contact the IRB Executive Director or Executive Chair to request a consultant's review.

3.2 Notification of the Board

When the expedited review procedure is used, all regular members will be informed at the next convened meeting through publication on the IRB agenda of actions taken by the designated IRB reviewer.

3.3 Documentation

The information received by the Primary Reviewer for expedited review is the same information provided to the Primary reviewer for review at a convened IRB meeting.

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If the study qualifies for review via expedited review, the designated IRB reviewer will document his/her determination of the applicable expedited review category. Consistent with review by a convened IRB, expedited reviewer will consider:

- all the criteria for review found at 45 CFR 46.111 and 21 CFR 56.111.
- all requirements found at Subparts B, C, and D, when applicable.
- the requirements for informed consent including altering or waiving the requirement for consent.

The IRB's agenda and minutes will include documentation of the studies that were reviewed via expedited review including a brief description of the research, the designated IRB reviewer who approved the research and the approval date.

3.4 Additional Items that May be Reviewed by the Chair or Designee

3.4.1 Withheld Approval Pending Minor Revisions or Conditional Reapprovals

Minor revisions to consent documents and documentation submitted as a result of convened IRB review and as a condition to final approval may be reviewed by the Executive Chair, IRB Executive Director, IRB Associate Director, IRB Chair or his/her designee or any IRB experienced member designated by the IRB Chair.

However, when the convened IRBs requested substantive clarifications or modifications that were directly relevant to the determinations required by the IRBs, the protocol will go back to a convened IRB and not be approved by the IRB Chair or member on behalf of the convened IRB.

3.4.2 Continuing Review

The Executive Chair, IRB Executive Director, IRB Associate Director, IRB chairperson or his/her designee may use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Any protocol revision that entails more than a minimal risk to the participant as determined by the Executive chairperson, IRB chairperson or his/her designee must be reviewed by the convened IRB at a convened meeting. Addition of procedures that involve increased risk or discomfort may not be considered minor changes. Examples of the kinds of minor changes that may be eligible for expedited review are provided in the Guide to Daily Operations RR 402.

Revisions to Informed Consent Documents: Minor changes to informed consent documents that do not affect the rights and welfare of study subjects, or do not involve increased risk or significant changes in study procedures may be reviewed and approved by the Executive chairperson, IRB chairperson or his/her designee.

Advertisements: The Executive chairperson or his/her designee may approve new or revised recruitment advertisements, recruitment flyers, and audio or video recruitment materials.

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4. REFERENCES

45 CFR 46.102(i); 21 CFR 56.102(i); 45 CFR 46.110; 21 CFR 56.110; Federal Register Vol. 63, No. 216, 11/9/98, pp. 60353-60356; 45 CFR 46.111; 21 CFR 56.111

Title	RR 402 Expedited Review
Date Last Reviewed	16 April 2009
Version	7.0, 16 April 2009
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RR 403 INITIAL REVIEWS: CRITERIA FOR IRB APPROVAL

1. PURPOSE

This policy elucidates the minimal requirements that all research proposals that involve human subject participation must meet in order to be approved for conduct at the University of Pennsylvania.

2. POLICY

All research proposals that intend to enroll human subjects must meet certain criteria before study related procedures can be initiated. The criteria are based on the principles of justice, beneficence and autonomy as discussed in the Belmont Report and are specified below. In addition, certain other criteria that are unique to the University of Pennsylvania may apply and must be met as well before any involvement of human subjects may begin.

3. SPECIFIC POLICIES

3.1 Minimal Criteria for Approval of Research

In order for a research project to be approved, the IRB must find that:

3.1.1 Risks to subjects are minimized:

By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

3.1.2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies those subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3.1.3 Selection of subjects is equitable. In making this assessment, the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.

3.1.4 Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by appropriate local, state and federal regulations.

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3.1.5 Informed consent will be appropriately documented as required by local, state and federal regulations.

3.1.6 Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

3.1.7 Where appropriate, there is adequate provision to protect the privacy of subjects and to maintain the confidentiality of data.

3.1.8 When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence or international sites are used, additional safeguards have been included in the study, and in the IRB review process to protect the rights and welfare of these subjects.

3.1.9 The IRB determines that the provisions are adequate to protect the privacy interests of subjects.

3.1.10 The IRB determines that the provisions are adequate to protect the confidentiality of data.

3.1.11 For repository activities, the IRB makes determinations concerning the regulatory status and appropriate use of stored biologic samples.

3.2 Additional Criteria for Studies Involving Protected Health Information

Studies proposing access to or collection of protected health information within the covered entities of the University of Pennsylvania require consideration of additional items to protect the privacy of the protected health information. Therefore the IRB must find that:

3.2.1 Appropriate authorization is obtained from human subjects or their effective representative for the use or disclosure of their protected health information;

3.2.2 The IRB has approved a waiver of such authorization;

3.2.3 The protected health information will be contained in a limited data set with appropriate safeguards to maintain privacy; or,

3.2.4 The protected health information will be de-identified.

3.3 Other Criteria

The IRB may require verification of information submitted by an investigator. The need to verify any information will be determined by the IRB at a convened meeting. The purpose of the verification will be to provide necessary protection to subjects when deemed appropriate by the IRB.

3.4 Reliance on Other IRBs for Review and Approval of Research Conducted at the University of Pennsylvania

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The IRB may enter into joint review arrangements, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort as allowed and upon modification of the Institutional FWA.

4. REFERENCES

45 CFR 46.111; 21 CFR 56.111; OHRP Guidance on Engagement of Institutions in Human Subjects Research, October 16, 2008; OHRP Frequently Asked Questions: Assurance Process; OHRP Correspondence: Determining when institutions are engaged in research, January 13, 2009

Title	RR 403 Initial Review: Criteria for IRB Approval
Date Last Reviewed/Revised	16 April 2009
Version	7.0, 16 April 2009
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RR 404 CONTINUING REVIEW

1. PURPOSE

This section elucidates the policy for the continuing review that occurs after approval and prior to review for renewal of IRB approval.

2. POLICY

No investigator has a right to conduct research within this institution. Rather, it is a privilege granted by society as a whole and the Trustees of the University of Pennsylvania in particular.

IRB approval may be withdrawn at any time if warranted by the conduct of the research. The regulations authorize the IRB to establish procedures for the concurrent monitoring of research activities involving human subjects. Periodic (continuing or ongoing) review of research activities is necessary to determine whether approval should be continued or withdrawn. All non-exempt research involving human subjects must be reviewed (renewed) no less than once per year.

No research related activities may occur after the protocol expiration date unless the PI contacts the Office of Regulatory Affairs, IRB and the Executive Chair (or authorized designee) determines that it is in the best interest of subjects to continue during the lapse in IRB approval.

IRB approval for the conduct of a study may be withdrawn at any time if the risks to the subjects are determined to be unreasonably high. For example, more than an expected number of adverse events, unexpected serious adverse events; or evidence that the investigator is not conducting the investigation in compliance with IRB or University guidelines. Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated. Continuing review includes, but may not be limited to the following activities:

- Site Visits and Third Party Verification
- Review of Serious and Unexpected Adverse Events and Unanticipated Problems Posing Risks to Subjects or Others
- Review of Significant New Findings
- Modifications

3. SPECIFIC POLICIES

3.1 Site Visits/Audits and Third Party Verification

The IRB has the authority to observe, or have a third party observe, the consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and within the University Policies and Procedures and site-specific procedures as appropriate. Under the direction of the IRB Associate Director, IRB

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personnel or members may perform site visits or use another party either affiliated with the institution or not, to verify information in the study application, or in any interim, continuing review or renewal submissions.

The IRB will consider the following criteria to determine if a site visit or third party verification process is required:

- The research involves vulnerable populations or high risk procedures.
- The investigator has a history of serious or continuing non-compliance related to continuing review in the past three years.
- The IRB has reason to doubt the veracity of the information provided by the investigator.
- The information provided by the investigator is inconsistent with other information known to the IRB and the inconsistency cannot be resolved through communication with the investigator.
- Any other reason where the IRB believes verification should be required.

Other means of verification. Sponsors may be asked to submit copies of monitoring reports. The IRB may conduct interviews with screened and/or enrolled subjects as deemed necessary.

3.2 Unanticipated Problems Involving Risks to Subjects or Others and Other Reportable Events

Consistent with federal regulations, the University of Pennsylvania requires reporting to the IRB of unanticipated problems posing risks to subjects or others. Unanticipated problems are: (1) unforeseen; and (2) indicate that participants are at increased risk of harm.

The IRB requires researchers to submit reports of the following problems within 10 working days with one exception. The one exception for prompt reporting within 10 days applies to death of a research participant as noted below.

3.2.1 Adverse Event (regardless of whether the event is serious or non-serious, on-site or off-site) that occurs any time during or after the research study, which in the opinion of the principal investigator is both unexpected and related to research procedures.

An event is “unexpected” when its specificity and severity are not accurately reflected in the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts);

An event is “related to the research procedures” if the event is deemed probably or definitely related.

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If the adverse event involved an unexpected death; and other participants or others may be at increased risk of harm, the investigator is required to report the death to the IRB within three days.

3.2.2 Unanticipated adverse device effect. Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

3.2.3 Information that indicates a change to the risks or potential benefits of the research, in terms of severity or frequency. For example:

- An interim analysis indicates that participants have a lower rate of response to treatment than initially expected.
- Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected.
- A paper is published from another study that shows that an arm of the research study is of no therapeutic value.

3.2.4 Any adverse event that represents a serious unexpected problem that is rare in absence of drug exposure (agranulocytosis, hepatic necrosis, or Stevens-Johnson syndrome).

3.2.5 Adverse event that would cause the sponsor to modify the investigator's brochure, protocol, or informed consent to assure the protection of human subjects.

3.2.6 Withdrawal from marketing for safety concerns of a drug, device, or biologic used in a research protocol.

3.2.7 Change to the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant.

Other Reportable Events

3.2.8 Complaint of a participant when the complaint indicates unexpected risks or the complaint cannot be resolved by the research team.

3.2.9 Violation, meaning an accidental or unintentional change to the IRB approved protocol) that placed one or more participants at increased risk, or has the potential to occur again.

3.2.10 Breach of confidentiality.

3.2.11 Incarceration of a participant when the research was not previously approved under Subpart C and the investigator believes it is in the best interest of the subject to remain on the study.

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The IRB will accept other reports when the investigator is unsure whether the event should be reported, and the IRB will review such reports to determine whether the event meets the threshold for an unanticipated event presenting risk to the participant.

Principal investigators will submit a written report of the above events. Initial reports may be accepted by other means such as e-mail, or phone with a follow up written report.

The IRB staff, when necessary in conjunction with the IRB chair, review reports and decide whether the event meets the definition of an unanticipated problem increasing risks to subjects or others.

Events that meet these criteria will be considered unanticipated problems involving risks to participants or others, will be reviewed by the convened IRB, and will be reported according to CO 602.

The IRB Administrator selects the primary reviewer. When, possible the IRB member assigned to the initial primary review will review the event. Otherwise, reviewers will be selected based on their, education, experience, and areas of expertise.

Primary reviewers will receive the sponsor protocol, investigator brochure, original IRB application form, consent document, copy of the report form, any supplemental information

All other IRB members will receive the original application form, consent document, copy of the report form, any supplemental information.

The IRB may request a consultant opinion or engage the division or department chair to collect additional information on the event.

The IRB considers the following actions:

- Accept report or with no additional requirements.
- Approve investigator’s proposed changes.
- Administrative hold on the study pending IRB receipt of further information from the PI in a time period not to exceed 90 days.
- Modification of the protocol.
- Modification of the information disclosed during the consent process.
- Providing additional information to current participant the information may relate to the participant’s willingness to continue participation.
- Making arrangements for clinical care outside the research or additional follow-up for participants.
- Providing additional information to past participants.

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- Requiring current participants to re-consent to participation.
- Alteration of the frequency of continuing review.
- Observation of the research or the consent process.
- Requiring additional training of the investigator.
- Notification of investigators at other sites.
- Obtaining additional information.
- Termination or suspension of the research. If this action is taken, the IRB Executive Director will notify the Institutional Official to initiate any reporting actions. If the IRB does not consider the event to represent an unanticipated problem involving risks to participants or others, no further action needs to be taken.

3.3 Modifications

Federal regulations require that all modifications in approved research, during the period for which approval has already been given, may not be initiated without prior IRB review and approval except where necessary to eliminate apparent immediate hazards to human subjects. Sometimes modifications are noted or recognized after they occur. These changes will be reviewed by the IRB as events that may represent unanticipated problems involving risks to participants or others and to determine whether the change was consistent with ensuring the participants' continued welfare.

3.3.1 The IRB categorizes modifications into 3 types: Amendments, Deviations, and Exceptions that require reporting to the IRB.

<u>Amendment</u>

An amendment is a permanent, intentional action or process that revises/amends/modifies a previously approved research protocol. Information relating to protocol amendments will be provided to research subjects when the information may relate to their willingness to continue to be a part of the research. Investigators or sponsors must submit requests for changes to the IRB in writing. Upon receipt of the protocol amendment, an IRB Administrator with the assistance of the IRB Executive Chair, or Senior IRB Administrative staff determine the appropriate level of review.

Minor modifications are defined as those that do not materially affect an assessment of the risks and benefits of the study and do not substantially change the specific aims/design of the study. Representative minor modifications include but are not limited to:

- The addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol;
- A minor increase or decrease in the number of participants;

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- Narrowing the inclusion criteria;
- Broadening the exclusion criteria;
- Changes to the dosage form (e.g. tablet to capsule or oral liquid) of an administered drug (when the dose and route of administration remain constant);
- Decreasing the number of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations;
- An increase in the number of study visits for the purpose of increased safety monitoring;
- A decrease in the number of study visits, provided the decrease does not affect the collection of information related to safety evaluations;
- Changes in remuneration;
- Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement;
- The addition or deletion of qualified investigators;
- The addition or deletion of study sites;
- Minor changes specifically requested by other University Committees with jurisdiction over research.

Exception

A one time, intentional action or process that departs from the IRB approved study protocol, intended for one occurrence.

If the action disrupts the study progress, such that the study design and results would be compromised, and the action compromises the safety and welfare of study subjects, prior documented IRB approval is required.

Deviation

A one time, unintentional action or process that departs from the IRB approved study protocol, involving one incident and identified retrospectively, after the event occurred. If the impact on the protocol disrupts the study design or compromises the safety and welfare of the subjects, the deviation must be reported to the IRB within 10 business days.

When the IRB reviews the exceptions and deviations, a determination will be made as to whether information related to protocol changes should be provided to participants when such information might relate to their willingness to continue to

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take part in the research. The investigator will be advised if subjects need to be informed.

3.4 Significant New Findings

During the course of a study, the IRB may review reports generated from the DSMB, adverse events, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit balance is still acceptable, whether or not new information needs to be conveyed to subjects, or if a segment of the population may be bearing an undue burden of research risk or being denied access to promising therapy. Such significant new findings will be reviewed by the Executive Chairperson, chairperson or their designee who shall decide whether such new information merits review by the IRB.

3.5 Reports from Employees, Staff and Faculty

It is the responsibility of the investigative team, medical staff, nursing staff, or any other employee of this institution to promptly report to the IRB any findings, results, occurrence, or new information about a study being conducted at any facility under the jurisdiction of the IRB that could affect the rights and welfare of research subjects. It is the responsibility of the IRB staff and members to act on any such information in order to protect research subjects.

3.6 Reports of Serious or Continuing Noncompliance Federal Regulation; or the Requirements or Determinations of the IRB

Reports of serious or continuing noncompliance or the requirements or determinations of the IRB will be handled in accordance with SOPs 408 and 409.

3.7 Suspension or Termination of IRB Approval

A decision to suspend or terminate a protocol must include an explicit consideration for the rights and welfare of subjects already enrolled in the study. If the suspension or termination is imposed on the investigator, the IRB Executive Chair may be consulted about whether and how to continue the care of enrolled subjects. The matter will be discussed at the next convened meeting of the IRB.

Any suspensions or terminations of approval shall include a statement of the reasons for the IRB's action and shall be promptly reported by the IRB to the investigator, IRB Executive Chair and Institutional Official. The timeframe for notification to the institutional official, sponsors, and regulatory agencies will depend on the urgency of the matter. Situations presenting immediate, unforeseen risk to subjects will be reported immediately to the institutional official and sponsors. When the research is sponsored or supported by the Department of Health and Human Services, the Institutional Official will notify OHRP. For FDA regulated research, the Institutional Official will notify FDA in writing after the IRB has considered the matter at the next convened meeting.

Enrolled subjects will be notified if a protocol in which they are enrolled is suspended or terminated. The IRB will determine at a convened meeting how and when the notification will take place. The IRB will consider whether to notify former subjects if the

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reason for termination or suspension was associated with risks not disclosed in the consent process.

4. REFERENCES

45 CFR 46.103; 21 CFR 56.108; 45 CFR 46.109; 21 CFR 56.109; 45 CFR 45.115; 21 CFR 56.115; OHRP Guidance on Continuing Review, January 15, 2007; FDA Information Sheets, Continuing Review after Study Approval; OHRP Guidance on Reporting and Reviewing Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others, January 15, 2007; FDA Final Guidance on Adverse Event Reporting to IRBs, January 2009

Title	RR 404 Continuing Review
Date Last Reviewed	16 April 2009
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RR 405 CRITERIA FOR RENEWAL

1. PURPOSE

This section elucidates the policy for the continuing review prior to the expiration of the IRB approval period.

2. POLICY STATEMENT

The IRB conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year, and has the authority to observe or have a third party observe the consent process and the research.

3. SPECIFIC POLICIES

3.1 Interval for Review for Purpose of Renewal

The IRBs must conduct continuing review of protocols for purposes of renewal of the IRB approval period at intervals appropriate to the degree of risk, which is determined at the time of initial review, but not less than once per year. “Not less than once per year" means that the research must be reviewed on or before the one-year anniversary date of the previous IRB review, even though the research activity may not begin until some time after the IRB has given approval.

The IRB may approve a protocol for a shorter period if warranted by the risks presented to participants. The IRB may approve a study for 6 months or may stipulate the approval on further IRB review after a defined number of participants have been enrolled (*e.g.*, review after the first three subjects receive a Phase I drug that has never been tested in humans). The IRB will generally consider review more often than annually for: (a) novel high-risk study using new therapeutic modality; (b) phase I studies of a new drug or biologic that has never been tested in humans; (c) studies involving a novel significant risk medical device that has never been tested in humans; and (d) other high-risk studies as IRB members deem appropriate including research for which the IRB determines that reports to the IRB of monitoring data should be more frequent than annually.

Investigators or qualified designees are required to submit a Request for Continuing Renewal Form and other materials outlined on the Form. The report should normally be filed eight weeks before the study approval period ends.

3.2 Extensions of Approval Period

There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted. If an investigator fails to provide continuing review information to the IRB, or the IRB has not reviewed and approved a research study before the expiration date specified by the IRB, no research related activities may occur after the protocol expiration date unless the PI contacts the Office of Regulatory Affairs and the IRB Executive Chair (or authorized designee) determines that it is in the best interest of individual subjects to continue during the lapse in IRB approval.

3.3 Criteria for Renewal

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Continuing review must be substantive and meaningful. The IRB (or the reviewer for protocols reviewed under an expedited procedure) must determine that:

- the risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
- the selection of subjects continues to be reasonable in relation to anticipated benefits;
- informed consent continues to be appropriately documented;
- there are:
  - provisions for safety monitoring of the data,
  - protections to ensure the privacy of subjects and confidentiality of data, and
  - appropriate safeguards for vulnerable populations.

Because it may be only after research has begun that the real risks can be evaluated and the preliminary results used to compute the actual risk/benefit ratio; the IRB can then determine whether or not the study can be renewed at the same risk/benefit, or if new information has changed that determination.

In order to determine the status of the study, the following will be reviewed:

3.3.1 Consent Document: Each member of the IRB shall review the currently approved consent document and must ensure that the information is still accurate and complete. Any significant new findings that may relate to the subject's willingness to continue participation should be provided to the subject in an updated consent document.

3.3.2 Current Approved Protocol including any amendments to Protocol since initial review. A copy of the protocol will be sent to primary reviewer of the continuing review. Amendments to a research protocol should be submitted on an ongoing basis during the course of the study. They may be submitted at the time of continuing review. A separate cover letter describing the amendment and all appropriate documentation (revised consent form) must accompany the continuing review application.

3.3.3 Continuing IRB review is required unless the project is complete with no subjects in follow up and no further contact with participants and all data analysis that requires contact with records or specimens linked to privately identified information is complete.

3.3.4 Continuing Review of DSMB-Monitored Clinical Trials. When a clinical trial is subject to oversight by a Data Safety Monitoring Board (DSMB), whose responsibilities include review of adverse events, interim findings and relevant literature (e.g. DSMBs operating in accordance with the National Cancer Institute Policy for Data and Safety Monitoring of Clinical Trials), the IRB conducting continuing review may rely on a current statement from the DSMB indicating that it has reviewed study-wide adverse events, interim findings and any recent literature

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that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

3.3.5 Request for Continuing Review Form: All IRB members shall receive a request for continuing review form prepared and submitted by the principal investigator or designee.

3.4 Possible Outcomes of Continuing Review

As an outcome of continuing review, the IRB may authorize continuation of the research, require that the research be modified or halted altogether. The IRB may need to impose special precautions or relax special requirements it had previously imposed on the research protocol such as frequency of monitoring, requirement for interim reports or duration of IRB approval period (so long as the approval period does not exceed one year . Any changes required to obtain continued renewal approval shall be provided to the investigators by the IRB staff.

3.5 Expedited Review for Renewal

A protocol that was originally reviewed using expedited review procedures may receive its continuing review on an expedited basis when one of the following conditions is met:

3.5.1 Where the research was originally reviewed using an expedited review process and the research activities continues to meet the applicability criteria.

3.5.2 Research was previously reviewed by the convened IRB where one of the following conditions is met:

- The research is permanently closed to enrollment of new subject; all research related interventions have been completed; and the study remains open only for long-term follow up;
- No subjects have been enrolled and no additional risks have been identified; or,
- The remaining research activities are limited to data analysis.

For multi-center trials “no subjects enrolled” means that no subjects have ever been enrolled at the University of Pennsylvania; and “no additional risks have been identified” means that no additional risks have been identified at any site.

A protocol that was determined by the full IRB to qualify for expedited renewal at the time of initial review (see categories of expedited review) may be reviewed and re-approved using an expedited review mechanism.

3.5.3 Where the research is not conducted under an investigational new drug application or investigational device exemption and where other expedited review categories do not apply but the IRB has determined that the research involves no more than minimal risk and no additional risks have been identified.

When conducting research under an expedited review procedure, the Executive chairperson, chairperson or his or her designee conducts the review on behalf of the full

IRB using the same criteria for renewal as stated in this section 3.3 of this policy. If the expedited reviewer feels that there has been a change to the risks so that they now are more than minimal as determined by the IRB, he or she may refer the study to the full board for review.

3.6 How the Continuing Review Date is Determined

When the IRB has determined that continuing review will occur no sooner than within 1 year, the date of continuing review is determined by using the date the protocol was reviewed and approved by the convened IRB or approved via an expedited mechanism. When continuing review occurs annually and the IRB approves the research within 30 days prior to the expiration date, the IRB may retain the original anniversary date to determine the next continuing review date.

4. REFERENCES

45 CFR 46.109(c); 21 CFR 56.109(f); OHRP Guidance on Continuing Review, January 15, 2007; FDA Information Sheets, Continuing Review after Study Approval

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RR 406 STUDY COMPLETION

1. PURPOSE

This section elucidates the policy for the closing a research project or protocol.

2. POLICY STATEMENT

The completion of the study is a change in activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report/notice to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

3. SPECIFIC POLICIES

3.1 Determining When a Project can be Closed

3.1.1 Externally or internally funded protocols: When the project is complete with no subjects in follow up and no further contact with participants and all data analysis that requires contact with records or specimens linked to privately identified information is complete.
3.1.2 Multi-site industry supported clinical trials may be closed when data collection and follow-up is complete at the institutional site and the industry monitor has closed the site.

3.2 Completion Reports

Final Reports should be submitted within 30 days after completion of the study. Final reports may be submitted in any format that provides adequate information about the status of the study, such as computer printouts, telephone reports, letters, etc. Final reports may be submitted by the investigator or his or her designee. The IRB Administrator will review all reports of study completion and, if needed, request further information from the investigator to clarify any questions that may arise.

Notice of the submission of Final Reports or closures will be presented to the Board at the next scheduled meeting; and copies of the reports and any supplement information will be made available for the members upon request.

4. REFERENCES

21 CFR 56.108 (a)(3); 45 CFR 46.103(b)(5)

Title	RR 406 Study Completion
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RR 407 CATEGORIES OF ACTION

1. PURPOSE

This section elucidates the actions the IRB may take as resulting from its review of research.

2. POLICY

As a result of its review, the IRBs may determine to approve or disapprove the proposed research activity, or to require modifications to the project/protocol/documents in order to secure IRB approval of the research activity. Except when the expedited review procedure is used, these actions will be taken by a vote of a majority of the regular and alternate members present, except for those members present but unable to vote in accordance with IRB's conflict of interest policies. When reviewed via expedited review, the Executive Chairperson, chairperson or their designee can take any of the following actions except to disapprove a study.

3. SPECIFIC POLICIES

3.1 Determinations: Initial Review

Initial Review: The IRB may make one of the following determinations as a result of its review of research submitted to the convened IRB for initial review:

3.1.1 Approval

When an acceptable risk/benefit ratio exists and the regulatory criteria required for approval are deemed acceptable, protocol is approved as submitted.

3.1.2 Withheld Approval Pending Changes

The IRB determines that the protocol will meet the regulatory criteria for approval provided the investigator agrees to make changes to the IRB application including the informed consent document.

The IRB Executive Chair, Chair or another designated IRB member may subsequently approve the revised research protocol on behalf of the IRB under an expedited review procedure. Research may not be initiated until a letter of IRB approval is received and other applicable committee reviews are satisfied.

When the IRB requires substantive changes that are directly relevant to the determinations required by the IRB under federal regulations at §_.111, the IRB may not grant withheld approval of the protocol.

3.1.3 Tabled

The IRB requires substantive changes that are directly relevant to the determinations required by the IRB under federal regulations at §_.111, the IRB will table the approval of the protocol pending subsequent review by the convened IRB of the responsive material.

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3.1.4 Disapproved

The IRB determines that the research does not meet the regulatory criteria for approval and cannot provide modifications that may allow the protocol to be approved. The IRB will notify the investigator in writing of the reasons for the decision and will give the investigator an opportunity to respond in person or in writing.

3.2 Determinations: Continuing Review (including modification)

3.2.1 Approval

When an acceptable risk/benefit ratio exists and the criteria required for approval are deemed acceptable, protocol is approved as submitted.

3.2.2 Conditional Approval

When the IRB determines requires minor modification to the protocol or accompaning documents.

3.2.3 Suspension

Study is suspended pending further clarification of issues that deal with the criteria at §_.111.

4. REFERENCES

45 CFR 46.109(a); 21 CFR 56.109(a); 45 CFR 46.111; 21 CFR 56.111

Title	RR 407 Categories of Action
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RR 408 NONCOMPLIANCE

1. PURPOSE

This policy affirms the standards of conduct, elucidates the policy for responding to reports of noncompliance and defines the actions the IRB may take as a result of its review of the reports.

2. POLICY

Penn pledges to promote and uphold the highest ethical standards in the conduct of human research. Employees and agents of the organization are required to comply with federal regulations and the requirements and determinations of the IRB.

All employees and agents of the University of Pennsylvania share the responsibility for reporting incidences of noncompliance with the regulations or the requirements or determinations of the IRB.

3. SPECIFIC POLICIES

3.1 Definitions

3.1.1 Noncompliance is defined as a violation of any federal, state, or local regulation that governs human research; any university policy on human research; any deviation from the protocol approved by the IRB or stipulations imposed by the IRB as a condition of approval.

3.1.2. Serious noncompliance is noncompliance that may affect subject safety; increase risks to subjects; affect the integrity of the data; violate the rights and welfare of subjects; or affect the subject's willingness to participate in research.

3.1.3 Continuing noncompliance means a pattern of noncompliance that indicates a lack of understanding about the regulations or ethical requirements that may affect the rights and welfare of participants. The pattern of noncompliance is assessed by the number of incidents occurring during the course of a protocol, and whether the same noncompliant action was repeated or many different noncompliant events occurred.

The frequency of noncompliance is assessed mainly by the number of incidents occurring during the course of a protocol, and would also take account of whether the same noncompliant action was repeated or many different noncompliant events occurred.

3.1.4 Allegation of noncompliance: A report of noncompliance that represents an unproven assertion.

3.1.5 Finding of noncompliance: A report of noncompliance that is true or an allegation of noncompliance that is determined to be true.

3.2 Reporting Concerns

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3.2.1 Reports of noncompliance in human research may come from many sources including, but not limited to, an investigator (as a self-report); a study monitor; university or school based compliance and audit offices; a sponsor; a research subject; a department chair; a member of the research team; or a person not directly involved with the research.

3.2.2 Persons raising such concerns are encouraged to express them in writing. However, verbal concerns will be received and should be documented on the Compliance Intake Form.

3.2.3 Reports of audit findings indicating serious or continuing noncompliance may also come from many sources including the Ben-Tips hotline.

Within the School of Medicine, the Vice Provost has delegated to the Office of Human Research (OHR) the responsibility for conducting routine and directed compliance audits within the School. When an OHR audit findings indicate potential serious or continuing noncompliance, the OHR will submit to the Vice Provost for Research through the IRB a copy of the audit findings, and any management plan constructed by the OHR. Reports from any other school based audit programs will be communicated in writing to the IRB.

3.3 Audits and Compliance Reviews

Audits and compliance reviews are conducted in the form of directed audits and periodic compliance reviews. These audits and reviews are designed to assess compliance with local, State, and Federal laws, research participant safety, and IRB policies and procedures.

3.3.1 Directed Audits**.** Directed audits are conducted to assess the Investigator's compliance with Federal, State, and local law, university and IRB policies and to identify areas for improvement. Triggers for audit activities may include:

- Any IRB committee directives or concerns;
- A response to an externally initiated complaint (OHRP, FDA or Sponsor) of potential protocol violations or regulatory noncompliance;
- A response to an internally initiated complaint or concern (a participant, a family member, Institutional personnel); or
- An Investigator with a history of poor adherence to Penn policies and procedures.

3.3.2 Periodic Compliance Reviews. Periodic compliance reviews are conducted using a systematic method to review IRB-approved research or IRB records/activities on a regular basis. The above-described periodic compliance review activities may include but are not limited to the following:

- Requesting progress reports from Investigators;
- Examining the entire research project;

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- Contacting research participants
- Assigning observers to the sites where research involving human research participants and/or the informed consent process is being conducted;
- Auditing advertisements and other recruiting materials;
- Reviewing projects to verify that the Investigator has not initiated unapproved changes since previous review;
- Monitor conflict of interest concerns to assure the consent documents include the appropriate information and disclosures;
- Examining HIPAA authorizations.

3.4 Evaluation

3.4.1 The Associate Director is responsible for the initial review of allegations of noncompliance, review of employee, staff, and faculty reports and complaints and review of audit findings that indicate potential or serious noncompliance.

3.4.2 Allegations of noncompliance

When an allegation of noncompliance is referred to the IRB, the IRB Associate Director conducts the initial review to verify the veracity of the allegation.

The Associate Director may choose any of the following methods to gather the required information:

- Conduct the initial review alone.
- Conduct the initial review in coordination with the IRB Executive Chair, IRB Chair, or IRB Executive Director.
- Convene a subcommittee of the IRB.
- Request advice from the Office of General Counsel, University or School Offices of Audit and Compliance, or outside consultants.
- The individual(s) or subcommittee conducting the investigative process may take any of the following actions as they deem necessary to verify the veracity of any allegations and the seriousness or number of occurrences of the actions:
- Review any written materials.
- Interview knowledgeable sources.
- Collect relevant documentation.

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A written record of findings and evidence will be made by the IRB Associate Director. The report will include an assessment of whether the preponderance of evidence shows that any of the **allegations** of noncompliance are **findings** of noncompliance.

If the investigation results in findings of noncompliance, the Process Flowchart for reports of serious and continuing noncompliance will be followed.

3.4.3 Noncompliance that is not serious or not continuing.

If it is determined by the Associate Director or investigative team that (1) the noncompliance was clearly not serious and not continuing, (2) the research staff recognized the noncompliance, and (3) the research staff took appropriate corrective actions, then the report will be forwarded to the IRB Executive Director. No further action is required.

If it is determined by the Associate Director or investigative team that (1) the noncompliance was clearly not serious and not continuing, but the research staff did not recognize the noncompliance or the research staff did not take appropriate corrective actions, the Associate Director will report the event to the PI of the event and offer guidance on the appropriate corrective action plan. The Associate Director may also request a Directed Audit as outlined in 3.3.1 above or may refer the matter to the convened IRB.

3.4.4 Noncompliance is serious or continuing.

The Associate Director is responsible for obtaining as much information as possible from the individual who initially reports the incident and for the initial fact finding process to decide whether each incident of noncompliance was serious or continuing.

If the incident is considered serious or continuing based on the Associate Director or investigative team review, then the Associate Director will follow the steps outlined in the Process Flow Chart and will document the process on the Compliance Intake Form.

The IRB will receive a copy of the Compliance Intake Form and a copy of the protocol, consent form, and the initial application form. The Associate Director or designee will present the report to the convened IRB. The convened IRB determine will review the report and determine the appropriate way to remedy the noncompliance as outlined in 3.5.

3.5 Actions that the IRB Considers in Responding to Serious or Continuing Noncompliance

3.5.1. The IRB may take the following actions in response to serious or continuing noncompliance:

- No action
- Modification of the research protocol

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- Modification of the information disclosed during the consent process
- Additional information provided to past participants
- Notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research)
- Requirement that current participants re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of the consent process
- Suspension of the research
- Termination of the research
- Obtaining more information pending a final decision
- Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)

3.5.2 IRB staff administrator will document the results of the IRB's determinations in the meeting minutes. The IRB will notify the investigator in writing of the results of the investigation and of any remedial actions required by the IRB. The letter will include a request for the investigator to respond in writing. The IRB will review the response. The response may be reviewed using expedited procedures or may be referred to the convened IRB.

3.5.3 The IRB minutes will include a description of the nature of the event, the findings, actions taken, and plans for continued investigation or action.

3.6 Notifications

3.6.1 If the noncompliance is determined to be serious or continuing, CO 602 will be followed.

4. REFERENCES

45 CFR 46.103(b)(4)&(5); 21 CFR 56.108(b)

Title	RR 408 Noncompliance
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RR 409 ADMINISTRATIVE HOLDS, TERMINATIONS, AND SUSPENSIONS OF IRB APPROVAL

1. PURPOSE

This policy describes the IRB actions associated with suspending or terminating previously approved research.

2. POLICY STATEMENT

Federal regulations require that the IRB have the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to participants. Suspensions and terminations represent an action by the IRB to temporarily or permanently withdraw approval for some or all research procedures. This policy describes the IRB actions associated with suspending or terminating previously approved research.

3. SPECIFIC POLICIES

3.1.1 The following officials are authorized to suspend IRB approval pending review by the IRB responsible for continuing review of the protocol: the Vice Provost for Research, Deans of Schools, the Executive IRB, and the Chair of the IRB responsible for continuing review of the protocol, the Institutional Director(s) of Research Compliance, and any other Penn officials who is authorized to take such action by virtue of his or her office or of a policy or procedure of the relevant organization.

The University of Pennsylvania official who suspends a protocol shall immediately notify the Principal Investigator of:

- The requirement to suspend the study or to halt the portion of the IRB approved protocol that poses immediate, material risk to participant health and welfare;
- The reasons for the suspension;
- The opportunity to respond in person or in writing to the official and IRB on the suspension; and,
- The obligation to immediately report the suspension and its basis to the IRB.

The IRB Associate Director will report the suspension to the Vice Provost for Research and will immediately initiate the appropriate procedure for review of the basis for the suspension.

If the suspension of some or all of the protocol involves the withdrawal from the research or modification of participation of current participants, the IRB will direct the investigator to contact the participants to:

- Describe any monitoring and follow-up for safety reasons that will be conducted and

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- Provide contact information for the Principal Investigator and the IRB where the participant may report any adverse events or unanticipated problems.

3.1 Administrative Hold

A voluntary action initiated by the investigator to place specific research activities on temporary hold. When a study is currently approved by the IRB, the PI may voluntarily place the study on hold as follows:

Administrative hold of screening/enrollment;
Administrative hold of interaction/intervention; or
Administrative hold of follow-up.

The investigator will notify the IRB in writing of its decision for Administrative Hold. The notification will include the criteria for the Administrative Hold and will notify the IRB when research related activities resume.

3.2 Sponsor-Imposed Suspension

A determination from the sponsor of the study to place specific research activities on hold. This determination may be made for interim data analysis; inadequate drug availability; in response to a DSMB report/recommendation; or a pre-planned stopping criteria. The investigator notifies the IRB in writing of sponsor-imposed suspensions.

3.3 Suspension for Cause

An action to stop temporarily some or all research procedures pending future action by the IRB or by the Investigator or his/her study personnel. The IRB reviews a study for suspension at convened IRB meeting. Examples of these types of circumstances include:

- Falsification of study safety data;
- Failure to comply with prior conditions imposed in writing by the IRB under suspension of the study;
- Repeated or deliberate failure to obtain or document informed consent from human participants, which may include:

  Repeated or deliberate omission of a description of serious risks of the experimental therapy when obtaining informed consent; and/or

  Repeated or deliberate failure to provide informed consent in a language understandable to the subject;

- Repeated or deliberate failure to limit administration of the investigational drug or device to those participants under the Investigator's supervision;
- Repeated or deliberate failure to comply with conditions placed on the study by the University, IRB, sponsor, or FDA;

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- Repeated or deliberate failure to obtain prior review and approval of new protocols and on-going human subjects research by the IRB;

- Repeated or deliberate failure to maintain accurate study records or submit required adverse event reports to the IRB;

- Repeated or deliberate falsification or concealment of study records, e.g., by substituting in study records the results of biological samples from participants who met the inclusion criteria for samples of participants who did not meet the inclusion criteria, or by fabricating participants.

In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or expertise in the specific area of concern.

The IRB notifies the Investigator in writing of its decision to suspend the study for cause and provide a rationale for its actions. This letter includes an opportunity for the PI to respond to the IRB's determinations and to attend an IRB meeting to discuss the suspension and provide clarification of the issues.

3.4.1 The IRB will take the appropriate actions to protect the rights and welfare of currently enrolled subjects in suspended or terminated research. For example:

- Consider transfer of subjects to another investigator.

- Arrange for participants to be provided clinical care by the investigator or another physician.

- Arrange for subjects to continue in some research-related activities.

- Require specific procedures for withdrawal of enrolled subjects.

- Permit or require follow-up of subjects for safety reasons, and if so, require reporting of adverse events or outcomes to the IRB.

- The IRB may request the development of an education plan and/or the completion of a directed audit by the Office of Human Research.

- Suspensions are reinstated for approval after corrective actions are completed to the IRB's satisfaction. The IRB may approve the study with or without additional restrictions (e.g., mandating a data and safety monitoring committee to oversee the research at designated intervals, increase in the frequency of IRB review, observation of the consent process).

3.5 Termination for Cause

An action initiated by the IRB to stop permanently some or all research procedures.

The IRB reviews a study for Termination for Cause at a convened IRB meeting.

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In addition, the IRB may request an ad hoc review from an independent source with expertise in the type of research being conducted or expertise in the specific area of concern.

The IRB notifies the Investigator in writing of the decision to terminate the study for cause and provide a rationale for its actions. This letter includes an opportunity for the PI to respond to the Committee's determinations and to attend an IRB meeting to discuss the termination and provide clarification of the issues.

3.6 Reporting of Suspensions for Cause or Terminations

All Suspensions or Terminations are promptly reported per IRB Policy CO 602. The institution may determine that suspensions or terminations associated with a particular study or an Investigator are repetitive and warrant action for issues of serious and continuing non-compliance.

4. REFERENCES

45 CFR 46.103(5)(ii); 21 CFR 56.108(b)(3)

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SC 500	REVIEW REQUIRING SPECIAL CONSIDERATION
501	VULNERABLE POPULATIONS
	Prisoners Children Pregnant Women, Fetuses & Neonates Other Vulnerable Groups
502	RESEARCH WITH TEST ARTICLES
	Research involving drugs or biologics Research involving medical devices Significant risk medical devices Nonsignificant risk medical devices Investigations exempted from IDE regulations Gene therapy research Prospective research in emergency settings Expanded access of an investigational drugs or devices Emergency use of an investigational article or product Humanitarian use devices

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SC 5O1 VULNERABLE POPULATIONS

1. PURPOSE

This section presents the policy concerning review of research that involves groups that could be potentially vulnerable to coercion in regard to autonomy, present conditions that may affect risk/benefit determinations or bearing unequal burden in research.

2. POLICY STATEMENT

The IRB shall apply additional protections as necessary to protect potentially vulnerable research subjects. Not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. The extent of additional protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations. In addition, when an IRB regularly reviews research involving a vulnerable population consideration will be given to inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

3. SPECIFIC POLICIES

3.1 Prisoners

If an investigator indicates that prisoners will participate in the research, or that subjects may reasonably be expected to be incarcerated at some time point during the study, the IRB will adhere to the requirements found at 45 CFR 46, Subpart C. A majority of the IRB (exclusive of prisoner members) has no association with the prison involved apart from membership on the IRB. At least one IRB member who is a prisoner or prisoner representative with appropriate background and experience to serve in that capacity is present at the meeting.

3.1.1 When Subjects Become Prisoners During a Research Protocol.

This policy applies whenever any human subject in a research protocol becomes a prisoner at any time during the protocol, *e.g.,* after the research has commenced. This is necessary because it is unlikely that review of the research and the consent document contemplated the constraints imposed by the possible future incarceration of the subject. If a subject becomes a prisoner after enrollment in research, the Principal Investigator is responsible for reporting in writing this situation to the IRB immediately.

At the earliest opportunity after receiving the Principal Investigator’s notice or otherwise becoming aware of the prisoner status of a subject the IRB willshould review the protocol again with a prisoner representative as a member of the IRB.

The IRB will take special consideration of the conditions of being a prisoner.
Upon this review, the IRB can either (a) approve the involvement of the prisoner-subject in the research in accordance with this policy and all applicable regulations; or (b) determine that this subject must be withdrawn from the research.

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Additionally, the IRB should confirm that, when appropriate, the informed consent process includes information regarding when subsequent incarceration may result in termination of the subject's participation by the investigator without regard to the subject's consent.

3.2 Children

3.2.1 Definition

Federal regulations define "children" as persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

Under Pennsylvania law, persons under the age of eighteen (18) generally meet this definition of "children", with the exceptions noted below. As a result, permission of the child's parent(s) or guardian(s) must generally be obtained prior to the participation child's participation in the research.

The following exceptions to the general rule apply, where a person under the age of 18 does not meet the federal definition of "child" and may provide legally effective consent to participate in research if either:

- The research involves the provision of medical care or treatment, (including care or treatment deemed to be experimental) and the person:

  has graduated from high school, or

  is married, or

  is or has been pregnant.

- The person is an emancipated minor. If an emancipated minor provides consent for himself or herself, the court order should be copied and included in the research records with the consent document.

3.2.2 All individuals defined as "children" will be afforded the protections under Subpart D, 45 CFR 46.401 - 409 and 21 CFR 50.50 - 54, Additional Protections for Children Involved as Subjects in Research and as delineated in IRB Policies.

Subpart D Protections are not applicable for minors who do not meet the definition of children. The IRB may consider these subjects potentially vulnerable and may choose to apply additional protections.

When a research protocol involves minors who do not meet the definition of children, the IRB will carefully balance the potential risks and benefits of the proposed research and will consult with the Office of General Counsel and the Vice Provost for Research as deemed necessary.

If the research includes enrollment of participants in other states or countries, the principal investigator is responsible for providing the IRB with sufficient information to verify the age at which participants in such jurisdictions have the ability to consent to

participation in research, including any medical treatments or procedures if applicable.

The IRB may, if it appears advisable, require the submission of an opinion rendered by an attorney from any applicable jurisdiction on age at which an individual can consent to participation in research.

3.2.3 Federal regulations at 45 CFR 46 Subpart D and 21 CFR 50 Subpart D define "guardian" as "an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care."

Pursuant Pennsylvania law, only the birth parent or a person adjudicated as an adoptive parent(s) or legal custodian may provide the legally effective consent on behalf of a child to general medical care.

Except for research involving no greater than minimal risk, if subject a court appointed guardian provides consent, documentation of the court order or legal authorization to consent to general medical care must be copied and included in the investigator's research records with the documentation of permission.

3.3 Pregnant Women, Fetuses, and Neonates

The University requires adherence to DHHS regulations regarding additional protections required for research involving pregnant women, fetuses, and neonates. In addition to the other responsibilities assigned to the IRBs under 45 CFR Part 46 Subpart A, the University of Pennsylvania requires each IRB to review research involving these subjects by applying the protections of 45 CFR 46 Subpart B.

Pennsylvania Law places additional restrictions on research on the fetus. The IRB will consult with the Office of General Counsel on a case-by-case basis for research protocols involving this class of subject.

3.4 Other vulnerable groups

Federal regulations require that the IRB consider additional protections for other vulnerable populations such as mentally disabled perrsons and economically or educationally disadvantaged individuals. The IRB will consider these additional protections as part of the criteria for approval.

Although the federal regulations do not list all vulnerable groups, the IRB considers vulnerable groups to include mentally impaired or disabled persons, employees of the sponsor or investigator or the University. The IRB will determine special protections for these groups on a case by case basis taking into account the risks and benefits and other protections afforded by institutional policies and state and federal law.

3.4.1. Adults with Impaired Decision-Making Capacity

Decisionally impaired adults are individuals who have a diminished capacity for judgment and reasoning due to a psychiatric, organic, developmental, or other

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disorder that affects cognitive or emotional functions. Other individuals may be considered decisionally impaired or have limited decision-making ability because they are under the influence of or dependent on drugs or alcohol, suffering from degenerative diseases affecting the brain, are terminally ill, or have severely disabling physical handicaps.

There are no regulations specific to research involving adults with impaired decision-making capacity. The IRB takes special care to consider issues such as the selection of participants, privacy and confidentiality, coercion and undue influence, and risk-benefit analysis. Decisions should be made with the utmost deference to the ethical principles underlying human research as set forth in the Belmont Report.

The National Bioethics Advisory Commission (NBAC) has issued 21 recommendations for IRBs, the research community, and Federal regulators to consider regarding the decision-making capacity of particularly vulnerable subjects.

The following criteria that should be taken into consideration for adult participants with impaired decision-making capacity involved in a research protocol:

The objectives of the research cannot be met by conducting the research in a population that does not have the disorder that may affect decision making capacity.

The research is designed for a disease or condition relevant to the vulnerable population under study.

The research is either minimal risk, more than minimal risk with a prospect of direct benefit, or more than minimal risk without a prospect of direct benefit, but of vital importance to the vulnerable population.

Adequate provisions are made for obtaining consent from the participant's legally authorized representative.

Adequate provisions are made for obtaining assent from the participant, unless the IRB determines that assent is not appropriate as a condition of participation or that some or all participants are not capable of providing assent.

The protocol must describe when and how the participants will be assessed for capacity for formal consent or assent and understanding of the proposed research, and the process for a second confirming assessment. Competency should be evaluated on an individual basis to avoid incorrect assumptions as to an individual's ability to make decisions. Criteria for determining competence might vary according to the degree of risk or discomfort presented by the research procedures and the extent to which therapeutic gain can be anticipated.

- The IRB will consider additional safeguards to protect participants. These include:

- Requiring the involvement of participant advocates

- Requiring independent monitoring

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- Requiring waiting periods
- Appointing a monitor to supervise the informed consent process

Such decisions may be based on the amount of risk involved in the research and the likelihood that participants will derive health benefits from their participation.

3.4.2 Reseach involving students or employees of the University.

When research involves students or employees of the University, the IRB requires the investigator to provide information regarding the measures that will be put into place to reduce the likelihood of coercion and to address confidentiality concerns.

4. REFERENCES

The Belmont Report; 45 CFR 46.111(b); 21 CFR 56.111(b); 45 CFR 46.107; 21 CFR 56.107; 45 CFR 46 Subpart B ; 45 CFR 46 Subpart C; 45 CFR 46 Subpart D ; 50 CFR Subpart D; OHRP FAQs prisoner research; OHRP FAQs on research involving children; *Research Involving Persons with Mental Disorders That May Affect Decision Making Capacity* (December 1998) http://bioethics.gov/; OPRR *Protecting Human Research Subjects Guidebook (1993)*, Chapter 6, Section J, "Students, Employees and Normal Volunteers". http://hhs.gov/ohrp/irb/irb_chapter6.htm

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SC 502 RESEARCH WITH TEST ARTICLES

1. PURPOSE

This section presents the policy concerning review of specific types of research that require additional considerations by the IRB

2. POLICY STATEMENT

Certain categories of research involve either methodologies that might require additional considerations or for which there are federally mandated determinations that IRBs are required to make and document. These categories of research include, but are not limited to:

- Clinical investigations involving drugs or biologics
- Clinical investigations involving medical devices
- Gene therapy research
- Prospective research in emergency settings
- Expanded access of an investigational drugs or devices
- Emergency use of an investigational article or product
- Humanitarian use devices

3. SPECIFIC POLICIES

3.1 Research Involving Drugs or Biologics

All research involving uses a FDA regulated drugs or biologics require submission of an Investigational New Drug Application to the FDA unless the research meets the criteria for exemption from the requirements.

Exemption determinations may be made by the IRB, the School of Medicine's Office of Human Research, the Abramson Cancer Center in accordance with written policies and procedures or may be determined by the FDA in response by the sponsor or Principal Investigator.

Exemption 1: A clinical investigation of a drug is exempt from the IND regulations if the drug is lawfully marketed in the United States and all of the following are true:

- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
- If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
- The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and

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- The investigation is conducted in compliance with the requirements of 312.7 (Promotion and charging for investigational drugs)

For sponsored research, applications for research on the use of a drug, unless that research is exempt from the IND regulations, must be accompanied by documentation from the FDA that includes a valid IND number. The IND number must either match the number on the sponsor protocol with the same title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA.

Exemption 2:

- A clinical investigation for an invitro diagnostic biological product that involves one or more of the following:
  - Blood grouping serum
  - Reagent read blood cells
  - Anti-human globilin
- The diagnostic test is intended to be used in a diagnostic procedure and conforms with the diagnosis made by another, medically established diagnostic procedure.
- The diagnostic test is shipped in compliance with 21 CFR 312.160.

Exemption 4: A clinical investigation involving use of a placebo is exempt from the requirements of 21 CFR 312 if the investigation does not otherwise require submission of an IND. Clinical investigations that are exempt from IND regulations still require IRB review and approval.

3.2 Research Involving Medical Devices

Research with devices falls into three categories:

- Investigations of significant risk devices to determine safety and effectiveness of the device
- Investigations of nonsignificant risk devices to determine safety and effectiveness of the device
- Investigations exempted from the IDE regulations

The convened IRB (or Executive Chair or designee if the review is expedited) will determine whether the study presents a significant risk or a non-significant risk of harm to study subjects. This assessment will be based on the information provided by the investigator and/or the sponsor.

The IRB's risk determination will be documented in the IRB meeting minutes. If an investigator submits a NSR research protocol that is determined by the IRB to be a SR study, the investigator and FDA will be notified in writing. No further action will be taken by the IRB on the research until the sponsor or investigator has met the requirements for a SR study described in 21 CFR 812.

3.2.1 Significant Risk Devices

Applications for research on the use of a significant risk device must be accompanied by documentation from the FDA that includes a valid IDE number. The IDE number must either match the number on the sponsor protocol with the same

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title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA.

3.2.2 Nonsignificant Risk Devices
When research is conducted to determine the safety or effectiveness of a device, the organization confirms that the device fulfills the requirements for an abbreviated IDE (21 CFR 812.2(b)(1)):

- The device is not a banned device;
- The sponsor labels the device in accordance with 21 CFR 812.5;
- The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
- The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation is waived;
- The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
- The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
- The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7); and
- The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

If the investigator applies to the IRB for a nonsignificant risk determination for a device study, but the IRB determines that the device is significant risk, the IRB will notify the investigator and the sponsor, if appropriate.

3.2.3 Investigations exempted from IDE regulations: Clinical investigations that are exempt from IDE regulations still require IRB review and approval. An investigation of a medical device in human subjects research that is exempt from the IDE regulations must fall into one of the following categories:

- A device legally marketed in the US that is used or investigated in accordance with the indications in the FDA-approved labeling.
- A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
- A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
- A diagnostic device (that is, an in vitro diagnostic device) if the testing:
    - Is noninvasive

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- Does not require an invasive sampling procedure that presents significant risk,
- Does not by design or intention introduce energy into a subject, and
- Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

- A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
- A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

3.3 Gene Therapy Research

Gene therapy research may require special considerations. If the project involves gene transfer (administration of recombinant vectors) to human subjects for other than clinical purpose review by the Recombinant DNA Advisory Committee (RAC) may be required. The FDA must review any such study prior to final IRB approval. In addition, the protocol will require review by the the University of Pennsylvania Biosafety Committee and may require review by the Vice Provost for Research Human Research Advisory Committee.

3.4 FDA Regulated Prospective Research in Emergency Settings

The IRB, with the concurrence of a licensed physician who is either a member of IRB or a consultant and who is not participating in the research being reviewed, may waive the requirement for informed consent in certain emergency research if it finds and documents the following:

The research activity is subject to the regulations codified by the Food and Drug Administration (FDA) at 21 CFR Part 50 and will be carried out under an investigational new drug application (IND) or investigational device exemption (IDE).

The application clearly identifies the protocols that will include participants who are unable to consent.

The protocol is performed under a separate IND or IDE and clearly identifies such protocols as protocols that may include participants who are unable to consent.

The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or and IDE for the same device product already exists.

3.3.1 The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

3.3.2 Obtaining informed consent is not feasible because:

The subjects will not be able to give their informed consent as a result of their medical condition;

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The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

3.3.3 Participation in the research holds out the prospect of direct benefit to the subjects because:

Subjects are facing a life-threatening situation that necessitates intervention;

Appropriate animal and other pre-clinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

3.3.4 The clinical investigation could not practicably be carried out without the waiver.

3.3.5 The proposed investigational or research plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.

The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

3.3.6 The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation.

3.3.7 Additional protections of the rights and welfare of the subjects will be provided, including, at least:

Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

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Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact, within the therapeutic window, the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The study plan must assure that, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

The study plan must assure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

3.3.8 If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided above of this section or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.

3.5 HHS Regulated Prospective Research in Emergency Settings

For research that not FDA regulated, requests for waivers of informed consent will be evaluated in accordance with 45 CFR 46.116 and 117 and the OHRP Guidance on Informed Consent Requirements in Emergency Research.

3.6 Emergency Use of Investigational Article or Product

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An investigational article may be used in an emergency prior to IRB review, provided that the patient is in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

Such emergency use is reported to the IRB within 5 working days, and any subsequent use of the test article is subject to IRB review.

In such a situation, obtaining informed consent shall be considered feasible except in certain emergency situations where the investigator has adequately documented the necessary exception under the guidelines described in 21 CFR 50.23. The investigator must submit documentation to the IRB for review by the IRB Executive Chair within 5 working days after emergency use of the test-article. In review of the documentation, the IRB will ensure that the investigator and a physician not otherwise participating in the clinical investigation have adequately certified the following in writing prior to use of the test-article:

> The human subject was confronted by a life-threatening situation necessitating the use of the test article.
>
> Informed consent could not be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
>
> Time was not sufficient to obtain consent from the subject's legal representative.
>
> There was available no alternative method of approved or generally recognized therapy that provided an equal or greater likelihood of saving the life of the subject.
>
> If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient, prior to administering the test-article, to obtain an independent physician's opinion, the determinations of the investigator must be reviewed in writing within 5 days after the use of the test article by a physician not otherwise participating in the clinical investigation. In this event, a copy of the independent review must be submitted to IRB within 5 working days after the use of the test article.

3.5.1 The IRB Executive Chair will review prior notifications to determine that the circumstances of the use follow FDA regulations.

3.5.2 Under FDA regulations, patients given emergency use test articles are considered research subjects and data from the emergency use may be used in research through reporting to the sponsor and the FDA. Under HHS regulations, whenever emergency care is initiated without prior IRB review and approval, the patient may *not* be considered to be a research subject. and the data derived from use of the test article may not be used in a prospective systematic investigation designed to develop or contribute to generalizable knowledge.

3.6 Humanitarian Use Devices

Humanitarian use devices (HUD) are intended to benefit patients by providing treatment or diagnosis of diseases that affect fewer than 4,000 individuals in the US per year. The

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IRB will conduct both initial and continuing review and approve the local use of a HUD. Researchers will submit the Humanitarian Device Application.

4. REFERENCES

21 CFR 812; 21 CFR 814; FDA Device Advice; FDA Information Sheets, Medical Devices; 21 CFR 50.24; Federal Register 61(192): 51531-51533; FDA Draft Guidance, Exception from Informed Consent Requirements for Emergency Research, August 29, 2006; OHRP Guidance, informed consent requirements in emergency research, October 31, 1996; IRB Guidance Significant Risk Device Determinations

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CO 600	COMMUNICATIONS
601	INVESTIGATIVE STAFF
602	OTHER ENTITIES

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CO 601 INVESTIGATIVE STAFF

1. PURPOSE

This policy describes the IRB actions that must be communicated to the investigator and the importance of open communication among IRBs, investigators, staff, and university committees and officials.

2. POLICY STATEMENT

It is important that staff, subjects, and other interested parties have a means of communicating information about the conduct of a research project directly to the appropriate institutional officials. It is vital that IRB members, department heads, and other officials with responsibility for oversight of research have open and ready access to the highest levels of authority within the institution. IRB staff and members do not have the opportunity to communicate directly with study subjects. The researcher and research staff interacts with subjects; therefore it is vital that open and frequent communication with the investigative team be maintained.

3. SPECIFIC POLICIES

3.1 Investigator Notifications

3.1.1 Initial Submission: The investigator will be notified in writing of the IRB's decision as soon as possible after the meeting. If the approval is withheld pending clarification, based upon receipt and review of requested materials or responses from the investigator or sponsor, the IRB must receive the response within 90 days of the date of notification; however, this period may be extended if the investigator/sponsor communicates a need for an extension.

3.1.2 Renewals and Revisions: Investigators will be notified in writing as soon as possible as to the action taken by the IRB for any continuing reviews or revisions.

3.1.3 Notification of Final Approval: Investigators will be notified in writing of the final approval. The IRB-approved consent form will be dated with the period of approval and submitted to the investigator with the final approval letter. Standard conditions for continued approval include, but are not necessarily limited to:

Informed consent is obtained and documented.

The IRB is notified of serious adverse events within appropriate periods.

Changes to the protocol, and deviations from the protocol are reported.

Continuing Review and Request for Reapproval Reports are submitted to the IRB.

3.1.4 Disapproval: correspondence will provide the reason(s) for disapproval andand will give the investigator an opportunity to respond in person and in writing to the IRB.

3.2 Investigator Appeal of IRB Action

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If an investigator disagrees with a determination of the IRB (substantive or procedural), the investigator may appeal to the Vice Provost for Research. An appeal must be in writing, state the decision being appealed and the basis of the appeal, and be filed within 30 calendar days of the decision. The Vice Provost may use his or her sole discretion to determine the process for the appeal and grant or deny the appeal, including:

Notifying the IRB of the appeal and requesting a response and relevant information from its records before making a decision.

Appointing a fact-finder to review the matter and prepare a report for review by the IRB.

Seeking assistance from consultants or internal administrative units such as the Office of the General Counsel who will report their findings to the IRB.

Requesting that the IRB consider additional information or actions in relation to the decision under appeal.

The investigator is bound by the IRB decision prior to and during the appeal. The decision on an appeal by the Vice Provost for Research is final.

If, after taking into consideration any additional information, the IRB decides to disapprove a protocol or requires protocol modifications as a condition for approval, neither the Vice Provost for Research, the Provost, nor any other any University of Pennsylvania official or committee may overturn the IRB's decision.

3.3. Noncompliance

The IRB, through the IRB Executive Director and the Executive Chairperson will notify the investigator in writing, detailing the alleged noncompliance, specifying corrective action, and stating the consequences. Copies of such correspondence shall also be sent to the sponsor, the individual's supervisor, Dean and the Vice-Provost for Research.

The IRB's responsibility is to protect the rights and welfare of research subjects, which could be placed at risk if there is scientific misconduct on the part of an investigator or any member of the investigative team. It is, therefore, the duty of the IRB to be receptive to and act on good faith allegations of scientific misconduct. Allegations of Misconduct in Science, as defined by University Policy must be referred to the Vice-Provost for Research.

4. REFERENCES

45 CFR 46.109; 21 CFR 56.109

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CO 602 REPORTING REQUIREMENTS

1. PURPOSE

This policy describes the IRB actions that must be communicated to various parties involved in the research program.

2. POLICY STATEMENT

The University of Pennsylvania complies with all applicable local, state, and federal regulations that pertain to reporting requirements. Federal regulations require institutions to have written procedures in place for prompt reporting to the IRB, appropriate institutional officials, and department and agency heads of:

- Unanticipated problems that involve risks to participants or others;
- Serious or continuing noncompliance with regulations; and,
- Suspension or termination of IRB approval of research; and

The specific procedures for investigating and making pertinent determinations concerning those situations are addressed in SOP RR 404.

The Institutional Official, IRB Executive Chair, IRB Executive Director, Office of the General Counsel will review the report.

3. SPECIFIC POLICIES

3.1 Communication to Institutional Official of IRB Actions

All IRB minutes shall be available to the Institutional Official via the shared computer drive and available, as requested in hard copy.

3.2 Communications to Others

3.2.1 Prospective Emergency Research: If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in 21 CFR 50.24 Exemption from Informed Consent Requirements for Emergency Research, notification of disapproval will be conveyed to the sponsor as well as the investigator.

3.2.2 Device studies: If the IRB determines that a study submitted as a non significant risk present significant risk, the IRB will notify the investigator.

3.2.3 Other Reportable Events:

The IRB determines that a problem represents an unanticipated problem that involves risks to participants or others;

The IRB or institutional official suspends or terminates its approval of research; or,

The IRB determines that noncompliance represents serious or continuing noncompliance.

3.3 Report Content

Following a complete investigation of the situation or incident, the IRB Executive Director will prepare a final report that includes the following:

- An overview of the situation or incident
- A description of the manner in which the investigation was conducted
- The findings of the investigation
- A full explanation as to why and how the incident occurred
- The actions taken, including any corrective actions
- Any sanctions taken

The IRB Executive Director, IRB Executive Chair, Chair, the Institutional Official, and the General Counsel, will review the report. The report will be signed by the Institutional Official.

3.4 Report Recipients

The unanticipated event reported by the Institutional Official, will be shared with government agencies and sponsors to the extent legally and contractually required, and with any others at the discretion of the IRB and the Institutional Official. The report will be sent to the following individuals and agencies:

- Office of Human Research Protections (OHRP) when the research is subject to regulation by the OHRP
- Food and Drug Administration (FDA) when the research is subject to regulation by the FDA
- Funding agency when funded by a government entity (e.g., the Departments of Defense, Education, and Justice require copies of such reports)
- Licensing and accrediting bodies, where the report or some portion thereof implicates standards or regulations administered by those bodies
- IRB Chair and members
- Principal investigator (PI)
- PI's Department Chair or supervisor

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- The Office of Research Services, when the research is funded by a grant or contract
- Any other external sponsor, when the research is sponsored
- A copy of the report is to be placed in the protocol file, as well as any other files that are maintained during an investigation to determine whether an event is reportable.

3.5 Reporting Timeframe

The Institutional Official will be notified within 5 working days of events that meet these reporting requirements.

Within 30 days of the notification, the Institutional Official will report the event to appropriate federal department and agency heads. If additional time is necessary to complete the final report, the time frame is to the extent practicable to be specified in the initial report. If federally funded, the Institutional Official will submit any report on behalf of the institution.

4. REFERENCES

45 CFR 46.103; 21 CFR 56.108; FDA Reporting Requirements: suspension or termination of IRB approval; OHRP compliance overview

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IC 700	INFORMED CONSENT AND HIPAA AUTHORIZATION
701	GENERAL REQUIREMENTS AND DOCUMENTATION
702	EXEMPTIONS AND WAIVERS
703	DOCUMENTATION
704	ASSENT
705	SURROGATE CONSENT

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IC 701 GENERAL REQUIREMENTS AND DOCUMENTATION OF INFORMED CONSENT

1. PURPOSE

This policy describes the general requirements for obtaining informed consent and subject authorization and for documentation of informed consent and subject authorization.

2. POLICY STATEMENT

Informed consent must be legally effective and prospectively obtained. Except as described at IC 702 no investigator may involve a human being as a research subject unless he or she has obtained legally effective informed consent of the subject or the subject's legally authorized representative. Consent shall be sought only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

Subject authorization must be obtained for prospective use or disclosure of protected health information for research conducted within one or more of the covered entities of the University of Pennsylvania. Except as described at IC 702 no investigator may involve a human being as a research subject unless he or she has obtained legally effective authorization of the subject or the subject's legally effective representative.

The IRB requires documentation of informed consent by use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. Authorization may be obtained by the use of a separate HIPAA Authorization Form, or combined with an IRB-approved informed consent document.

3. SPECIFIC POLICIES

3.1 The Consent Form May be:

3.1.1 A written consent document that embodies the elements of informed consent and if necessary the required elements of HIPAA authorization. This form may be read to the subject or the subject's legally authorized representative, but, in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed. Each participant shall receive a copy of the signed consent document or signed combined consent authorization document.

3.1.2 A "short form" written consent document stating that the elements of informed consent as required have been presented orally to the subject or the subject's legally authorized representative. The short form may be used when an investigator unexpectedly encounters a subject who does not speak English. When this method is used, there will be an impartial witness to the oral presentation. The IRB will approve the translated short form. Only the subject or the representative signs the short form itself. However, the witness will sign both the short form and a copy of the summary, and the person actually obtaining the consent will sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the signed short form.

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3.2 Required Elements of Informed Consent:

3.2.1 A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental or investigational.

3.2.2 A description of any reasonably foreseeable risks or discomforts to the subject.

3.2.3 A description of any benefits to the subject or to others which may reasonably be expected from the research.

3.2.4 A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

3.2.5 A statement describing the extent to which, if any, the confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration and representatives of the IRB may inspect the records.

3.2.6 For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained. The informed consent document must not waive or appear to waive the rights of the participant or release or appear to release those conducting the study from liability for negligence.

3.2.7 An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

3.2.8 A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

3.3. Additional Elements

3.3.1 When appropriate, one or more of the following elements of information shall also be provided to each subject:

A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant) which are currently unforeseeable.

Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

Any additional costs to the subject that may result from participation in the research.

The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

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The approximate number of subjects involved in the study.

3.4 Other Requirements

3.4.1 Second Person

The language of the consent document should be in the second person style so the consent form conveys a dialogue with information being provided and that there is a choice to be made by the subject rather than presumption of the subject's consent with the use of the first person style.

3.4.2 Lay Language

The information provided in the informed consent documents must be in language understandable to the subject. The informed consent document should not include complex language that would not be understandable to all subjects. Technical and scientific terms should be adequately explained using common or lay terminology.

3.4.3 Exculpatory Language

Informed consent documents may not contain any exculpatory language through which the subject is made to waive or appear to waive legal rights or releases or appears to release the investigator, the sponsor, the university from liability for negligence.

3.4.4 FDA-Regulated Test Articles

For all research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent documents should include a statement that the purpose of the study includes evaluation of the safety or the safety and the effectiveness of the test article. The consent form must also include a statement that the FDA has access to the subject's medical records.

3.4.5 IRB review of consent process.

The IRB will take the following into consideration when reviewing the protocol and consent form:

Who will conduct the consent process.

Matters of timing of obtaining informed consent and any waiting period between informing the subject and obtaining consent.

That the process provides ample time for the person conducting the consent interview and the prospective subject to exchange information and ask questions.

3.4.6 Translations of consent documents will also be submitted for IRB approval and will be reviewed in an expedited manner. There are two options available to obtain approval of translated consent forms.

Option #1: The IRB-approved consent form is translated by the sponsor or site and submitted to the IRB. The IRB will have a member or consultant fluent in the language of the consent; review the translated document for accuracy. In their opinion it must match the English version.

Option #2: The investigator (or sponsor) may submit the IRB-approved version of the consent to a translator for translation. A second translator may then back translate the consent to the original English. Both original and back-translated consent must be submitted.

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Option #3: The translator will submit a signed statement that the consent document is a true and accurate translation.

3.5 Observation of the Informed Consent Process

The IRBs have procedures for observation of the informed consent process in ongoing research, when appropriate. As part of the IRB oversight options, an IRB may require that a staff member or an outside third party observe the consenting of research participants to determine:

Whether the informed consent process has been appropriately completed and documented.

An IRB may require that selected protocols have one or more informed consent process situations be observed. Examples of protocols that may require observation of the consent process include:

High risk studies;

Studies that involve particularly complicated procedures or interventions;

Studies involving potentially vulnerable populations (e.g., ICU patients, children); or,

Studies involving study staff with minimal experience in administering consent to potential study participants.

4. REFERENCES

45 CFR 46.116; 21 CFR 50.20; FDA's Information Sheets: guide to informed consent; OPRR Guidance, obtaining and documenting informed consent of subjects who do not speak English

Title	IC 701 General Requirements and Documentation of Informed Consent
Date Last Reviewed	16 April 2009
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IC 702 EXEMPTIONS AND WAIVERS

1. PURPOSE

This policy describes the requirements for waiver of certain or all elements of informed consent procedures and waiver of requirements for obtaining informed consent.

2. POLICY STATEMENT

The IRB may approve a consent procedure, which does not include, or which alters some or all of the elements of informed consent (above), or waives the requirement to obtain informed consent if the IRB finds that the research meets specific criteria.

For FDA regulated research, the IRB may not waive informed consent except under the narrow provisions in 21 CFR 50.23 governing emergency research and as clarified in the FDA's Guidance on Informed Consent for *in vitro* Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, April 25, 2006.

3. SPECIFIC POLICIES

3.1 Exemptions or Waivers of One or More Requirements of Informed consent

The IRB may approve an informed consent procedure which does not include, or which alters, some or all of the elements of informed consent or waives the requirement to obtain informed consent provided the IRB finds and documents that:

- the research involves no more than minimal risk to the subjects and,
- the waiver or alteration will not adversely affect the rights and welfare of the subjects and;
- whenever appropriate, the subjects will be provided with additional pertinent information after participation; and, the research could not be practicably be carried out without the waiver or alteration.

4. REFERENCES

45 CFR 46.116; 45 CFR 46.117; 21 CRF 50; 21 CFR 50.23; FDA Guidance on Informed Consent for *in vitro* Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, April 25, 2006

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IC 703 DOCUMENTATION

1. PURPOSE

This policy describes the requirements for documentation of informed consent and circumstances when the IRB may waive the requirement to document informed consent.

2. POLICY STATEMENT

Unless specifically waived by the IRB, all subjects, or their legally authorized representatives, must document that they are consenting to participate in any research project that is conducted at the University of Pennsylvania.

3. SPECIFIC POLICIES

Documentation of Informed Consent

Each subject or his/her legally authorized representative must sign and date a copy of the current IRB-approved consent form prior to enrollment or any participation in any phase of the study, unless the requirement is waived by the IRB as allowed, and be given a copy of the signed document.

The IRB may approve procedures for documentation of informed consent that involve (a) a written consent form signed by the subject; (b) a short form written consent form with oral presentation; or (c) in limited circumstances, waiver of signed written consent form.

Each of these three options is described in detail below. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent in protocols that it reviews. Generally, only option (a) will be appropriate.

3.1 Written Consent Form Signed by Subject or Legally Authorized Representative

In most circumstances, the IRB requires that informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. The investigator should allow the subject or the legally authorized representative adequate opportunity to read the consent document before it is signed. A copy of the document must be given to the person signing the form.

3.1.1 Mentally disabled or cognitively impaired subjects: Studies involving subjects who may have impaired decision-making capabilities may take place over extended periods. The IRB should consider whether periodic re-consenting of individuals should be required to ensure that a subject’s continued involvement is voluntary. The IRB may require that investigators re-consent subjects after taking into account the study’s anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB should consider whether and when to require a reassessment of decision-making capacity.

3.1.2 The written informed consent document should embody, in language understandable to the subjects of the study, all the elements necessary for legally effective informed consent (see above).

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3.1.3 Subjects who do not understand English should be presented with an informed consent document written in a language understandable to them.

3.2 Oral Presentation Using Short Form

The written informed consent document should embody, in language understandable to the participant, all the elements necessary for legally effective informed consent. Participants who do not speak English should be presented with an informed consent document written in a language understandable to them.

As an alternative to standard written informed consent documents, oral presentation of informed consent information may be used.
In such cases, the subject must be provided with both:

A short form written informed consent document stating that the elements of consent have been presented orally to the subject or the subject's legally authorized representative; and,

A written summary of the information that is presented orally.

3.2.1 A witness to the oral presentation is required. The witness must sign both the short form written informed consent document and a copy of the written summary. When this method is used the IRB must review the written summary.

3.2.2 The subject or the legally authorized representative must sign the short form written consent document.

3.2.3 The person obtaining consent must sign a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.

3.2.4 Subjects Who Do Not Speak English. Where informed consent is documented using this short form procedure for non-English speaking subjects, the written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent.

When this procedure is used with subjects who do not speak English, (i) the oral presentation and the short form written informed consent document should be in a language understandable to the subject; (ii) the IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject.

The IRB will receive all foreign language versions of the short form as a condition of approval. The information in the protocol must match the information in the informed consent. Expedited review of these versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

3.3 Waiver of Documentation

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The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if the IRB finds that the only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from breach of confidentiality.

The IRB may waive the requirement for the investigator to obtain written informed consent if the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the Principal Investigator to provide subjects with a written statement regarding the research.

3.4 Use of Facsimile or Mail to Document Informed Consent

The IRB may approve a process that allows the informed consent document to be delivered by mail or facsimile to the potential subject or the potential subject's legally authorized representative and to conduct the consent interview by telephone when the subject or the legally authorized representative can read the consent document as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

4. REFERENCES

46 CFR 46.117; 21 CFR 50.27; FDA Information Sheets, a guide to informed consent

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IC 704 ASSENT

1. PURPOSE

This policy describes the requirements for assent of cognitively impaired adults and of children.

2. POLICY STATEMENT

The principle of respect for persons requires that the choice of an autonomous person be respected. Under the usual conditions of clinical research, this is accomplished by soliciting the informed consent of the prospective research subject. When prospective subjects have diminished capacity to consent , the consent of the parent or legally authorized representative is required (see IC705). However, any individual capable of some degree of understanding (generally, a child of seven or older) should participate in research only with assent. When assent is required, however, the decision of the individual assenting should be binding.

The Department of Health and Human Services' (DHHS) Regulations for the Protection of Human Subjects (Title 45, Part 46 Subpart D of the Code of Federal Regulations)and the Food and Drug Administration (FDA) regulations for the Protection of Human Subjects (Title 21, Part 50, Subpart D) set standards for the informed consent process and assign Institutional Review Boards with the responsibility for ensuring that any research or clinical trials involving children meet the following criteria.

3. SPECIFIC POLICIES

3.1 Use of Assent:

In instances where the subject may not be capable of giving informed consent the IRB must find that adequate provisions are made for soliciting the assent of the subject when in the judgment of the IRB, the subject is capable of providing assent.

3.1.1 "Assent" means a subject's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

3.1.2 In determining whether subjects are capable of assenting, the investigator and the IRB shall take into account the age, maturity, and psychological state of the subject involved. This judgment may be made for all subjects to be involved in research under a particular protocol, or for each subject, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the subjects is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the subject and is available only in the context of the research, the assent of the subject is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived as stated in section IC 702.3.1.

3.1.3. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

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3.2 Parental Permission and Assent for Research involving Children

3.2.1 When children are involved in research, the regulations require the **assent** of the child and the **permission** of the parent(s), in place of the consent of the subjects.

Given that children have not reached their full intellectual and emotional capacities and are legally unable to give valid consent, involving children in research requires the permission of their parents or legally authorized representatives. The IRB will determine whether the permission of both parents is necessary, and the conditions under which one parent may be considered "not reasonably available". In addition, the IRB will determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.

3.2.2 For research that is FDA regulated, children may be subjects of research only if informed consent is obtained from the parents or legal guardian. For other research, parental permission may be waived in accordance with 45 CFR 46.116(c)(2)(d).

The regulations provide that an IRB may find that the permission of one parent is sufficient for research to be conducted if the research is no more (minimal risk or if the research involves greater than minimal risk but presents the prospect of direct benefit to individual subjects). Where research is covered by §46.406 - 46.407 of the HHS regulations or §50.53 - §50.54 of the FDA regulations, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

3.2.3 The IRB will determine for each protocol - depending on such factors as the nature of the research and the age, status, and condition of the proposed subjects - whether all or some of the children are capable of assenting to participation. Where appropriate, the IRB may choose to review on a case-by-case basis whether assent should be sought from given individual subjects.

When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary. Additionally, in such circumstances a child's dissent, which should normally be respected, may be overruled by the child's parents, at the IRB's discretion.

When the IRB determines that the assent of the child is required, it will also determine that the provisions for obtaining and documenting assent are adequate.
3.2.4 The IRB will comply all federal regulations and also with state and local law.

4. REFERENCES

45 CFR 46.408 Subpart D; 21 CFR 50.55 Subpart D

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IC 705 SURROGATE CONSENT

1. PURPOSE

The purpose of this Policy is to provide guidelines for the IRB and investigators in proposing, conducting and reviewing research in subjects with decisional impairments.

Informed Consent

Federal regulations require that the researcher obtain the legally effective informed consent of the subject or the subject's legally authorized representative prior to medical research. Federal law defers to state law to determine what surrogate is legally authorized to substitute consent. Pennsylvania law requires the informed consent of the subject or the subject's authorized representative before the administration of an experimental medication, the use of an experimental device, or the use of an approved medication or device in an experimental manner. Pennsylvania law also authorizes substituted consent to the performance of experimental biomedical or behavioral medical procedure or participation in any biomedical or behavioral experiment by the subject's court-appointed guardian pursuant to a court order issued after fact finding. Finally, Pennsylvania statutory law further authorizes a person named in the subject's power of attorney to consent to medical, therapeutic and surgical procedures.

While Pennsylvania statutory law does not explicitly authorize substituted consent in the absence of a power of attorney or court-appointed guardian, case law strongly supports substituted consent by close family members when patients lack capacity to make medical decisions. When the subject is unable to give informed consent, the subject's close family member or significant partner is in the best position to determine the wishes of the subject regarding participation in therapeutic research.

If the research poses no more than minimal risk, the investigator and IRB may consider waiver of the requirement for informed consent as described in Policy 702.

2. POLICY STATEMENT

It is the policy of the University of Pennsylvania Institutional Review Boards to protect the research subject's right to autonomy. It is also the IRB's policy to protect those with diminished autonomy or reduced capacity to consent to research or to provide authorization for the use and/or disclosure of their protected health information.

However, the IRB recognizes that substituted consent is necessary in order to offer experimental treatments to subjects incapable of making autonomous choices where the research poses more than minimal risk, but where the risks to the subject are reasonable in relationship to any anticipated benefits to subjects, and to the importance of the knowledge that may reasonably be expected to result from the research. Accordingly, the following procedure will be followed when the researcher determines that a patient is unable to give informed consent for participation in research and/or is unable to give a HIPAA Authorization.

3. SPECIFIC POLICIES

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3.1 Submission and Review of Protocols Involving Subjects Unable to Provide Informed Consent for biomedical research.

3.1.1 The investigator shall be responsible for making the determination as to whether the research protocol shall or shall not enroll subjects incapable of giving informed consent.

3.1.2 If it is anticipated that the research will involve individuals with diminished capacity to consent, the protocol shall describe the process by which the investigator will determine and document the individual's ability to provide consent. The protocol shall also describe the process by which the investigator shall obtain assent/surrogate consent.

3.1.3 The IRB shall review such protocols and determine and document whether:

- the risks to the subjects are reasonable in relationship to any anticipated benefits to subjects and to the importance of the knowledge that may reasonably be expected to result; and,
- the description of the informed consent process to be used is appropriate to the risk of the protocol as assigned by the IRB; and,
- the appropriateness of the assent/surrogate consent content and process; and,
- the appropriateness and effectiveness of the HIPAA Authorization if included as part of the informed consent or assent; and,
- all other aspects of the proposed research as provided in Policies RR 402-404 are appropriate.

3.1.4 If the IRB determines that the risk to the subject is greater than minimal risk, it may require additional safeguards to insure that the rights of such subjects are protected. Such additional protections may include, but are not limited to:

Witnessing of assent/informed surrogate consent by a third party.

Independent assessment of subject's ability to assent, and/or surrogates ability to consent by an independent subject advocate or subject's primary care physician consistent with legal requirements.

Independent documentation of the informed consent process.

The appropriateness of the individual serving as the personal representative/ surrogate.

Other safeguards as appropriate.

3.1.5 The IRB shall not approve any research involving the use of surrogate consent if they determine that the risk to the subject is high in relationship to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

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3.2 Determination of Subjects Ability to Provide Informed Consent in a Research Study

3.2.1 The investigator shall be responsible for determining whether an individual subject can provide informed consent.

3.2.2 The investigator will document in the research record, as thoroughly as possible, the reason for the subject's inability to provide informed consent.

3.2.3 The investigator shall apply and document any additional safeguards as directed by the IRB.

3.3 Individuals Able to Provide Effective Surrogate Consent and/or Surrogate

3.3.1 For research conducted in the Commonwealth of Pennsylvania, following individuals may be considered legally authorized representatives of the subject and capable of providing surrogate consent:

- A court-appointed guardian authorized to consent to the subject's participation in the protocol in a current court order issued within the subject's jurisdiction.
- A health care agent appointed by the subject in a power of attorney.
- A "health care representative" when the subject cannot speak for themselves and where there has been no guardian appointed by the court or health care power of attorney designated by the patient. (PA Act 169). Any member of the following classes, in descending order of priority, who is reasonably available may act as the subject's health care representative.
    - The spouse (unless an action for divorce is pending) and adult child or children of another relationship.
    - Adult children (18 years of age or older).
    - A parent.
    - An adult sibling.
    - An adult grandchild
    - An adult who has knowledge of the patient's preferences and values, including but not limited to religious and moral beliefs, wto assess how the patient would make decisions.

3.3.2 For human subjects research conducted in other states or internationally, requests for the use of surrogate consent will be considered by the IRB in accordance with local state or international law. The investigator or the IRB will contact the legal advisor to the IRB within the Office of General Counsel to assist in determining who under local law may serve as a legally authorized individual.

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3.4 Responsibilities of the Authorized Individual in the Surrogate Consent Process

3.4.1 The surrogate should base his or her decision on the subject's expressed wishes or, if unknown, what the subject would have desired in light of his or her

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prognosis, values, and beliefs. In the event of a disagreement among potential patient surrogates, an attempt to reach consensus shall be made through the intervention of a subject advocate appointed by the IRB if available. If consensus is not possible, a court appointed guardian should be obtained before the subject is enrolled in the study. When a surrogate provides consent, for a subject's participation in a research project it is preferable for that surrogate to remain the responsible party for all subsequent research decisions including but not limited to withdrawal of consent.

3.5 Requirement for Re-Consent

3.5.1 If at any time after the subject is enrolled in a study through surrogate consent, he or she regains the capacity to provide informed consent, the investigator shall obtain the legally effective informed consent of the subject for continued participation in the research.

3.5.2 Decision-making capacity of subjects may fluctuate. The consent process should be ongoing and involve the legally effective representative if at any time the investigator believes that the subject is unable to provide informed consent for continuing in a research project in which the subject initially gave informed consent.

4. REFERENCES

Fiori, 543 Pa. 592, 673 A.2d 905 (1996); PA Act 169

Title	IC 705 Surrogate Consent
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3624 Market Street, Suite 301 South, Philadelphia, PA 19104-6006

RI 800	RESPONSIBILITIES OF INVESTIGATORS
801	IRB-REQUIRED INVESTIGATOR ACTIONS
802	PRINCIPAL INVESTIGATORS

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RI 801 IRB-REQUIRED INVESTIGATOR ACTIONS

1. PURPOSE

This policy describes what the IRB requires of investigators in the conduct of research.

2. POLICY STATEMENT

The regulations require that organizations have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and appropriate federal officials of unanticipated problems involving risks to participants or others, defined as an untoward event that is serious, unexpected and related to the research. Events meeting the definition must be reported under this policy to the appropriate regulatory oversight agency. For research subject to the FDA regulations, reportable events include a subset of serious adverse events as defined by FDA regulations.

It is the Investigator's responsibility to keep the IRB informed of unexpected, protocol related, non-serious and serious adverse events or unanticipated problems that pose risk to subjects or others. An investigator is responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events. Investigators are also responsible for informing government funding agencies and other sponsors of any unanticipated serious events, as appropriate.

3. SPECIFIC POLICIES

3.1 IRB Review of Research

All human subjects research that is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania in connection with his or her institutional responsibilities must be reviewed by the IRB.

3.2 Informed Consent

The investigator must obtain informed consent from participants prior to their enrollment into the research unless the IRB has waived this requirement. The investigator must use the informed consent document approved by the IRB. Approval dates are indicated on the first page of the consent document. Consent documents are valid only during the dates indicated on the form; and the investigator may use the forms only during the period for which they are valid. Investigators must follow University guidelines for obtaining consent.

3.3 Reporting of Unanticipated Problems Increasing Risks to Subjects or Other Reportable Events

The IRB must be informed of unanticipated problems involving risks to subjects or others and other reportable events as defined by SOP RR 404.

3.4 Changes in Approved Research

Changes in approved research, during the period for which approval has already been given, may not be initiated without IRB review and approval except where necessary to

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eliminate apparent immediate hazards to human subjects. Investigators or sponsors must submit requests for changes to the IRB in writing. Upon receipt of the protocol change, the IRB Chair or designee will determine if the revision meets the criteria for expedited review. Minor changes involving no more than minimal risk to the subject will be reviewed by the expedited review process.

3.5 Periodic and Final Reports

The length of time approval is given to a research protocol will be no more than one year, and is dependent on the risk involved with the research. Investigators are responsible for requesting renewal in anticipation of the expiration of the approval period. Investigators or their designees and or sponsors are required to provide a periodic report regarding their investigation prior to the end of the approval period, or upon completion of the study. In addition, if so determined by the Board, the investigator is required to submit Interim Reports within 14 days of the date determined for interim review at the time of the initial IRB review. For renewal of approval, an IRB Continuing Review Form will be provided to the investigator within 90 days from study expiration date, however, the investigator is not required to utilize this form to report completion of the study. The sponsor and/or the investigator or his/her designee may submit final reports of study completion.

3.6 Student Conducted Research

Directed or independent Research Projects (e.g., honors or graduate theses), which employ systematic data collection with the intent to contribute to generalizable knowledge require IRB review and approval.

For example, activities that must be reviewed and approved by the IRB include: (i) All master's theses and doctoral dissertations that involve human subjects; and (ii) All projects that involve human subjects and for which findings may be published or otherwise disseminated.

Classroom activities, the goal of which is to provide training in research methodology do not require IRB review and approval. Examples are provided in the IRB Guidance: Is IRB Review Required?

All students/fellows applying for IRB review must obtain the signature of their faculty advisor on the Signature Page of their application.

3.7 Financial Conflicts of Interest

The protection of human subjects requires objectivity in communicating risks, selecting subjects, promoting informed consent, and gathering, analyzing and reporting data.

All investigators must report on their application to the IRB whether they or any other person responsible for the design, conduct, or reporting of the research has any economic interest in, or acts as an officer or a director of any outside entity whose financial interests would reasonably appear to be affected by, the research. The IRB will determine whether such conflicts will be disclosed to participants and will refer disclosures of financial conflicts of interest to the Research Conflicts of Interest Standing

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Committee for management. IRB approval will be contingent upon review and approval of the management plan, if applicable.

4. REFERENCES

None

Title	RI 801 IRB Required Investigator Actions
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RI 802 PRINCIPAL INVESTIGATORS

1. PURPOSE

This policy describes those individuals who may serve as principal investigators on research protocols involving human subjects.

2. POLICY STATEMENT

All research involving the use of human subjects conducted at the University of Pennsylvania must be conducted by individuals appropriately trained and knowledgeable concerning the protection of human subjects.

3. SPECIFIC POLICIES

3.1 Faculty

All human subjects research that is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania in connection with his or her institutional responsibilities must be under the direct supervision of a member of the Standing Faculty, Clinician-Educator or Associate Faculty of the University. Generally, faculty members are considered to be sufficiently knowledgeable to supervise and/or conduct research as determined by their appointment. However, the IRB may at its discretion determine that a faculty member lacks sufficient expertise to carry out any particular research project based on the risks and benefits to the research subjects.

When all research activities take place at the Philadelphia Veterans Administration Medical Center (VAMC) and the research is conducted by an investigator whose academic appointment is at the University of Pennsylvania but whose primary hospital appointment is at the VAMC, the research proposal does not have to be submitted to the Penn IRB.

When all research activities take place at the Children's Hospital of Philadelphia (CHOP) and the research is conducted by an investigator whose academic appointment is at the University of Pennsylvania but whose primary hospital appointment is at the CHOP, the research proposal does not have to be submitted to the Penn IRB. Other exceptions are elaborated in the CHOP-Penn IRB Reciprocity Agreement.

3.2 Non Faculty, Academic Support Staff, Postdoctoral Fellows, Graduate Students, and Undergraduate Students

Research conducted by University students or employees must be under the direction of a faculty member as defined in 3.1.

3.3 Other Individuals

Individuals not meeting the above criteria as principal investigators may, by demonstrating sufficient cause and necessary expertise, petition the IRB Executive Director for permission to submit an application for approval to serve as a principal

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investigator of a human research protocol. Such agreement shall be in writing and require the individual to comply with all relevant IRB and University policies for the conduct of research involving human subjects.

3.6 Training of Investigators

The IRB shall establish standards of training required for all individuals engaged in human research.

4. REFERENCES

None

Title	RI 802 Principal Investigators
Date Last Reviewed	16 April 2009
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QA 900	QUALITY ASSURANCE
901	QA/QC PROGRAM
902	AUDITS BY REGULATORY AGENCIES

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QA 901 QUALITY ASSURANCE AND IMPROVEMENT PROGRAM

1. PURPOSE

This section states the policy concerning quality assurance measures for the IRB.

2. POLICY STATEMENT

Quality assurance and inprovement of the daily operations of the IRB ensure that they effectively support the IRB's mandate. Therefore, the QA/Qi program consists of three components:

- Periodic review of IRB records; and,
- Regular review and assessment of procedures.
- Training and continuing education of IRB staff.

3. SPECIFIC POLICIES

The IRB Executive Director has the authority to implement a QA/QI program and act on identified deficiencies by implementing corrective action via revisions to the Guide to Daily Operations or recommending changes to the SOPs. The IRB Associate Director is responsible for oversight of the IRB's quality improvement activities.

4. REFERENCES

None

Title	QA 901 QA/QC Program
Date Last Reviewed/Revised	16 April 2009
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QA 902 AUDITS BY REGULATORY AGENCIES

1. PURPOSE

This section states the policy concerning preparation for regulatory audits of the IRB and appropriate behavior toward regulators

2. POLICY STATEMENT

Quality assurance and control of the daily operations of the IRB insure that they effectively support the IRB's mandate. Therefore, the IRB must have in place mechanisms and policies for dealing with external auditing and accrediting agencies.

3. SPECIFIC POLICIES

3.1 Preparing for an audit

Certain regulatory and/or accrediting agencies have the authority to audit the operations of IRBs. These include: FDA, OHRP, sponsors or funding entities of research, or others who may also be authorized by regulations or agreement with the University to audit specific documents and procedures.

For external audits involving OHRP or FDA, the following must be notified immediately:

- Vice Provost for Research
- IRB Executive Chair
- Hospital administration if applicable
- Medical Records Supervisor, if applicable

The IRB Executive Director and IRB staff designated to participate in the audit are required to follow the steps outlined by this institution for preparing the site for an audit.

3.2 Participating in an Audit

Researchers and IRB staff members are expected to know and follow the procedures outlined by this institution for the conduct of an internal or external audit of specific studies or study sites.

Prior to being granted access to IRB documentation, inspectors or auditors must exhibit proof of their authority or authorization to conduct an audit to access IRB documents, and no entity other than those listed on the consent forms may have access to any document that includes subject identifiers. The IRB Executive Director is responsible for ensuring the redaction of such information from files prior to an audit as may be required.

Auditors will be provided with adequate working area to conduct an audit and IRB staff and members must make every reasonable effort to be available and to accommodate and expedite the requests of such auditors.

Documents may be copied and taken off-site only by individuals authorized in writing by the Office of General Counsel or the Vice Provost for Research to do so.

3.3 Follow-up after an Audit

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Reports of the audit, either verbal or written, should be addressed by the principal investigator or other appropriate individuals or offices, as soon as possible after site-specific audits. Reports of the audit directed to the operation of the IRB should be presented to the Vice Provost for Research and addressed as soon as possible.

4. REFERENCES

None

Title	QA 902 Audits by Regulatory Agencies
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Peer review

From Wikipedia, the free encyclopedia

For Wikipedia's Peer Review area, see Wikipedia:Peer review.

For other uses, see Peer review (disambiguation).

It has been suggested that *Open peer review* be merged into this article or section. (Discuss)

It has been suggested that *Independent review* be merged into this article or section. (Discuss)

This article has multiple issues. Please help **improve it** or discuss these issues on the **talk page**.

- It needs **additional references or sources for verification.** Tagged since July 2009.
- It may need **reorganization** to meet Wikipedia's quality standards. Tagged since October 2010.
- It contains too much **jargon** and may need simplification or further explanation. Tagged since October 2010.
- Its **lead section** requires expansion. Tagged since April 2010.

Peer review is a generic term that is used to describe a process of self-regulation by a profession or a process of evaluation involving qualified individuals with the related field. Peer review methods are employed to maintain standards, improve performance, and provide credibility. In academia, the term is often used to denote a prepublication reviews of academic papers; reviewing an academic paper is often called *refereeing*.

Contents [hide]

Terminology [edit]

The process and content of peer review may vary substantially depending on the profession and the purpose of the review. The key elements **Peer** and **Review** define and describe the term.

Peer [edit]

1. Someone “of equal standing with another … especially belonging to the same societal group… or [having the same] status” [1]
2. “A noble with a hereditary title, i.e., a peerage, and in times past, with certain rights and privileges not enjoyed by commoners.” [2]

Review [edit]

1. A critical inspection or examination
2. A second or repeated viewing of past events, circumstances or facts.[3]

Peer review can be categorized by the type of activity and by the field or profession in which the activity occurs. The following terms could be used to make these distinctions, but generally those in any given field just rely on the generic term. Even when qualifiers are applied, they may be used inconsistently. For example, **Clinical peer review** has been used to refer specifically to Physician peer review,[4] to the peer evaluation of clinical teaching skills for both physicians and nurses,[5][6] to scientific peer review of journal articles, and to the secondary rating of the clinical value of articles in peer reviewed journals.[7] Similarly, Medical peer review has been used by the American Medical Association (AMA) to refer not only to the process of improving quality and safety in healthcare organizations ,[8] but also to process by which adverse actions involving clinical privileges or professional society membership may be pursued.[9] Thus, the terminology has poor standardization and specificity, particularly as a database search term.

Professional peer review [edit]

Professional peer review focuses on the performance of professionals, with a view to improving quality, upholding standards, or providing certification. Professional peer review activity is widespread in the field of health care, where it may be termed "clinical peer review" or "medical peer review".

Further, since peer review activity is commonly segmented by clinical discipline, there is also physician peer review, nursing peer review, dentistry peer review,[10] etc. Many other professional fields have some level of peer review process: accounting,[11] law,[12][13] engineering (e.g., software peer review, technical peer review), aviation, and even forest fire management.[14] In academia, peer review is common in decisions related to faculty advancement and tenure. Peer review is used in education to achieve certain learning objectives, particularly as a tool to reach higher order processes in the affective and cognitive domains as defined by *Bloom's Taxonomy*. This may take a variety of forms, including closely mimicking the scholarly peer review processes used in science and medicine.[15]

Scholarly peer review [edit]

A reviewer at the National Institutes of Health evaluates a grant proposal.

Scholarly peer review (also known as **refereeing**) is the process of subjecting an author's scholarly work, research, or ideas to the scrutiny of others who are experts in the same field, before a paper describing this work is published in a journal. Peer review requires a community of experts in a given (and often narrowly defined) field, who are qualified and able to perform impartial review. Impartial review, especially of work in less narrowly defined or inter-disciplinary fields, may be difficult to accomplish; and the significance (good or bad) of an idea may never be widely appreciated among its contemporaries. Although generally considered essential to academic quality, and used in most important scientific publications, peer review has been criticized as ineffective, slow, and misunderstood (see anonymous peer review and open peer review). Recently there have been some experiments with wiki-style, signed, peer reviews, for example in an issue of the *Shakespeare Quarterly*.[16]

Pragmatically, peer review refers to the work done during the screening of submitted manuscripts and funding applications. This process encourages authors to meet the accepted standards of their discipline and prevents the dissemination of irrelevant findings, unwarranted claims, unacceptable interpretations, and personal views. Publications that have not undergone peer review are likely to be regarded with suspicion by scholars and professionals.

Justification [edit]

It is difficult for authors and researchers, whether individually or in a team, to spot every mistake or flaw in a complicated piece of work. This is not necessarily a reflection on those concerned, but because with a new and perhaps eclectic subject, an opportunity for improvement may be more obvious to someone with special expertise or who simply looks at it with a fresh eye. Therefore, showing work to others increases the probability that weaknesses will be identified and improved. For both grant-funding and publication in a scholarly journal, it is also normally a requirement that the subject is both novel and substantial.[*dubious* – *discuss*]

Furthermore, the decision whether or not to publish a scholarly article, or what should be modified before publication, lies with the editor of the journal to which the manuscript has been submitted. Similarly, the decision whether or not to fund a proposed project rests with an official of the funding agency. These individuals usually refer to the opinion of one or more reviewers in making their decision. This is primarily for three reasons:

- Workload. A small group of editors/assessors cannot devote sufficient time to each of the many

articles submitted to many journals.
- Diversity of opinion. Were the editor/assessor to judge all submitted material themselves, approved material would solely reflect their opinion.
- Limited expertise. An editor/assessor cannot be expected to be sufficiently expert in all areas covered by a single journal or funding agency to adequately judge all submitted material.

Thus it is normal for manuscripts and grant proposals to be sent to one or more external reviewers for comment.

Reviewers are typically anonymous and independent, to help foster unvarnished criticism, and to discourage cronyism in funding and publication decisions. However, US government guidelines governing peer review for federal regulatory agencies require that reviewer's identity be disclosed under some circumstances. Anonymity may be unilateral or reciprocal (single- or double-blinded reviewing).

Since reviewers are normally selected from experts in the fields discussed in the article, the process of peer review is considered critical to establishing a reliable body of research and knowledge. Scholars reading the published articles can only be expert in a limited area; they rely, to some degree, on the peer-review process to provide reliable and credible research that they can build upon for subsequent or related research. As a result, significant scandal ensues when an author is found to have falsified the research included in an article, as many other scholars, and the field of study itself, may have relied upon the original research (see Peer review failures below).

Procedure [edit]

In the case of proposed publications, an editor sends advance copies of an author's work or ideas to researchers or scholars who are experts in the field (known as "referees" or "reviewers"), nowadays normally by e-mail or through a web-based manuscript processing system. Usually, there are two or three referees for a given article.

These referees each return an evaluation of the work to the editor, noting weaknesses or problems along with suggestions for improvement. Typically, most of the referees' comments are eventually seen by the author; scientific journals observe this convention universally. The editor, usually familiar with the field of the manuscript (although typically not in as much depth as the referees, who are specialists), then evaluates the referees' comments, her or his own opinion of the manuscript, and the context of the scope of the journal or level of the book and readership, before passing a decision back to the author(s), usually with the referees' comments.

Referees' evaluations usually include an explicit recommendation of what to do with the manuscript or proposal, often chosen from options provided by the journal or funding agency. Most recommendations are along the lines of the following:

- to unconditionally accept the manuscript or proposal,
- to accept it in the event that its authors improve it in certain ways,
- to reject it, but encourage revision and invite resubmission,
- to reject it outright.

During this process, the role of the referees is advisory, and the editor is typically under no formal obligation to accept the opinions of the referees. Furthermore, in scientific publication, the referees do not act as a group, do not communicate with each other, and typically are not aware of each others identities or evaluations. There is usually no requirement that the referees achieve consensus. Thus the group dynamics are substantially different from that of a jury.

In situations where the referees disagree substantially about the quality of a work, there are a number of strategies for reaching a decision. When an editor receives very positive and very negative reviews for the same manuscript, the editor often will solicit one or more additional reviews as a tie-breaker. As another strategy in the case of ties, editors may invite authors to reply to a referee's

criticisms and permit a compelling rebuttal to break the tie. If an editor does not feel confident to weigh the persuasiveness of a rebuttal, the editor may solicit a response from the referee who made the original criticism. In rare instances, an editor will convey communications back and forth between authors and a referee, in effect allowing them to debate a point. Even in these cases, however, editors do not allow referees to confer with each other, though the reviewer may see earlier comments submitted by other reviewers. The goal of the process is explicitly not to reach consensus or to persuade anyone to change their opinions. Some medical journals, however (usually following the open access model), have begun posting on the Internet the pre-publication history of each individual article, from the original submission to reviewers' reports, authors' comments, and revised manuscripts.

Traditionally, reviewers would remain anonymous to the authors, but this standard is slowly changing. In some academic fields, most journals now offer the reviewer the option of remaining anonymous or not, or a referee may opt to sign a review, thereby relinquishing anonymity. Published papers sometimes contain, in the acknowledgments section, thanks to anonymous or named referees who helped improve the paper.

Some university presses undertake peer review of books. After positive review by two or three independent referees, a university press sends the manuscript to the press's editorial board, a committee of faculty members, for final approval.[17] Such a review process is a requirement for full membership of the Association of American University Presses.[18]

In some disciplines there exist refereed venues (such as conferences and workshops). To be admitted to speak, scholars and scientists must submit papers (generally short, often 15 pages or less) in advance. These papers are reviewed by a "program committee" (the equivalent of an editorial board), which generally requests inputs from referees. The hard deadlines set by the conferences tend to limit the options to either accepting or rejecting the paper.

Recruiting referees [edit]

At a journal or book publisher, the task of picking reviewers typically falls to an editor.[19] When a manuscript arrives, an editor solicits reviews from scholars or other experts who may or may not have already expressed a willingness to referee for that journal or book division. Granting agencies typically recruit a panel or committee of reviewers in advance of the arrival of applications.

Typically referees are not selected from among the authors' close colleagues, students, or friends. Referees are supposed to inform the editor of any conflict of interests that might arise. Journals or individual editors often invite a manuscript's authors to name people whom they consider qualified to referee their work. Indeed, for a number of journals this is a requirement of submission. Authors are sometimes also invited to name natural candidates who should be *disqualified*, in which case they may be asked to provide justification (typically expressed in terms of conflict of interest). In some disciplines, scholars listed in an "acknowledgments" section are not allowed to serve as referees (hence the occasional practice of using this section to disqualify potentially negative reviewers[*citation needed*]).

Editors solicit author input in selecting referees because academic writing typically is very specialized. Editors often oversee many specialties, and can not be experts in all of them. But after an editor selects referees from the pool of candidates, the editor typically is obliged not to disclose the referees' identities to the authors, and in scientific journals, to each other (see Anonymous peer review). Policies on such matters differ among academic disciplines.

Recruiting referees is a political art, because referees, and often editors, are usually not paid, and reviewing takes time away from the referee's main activities, such as his or her own research. To the would-be recruiter's advantage, most potential referees are authors themselves, or at least readers, who know that the publication system requires that experts donate their time. Referees also have the opportunity to prevent work that does not meet the standards of the field from being published, which

is a position of some responsibility. Editors are at a special advantage in recruiting a scholar when they have overseen the publication of his or her work, or if the scholar is one who hopes to submit manuscripts to that editor's publication in the future. Granting agencies, similarly, tend to seek referees among their present or former grantees. Serving as a referee can even be a condition of a grant, or professional association membership.

Another difficulty that peer review organizers face is that, with respect to some manuscripts or proposals, there may be few scholars who truly qualify as experts. Such a circumstance often frustrates the goals of reviewer anonymity and the avoidance of conflicts of interest. It also increases the chances that an organizer will not be able to recruit true experts – people who have themselves done work similar to that under review, and who can read between the lines. Low-prestige or local journals and granting agencies that award little money are especially handicapped with regard to recruiting experts.

Finally, anonymity adds to the difficulty in finding reviewers in another way. In scientific circles, credentials and reputation are important, and while being a referee for a prestigious journal is considered an honor, the anonymity restrictions make it impossible to publicly state that one was a referee for a particular article. However, credentials and reputation are principally established by publications, not by refereeing; and in some fields refereeing may not be anonymous.

Different styles of review [edit]

Peer review can be *rigorous*, in terms of the skill brought to bear, without being highly *stringent*. An agency may be flush with money to give away, for example, or a journal may have few impressive manuscripts to choose from, so there may be little incentive for selection. Conversely, when either funds or publication space is limited, peer review may be used to select an extremely small number of proposals or manuscripts.

Often the decision of what counts as "good enough" falls entirely to the editor or organizer of the review. In other cases, referees will each be asked to make the call, with only general guidance from the coordinator on what stringency to apply.

Very general journals such as *Science* and *Nature* have extremely stringent standards for publication, and will reject papers that report good quality scientific work if editors feel the work is not a breakthrough in the field. Such journals generally have a two-tier reviewing system. In the first stage, members of the editorial board verify that the paper's findings — if correct — would be ground-breaking enough to warrant publication in *Science* or *Nature*. Top journals in other fields have similar policies, for instance the *Journal of the ACM*.[20] Most papers are rejected at this stage. Papers that do pass this 'pre-reviewing' are sent out for in-depth review to outside referees. Even after all reviewers recommend publication and all reviewer criticisms/suggestions for changes have been met, papers may still be returned to the authors for shortening to meet the journal's length limits. With the advent of electronic journal editions, overflow material may be stored in the journal's online Electronic Supporting Information archive.

A similar emphasis on novelty exists in general area journals such as the *Journal of the American Chemical Society* (*JACS*). However, these journals generally send out all papers (except blatantly inappropriate ones) for peer reviewing to multiple reviewers. The reviewers are specifically queried not just on the scientific quality and correctness, but also on whether the findings are of interest to the general area readership (chemists of all disciplines, in the case of *JACS*) or only to a specialist subgroup. In the latter case, the recommendation is usually for publication in a more specialized journal. The editor may offer to authors the option of having the manuscript and reviews forwarded to such a journal with the same publishers (perhaps, in the example given, the *Journal of Organic Chemistry*); if the reviewer reports warrant such a decision, the editor of such a journal may accept the forwarded manuscript without further reviewing.

Specialized scientific journals such as the aforementioned chemistry journals, *Astrophysical Journal*,

and the *Physical Review* series use peer review primarily to filter out obvious mistakes and incompetence, as well as plagiarism, overly derivative work, and straightforward applications of known methods. Different publication rates reflect these different criteria: *Nature* publishes about 5 percent of received papers, while *Astrophysical Journal* publishes about 70 percent. Some open access journals such as Biology Direct have the policy of making the reviewers' reports public by publishing the reports together with the manuscripts.

Screening by peers may be more or less laissez-faire depending on the discipline. Physicists, for example, tend to think that decisions about the worthiness of an article are best left to the marketplace. Yet even within such a culture peer review serves to ensure high standards in what is published. Outright errors are detected and authors receive both edits and suggestions.

To preserve the integrity of the peer-review process, submitting authors may not be informed of who reviews their papers; sometimes, they might not even know the identity of the associate editor who is responsible for the paper. In many cases, alternatively called "masked" or "double-masked" review (or "blind" or "double-blind" review), the identity of the authors is concealed from the reviewers, lest the knowledge of authorship bias their review; in such cases, however, the associate editor responsible for the paper does know who the author is. Sometimes the scenario where the reviewers do know who the authors are is called "single-blinded" to distinguish it from the "double-blinded" process. In double-blind review, the authors are required to remove any reference that may point to them as the authors of the paper.

In many fields of study, single-blinding is the normative practice; however, in others, such as information systems, it is almost unheard of, and double-blinding is the norm. While the anonymity of reviewers is almost universally preserved, open peer review is a relatively novel exception to this principle, where reviewers are revealed to the authors.

Critics of the double-blind process point out that, despite the extra editorial effort to ensure anonymity, the process often fails to do so, since certain approaches, methods, writing styles, notations, etc., may point to a certain group of people in a research stream, and even to a particular person.[21][22] Proponents of double-blind review argue that it performs at least as well as single-blind, and that it generates a better perception of fairness and equality in global scientific funding and publishing.[23]

Proponents also argue that if the reviewers of a paper are unknown to each other, the associate editor responsible for the paper can easily verify the objectivity of the reviews. Single-blind review is thus strongly dependent upon the goodwill of the participants.

A conflict of interest arises when a reviewer and author have a disproportionate amount of respect (or disrespect) for each other. As an alternative to single-blind and double-blind review, authors and reviewers are encouraged to declare their conflicts of interest when the names of authors and sometimes reviewers are known to the other. When conflicts are reported, the conflicting reviewer is prohibited from reviewing and discussing the manuscript. The incentive for reviewers to declare their conflicts of interest is a matter of professional ethics and individual integrity. While their reviews are not public, these reviews are a matter of record and the reviewer's credibility depends upon how they represent themselves among their peers. Some software engineering journals, such as the IEEE Transactions on Software Engineering, use non-blind reviews with reporting to editors of conflicts of interest by both authors and reviewers.

A more rigorous standard of accountability is known as an audit. Because reviewers are not paid, they cannot be expected to put as much time and effort into a review as an audit requires. Most journals (and grant agencies like NSF) have a policy that authors must archive their data and methods in the event another researcher wishes to replicate or audit the research after publication[*citation needed*]. Unfortunately, the archiving policies are often ignored by researchers.

Prepublication reviews [edit]

Anonymous peer review [edit]

Anonymous peer review, also called **blind review**, is a system of prepublication peer review of scientific articles or papers for journals or academic conferences by reviewers who are known to the journal editor or conference organizer but whose names are not given to the article's author. The reviewers do not know the author's identity, as any identifying information is stripped from the document before review. The system is intended to reduce or eliminate bias, although this has been challenged - for example Eugene Koonin, a senior investigator at the National Center for Biotechnology Information, asserts that the system has "well-known ills"[24] and advocates "open peer review".

Open peer review [edit]

Main article: Open peer review

Open peer review describes a scientific literature concept and process, central to which is the various transparency and disclosure of the identities of those reviewing scientific publications. The concept thus represents a departure from, and an alternative to, the incumbent anonymous peer review process, in which non-disclosure of these identities toward the public - and toward the authors of the work under review - is default practice. The open peer review concept appears to constitute a response to modern criticisms of the incumbent system; ergo, its emergence may be partially attributed to these phenomena.

Postpublication reviews [edit]

The process of peer review does not end after a paper completes the peer review process. After being put to press, and after 'the ink is dry', the process of peer review continues as publications are read. Readers will often send letters to the editor of a journal, or correspond with the editor via an on-line journal club. In this way, all 'peers' may offer review and critique of published literature. A variation on this theme is open peer commentary; journals using this process solicit and publish non-anonymous commentaries on the "target paper" together with the paper, and with original authors' reply as a matter of course. The introduction of the "epub ahead of print" practice in many journals has made possible the simultaneous publication of unsolicited letters to the editor together with the original paper in the print issue.

Criticism of peer review [edit]

This section **needs additional citations for verification.**
Please help improve this article by adding reliable references. Unsourced material may be challenged and removed. *(October 2009)*

One of the most common complaints about the peer review process is that it is slow, and that it typically takes several months or even several years in some fields for a submitted paper to appear in print[*citation needed*]. In practice, much of the communication about new results in some fields such as astronomy and economics no longer takes place through peer-reviewed papers, but rather through preprints submitted onto electronic servers such as arXiv.org[*citation needed*]. However, such preprints are often also submitted to refereed journals, and in many cases have, at the time of electronic submission, already passed through the peer review process and been accepted for publication.[*citation needed*]

While passing the peer review process is often considered in the scientific community to be a certification of validity[*citation needed*], it is not without its problems. Drummond Rennie, deputy editor of *Journal of the American Medical Association* is an organizer of the International Congress on Peer Review and Biomedical Publication, which has been held every four years since 1986.[25] He

remarks,

> There seems to be no study too fragmented, no hypothesis too trivial, no literature too biased or too egotistical, no design too warped, no methodology too bungled, no presentation of results too inaccurate, too obscure, and too contradictory, no analysis too self-serving, no argument too circular, no conclusions too trifling or too unjustified, and no grammar and syntax too offensive for a paper to end up in print.

Richard Horton, editor of the British medical journal *The Lancet*, has said that

> The mistake, of course, is to have thought that peer review was any more than a crude means of discovering the acceptability — not the validity — of a new finding. Editors and scientists alike insist on the pivotal importance of peer review. We portray peer review to the public as a quasi-sacred process that helps to make science our most objective truth teller. But we know that the system of peer review is biased, unjust, unaccountable, incomplete, easily fixed, often insulting, usually ignorant, occasionally foolish, and frequently wrong.[26]

Allegations of bias and suppression [edit]

The interposition of editors and reviewers between authors and readers always raises the possibility that the intermediators may serve as gatekeepers.[27] Some sociologists of science argue that peer review makes the ability to publish susceptible to control by elites and to personal jealousy.[28] The peer review process may suppress dissent against "mainstream" theories.[29][30][31] Reviewers tend to be especially critical of conclusions that contradict their own views,[32] and lenient towards those that accord with them. At the same time, established scientists are more likely than less established ones to be sought out as referees, particularly by high-prestige journals or publishers. As a result, it has been argued[*by whom?*], ideas that harmonize with the established experts' are more likely to see print and to appear in premier journals than are iconoclastic or revolutionary ones, which accords with Thomas Kuhn's well-known observations regarding scientific revolutions.[33]

Others[*who?*] have pointed out that there is a very large number of scientific journals in which one can publish, making total control of information difficult[*citation needed*]. In addition, the decision-making process of peer review, in which each referee gives their opinion separately and without consultation with the other referees, is intended to mitigate some of these problems[*citation needed*]. Some have suggested that:

> "... peer review does not thwart new ideas. Journal editors and the 'scientific establishment' are not hostile to new discoveries. Science thrives on discovery and scientific journals compete to publish new breakthroughs."[34]

Peer review failures [edit]

> *Main article: Peer review failure*

Peer review failures occur when a peer-reviewed article contains obvious fundamental errors that undermine at least one of its main conclusions. Many journals have no procedure to deal with peer review failures beyond publishing letters to the editor.[35]

Peer review in scientific journals assumes that the article reviewed has been honestly written, and the process is not designed to detect fraud.[36]

The reviewers usually do not have full access to the data from which the paper has been written and some elements have to be taken on trust. It is not usually practical for the reviewer to reproduce the author's work. Publication of incorrect results does not in itself indicate a peer review failure.[*citation needed*]

Dynamic and open peer review [edit]

Main article: Open peer review

It has been suggested that traditional anonymous peer review lacks accountability, can lead to abuse by reviewers, and may be biased and inconsistent,[37] alongside other flaws.[38][39] In response to these criticisms, other systems of peer review with various degrees of "openness" have been suggested.

Starting in the 1990s, several scientific journals (including the high impact journal *Nature* in 2006) started experiments with hybrid peer review processes, often allowing open peer reviews in parallel to the traditional model. The initial evidence of the effect of open peer review upon the quality of reviews, the tone and the time spent on reviewing was mixed, although it does seem that under open peer review, more of those who are invited to review decline to do so.[40][41]

Throughout the 2000s first academic journals based solely on the concept of open peer review were launched (see e.g. *Philica*). An extension of peer review beyond the date of publication is Open Peer Commentary, whereby expert commentaries are solicited on published articles, and the authors are encouraged to respond.

Peer review of government policy [edit]

The technique of peer review is also used to improve government policy. In particular, the European Union uses it as a tool in the 'Open Method of Co-ordination' of policies in the fields of employment and social inclusion.

A program of peer reviews in active labour market policy[42] started in 1999, and was followed in 2004 by one in social inclusion.[43] Each program sponsors about eight peer review meetings in each year, in which a 'host country' lays a given policy or initiative open to examination by half a dozen other countries and relevant European-level NGOs. These usually meet over two days and include visits to local sites where the policy can be seen in operation. The meeting is preceded by the compilation of an expert report on which participating 'peer countries' submit comments. The results are published on the web.

Further information: U.S. Government peer review policies

History [edit]

The first recorded editorial prepublication peer review process was at The Royal Society in 1665 by the founding editor of Philosophical Transactions of the Royal Society, Henry Oldenburg.[44][45][46] In the 20th century peer-review became common for science funding allocations. This process appears to have developed independently from the editorial peer review.[47]

The first peer-reviewed publication may have been the *Medical Essays and Observations* published by the Royal Society of Edinburgh in 1731. The present-day peer review system evolved from this 18th century process.[48]

A professional peer review process is found in the *Ethics of the Physician* written by Ishaq bin Ali al-Rahwi (854–931) of al-Raha, Syria. His work, as well as later Arabic medical manuals, state that a visiting physician must always make duplicate notes of a patient's condition on every visit. When the patient was cured or had died, the notes of the physician were examined by a local medical council of other physicians, who would review the practicing physician's notes to decide whether his/her performance have met the required standards of medical care. If their reviews were negative, the practicing physician could face a lawsuit from a maltreated patient.[49][*verification needed*]

Peer review has been a touchstone of modern scientific method only since the middle of the 20th century, the only exception being medicine. Before then, its application was lax in other scientific

fields. For example, Albert Einstein's revolutionary "Annus Mirabilis" papers in the 1905 issue of *Annalen der Physik* were not peer-reviewed by anyone other than the journal's editor in chief, Max Planck (the father of quantum theory), and its co-editor, Wilhelm Wien. Although clearly peers (both won Nobel prizes in physics), a formal panel of reviewers was not sought, as is done for many scientific journals today. Established authors and editors were given more latitude in their journalistic discretion, back then. In a recent editorial in *Nature*, it was stated that "in journals in those days, the burden of proof was generally on the opponents rather than the proponents of new ideas."[50]

See also [edit]

- Academic conference
- Academic journal
- Abstract management
- Adversarial review
- Journal club
- JournalReview.org
- Objectivity (philosophy)
- Open Peer Commentary
- Physician peer review
- Publication bias
- Scholarly method
- Sham peer review
- Sokal affair
- Software peer review
- Sternberg peer review controversy
- Technical peer review

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Peer Review Process

On This Page:

Overview

NIH policy is intended to ensure that grant applications submitted to the NIH are evaluated on the basis of a process that is fair, equitable, timely, and free of bias. The NIH dual peer review system is mandated by statute in accordance with section 492 of the Public Health Service Act and federal regulations governing "Scientific Peer Review of Research Grant Applications and Research and Development Contract Projects" (42 CFR Part 52h).

The first level of review is carried out by a Scientific Review Group (SRG) composed primarily of non-federal scientists who have expertise in relevant scientific disciplines and current research areas. The second level of review is performed by Institute and Center (IC) National Advisory Councils or Boards. Councils are composed of both scientific and lay members chosen for their expertise, interest, or activity in matters related to health and disease. Only applications that are favorably recommended by both the SRG and the Advisory Council may be recommended for funding.

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First Level of Review

Initial peer review meetings are administered by either the Center for Scientific Review (CSR) or another NIH IC. The focus of review is specified in the Funding Opportunity Announcement. Peer review meetings are announced in the Federal Register. The meetings are closed to the public, although some meetings may have an open session; the Federal Register provides the details of each meeting.

A. Peer Review Roles and Meeting Overview

Scientific Review Officer:

Each SRG is led by a Scientific Review Officer [(SRO), formerly Scientific Review Administrator (SRA)]. The SRO is an extramural staff scientist and the Designated Federal Official responsible for ensuring that each application receives an objective and fair initial peer review, and that all applicable laws, regulations, and policies are followed.

SROs:

- Analyze the content of each application, and check for completeness.
- Document and manage conflicts of interest.
- Recruit qualified reviewers based on scientific and technical qualifications and other considerations, including:
  - Authority in their scientific field (42 CFR 52h.4)
  - Dedication to high quality, fair, and objective reviews
  - Ability to work collegially in a group setting

Related Resources

Guides, Tips, and Tutorials:
- NIH Peer Review Revealed - YouTube EXIT Disclaimer
- Enhancing Peer Review at NIH
- Information for New Grantees
- NIH Guide for Grants and Contracts (Funding Opportunities)
- Planning Your Application (Helpful Tips)
- Writing Your Application (Helpful Tips)

- Experience in research grant review
- Balanced representation

- Assign applications to reviewers for critique preparation and assignment of individual criterion scores.
- Attend and oversee administrative and regulatory aspects of peer review meetings.
- Prepare summary statements for all applications reviewed.

SRG Members

Chair:

- Serves as moderator of the discussion of scientific and technical merit of the applications under review.
- Is also a peer reviewer for the meeting.

Reviewers:

- Declare Conflicts of Interest with specific applications following NIH guidance
- Receive access to the grant applications approximately six weeks prior to the peer review meeting.
- Prepare a written critique (using Review Critique Fill-able Templates) for each application assigned per the SRO, based on review criteria and judgment of merit.
- Assign a numerical score to each review criterion
- Make recommendations concerning the scientific and technical merit of applications under review, in the form of final written comments and numerical scores.
- Make recommendations concerning protections for human subjects; inclusion of women, minorities, and children in clinical research; welfare of vertebrate animals; and other areas as applicable for the application (see guidance for reviewers on Human Subjects Protection and Inclusion, Human Embryonic Stem Cells, and Vertebrate Animals).
- Make recommendations concerning appropriateness of budget requests (see Budget Information for Reviewers).

Other NIH Staff

- Federal officials who have need-to-know or pertinent related responsibilities are permitted to attend closed review meetings.
- NIH IC or other federal staff members wishing to attend an SRG meeting must have advance approval from the responsible SRO. These individuals may provide programmatic or grants management input at the SRO's discretion.

Peer Review Meeting Procedures

- Applications are reviewed based on established review criteria (see below).
- Assigned reviewers summarize their prepared critiques for the group.
- An open discussion follows.
- Final scoring of overall impact/priority scores is conducted by private ballot.

B. Peer Review Criteria and Considerations

Enhanced review criteria were announced in NOT-OD-09-025 for the evaluation of applications for research grants and cooperative agreements received for potential FY2010 funding and thereafter. A Side-by-Side Comparison of Enhanced and Former Review Criteria is available for reference. Enhanced review criteria for other types of applications are available through the Review Criteria at a Glance document.

Enhanced Review Criteria for Research Grants and Cooperative Agreements

The mission of the NIH is to support science in pursuit of knowledge about the biology and behavior of living systems and to apply that knowledge to extend healthy life and reduce the burdens of illness and disability. As part of this mission, applications submitted to the NIH for grants or cooperative agreements to support biomedical and behavioral research are

evaluated for scientific and technical merit through the NIH peer review system.

Overall Impact. Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria, and additional review criteria (as applicable for the project proposed).

Scored Review Criteria. Reviewers will consider each of the review criteria below in the determination of scientific and technical merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance. Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Investigator(s). Are the PD/PIs, collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, or in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

Innovation. Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Approach. Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

Environment. Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Additional Review Criteria. As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit and in providing an overall impact/priority score, but will not give separate scores for these items.

Protections for Human Subjects
Inclusion of Women, Minorities, and Children
Vertebrate Animals
Biohazards
Resubmission
Renewal
Revision

Additional Review Considerations. As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items and should not consider them in providing an overall impact/priority score.

Applications from Foreign Organizations
Select Agent
Resource Sharing Plans
Budget and Period Support

C. Scoring

The scoring system described below was implemented for applications submitted for funding consideration for FY2010 and thereafter (NOT-OD-09-024)

Before the SRG meeting, each reviewer and discussant assigned to an application will give a separate score for each of five review criteria (i.e., Significance, Investigator(s), Innovation, Approach, and Environment for research grants and cooperative agreements; see above). For all applications, even those not discussed by the full committee, the individual scores of the assigned reviewers and discussant(s) for these criteria are reported to the applicant.

In addition, each reviewer and discussant assigned to an application gives a preliminary overall impact/priority score for that application. The preliminary scores are used to determine which applications will be discussed in full. For each application that is discussed at the meeting, a final impact/priority score is given by each eligible committee member (without conflicts of interest) including the assigned reviewers. Each member's score reflects his/her evaluation of the overall impact that the project is likely to have on the research field(s) involved, rather than being a calculation of the reviewer's scores for each criterion.

The scoring system utilizes a 9-point rating scale (1 = exceptional; 9 = poor). The final overall impact/priority score for each discussed application is determined by calculating the mean score from all the eligible members' impact/priority scores, and multiplying the average by 10; the final overall impact/priority score is reported on the summary statement. Thus, the final overall impact/priority scores range from 10 (high impact) through 90 (low impact). Numerical impact/priority scores are not reported for applications that are not discussed (ND), which may be reported as *.* on the face page of the summary statement and typically rank in the bottom half of the applications.

Applicants should contact the Program Officer for the application to seek additional feedback on the score and summary statement.

An application may be designated Not Recommended for Further Consideration (NRFC) by the Scientific Review Group if it lacks significant and substantial merit; presents serious ethical problems in the protection of human subjects from research risks; or presents serious ethical problems in the use of vertebrate animals, biohazards, and/or select agents. Applications designated as NRFC do not proceed to the second level of peer review (National Advisory Council/Board) because they cannot be funded.

The following guidance has been given to reviewers to determine individual review criterion and overall impact/priority scores:

Impact	Score	Descriptor	Additional Guidance on Strengths/Weaknesses
High	1	Exceptional	Exceptionally strong with essentially no weaknesses
	2	Outstanding	Extremely strong with negligible weaknesses
	3	Excellent	Very strong with only some minor weaknesses
Medium	4	Very Good	Strong but with numerous minor weaknesses
	5	Good	Strong but with at least one moderate weakness
	6	Satisfactory	Some strengths but also some moderate weaknesses
Low	7	Fair	Some strengths but with at least one major weakness
	8	Marginal	A few strengths and a few major weaknesses
	9	Poor	Very few strengths and numerous major weaknesses
Non-numeric score options: NR = Not Recommended for Further Consideration, DF = Deferred, AB = Abstention, CF = Conflict, NP = Not Present, ND = Not Discussed			
Minor Weakness: An easily addressable weakness that does not substantially lessen impact			

Moderate Weakness: A weakness that lessens impact
Major Weakness: A weakness that severely limits impact

D. Summary Statement

Applications that are not discussed at the meeting will be given the designation "ND" as an overall impact/priority score, but the applicant, as well as NIH staff, will see the scores from the assigned reviewers and discussants for each of the review criteria as additional feedback on their summary statement.

Understanding the Percentile

- A percentile is the approximate percentage of applications that received a better overall impact/priority score from the study section during the past year.
- All percentiles are reported as whole numbers
- Only a subset of all applications receive percentiles. Which types of applications are percentiled varies across different NIH Institutes and Centers.
- The summary statement will identify the base that was used to determine the percentile.

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Second Level of Review - Advisory Council or Board

Who Reviews the Application?

The Advisory Council/Board of the potential awarding IC performs the second level of review. Advisory Councils/Boards are composed of scientists from the extramural research community and public representatives (NIH Federal Advisory Committee Information). Members are chosen by the respective IC and are approved by the Department of Health and Human Services. For certain committees, members are appointed by the President of the United States.

Recommendation Process

- NIH program staff members examine applications, their overall impact/priority scores, percentile rankings and their summary statements and consider these against the IC's needs.
- Program staff provide a grant-funding plan to the Advisory Board/Council.
- The Advisory Board/Council also considers the IC's goals and needs and advises the IC director.
- The IC director makes final funding decisions based on staff and Advisory Council/Board advice.

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Post-Review

Not Funded – What Next?

The NIH receives thousands of applications for each application receipt round. Funding on the first attempt is difficult, but not impossible. If an application does not result in funding, NIH has resources to help applicants prepare a possible resubmission. Applications in response to a specific initiative with set aside money typically cannot be resubmitted, but the Program Officer should be consulted about next steps.

Fundable Score – What Next?

If an application results in an award, the applicant will be working closely with the IC program officer on scientific and programmatic matters and a grants management officer on budgetary or administrative issues

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More Details

For more details about Peer Review, visit Peer Review Policies & Practices.


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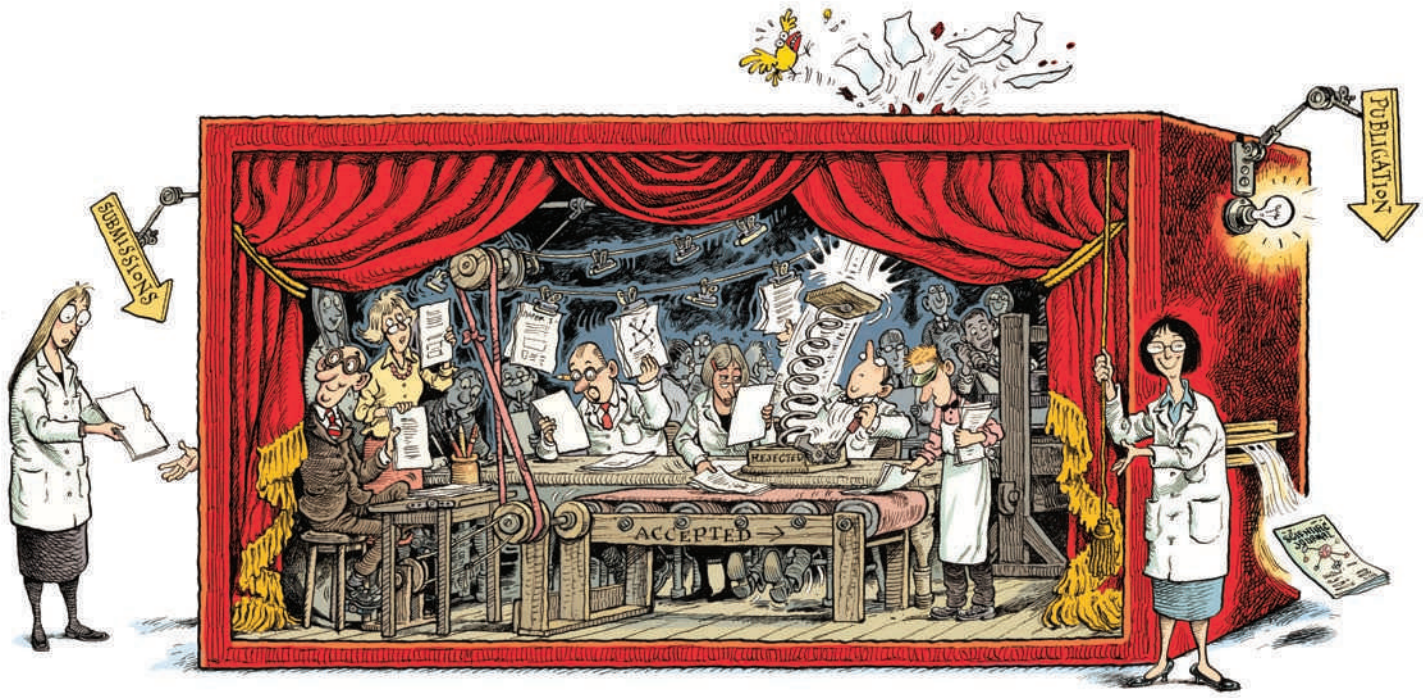


ILLUSTRATION BY DAVID PARKINS

Transparency showcases strength of peer review

Bernd Pulverer reflects on his experience at *The EMBO Journal* of publishing referees' reports, authors' responses and editors' comments alongside papers, as other EMBO publications adopt the same policy.

Two years ago at *The EMBO Journal* we added transparency to peer review. We invited authors to allow inclusion of 'peer-review process files' alongside their published papers. Almost all have agreed. Now, more than 400 primary papers published in the journal showcase details of the editorial process: referee comments from every round of revision, editorial decision letters, the authors' response, as well as a detailed timeline of submission, decisions, revisions and publication[1,2] (see go.nature.com/nbus3f for an example of an *EMBO J.* process file).

In our view, these augmented papers are testament to the fact that carefully administered peer review works — works well, in fact. We were initially concerned that some authors and referees might be discouraged from contributing to the journal and so, until now, have made the files relatively hard to find. But, given the positive response from the community, we are this month extending the policy to all four European Molecular Biology Organization (EMBO) scientific publications — *The EMBO Journal*, *EMBO Reports*, *Molecular Systems Biology* and *EMBO Molecular Medicine* — and making the process files much more visible online.

The perennial concerns voiced about peer review and decisions made by professional editors — as opposed to part-time academic editors — stimulated us to think about how we might improve the process at EMBO. As a first step, we did a detailed annual analysis of where manuscripts rejected at our journal were eventually published, a summary of which we now publish annually (see go.nature.com/4y7fwp). This supported our sense that editorial decisions are generally informed and fair. For example, only 1% of manuscripts rejected in 2008 ended up in ▶

journals with an impact factor two points or more above that of *The EMBO Journal*; and only 9% have a citation rate higher than the average paper in the journal.

Our second thought was that a huge amount of effort goes into peer review — effort that remains largely invisible. Many an editor and referee will attest to how much the process can improve a published paper — painful as it may be to go through. Referees can be the best writers of published analyses of single papers, such as *Science*'s Perspectives and *Nature*'s News & Views. So why hide all their incisive, constructive comments, which can remain pertinent even after revision and publication?

An obvious solution was to publish our anonymous referee reports. It would showcase the quality and thoughtfulness of the majority of reports. And it would add interesting points about suggested further experiments, alternative interpretations and, sometimes, limitations.

Another appeal of this path was that peer review is rarely formally taught, yet so much depends on it. We hoped that the peer-review process files might serve as a teaching tool. Finally, a clear potential benefit was to fortify the peer-review process. Referees might feel compelled to take extra care when writing their report, as the report would be published, albeit anonymously.

It was immediately apparent that, for completeness, we'd have to post all referee reports on a paper, followed by the author response. In the spirit of transparency and accountability, and with the hope of addressing grumblings about professional editors, we decided to add editorial decision letters. We'd only correct simple typos in the reports, but we'd allow removal of data that were provided solely to address a referee's point, as they might be required for future publications.

IMPACT ASSESSMENT

The policy kicked off in January 2009 (ref. 1). We invite authors to opt out of the system at any stage, and referees are made aware at invitation that their comments will be posted in case of acceptance. In September this year we decided to discourage 'confidential comments for the editor' by referees, which are commonplace at many biological sciences journals[2]. Legitimate confidential comments are allowed — for example, notes about biosecurity or conflicts of interest. But we want to move away from anything that gives rejected authors the sense that something went on behind the scenes that led to their rejection.

NATURE.COM
See Nature's blog on peer review
go.nature.com/nqlawg

At the time, *Biology Direct* and a number of BioMed Central journals already included published reports and author responses. Nevertheless, as with any change to a long-established system, there were significant risks. Would we discourage trusted referees? Would they fear that their identities might be revealed, and would they write less incisive or less critical reports as a result? Would authors resent the airing of — in the words of one referee — the 'dirty washing' leading up to acceptance? What if reports were rude or even defamatory? Would divergent referee reports lend ammunition to those that believe the system is failing? More pragmatically, would producing the files increase our editorial costs significantly, and would this additional step slow down the publication process in a field in which every day can count?

The experience has been overwhelmingly positive. The number of submissions to the journal remains steady and just 5.3% of authors have opted out, few of them citing philosophical objections to the policy[2]. The objectors cite a reluctance to add to the already excessive literature or a perception that an otherwise excellent piece of work can be marred by prominent comments on small mistakes or limitations.

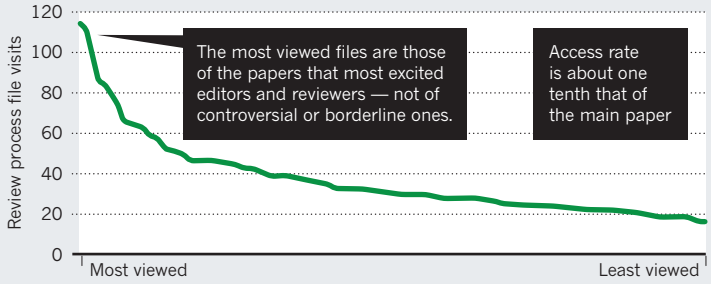
The rate of acceptance of invitations to review a paper has remained the same, and very few invited referees decline explicitly because of the policy. In one case, a referee who had failed to read to the end of his invitation letter in the first round did decline to re-review the revised manuscript, but agreed to post the first set of comments. Nor have we seen a significant change in the quality of referees' reports or authors' responses — for better or for worse. Several referees have acknowledged that they spend more time on phrasing their reports now and this is certainly true for my own two-finger-typed decision letters! And we estimate that each file takes around 1½ hours for our administrators and editors to produce.

Many of the process files include divergent referee opinions, but we feel that the reader is well aware that journals invite a referee panel with complementary expertise and thus different vantage points. It hasn't happened yet, but if we felt a referee's report was too aggressive, we'd go back to the reviewer to suggest a rethink, noting the possible publication of the comment.

So does anyone actually notice the process files? The numbers show that the access rate is about one-tenth that of the main paper and that almost all peer-review process files have been viewed. Access to the files correlates with access to the whole article. The most viewed files are those of the papers that most excited the editors and reviewers — not of controversial or borderline papers (see graph). We haven't been collecting data on how long readers spend looking at the files, but plan to. And now we've made the files much more visible and open access, we expect an uptick in access. Meanwhile, other journals, including the *European Journal of Cell Biology* have been taking note and are implementing similar enhancements.

PEER REVIEW PROCESS FILES ARE BEING NOTICED

Web access between April and July 2010 to the 100 most visited process files (referees' reports, editors' letters and authors' responses).



One crucial limitation of the policy is, of course, that we do not release reports on manuscripts that end up being rejected. It goes without saying that these are often the more interesting cases to consider. However, a workable way to redress this shortcoming has eluded us. A partial solution we're pursuing instead follows the example of the Neuroscience Peer Review Consortium. This cooperative of 37 journals has agreed to share referee reports if an author desires. 'Review recycling' is in our view an important way to address a key bottleneck in the publishing process.

WHERE NEXT?

To mix metaphors, we feel we have pried open the black box of peer review with this initiative — and shown that it is not Pandora's box. Now, like many others interested in optimizing the scientific publishing and grant-review processes, we are considering several other enhancements to traditional 'single-blinded' peer review. We remain convinced that a high level of quality assessment is essential to filter and validate the increasingly vast and diverse literature.

Many journals now allow post-publication commenting, often curated and usually signed. Despite the ubiquity of social media, commenting on scientific reports has not yet reached a level at which it could give peer review a run for its money. Inspired by the physical and computational sciences, where pre-publication commenting is commonplace, *Nature* ran an interesting trial a few

years ago in which authors were invited to open up their manuscripts to pre-publication scrutiny during a 'traditional' peer-review process. Around 70 authors participated and the editors carefully compared the input received in this and a peer-review-alone approach. In no instance did commenting add significant value[3,4] (see go.nature.com/n67mfk for the report).

Nevertheless, *Nature* opened all its published content for readers' online comments in March 2010. Comments, even on high-profile papers, remain sparse, however, even in journals such as *PLoS ONE* that specifically set out to supplement their assessment process with comments. Everyone is busy, and few may wish to risk outing themselves as critics without tangible benefit.

If peer review benefits from anonymity, why not also mask the author's identity ('double-blinded' review)? We remain interested in this possibility, but fail to see how to implement it without adding delays or requesting anonymized manuscripts for initial peer review (removal of author names does not suffice to anonymize a manuscript from one's peers). Conversely, why not add accountability by asking referees to sign their reports? The *British Medical Journal*, among others, has bravely pursued this path, and its editors claim that neither their referee pool nor their reports have changed[5]. In our view, the stakes often remain too high for this in the competitive world of biological research. Can a rookie investigator really be expected to write a critical report on a manuscript submitted by an eminent colleague who may well review their next grant? Can an author who has been asked to revise a paper significantly be relied on not to persuade the referee to back down?

"Online comments, even on high-profile papers, remain sparse"

Last month we started to encourage referees to comment on each other's reports, where they feel this would aid the editorial decision. Comments are only expected in cases in which a referee has taken a particularly extreme line or made a mistake, or if a referee wants to underline an essential point made by a colleague that they had missed. In line with some other journals, we have also implemented another change: we now explicitly prompt reviewers to declare the common practice of delegating peer review to others in the lab. We request that reports are vetted by the invited referee and that co-referees are named. We regard this as an essential component of good mentorship.

Most successful scientists spend a good fraction of their time reviewing papers. Yet, there is little tangible individual credit derived from the anonymous and voluntary contribution to this cornerstone of the research system. Thankfully, the remarkable culture of willingness to help colleagues and journals through peer review remains healthy, despite ever-increasing publication rates. Nevertheless, we are keenly pursing means to allow funding agencies and tenure committees to take this essential activity into account, and we welcome suggestions and collaborations on this and other possible enhancements. Peer review is the most remarkable manifestation of a collaborative spirit of science and needs to be nurtured and fortified where necessary. ■

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2. Pulverer, B. *EMBO J.* **29** (in the press).
3. Editorial *Nature* **444,** 971–972 (2006).
4 Editorial *Nature Cell Biol.* **9,** 1 (2007).
5. Smith, R. *Br. Med. J.* **318,** 4 (1999).

RESPONSIBLE CONDUCT OF BIOMEDICAL RESEARCH:

A Handbook for Biomedical Graduate Studies Students

Fourth Edition

BIOMEDICAL GRADUATE STUDIES PROGRAM
UNIVERSITY of PENNSYLVANIA

PREFACE TO THE FOURTH EDITION

Scientists agree that a trainee in biomedical research should be taught to maintain the highest standards of scientific integrity and ethical behavior in all phases of the conduct of research. Scientists and trainees should also be aware of the potential for subjectivity, unconscious bias and conflicts of interest that accompany the collection and treatment of data, the attribution of responsibility and credit, the mentoring of students and fellows, and the use of human and animal subjects for research. Scientific data collected and reported with the greatest care and ethical considerations may yet contain unrecognized errors due to the limitations of knowledge or technology. The requirement for high standards of scientific integrity and ethical behavior is important for a number of reasons. Scientists must be able to trust one another's work, since advances in science rely on the integrity of the research record. Furthermore, most research is carried out using public funds and thus the public should have confidence that this is money well-spent.

The goal of BGS's training in Responsible Conduct of Research (RCR) is to make graduate students aware of the rules, regulations and guidelines governing research and to minimize the potential problems associated with carrying out research. While these problems cannot be totally eliminated, they should be recognized, openly acknowledged and constructively addressed by discussions among scientists and with trainees. The incidence and consequences of misconduct can be sharply reduced by both good habits of research and by an increased understanding of what constitutes accepted responsible conduct. Education of this nature is the major goal of the RCR training program at the University of Pennsylvania.

The fourth edition of the handbook on RCR has been modified considerably, and is intended as a companion to the excellent publication, *ON BEING A SCIENTIST: third edition* (National Academy Press, Washington, DC 2009) and *Teaching the Responsible Conduct of Research Through a Case Study Approach (*a handbook prepared by the Association of American Medical Colleges, Korenman and Shipp, eds., 1994). These documents utilize a case study approach to initiate discussions of relevant issues in the conduct and training of biomedical research. The revised handbook includes additional material unique to the training of young investigators, provides practical information on the guidelines and procedures regarding alleged misconduct at the University of Pennsylvania, and includes examples of perspectives on the ethical conduct of research from the scientific community.

I would like to thank the faculty and staff of the University who assisted in editing this handbook and in developing the RCR training program. I am particularly grateful to Drs. Jane Glick and Glen Gaulton for compiling the previous three editions, to Dr. Hillary Nelson for providing material for this edition and for identifying the best available sources for RCR training and case studies and to Colleen Dunn and Judy Jackson in the BGS office for the many hours they spent executing the revised BGS RCR training and for proof-reading this document. I am also grateful to Dr. Stanley Korenman, UCLA Health System and the Association of American Medical Colleges for granting permission touse case studies and text from *Teaching the Responsible Conduct of Research through a Case Study Approach,* Korenman, S.G. and Shipp, A., eds. (AAMC, Washington, DC 1994), and to the U.S. Department of Health and Human Services, Office of Research Integrity, Nicholas Steneck, Ph.D., *ORI Introduction to the Responsible Conduct of Research (2007)* (http://ori.hhs.gov/documents/rcrintro.pdf).

Susan R. Ross, Ph.D.
University of Pennsylvania School of Medicine

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I. INTRODUCTION

The training program in Responsible Conduct of Research (RCR) has three major educational components: web-based training, program literature, and small group discussion workshops. Participation in all phases of the training program is mandatory for all graduate students in the Biomedical Graduate Studies programs.

The program is introduced through on-line RCR training available on the BGS website at http://www.med.upenn.edu/bgs/rcr.shtml. The training is designed to provide all participants with an introduction to RCR, particularly in biomedical research. The topics covered are:

A. Research Misconduct
B. Data Acquisition, Management, Sharing and Ownership
C. Mentoring
D. Collaboration
E. Conflicts of Interest
F. Publication Practices, Responsible Authorship and Peer Review
G. Human Subjects
H. Animal Welfare

All first-year graduate students must complete the introductory web-based training and pass the web-based quiz. In addition to the topic presentations, there are several RCR case studies on the web site. These are good introductions to the case study method that is the basis of RCR training for graduate students beyond the first year.

This document (RESPONSIBLE CONDUCT OF BIOMEDICAL RESEARCH: A Handbook for Biomedical Graduate Studies Students, Biomedical Graduates Studies, University of Pennsylvania, Philadelphia, PA, 2010) is the primary resource for the case study portion of the training program. It was originally written as a companion to ON BEING A SCIENTIST: A Guide to Responsible Conduct in Research, third edition (published by the National Academy Press, Washington, DC, 2009). That document is available on the web at http://www.nap.edu/catalog/12192.html. These documents utilize a case study approach to inform, stimulate discussion among and thereby educate program participants. The BGS Handbook includes a number of topics that are not included in ON BEING A SCIENTIST but that are judged to be important to the training of graduate students at the University of Pennsylvania. The BGS Handbook also includes a practical guide to acquaint students with the guidelines and procedures regarding alleged misconduct at the University of Pennsylvania and to define the appropriate sources for contact when questions arise. Copies of these booklets are available through links on the BGS web site. More detailed reference material is also available in the BGS office, 160 BRB II/III, 215-898-1030.

The final component of the training program for second, third and fourth year BGS students is topic-specific, on-line training, using the Collaborative Institutional Training Initiative (CITI), Responsible Conduct of Research Program, followed by small group discussions using a case-based study approach. Small group workshops of about 12 students are organized with two faculty preceptors each. The workshops meet for a minimum of one and one-half hours. During these workshops, students and faculty become engaged in a process of discovery together. In respect to research integrity, this includes not only learning facts, but recognizing potential ambiguities in the responsible conduct of research. The small group workshops also reveal the instructors' and students' own attitudes and prejudices, and recognition of conflicting ethical principles. This method also provides the opportunity to directly illustrate the avoidance

of misconduct through good laboratory practice. The participation of active investigators is essential in this exercise. Their involvement lends credibility to the process and may even influence the investigator's own practices.

Graduate students are expected to move through a progression of case studies that consider a specific set of topics. Second year students consider research misconduct, plagiarism, data management and lab notebooks. Third year students consider issues relating to mentoring and lab supervision, collaboration, animals and human subjects. Fourth year students discuss issues of publication practices, authorship, peer review and conflicts of interest. The cases given below are grouped accordingly, although many of the cases touch on more than one issue that may bridge topics considered in different years. Graduate students in years five and beyond have different choices for fulfilling their requirement, which may include attending University sanctioned bioethics seminars, courses or symposia sponsored by the Center for Bioethics (see http//www.bioethics.upenn.edu). Attendance at these events must be registered with the BGS office. Another option for upper level students is to co-facilitate a workshop for the second, third or fourth year students along with a faculty facilitator. This can be arranged through the BGS office.

II. A CASE STUDY APPROACH TO TRAINING OF RESPONSIBLE CONDUCT OF RESEARCH

(adapted from *Teaching the Responsible Conduct of Research Through A Case Study Approach (©1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission), Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health, and the Federal Policy on Research Misconduct*) (http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/Conduct%20Research%206-11-07.pdf)

A. Research Misconduct and Plagiarism Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records (both physical and electronic), progress reports, abstracts, theses, internal (group meetings, thesis committee meetings, etc.) and external (national/international conferences, seminars, job interviews) oral or poster presentations, internal reports, and journal articles. Fabrication is making up data or results and recording or reporting them. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit; this includes internet sources. For a detailed definition of plagiarism, see Appendix A of this document. Research misconduct does not include honest error or differences of opinion. A finding of research misconduct requires that there be a significant departure from accepted practices of the relevant research community, that the misconduct be committed intentionally, knowingly, or recklessly, and that the allegation be proven by a preponderance of evidence.

Case Studies on Research Misconduct and Plagiarism

Case #1 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Dr. Alice Charles, a mid-career scientist, was revising and updating a book chapter. This led her to review other articles on the same subject to help determine what new material to cover. During the course of her reading, she came upon a chapter in a major text by Dr. Chris Long, a departmental chair at a leading medical school, which contained long passages from her previous chapter without attribution.

Dr. Charles called Dr. Long and confronted him with her finding. At first, he vehemently denied having used any of Dr. Charles's text inappropriately. Dr. Charles then emailed Dr. Long copies of the offending passages. After some delay, Dr. Long finally responded, acknowledging that the language was indeed remarkably similar. Dr. Long noted that he had engaged younger members of his research group to write portions of the chapter because he was very busy at the time that the deadline was approaching. Furthermore, to defend himself, he pointed out that much of the original research on which her chapter was based was derived from the work of his laboratory. He admitted only to negligence in not adequately monitoring the activities of his subordinates.

Dr. Charles replied that the subordinates were not acknowledged in Dr. Long's chapter either, and that admission of plagiarism required more than an apology. She indicated her intention to report the matter to Dr. Long's Dean and the editor of the text.

Questions

1. Did Dr. Charles act appropriately? Would you have done anything differently? Considering the difference in status between herself and Dr. Long, was she taking a professional risk?
2. Did Dr. Long do anything wrong? What if he were copying his own previous writings?
3. How would you have handled this matter if you were Dr. Long and were confronted with Dr. Charles's revelations?
4. If you were Dr. Long's Dean, how would you handle Dr. Charles's letter, which contained copies of the plagiarized texts?
5. Upon hearing Dr. Charles's complaint, what would you do as editor of Dr. Long's textbook?

Case #2 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled “Teaching Research Ethics: A Workshop at Indiana University”.).

Charlie West completed his doctorate in biology two years ago and is in his last year as a postdoctoral fellow in Professor Wilson’s laboratory. The last few months have been both good and bad. West and his wife were thrilled by the birth of their first child six months ago, and research has been going well. There are just a few relatively straightforward controls to be run before he and Wilson can submit a manuscript they have been preparing. In addition, West had five job interviews and was then offered a position at Heartland State University, which he has accepted.

However, his success has also caused some problems. With all the preparation and traveling for interviews plus the new responsibilities of parenting, West hasn’t had the time or energy to do very much work in the lab lately. There’s another factor as well. West promised Wilson that

he'd take care of those controls as soon as he finished interviewing but he hasn't done them yet because he's been writing a grant application. During West's second visit to Heartland, the biology department chair made it clear that West is expected to bring in external funding for the research he plans to begin at HSU in a little over a year. The chair told West, "The sooner you get a grant, the better your chances for tenure."

For his post doc, West decided to switch fields in order to learn some new techniques, but for his job he plans to return to research very close to what he did for his Ph.D. In fact, his job seminar was all based on his grad research, not the work he has done as a post doc. West has an idea for a project that everyone he has consulted agrees has great potential. He is very excited about his planned research, and is highly confident that it will be successful both with the funding agency and in the lab. The only problem seems to be getting the grant written.

Unfortunately, since this is West's first grant application, writing it is proving to be far more time-consuming than he expected. He started a couple of months ago and has written the Approach section of the Research Strategy section. All the special forms, facilities statements, biographies, supporting letters, and the budget are now done, but that still leaves the Significance and Innovation sections of the text. It seems that every time he gets set to work on the grant proposal, something goes wrong. Last week he discovered that he had forgotten the animal use forms and had to rush about getting his protocol finalized and approved. A few days ago his baby daughter was up all night with an earache. Then, just this morning, Wilson was pressing him for experimental results. "Look, Charlie," he said, "I know you've been busy, but those experiments can't wait any longer. It's been eight or ten weeks since you finished interviewing and the paper still isn't ready to submit. If we don't get moving we're going to get scooped by Joe Atkins' lab. Neither of us can afford to lose an important publication like this, especially you at this stage of your career. I want to see you at the bench tomorrow. Besides, I'm supporting you on my grant to do research in my lab, not to try to pull in money for HSU."

The NIH grant application deadline for which West has been aiming, one that could give him funding just after he arrives at HSU, is now only three days away, and it's already 10 pm. As he goes through his files, frantically pulling out relevant articles while feeling fairly sure that there is no way he can get the writing done in time, he comes across a grant proposal on a similar topic that he had helped a professor review while he was a graduate student. The professor had also pointed out that it was a model proposal — scientifically sound and extremely well-written. As he looks at the photocopy he kept, West realizes that the Significance and Innovation sections of this older grant would fill in 90% of the information he needs. He could easily write the other 10% in three days. Reasoning that grant proposals are funded mostly on the quality of the proposed work, West decides to copy and paste theSignificance and Innovation sections from the old grant, add his own Research Strategy section and update the Reference section with papers that have been published in the last two years, and be done with it. This way everyone should be happy.

Questions

1. Should West use the material this way? Why or why not?
2. Should West have kept a copy of the proposal?

Case #3 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Professor Diane Archer is a tenured member of a biology department at a major Midwestern university. She has been in the department for 15 years, and during that time she has supervised the work of 20 Ph.D. students. As part of the mentoring process, she has worked closely with her students, teaching them the ropes of writing grant proposals and on occasion inviting students to assist her in reviewing NIH grant applications.

Professor Archer is currently in her last year on an NIH study section. As she is reviewing a group of proposals, she comes upon one written by Charlie West, a former graduate student of one of her close departmental colleagues. Archer knows and remembers Charlie West because she had solicited his help two years earlier in reviewing a proposal closely related to West's own area of research. As she now reads West's proposal, Archer is impressed with the scientific soundness and fine writing style in the Significance and Innovation sections. She notes, however, the extremely terse and awkward phrasing in the Approach section. Perplexed by this shift in style, Archer retrieves from her files the grant proposal West had reviewed with her two years earlier. She is dismayed to see that West has used verbatim virtually the entire Significance and Innovation sections of the earlier proposal for his own current proposal.

Archer is torn. If she reports her discovery of West's plagiarism to the NIH, she knows she will have thrown this young scientist's otherwise promising scientific career into jeopardy. If, however, she says nothing, she will be shirking her responsibility to the NIH, as well as risking her own professional reputation, should the plagiarism be detected later. She decides to contact West directly, and confront him with her finding. She plans to advise West that what he has done constitutes plagiarism and suggest to him that he withdraw the proposal.

If West agrees, and withdraws the grant application, Archer feels she need take this incident no further.

Questions

1. Should Archer proceed with her plan to contact West? Why or why not? Is there anyone else she needs to contact?
2. Should Archer have solicited West's assistance in reviewing the grant?
3. Should Archer have kept grants that she had reviewed in her files?

Case #4 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Alan Yeager has completed a series of experiments characterizing the receptor for a new class of hormones. During the course of his work, he studied binding characteristics and hormonal responses in tissue culture and in vitro, utilizing gels to characterize the molecular weights of receptor variants. This was exciting work for a second-year graduate student doing his first project. One day, Alan's laboratory chief asked him to prepare an abstract for an upcoming meeting and a paper for publication, both to be based on the work Alan had been doing. The abstract was due in one week.

As Alan examined his accumulated data, he noted that a number of cell culture plates failed to respond to the hormonal stimulus and that there was considerable variability in the dose-response relationship. Furthermore, on reexamination, he noted that a number of his gels were not very aesthetic in appearance, yet he was sure that they demonstrated the molecular weight, agonist binding, and subunit characteristics of the receptor.

Alan mentioned his distress to Pam Alden, a fifth-year graduate student, who said, "Why don't you clean up your data? You'll never get the paper published unless you do. We always clean up the data around here." She then suggested that the four culture points failing to show a response be dropped because the cells were probably dead. She also pointed out that he might eliminate the top data point at the 45 minute interval as an outlier. She examined the gels and suggested using Adobe Photoshop™ to improve the quality of the pictures, including the duplication of one of the nicer gel lanes to replace another that turned out poorly, but showed essentially the same result. "That will greatly improve your chances of publication," she said. Alan replied, "Maybe I should repeat a few of the experiments or try to improve the culture conditions?" "No," said Pam, "If you're convinced of your results, why go through the time, expense, and uncertainty of more repetitions? You'll never complete an experiment in time for the abstract, anyhow." Somewhat dismayed, Alan thanked her and turned back to his work.

Questions

1. What do you think about Pam's comments on publication practices and her suggestions for "cleaning up" the data?
2. How should Alan go about determining which points to include and which to exclude?
3. What other course(s) of action would you recommend to Alan?
4. Pam's perception about improving the chances of publication by "cleaning up" the data is not uncommon. How might journal editors and reviewers work toward correcting this perception?

Case #5 (©ASM Press. This case is from Francis L. Macrina (2000): Scientific Integrity, 2nd edition, published by ASM Press. Appropriate permission being processed.)

Jim, a new assistant professor, is getting ready to submit his first paper since joining the faculty. He reviews one of the figures for this paper which is a photo of an ethidium bromide-stained agarose gel. The gel contains the products of polymerase chain reaction (PCR)-amplified whole cell DNA. The photo displays the predicted 3 kb DNA fragment. Jim comments that a second minor signal was also evident on the original gel. Based on its size, Jim believes that this second fragment represents a very exciting discovery, but it needs considerable additional work. This second fragment cannot be seen in the photograph because Jim discloses that he has deliberately cropped the photo to obscure the second fragment. He says he did this because he is worried that competing groups in larger, more established labs will interpret the potential of the second fragment and they will "scoop" him. He has prepared a figure legend that says: "a second minor signal of unexplained origin was present in this experiment but is not shown in the figure". But, the figure legend does not include the size of the unexplained fragment. Thus, he argues he'll be telling the truth while, at the same time, he'll be protecting himself from his competition.

Questions

1. Are Jim's actions appropriate?

2. Is he simply playing fairly in the hotly competitive arena of biomedical research, falling victim to self-deception or perpetrating scientific fraud?

B. Data Acquisition, Management, Sharing and Ownership Research data, including detailed experimental protocols, all primary data, and procedures of reduction and analysis are the essential components of scientific progress. Scientific integrity is inseparable from meticulous attention to the acquisition and maintenance of these research data.

The results of research should be carefully recorded in a form that will allow continuous access for analysis and review. Attention should be given to annotating and indexing notebooks and documenting computerized information to facilitate detailed review of data. All data, even from observations and experiments not directly leading to publication, should be treated comparably. All research data should be available to scientific collaborators and supervisors for immediate review, consistent with requirements of confidentiality. Investigators should be aware that research data are legal documents for purposes such as establishing patent rights or the veracity of published results when the data are challenged. The data are subject to subpoena by congressional committees and the courts.

Research data, including the primary experimental results, should be retained for a sufficient period to allow analysis and repetition by others of published material resulting from those data. In general, five to seven years is specified as the minimum period of retention but this may vary under different circumstances.

In most cases, such as with federally-funded research, the university owns the data, not the faculty, graduate students, postdoctoral fellows or staff who perform the research (see Appendix B). Notebooks, other research data, and supporting materials, such as unique reagents, belong to the university, and are entrusted to the laboratory in which they were developed. Departing investigators may take copies of notebooks or other data for further work if approved by the responsible principal investigator. For industry-sponsored research, data may belong to the sponsor. This is usually negotiated with by the investigator and the university with the industry sponsor prior to initiating the research.

Data management, including the decision to publish, is the responsibility of the principal investigator. After publication, the research data and any unique reagents that form the basis of that communication should promptly and completely be made available to all responsible scientists seeking further information. Exceptions may be necessary to maintain confidentiality of clinical data or if unique materials were obtained under agreements that preclude their dissemination.

Sharing of reagents/resources is an important part of the scientific enterprise and is required by federal funding agencies and most journals. Reagents/resource sharing allows other investigators to both repeat and extend studies and thereby advance research. This includes not only reagents/resources such as plasmids and novel chemical reagents, but model organisms such as transgenic mice. Similarly, genome-wide association study data funded by the federal government are required to be made publically available. For more information on these policies, see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html, NIH Guide NOT-OD-04-042 and http://grants.nih.gov/grants/gwas/.

Authors should not lose sight of the principle that a major purpose of publication is to allow repetition or extension of the research findings. The information given, its accuracy, and the

extent of detailed description should be sufficient to allow others to repeat the experiments successfully. "Any responsible scientist seeking further information is to be shown the research data promptly and completely, once the findings have been published."[1] In this sense, research data lose their privacy once the findings have been made public; NIH data are expected to be retained and available for review for a minimum of five to seven years after publication. It is a shock to learn that some scientists who are accused of falsifying data claim without much apology or explanation to have lost or deliberately discarded the notebooks or primary data. In our academic experience, ordinary scientists are exceedingly reluctant to discard notebooks, even to the point of compulsion. The obligation to produce original data upon challenge is not one that can be shrugged off by any serious scientist.

The current NIH Public Access Policy (http://publicaccess.nih.gov/policy.htm) also requires that "*all investigators funded by the NIH submit or have submitted for them to the National Library of Medicine's PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication: Provided, that the NIH shall implement the public access policy in a manner consistent with copyright law."*

For more detailed information on ownership of research and authorship, see Appendix B.

Case Studies on Data Management and Lab Notebooks

Case #6 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Jessica Banks, a postdoctoral fellow in Professor Brian Hayward's lab, is about to leave for her new job. When starting research in Hayward's lab, Banks divided her time among three projects. Then in her second year, after consultation with Hayward, she decided to continue and expand upon one of the three lines of investigation as her main project. This was also the project most closely related to Hayward's grant at the time. Later, Banks's early results were included in Hayward's grant renewal. The other two promising lines of research were left incomplete.

Banks's new job is a tenure-track position in a mid-sized Western liberal arts college. Shortly before leaving for her job, she comes into the lab to pick up her notebooks. Although her new faculty position will place a heavy emphasis on teaching, she is looking forward to continuing to do some research as well. In particular, she is eager to pick up where she left off with the two uncompleted projects she worked on before.

Professor Hayward meets Banks on her way into the lab, and their genial conversation abruptly changes when she mentions she has come to take her notebooks. Hayward exclaims, "You can't take those notebooks away — they belong to the lab!" Banks is confused. "But I did the work, and I wanted to follow up on it. I can't do that without the notebooks."

Professor Hayward is adamant. "I'm sorry, but you should understand this. This lab is a joint enterprise, and all the work you did was funded by money I brought in via grants. The notebooks don't belong to you, nor to me; they belong to the lab, and the work will be continued in this lab. I've already talked to one of the new students about working on those projects this fall." Banks, seeing her plans fall apart around her, protests, but Hayward is implacable. After a

few minutes, she stalks away, without the notebooks.

Later that afternoon, Banks gets together with her labmate Paul Larson, and during their conversation, she tells him about her run-in with Hayward. “Look,” says Larson. “Hayward has no right to deny you access to the information in the notebooks. Even if the books should remain in the lab, you did the work that generated all the data.” “I know!” says Banks. “But Hayward wouldn’t listen to that argument when I made it.” “Here’s my suggestion,” says Larson after some reflection. “Just stop by the lab and photocopy the books some time during the weekend. I happen to know Hayward will be out of town, so he’ll never know. That’s the fair thing to do: He gets to keep the notebooks in his lab, and you get a copy of the data you collected.”

Banks seems uncertain, but says she’ll think about Larson’s suggestion and decide before the weekend.

Questions

1. Should Banks photocopy the notebooks? Why or why not?
2. Can you think of another approach Jessica might take to get copies of the notebook?
3. How might this conflict have been avoided in the first place?

C. Mentoring and Respectful Workplace (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* *), Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health and The University of Pennsylvania Affirmative Action and Equal Opportunity Handbook)***:** Research training is a complex process, the central aspect of which is an extended period of research carried out under the supervision of an experienced scientific mentor. This supervised research experience represents not merely performance of tasks assigned by the supervisor, but rather a process wherein the trainee takes on an increasingly independent role in the choice of research projects, development of hypotheses and the performance of the work. Indeed, if training is to prepare a young scientist for a successful career as a research investigator, it must be geared toward providing the trainee with the aforementioned skills and experience. It is particularly critical that the mentor recognize that the trainee is not simply an additional laboratory worker.

Each trainee should have at least one designated primary scientific mentor, although particularly in newer, inter-disciplinary fields, it is becoming more common for trainees to have two mentors, each with expertise in different disciplines. It is the responsibility of mentors to provide a training environment in which the trainee has the opportunity to acquire both the conceptual and technical skills of the field. In this setting, the trainee should undertake a significant piece of research, chosen usually as the result of discussions between the mentor(s) and the trainee, which has the potential to yield new knowledge of importance in that field. The mentor has the responsibility to monitor the trainee's progress closely and to interact personally with the trainee on a regular basis in such a way as to make the training experience a meaningful one. Styles of research differ, both among fields and among investigators in a given field, so that no specific rules should be made about the number of trainees that is appropriate for a single mentor to supervise. Nonetheless, mentors should limit the number of

Students should be aware that copyright infringement extends to theses. If one includes figures or text from published manuscripts without alteration in one's thesis, permission must be obtained from the publisher. The ability to do on-line searches for particular text makes it exceptionally easy to identify plagiarism and self-plagiarism, as well as copyright infringement.

B. Ownership of Research

Taken from: Office of Research Integrity, Nicholas Steneck, Ph.D., *ORI Introduction to the Responsible Conduct of Research (2007)* (http://ori.hhs.gov/documents/rcrintro.pdf
Research produces data. As a product, common sense might suggest that the person who conducts the research should own the product—the data. In fact, conditions imposed by funders, research institutions, and data sources may dictate otherwise.

Funders. Funders provide support for research for different reasons. Government is interested in improving the general health and welfare of society. Private companies are interested in profits, along with benefits to society. Philanthropic organizations are interested in advancing particular causes. These different interests translate into different ownership claims. Typically:

- Government gives research institutions the right to use data collected with public funds as an incentive to put research to use for the public good (see the discussion of the Bayh-Dole Act, Chapter 5).

- Private companies seek to retain the right to the commercial use of data.

- Philanthropic organizations retain or give away ownership rights depending on their interests.

Since the claims of funders can and do vary considerably, researchers must be aware of their obligations to them before they begin collecting data. With government funding, it is important to distinguish between grants and contracts. Under grants, researchers must carry out the research as planned and submit reports, but control of the data remains with the institution that received the funds (see below). Contracts require the researcher to deliver a product or service, which is then usually owned and controlled by the government. If your research is supported with government funds, make sure you know whether you are working under a grant or a contract. The difference is significant and could determine who has the right to publish and use your results.

At Penn, faculty, graduate students, postdoctoral fellows or staff performing research in a university do not own the data collected. Employees work for hire for the university, which, in most cases, owns the rights to the data. Students and postdoctoral fellows sign a participation agreement that governs Research Property (http://www.med.upenn.edu/postdoc/documents/participation.agreement.pdf). Data and data books collected by undergraduates, post-baccalaureate students, graduate students, and postdoctoral fellows on a research project belong to the grantee institution. Students may not take their data when they leave without making appropriate arrangements. Retaining copies of data is allowed with permission and is usually good practice. When faculty members leave an institution, they have to negotiate with the university to keep their grants and data.

Copyright

From Wikipedia, the free encyclopedia

"Copyrighting" redirects here. For the use of words to promote or advertise something, see Copywriting.

"Copyrights" redirects here. For Wikipedia policy about copyright issues, see Wikipedia:Copyrights.

Copyright is a set of exclusive rights granted by the law of a jurisdiction to the author or creator of an original work, including the right to copy, distribute and adapt the work. Exceptions and limitations to these rights strive to balance the public interest in the wide distribution of the material produced and to encourage creativity. Exceptions include fair dealing and fair use, and such use does not require the permission of the copyright owner. All other uses require permission and copyright owners can license or permanently transfer or assign their exclusive rights to others. Copyright does not protect ideas, only their expression or fixation. In most jurisdictions, copyright arises upon fixation and does not need to be registered. Copyright protection applies for a specific period of time, after which the work is said to enter the public domain.

Intellectual property law

Primary rights

Copyright • Authors' rights • Related rights • Moral rights • Industrial design right • **Patent** • Utility model • **Trademark** • Geographical indication • **Trade secret**

Sui generis rights

Database right • Mask work • Plant breeders' rights • Supplementary protection certificate • Indigenous intellectual property

Related topics

Criticism • Orphan works • Public domain • more

The first copyright statute was the British Statute of Anne of 1709, the full title of which was: "An Act for the Encouragement of Learning, by vesting the Copies of Printed Books in the Authors or purchasers of such Copies, during the Times therein mentioned". Initially copyright only applied to published books, but over time copyright was extended to other uses, such as translations and derivative works. Copyright now covers a wide range of works, including maps, dramatic works, paintings, photographs, sound recordings, motion pictures and computer programs. Today, copyright laws have been standardized to some extent through international and regional agreements such as the Berne Convention and the European copyright directives. Although there are consistencies among nations' copyright laws, each jurisdiction has separate and distinct laws and regulations covering copyright. National copyright laws on licensing, transfer and assignment of copyright still vary greatly between countries and copyrighted works are licensed on a territorial basis. Some jurisdictions also recognize moral rights of creators, such as the right to be credited for the work.

Contents [hide]

Justification [edit]

Main article: Philosophy of copyright

The British Statute of Anne was the first act to directly protect the rights of authors.[1] Under US copyright law, the justification appears in Article I, Section 8 Clause 8 of the Constitution, known as the Copyright Clause. It empowers the United States Congress "To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."[2]

According to the World Intellectual Property Organisation the purpose of copyright is twofold:

> "To encourage a dynamic culture, while returning value to creators so that they can lead a dignified economic existence, and to provide widespread, affordable access to content for the [3]

public."

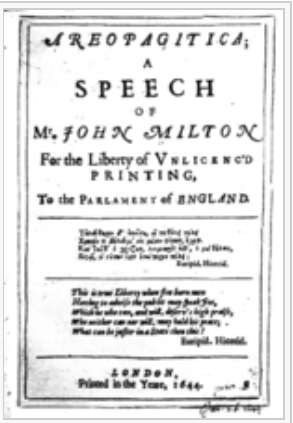
History [edit]

Main article: History of copyright law

Early European printers' monopoly [edit]

Pope Alexander VI issued a bull in 1501 against the unlicensed printing of books and in 1559 the Index Expurgatorius, or *List of Prohibited Books*, was issued for the first time.[4]

The origin of copyright law in most European countries lies in efforts by the church and governments to regulate and control printing,[5] which was widely established in the 15th and 16th centuries.[5] Before the invention of the printing press a writing, once created, could only be physically multiplied by the highly laborious and error-prone process of manual copying by scribes.[4] Printing allowed for multiple exact copies of a work, leading to a more rapid and widespread circulation of ideas and information (see print culture).[5]



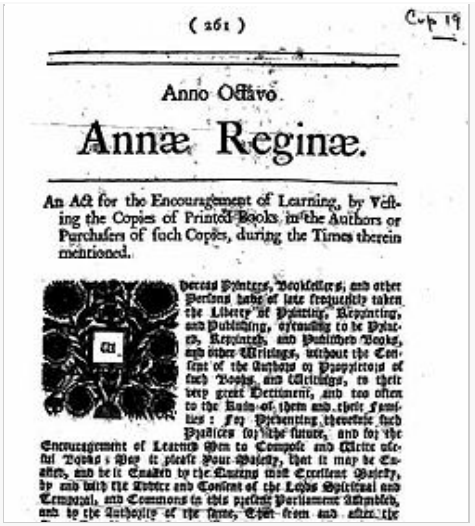
John Milton's 1644 edition of *Areopagitica*, long title *Areopagitica: A speech of Mr. John Milton for the liberty of unlicensed printing to the Parliament of England*, in it he argued forcefully against the Licensing Order of 1643.

While governments and church encouraged printing in many ways, which allowed the dissemination of Bibles and government information, works of dissent and criticism could also circulate rapidly. As a consequence, governments established controls over printers across Europe, requiring them to have official licences to trade and produce books. The licenses typically gave printers the exclusive right to print particular works for a fixed period of years, and enabled the printer to prevent others from printing or importing the same work during that period.[5] The notion that the expression of dissent should be tolerated, not censured or punished by law, developed alongside the rise of printing and the press. The Areopagitica, published in 1644 under the full title *Areopagitica: A speech of Mr. John Milton for the liberty of unlicensed printing to the Parliament of England*, was John Milton's response to the British parliament re-introducing government licensing of printers, hence publishers. In doing so, Milton articulated the main strands of future discussions about freedom of expression.[6] As the "menace" of printing spread, governments established centralised control mechanism[7] and in 1557 the British Crown thought to stem the flow of seditious and heretical books by chartering the Stationers' Company. The right to print was limited to the members of that guild, and thirty years later the Star Chamber was chartered to curtail the "greate enormities and abuses" of "dyvers contentyous and disorderlye persons professinge the arte or mystere of pryntinge or selling of books." The right to print was restricted to two universities and to the 21 existing printers in the city of London, which had 53 printing presses. The French crown also repressed printing, and printer Etienne Dolet was burned at the stake in 1546. As the British took control of type founding in 1637, printers fled to the Netherlands. Confrontation with authority made printers radical and rebellious, with 800 authors, printers and book dealers being incarcerated in the Bastille before it was stormed in 1789.[7]

Early British copyright law [edit]

Main article: Statute of Anne

In England the printers, known as stationers, formed a collective organisation, known as the Stationers' Company. In the 16th century the Stationers' Company was given the power to require all lawfully printed books to be entered into its register. Only members of the Stationers' Company could enter books into the register. This meant that the Stationers' Company achieved a dominant position over publishing in 17th century England (no equivalent arrangement formed in Scotland and Ireland). The monopoly came to an end in 1694, when the English Parliament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Anno Octavo

Annæ Reginæ.

An Act for the Encouragement of Learning, by vesting the Copies of Printed Books in the Authors or Purchasers of such Copies, during the Times therein mentioned.

The Statute of Anne came into force in 1710

did not renew the Stationers Company's power.[5] The newly established Parliament of Great Britain passed the first copyright statute, the Statute of Anne, full "An Act for the Encouragement of Learning, by vesting the Copies of Printed Books in the Authors or purchasers of such Copies, during the Times therein mentioned".[5]

The coming into force of the Statute of Anne in April 1710 marked a historic moment in the development of copyright law. As the world's first copyright statute it granted publishers of a book legal protection of 14 years with the commencement of the statute. It also granted 21 years of protection for any book already in print.[8] Unlike the monopoly granted to the Stationers' Company previously, the Statute of Anne was concerned with the reading public, the continued production of useful literature, and the advancement and spread of education. To encourage "learned men to compose and write useful books" the statute guaranteed the finite right to print and reprint those works. It established a pragmatic bargain involving authors, the booksellers and the public.[9] The Statute of Anne ended the old system whereby only literature that met the censorship standards administers by the booksellers could appear in print. The statute furthermore created a public domain for literature, as previously all literature belonged to the booksellers forever.[10]

Common law copyright [edit]

When the statutory copyright term provided for by the Statute of Anne began to expire in 1731 London booksellers thought to defend their dominant position by seeking injunctions from the Court of Chancery for works by authors that fell outside the statute's protection. At the same time the London booksellers lobbied parliament to extend the copyright term provided by the Statute of Anne. Eventually, in a case known as Midwinter v. Hamilton (1743–1748), the London booksellers turned to common law and starting a 30 year period known as the *battle of the booksellers*. The London booksellers argued that the Statute of Anne only supplemented and supported a pre-existing common law copyright. The dispute was argued out in a number of notable cases, including Millar v Kincaid (1749–1751), Tonson v Collins (1761–1762),[11] and Donaldson v Beckett (1774). Donaldson v Beckett eventually established that copyright was a "creature of statute", and that the rights and responsibilities in copyright were determined by legislation.[12] The Lords clearly voted against perpetual copyright[13] and by confirming that the copyright term, that is the length of time of work is in copyright, did expire according to statute the Lords also confirmed that a large number of works and books first published in Britain were in the public domain, either because the copyright term granted by statute had expired, or because they were first published before the Statute of Anne was enacted in 1709. This opened the market for cheap reprints of works from Shakespeare, John Milton and Geoffrey Chaucer, works now considered classics. The expansion of the public domain in books broke the dominance of the London booksellers and allowed for competition, with the number of London booksellers and publishers rising threefold from 111 to 308 between 1772 and 1802.[14]

Early French copyright law [edit]

Main article: French copyright law

In pre-revolutionary France all books needed to be approved by official censors and authors and publishers had to obtain a royal privilege before a book could be published. Royal privileges were exclusive and usually granted for six years, with the possibility of renewal. Over time it was established that the owner of a royal privilege has the sole right to obtain a renewal indefinitely. In 1761 the Royal Council awarded a royal privilege to the heirs of an author rather than the author's publisher, sparking a national debate on the nature of literary

property similar to that taking place in Britain during the battle of the booksellers.[15]

In 1777 a series of royal decrees reformed the royal privileges. The duration of privileges were set at a minimum duration of 10 years or the life of the author, which ever was longer. If the author obtained a privilege and did not transfer or sell it on, he could publish and sell copies of the book himself, and pass the privilege on to his heirs, who enjoyed an exclusive right into perpetuity. If the privilege was sold to a publisher, the exclusive right would only last the specified duration. The royal degrees prohibited the renewal of privileges and once the privilege had expired anyone could obtain a "permission simple" to print or sell copies of the work. Hence the public domain in books whose privilege had expired was expressly recognised.[15]

After the French Revolution a dispute over Comédie-Française being granted the exclusive right to the public performance of all dramatic works erupted and in 1791 the National Assembly abolished the privilege. Anyone was allowed to establish a public theatre and the National Assembly declared that the works of any author who had died more than five years ago were public property. In the same degree the National Assembly granted authors the exclusive right to authorise the public performance of their works during their lifetime, and extended that right to the authors' heirs and assignees for five years after the author's death. The National Assembly took the view that a published work was by its nature a public property, and that an author's rights are recognised as an exception to this principle, to compensate an author for his work.[15]

In 1793 a new law was passed giving authors, composers, and artists the exclusive right to sell and distribute their works, and the right was extended to their heirs and assigns for 10 years after the author's death. The National Assembly placed this law firmly on a natural right footing, calling the law the "Declaration of the Rights of Genius" and so evoking the famous Declaration of the Rights of Man and of the Citizen. However, author's rights were subject to the condition of making depositing copies of the work with the Bibliothèque Nationale and 19th Century commentators characterised the 1793 law as utilitarian and "a charitable grant from society".[15]

Early US copyright law [edit]

Main article: US copyright law

The Copyright Act of 1790 in the Columbian Centinel

The Statute of Anne did not apply to the American colonies. The colonies' economy was largely agrarian, hence copyright law was not a priority, resulting in only three private copyright acts being passed in America prior to 1783. Two of the acts were limited to seven years, the other was limited to a term of five years. In 1783 several authors' petitions persuaded the Continental Congress "that nothing is more properly a man's own than the fruit of his study, and that the protection and security of literary property would greatly tends to encourage genius and to promote useful discoveries." But under the Articles of Confederation, the Continental Congress had no authority to issue copyright, instead it passed a resolution encouraging the States to "secure to the authors or publishers of any new book not hitherto printed... the copy right of such books for a certain time not less than fourteen years from the first publication; and to secure to the said authors, if they shall survive the term first mentioned,... the copy right of such books for another term of time no less than fourteen years.[16] Three states had already enacted copyright statutes in 1783 prior to the Continental Congress resolution, and in the subsequent three years all of the remaining states except Delaware passed a copyright statute. Seven of the States followed the Statute of Anne and the Continental Congress' resolution by providing two fourteen year terms. The five remaining States granted copyright for single terms of fourteen, twenty and twenty one years, with no right of renewal.[17]

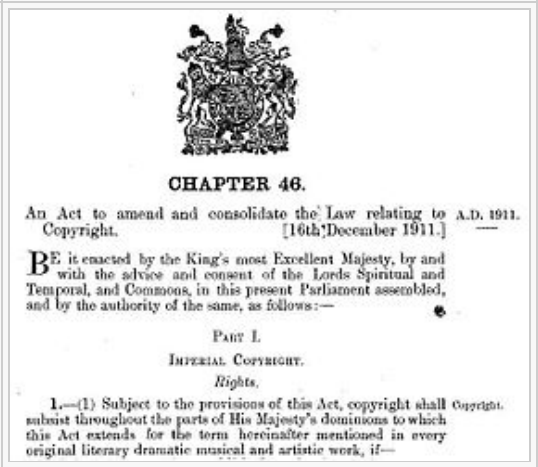
At the Constitutional Convention 1787 both James Madison of Virginia and Charles Pinckney of South Carolina submitted proposals that would allow Congress the power to grant copyright for a limited time. These proposals are the origin of the Copyright Clause in the United States Constitution, which allows the granting of copyright

and patents for a limited time to serve a utilitarian function, namely "to promote the progress of science and useful arts". The first federal copyright act, the Copyright Act of 1790 granted copyright for a term of "fourteen years from the time of recording the title thereof", with a right of renewal for another fourteen years if the author survived to the end of the first term. The act covered not only books, but also maps and charts. With exception of the provision on maps and charts the Copyright Act of 1790 is copied almost verbatim from the Statute of Anne.[17]

At the time works only received protection under federal statutory copyright if the statutory formalities, such as a proper copyright notice, were satisfied. If this was not the case the work immediately entered into the public domain. In 1834 the Supreme Court ruled in Wheaton v. Peters, a case similar to the British Donaldson v Beckett of 1774, that although the author of an unpublished work had a common law right to control the first publication of that work, the author did not have a common law right to control reproduction following the first publication of the work.[17]

Latin America [edit]

Latin American countries established national copyright laws following independence from the Spanish and Portuguese colonial powers. Latin American countries were among the first countries outside Europe to establish copyright law, with Brazil being the fourth country in the world to establish national copyright laws in 1804, after the UK, France and the United States. The foundation of Brazilian copyright law was the French Civil Code. Copyright law was initially established in Mexico following a Spanish court order in 1820 and in 1832 Mexico passed its first copyright statute. Copyright statutes had been established in eight Latin American countries by the 1850s.[18]



CHAPTER 46.

An Act to amend and consolidate the Law relating to Copyright. [16th December 1911.] A.D. 1911.

BE it enacted by the King's most Excellent Majesty, by and with the advice and consent of the Lords Spiritual and Temporal, and Commons, in this present Parliament assembled, and by the authority of the same, as follows:—

PART I.

IMPERIAL COPYRIGHT.

Rights.

1.—(1) Subject to the provisions of this Act, copyright shall subsist throughout the parts of His Majesty's dominions to which this Act extends for the term hereinafter mentioned in every original literary dramatic musical and artistic work, if— Copyright.

Cover page of the British Copyright Act 1911, also known as the Imperial Copyright Act of 1911. "Part I Imperial Copyright. Rights. 1.(1) Subject to the provisions of this Act, copyright shall subsist throughout the parts of His Majesty's dominions to which this Act extends for the term hereinafter mentioned in every original literary dramatic music and artists work, if..."

Africa, Asia, and the Pacific [edit]

Copyright law was introduced in African, Asian and Pacific countries in the late 19th Century by European colonial powers, especially Britain and France. After the 1884 Congress of Berlin European colonial powers imposed new laws and institutions in their colonies, including copyright laws. The British Empire introduced copyright law in its African and Asian colonies though the Copyright Act 1911, also known as the Imperial Copyright Act of 1911. Similarly France applied its copyright law throughout its colonies and the French National Institute for Intellectual Property (INPI) acted as the colonial intellectual property authority.[18] The introduction of copyright laws in colonies occurred in the context of colonial powers' desire to "civilize" their colonies and to protect the commercial interest of the colonial powers. While approaches varied, copyright laws were generally not adapted to fit local conditions.[19]

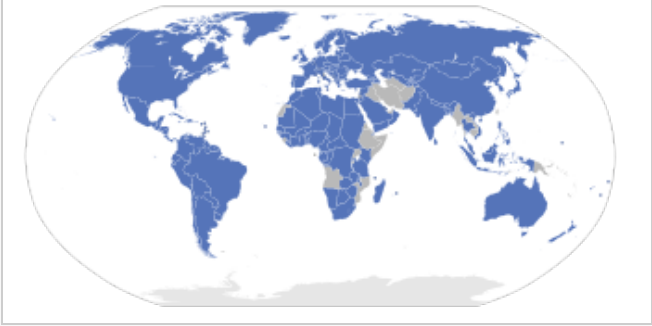
International copyright law [edit]

Main article: International copyright agreements

Berne Convention for the Protection of Literary and Artistic Works [edit]

Main article: Berne Convention for the Protection of Literary and Artistic Works

The Berne Convention was first established in 1886, and was subsequently re-negotiated in 1896 (Paris), 1908 (Berlin), 1928 (Rome), 1948 (Brussels), 1967 (Stockholm) and 1971 (Paris). The convention relates to literary and artistic works, which includes films, and the convention requires its member states to provide protection



Berne Convention signatory countries (in blue).

for every production in the literary, scientific and artistic domain. The Berne Convention has a number of core features, including the principle of *national treatment*, which holds that each member state to the Convention would give citizens of other member states the same rights of copyright that it gave to its own citizens (Article 3-5).[20]

Another core feature is the establishment of minimum standards of national copyright legislation in that each member state agrees to certain basic rules which their national laws must contain. Though member states can if they wish increase the amount of protection given to copyright owners. One important minimum rule was that the term of copyright was to be a minimum of the author's lifetime plus 50 years. Another important minimum rule established by the Berne Convention is that copyright arises with the creation of a work and does not depend upon any formality such as a system of public registration (Article 5(2)). At the time some countries did require registration of copyright, and when Britain implemented the Berne Convention in the Copyright Act 1911 it had to abolish its system of registration at Stationers' Hall.[20]

The Berne Convention focuses on authors as the key figure in copyright law and the stated purpose of the convention is "the protection of the rights of authors in their literary and artistic works" (Article 1), rather than the protection of publishers and other actors in the process of disseminating works to the public. In the 1928 revision the concept of moral rights was introduced (Article 10bis), giving authors the right to be identified as a such and to object to derogatory treatment of their works. These rights, unlike economic rights such as preventing reproduction, could not be transferred to others.[20]

The Berne Convention also enshrined limitations and exceptions to copyright, enabling the reproduction of literary and artistic works without the copyright owners prior permission. The detail of these exceptions was left to national copyright legislation, but the guiding principle is stated in Article 9 of the convention. The so called three-step test holds that an exception is only permitted "in certain special cases, provided that such reproduction does not conflict with a normal exploitation of the work and does not unreasonably prejudice the legitimate interests of the author". Free use of copyrighted work is expressly permitted in the case of quotations from lawfully published works, illustration for teaching purposes, and news reporting (Article 10).[20]

European copyright law [edit]

In the 1980s the European Community started to regard copyright as an element in the creation of a single market. Since 1991 the EU has passed a number of directives on copyright, designed to harmonise copyright laws in member states in certain key areas, such as computer programmes, databases and the internet. The directives aimed to reduce obstacles to the free movement of goods and services within the European Union, such as for example in rental rights, satellite broadcasting, copyright term and resale rights.[21] Key directives include the 1993 Copyright Duration Directive, the 2001 InfoSoc Directive, also known as Copyright Directive, and the 2004 Directive on the enforcement of intellectual property rights.

Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) [edit]

Main article: Agreement on Trade-Related Aspects of Intellectual Property Rights

Important developments on copyright at international level in the 1990s include the 1994 Agreement on Trade-Related Aspects of Intellectual Property Rights, known as TRIPS Agreement. TRIPS was negotiated at the end of the Uruguay Round of the General Agreement on Tariffs and Trade (GATT) and contains a number of provisions on copyright. Compliance with the TRIPS Agreement is required of states wishing to be members of the World Trade Organisation (WTO). States need to be signatory of the Berne Convention and comply with all its provisions, except for the provision on moral rights (Article 9(1)). States need to bring computer programs and databases within the scope of works covered by copyright law (Article 10). States need to provide for rental rights in at least computer programs and films (Article 11). Where copyright term, that is duration of copyright, is

calculated other than by reference to the life of a natural person, States need to give a minimum term of 50 years calculated from either the date of authorised publication or the creation of the work.[21]

Anti-Counterfeiting Trade Agreement [edit]

Main article: Anti-Counterfeiting Trade Agreement

The Anti-Counterfeiting Trade Agreement (ACTA) is a proposed plurilateral trade agreement which is claimed by its proponents to be in response "to the increase in global trade of counterfeit goods and pirated copyright protected works."[22] The scope of ACTA is broad, including counterfeit physical goods, as well as "internet distribution and information technology".[23]

In October 2007 the United States, the European Community, Switzerland and Japan announced that they would negotiate ACTA. Furthermore the following countries have joined the negotiations: Australia, the Republic of Korea, New Zealand, Mexico, Jordan, Morocco, Singapore, the United Arab Emirates and Canada.[23][24][25] The ACTA negotiations have been largely conducted in secrecy, with very little information being officially disclosed. However, on 22 May 2008 a discussion paper about the proposed agreement was uploaded to Wikileaks, and newspaper reports about the secret negotiations quickly followed.[25][26][27][28]

Copyright by country [edit]

Copyright laws have been standardized to some extent through international conventions such as the Berne Convention. Although there are consistencies among nations' intellectual property laws, each jurisdiction has separate and distinct laws and regulations about copyright.[1] The World Intellectual Property Organization summarizes each of its member states' intellectual property laws on its website.[29]

Copyright law by country

Europe

France · Germany · Ireland · Netherlands · Poland · Serbia · Spain · Switzerland · Turkey · United Kingdom

North America

Canada · United States

Indian subcontinent, South East Asia and Australia

Australia · Hong Kong · India · Japan · New Zealand · Pakistan · Phillippines · Thailand

Central Asia and Russia

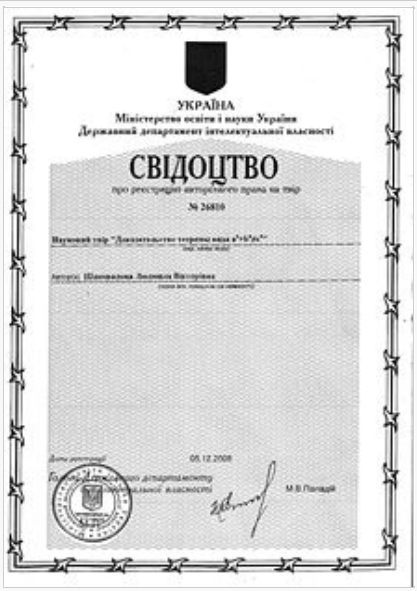
Russia · Tajikistan

Middle East

Egypt · Iran · Jordan

Africa

South Africa



A copyright certificate for proof of the Fermat theorem, issued by the State Department of Intellectual Property of Ukraine

Obtaining copyright [edit]

© is the copyright symbol in a copyright notice

Copyright law is different from country to country, and a copyright notice is required in about 20 countries for a work to be protected under copyright.[30] Before 1989, all published works in the US had to contain a copyright notice, the © symbol followed by the publication date and copyright owner's name, to be protected by copyright. This is no longer the case and use of a copyright notice is now optional in the US, though they are still used.[31]

In all countries that are members of the Berne Convention, copyright is automatic and need not be obtained through official registration with any government office. Once an idea has been reduced to tangible form, for example by securing it in a fixed medium (such as a drawing, sheet music, photograph, a videotape, or a computer file), the copyright holder is entitled to enforce his or her exclusive rights. However, while registration isn't needed to exercise copyright, in jurisdictions where the laws provide for registration, it serves as *prima facie* evidence of a valid copyright. The original copyright owner of the copyright may be the *employer* of the author rather than the author himself, if the work is a "work for hire".

Copyright term [edit]

Main article: Copyright term

See also: List of countries' copyright length

Copyright subsists for a variety of lengths in different jurisdictions. The length of the term can depend on several factors, including the type of work (e.g. musical composition or novel), whether the work has been published or not, and whether the work was created by an individual or a corporation. In most of the world, the default length of copyright is the life of the author plus either 50 or 70 years. In the United States, the term for most existing works is a fixed number of years after the date of creation or publication. In some countries (for example, the United States[32] and the United Kingdom),[33] copyrights expire at the end of the calendar year in question.

The length and requirements for copyright duration are subject to change by legislation, and since the early 20th century there have been a number of adjustments made in various countries, which can make determining the duration of a given copyright somewhat difficult. For example, the United States used to require copyrights to be renewed after 28 years to stay in force, and formerly required a copyright notice upon first publication to gain coverage. In Italy and France, there were post-wartime extensions that could increase the term by approximately 6 years in Italy and up to about 14 in France. Many countries have extended the length of their copyright terms (sometimes retroactively). International treaties establish minimum terms for copyrights, but individual countries may enforce longer terms than those.[34]

Exclusive rights granted by copyright [edit]

Copyright is literally, the right to copy, though in legal terms "the right to control copying" is more accurate. Copyright are exclusive statutory rights to exercise control over copying and other exploitation of the works for a specific period of time. The copyright owner is given two sets of rights: an exclusive, positive right to copy and exploit the copyrighted work, or license others to do so, and a negative right to prevent anyone else from doing so without consent, with the possibility of legal remedies if they do.[35]

Copyright initially only granted the exclusive right to copy a book, allowing anybody to use the book to, for example, make a translation, adaptation or public performance.[36] At the time print on paper was the only format in which most text based copyrighted works were distributed. Therefore, while the language of book contracts was typically very broad, the only exclusive rights that had any significant economic value were rights to distribute the work in print.[37] The exclusive rights granted by copyright law to copyright owners have been gradually expanded over time and now uses of the work such as dramatization, translations, and derivative works such as adaptations and transformations, fall within the scope of copyright.[36] With a few exceptions, the exclusive rights granted by copyright are strictly territorial in scope, as they are granted by copyright laws in different countries. Bilateral and multilateral treaties establish minimum exclusive rights in member states, meaning that there is some uniformity across Berne Convention member states.[38]

The print on paper format means that content is affixed onto paper and the content can't be easily or conveniently manipulated by the user. Duplication of printed works is time-consuming and generally produces a copy that is of lower quality. Developments in technology have created new formats, in addition to paper, and new means of distribution. Particularly digital formats distributed over computer networks have separated the content from its means of delivery. Users of content are now able to exercise many of the exclusive rights granted to copyright owners, such as reproduction, distribution and adaptation.[37]

Types of work subject to copyright [edit]

The types of work which are subject to copyright has been expanded over time. Initially only covering books, copyright law was revised in the 19th century to include maps, charts, engravings, prints, musical compositions, dramatic works, photographs, paintings, drawings and sculptures. In the 20th century copyright was expanded to cover motion pictures, computer programs, sound recordings, choreography and architectural works.[36]

Idea–expression divide [edit]

Main article: Idea-expression divide

Copyright law is typically designed to protect the fixed expression or manifestation of an idea rather than the fundamental idea itself. Copyright does not protect ideas, only their expression and in the Anglo-American law tradition the idea-expression divide is a legal concept which explains the appropriate function of copyright

laws.[39]

Related rights and neighboring rights [edit]

Main article: Related rights

Related rights is used to describe database rights, public lending rights (rental rights), artist resale rights and performers' rights. Related rights may also refer to copyright in broadcasts and sound recordings.[40] Related rights award copyright protection to works which are not author works, but rather technical media works which allowed author works to be communicated to a new audience in a different form. The substance of protection is usually not as great as there is for author works. In continental European copyright law, a system of *neighboring rights* has thus developed and the approach was reinforced by the creation of the Rome Convention for the Protection of Performers, Producers of Phonograms and Broadcasting Organizations in 1961.[41]

First-sale doctrine and exhaustion of rights [edit]

Main articles: First-sale doctrine and Exhaustion of rights

Copyright law does *not* restrict the owner of a copy from reselling legitimately obtained copies of copyrighted works, provided that those copies were originally produced by or with the permission of the copyright holder. It is therefore legal, for example, to resell a copyrighted book or CD. In the United States, this is known as the first-sale doctrine, and was established by the courts to clarify the legality of reselling books in second-hand bookstores. Some countries may have parallel importation restrictions that allow the copyright holder to control the resale market. This may mean for example that a copy of a book that does not infringe copyright in the country where it was printed **does** infringe copyright in a country into which it is imported for retailing. The first-sale doctrine is known as exhaustion of rights in other countries and is a principle that also applies, though somewhat differently, to patent and trademark rights. It is important to note that the first-sale doctrine permits the transfer of the particular legitimate copy involved. It does not permit making or distributing additional copies.

Limitations and exceptions [edit]

Main article: Limitations and exceptions to copyright

The expression "**limitations and exceptions**" refers to situations in which the exclusive rights granted to authors, or their assignees under copyright law do not apply or are limited for public interest reasons. They generally limit use of copyrighted material to certain cases that do not require permission from the rights holders, such as for commentary, criticism, news reporting, research, teaching or scholarship, archiving, access by the visually impaired etc. They essentially create a limitation, or an exception to the monopoly exclusive rights that are granted to the creator of a copyright work by law. Copyright theory teaches that the balance between monopoly granted to the creator, and the exceptions to this monopoly are at the heart of creativity. i.e. Exclusive rights stimulate investment and the production of creative works and simultaneously, exceptions to those rights create a balance that allows for the use of creative works to support innovation, creation, competition and the public interest.

Limitations and exceptions have a number of important public policy goals such as market failure, freedom of speech,[42] education and equality of access (such as by the visually impaired.)

Some view "limitations and exceptions" as "user rights" - seeing user rights provide an essential balance to the rights of copyright owners. There is no consensus amongst copyright experts as to whether they are "rights" or not. See for example the National Research Council's Digital Agenda Report, note 1. The concept of user rights has also been recognised by courts, including the Canadian Supreme Court in CCH Canadian Ltd v. Law Society of Upper Canada (2004 SCC 13), which classed "fair dealing" as such a user right. These kinds of disagreements in philosophy are quite common in the philosophy of copyright, where debates about jurisprudential reasoning tend to act as proxies for more substantial disagreements about good policy.

Changing Technology and Limitations and Exceptions [edit]

The scope of copyright limitations and exceptions became a subject of significant controversy within various nations in the late 1990s and early 2000s, largely due to the impact of digital technology, the changes in national copyright legislations for compliance with TRIPS, and the enactment of anti-circumvention rules in

response to the WIPO Copyright Treaty. Academics and defenders of copyright exceptions fear that technology, contract law undermining copyright law and copyright law not being amended, is reducing the scope of important exceptions and therefore harming creativity. This has resulted in a number of declarations on the importance of access to knowledge being important for creativity, such as the Adelphi Charter in 2005 and at a European level in May 2010 a declaration entitled Copyright for Creativity - A Declaration for Europe.[43] The declaration was supported by industry, artist, education and consumer groups. The declaration states that "While exclusive rights have been adapted and harmonised to meet the challenges of the knowledge economy, copyright's exceptions are radically out of line with the needs of the modern information society. The lack of harmonisation of exceptions hinders the circulation of knowledge based goods and services across Europe. The lack of flexibility within the current European exceptions regime also prevents us from adapting to a constantly changing technological environment."

Competition Law / Anti-Trust Law and Limitations and Exceptions [edit]

Copyright is typically thought of as a limited, legally sanctioned monopoly.[44] Because of this, copyright licensing may sometimes interfere too much in free and competitive markets.[45] These concerns are governed by legal doctrines such as competition law in the European Union, anti-trust law in the United States, and anti-monopoly law in Russia and Japan.[45] Competition issues may arise when the licensing party unfairly leverages market power, engages in price discrimination through its licensing terms, or otherwise uses a licensing agreement in a discriminatory or unfair manner.[44][45] Attempts to extend the copyright term granted by law – for example, by collecting royalties for use of the work after its copyright term has expired and it has passed into the public domain – raise such competition concerns.[44]

In April 1995, the US published "Antitrust Guidelines for the licensing of Intellectual Property" which apply to patents, copyright, and trade secrets. In January 1996, the European Union published Commission Regulation No.240/96 which applies to patents, copyright, and other intellectual property rights, especially regarding licenses. The guidelines apply *mutatis mutandis* to the extent possible.[46]

The interplay of copyright law and competition law is increasingly important in the digital world, as most countries laws allow private contracts to over-ride copyright law. Given that copyright law creates a legally sanctioned monopoly, balanced by "limitations and exceptions" that allow access without the permission of the copyright holder the over-riding of copyright law by private contracts can create monopoly activity. Well known limitations and exceptions include fair dealing in the UK and Canada, as well as the fair use doctrine in the US. The undermining of copyright law, and in particular limitations and exceptions to copyright by contract law is an issue frequently raised by libraries, and library groups such as International Federation of Library Associations and Institutions. As a result of this, this issue is increasingly being looked at and discussed at a national governmental level e.g UK [47] as well as international level such as WIPO - as part of the Development Agenda.

International Legal Instruments and Limitations and Exceptions [edit]

Limitations and exceptions are also the subject of significant regulation by global treaties. These treaties have harmonized the exclusive rights which must be provided by copyright laws, and the Berne three-step test operates to constrain the kinds of copyright exceptions and limitations which individual nations can enact. On the other hand, international copyright treaties place almost no *requirements* on national governments to provide exemptions from exclusive rights; a notable exception to this is Article 10(1) of the Berne Convention, which guarantees a limited right to make quotations from copyrighted works. Because of the lack of balance in international treaties in October 2004, WIPO agreed to adopt a significant proposal offered by Argentina and Brazil, the "Proposal for the Establishment of a Development Agenda for WIPO" also known simply as the "Development Agenda" - from the Geneva Declaration on the Future of the World Intellectual Property Organization.[48] This proposal was well supported by developing countries. A number of civil society bodies have been working on a draft Access to Knowledge,[49] or A2K, Treaty which they would like to see introduced.

Fair Use and Fair Dealing [edit]

Main articles: Fair use and Fair dealing

Copyright does not prohibit all copying or replication. In the United States, the fair use doctrine, codified by the Copyright Act of 1976 as 17 U.S.C. § 107, permits some copying and distribution without permission of the

copyright holder or payment to same. The statute does not clearly define fair use, but instead gives four non-exclusive factors to consider in a fair use analysis. Those factors are:

1. the purpose and character of the use;
2. the nature of the copyrighted work;
3. the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and
4. the effect of the use upon the potential market for or value of the copyrighted work.[50]

In the United Kingdom and many other Commonwealth countries, a similar notion of fair dealing was established by the courts or through legislation. The concept is sometimes not well defined; however in Canada, private copying for personal use has been expressly permitted by statute since 1999. In Australia, the fair dealing exceptions under the *Copyright Act 1968* (Cth) are a limited set of circumstances under which copyrighted material can be legally copied or adapted without the copyright holder's consent. Fair dealing uses are research and study; review and critique; parody and satire; news reportage and the giving of professional advice (i.e. legal advice). Under current Australian law it is still a breach of copyright to copy, reproduce or adapt copyright material for personal or private use without permission from the copyright owner. Other technical exemptions from infringement may also apply, such as the temporary reproduction of a work in machine readable form for a computer.

In the United States the AHRA (Audio Home Recording Act Codified in Section 10, 1992) prohibits action against consumers making noncommercial recordings of music, in return for royalties on both media and devices plus mandatory copy-control mechanisms on recorders.

> *Section 1008. Prohibition on certain infringement actions*
>
> *No action ever may be brought under this title alleging infringement of copyright based on the manufacture, importation, or distribution of a digital audio recording device, a digital audio recording medium, an analog recording device, or an analog recording medium, or based on the noncommercial use by a consumer of such a device or medium for making digital musical recordings or analog musical recordings.*

Later acts amended US Copyright law so that for certain purposes making 10 copies or more is construed to be commercial, but there is no general rule permitting such copying. Indeed making one complete copy of a work, or in many cases using a portion of it, for commercial purposes will not be considered fair use. The Digital Millennium Copyright Act prohibits the manufacture, importation, or distribution of devices whose intended use, or only significant commercial use, is to bypass an access or copy control put in place by a copyright owner. An appellate court has held that fair use is not a defense to engaging in such distribution.

Educational use is regarded as "fair use" in most jurisdictions, but the restrictions vary wildly from nation to nation.[51]

Recent Israeli District Court decision dated Sep. 2, 2009 [52][53] accepted the defence of fair use for a site linking to P2P live feeds of soccer matches. The main reasoning was based on the public importance of certain sporting events, i.e. - the public's rights as counter weight to the copyright holders rights.

Licensing, transfer, and assignment [edit]

Copyright may be bought and sold much like other properties.[54] In the individual licensing model the copyright owner authorizes the use of the work against remuneration and under the conditions specified by the license. The conditions of the license may be complex since the exclusive rights granted by copyright to the copyright owner can be split territorially or with respect to language, the sequence of uses may be fixed, the number of copies to be made and their subsequent use may also be specified. Furthermore sublicenses and representation agreements may also be made.[55]

DVD: All Rights Reserved

A contractual transfer of all or some of the rights in a copyrighted work is a known as a copyright license. A copyright assignment is an immediate and irrevocable transfer of the copyright owner's entire interest in all or some of the rights in the copyrighted work. Copyright licensing and assignment cover only the specified geographical region.

There are significant differences in national copyright laws with regards to copyright licensing and assignment.[44]

Copyright licenses, as a minimum, define the copyrighted works and rights subject to the license, the territories or geographic region in which the license applies, the term or length of the license, and the consideration (such as a one of payment or royalties) for the license. The exclusive rights granted by copyright law can all be licensed, but they vary depending on local law. Depending on how the work may be used different licenses need to be acquired. For example, the activity of distributing videocassettes of a motion picture will require the license for the right to reproduce the motion picture on a videocassette and the right to distribute the copies to the public. Because the ratio of a television screen is different from that of a wide-screen cinema, requiring the cutting of the wide-screen "ends", it may also be necessary to obtain a license for the right to modify the motion picture. If the motion picture is to be edited or modified the copyright owner may include control over or approval of the editing process, or of the final result. Existing contractual agreements between the copyright owner and the director, may also require approval from the director to any changes made to the copyrighted work.[56]

Different types of exclusive licenses exist, such as licenses that excludes the licensor from use of the licenced copyrighted work in the relevant region and for the stated time period. Or exclusive licenses may prevent the licensor from licensing other parties in the geographic region and during the license term. There are also various types of non-exclusive licenses, including the right of first refusal should the licensor elect to offer future licenses to third parties. If a licensing agreement does not specify that the license is exclusive it may nonetheless be deemed exclusive depending on the language of the contract. Depending on local laws the owner of an exclusive license may be deemed the "copyright owner" of that work and bring charges for copyright infringement.[57]

The term or length of the copyright license is not allowed to exceed the copyright term specified by local law. Licenses may establish various pay arrangements, such as royalties as a percentage of sales or as a stepped up or down percentage of sales, e.g. 5 percent of sales up to 50,000 units, 2.5 percent of sales in excess thereof. The trigger for royalty payments may be sales, or other factors, such as the number of "hits" or views on a website. Minimum royalty payments are arrangements whereby a minimum up-front payment is made and then recouped against the percentage of sales. The up-front payment may be non-refundable if sales royalties do not reach the amount of the payment.[57] Minimum royalty payment arrangements may be accompanied by marketing duties for the licensee, e.g. best effort and reasonable effort to market and promote the copyrighted work.[58]

Collective rights management [edit]

Main article: Collective rights management

Collective rights management is the licensing of copyright and related rights by organizations acting on behalf of rights owners. Collective management organisations, such as collecting societies, typically represent groups of copyright and related rights owners, such as authors, composers, publishers, writers, photographers, musicians and performers.[59] The following exclusive rights granted under copyright law are commonly collectively managed by collecting societies: the right to public performance, the right to broadcasting, the mechanical reproduction rights in recorded music, the performing rights in dramatical works, the rights of reprographic reproduction of literary and musical works, and related rights, for example the rights of performers and producers in recorded music when used in broadcasts.[60]

The collective management of copyright and related rights is undertaken by various types of collective management organisations, most commonly collecting societies. Collecting societies act on behalf of their members, which may be authors or performers, and issue copyright licenses to users authorising the use of the works of their members.[61] Other forms of collective management organisations include rights clearance centres and one-stop shops. One-stop shops are a coalition of collecting societies and rights clearance centres offering a centralised source for users to obtain licences. They have become popular in response to multi-media productions requiring users to obtain multiple licences for relevant copyright and related rights.[62]

Extended collective licensing [edit]

Main article: extended collective licensing

The first extended collective licensing (ECL) laws were established in Denmark, Finland, Iceland, Norway and Sweden in the 1960s.[63] ECL is a form of collective rights management whereby ECL laws allow for freely negotiated copyright licensing contracts for the exclusive rights granted by copyright. ECL laws are designed specifically for mass use, where negotiating alone will rarely allow a single right owner to fully financially benefit from their exclusive rights. Under ECL laws, collecting societies negotiate ECL agreements with users, such as a TV broadcaster, covering the types of copyrighted works for uses specified in the ECL licence.[64]

Subject to certain conditions collecting societies can under ECL law apply to represent all rights owners on a non-exclusive basis in a specific category of copyrighted works.[65] The collecting society can then negotiate an ECL agreement with a user for certain uses. This agreement applies to members of that collecting society, as well as non-members. ECL laws require that collecting societies treat rights owners who are non-members in the same way they treat their members. Non-members are also given the right to individual remuneration, ie royalty payment, by the collecting society, and the right to exclude their work from an ECL agreement.[66]

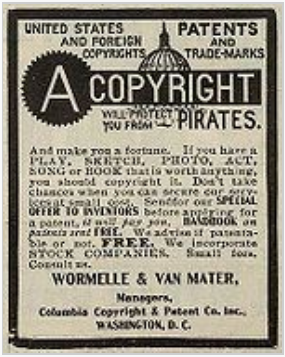
Compulsory licensing [edit]

Main article: Compulsory license

In some countries copyright law provides for compulsory licenses of copyrighted works for specific uses. In many cases the remuneration or royalties received for a copyrighted work under compulsory license are specified by local law, but may also be subject to negotiation. Compulsory licensing may be established through negotiates licenses that provide terms within the parameters of the compulsory license.[67] Article 11bis(2) and Article 13(1) of the Berne Convention for the Protection of Literary and Artistic Works provide the legal basis for compulsory licenses. They state that member states are free to determine the conditions under which certain exclusive rights may be exercised in their national laws. They also provide for the minimum requirements to be set when compulsory licenses are applied, namely that they must not prejudice the author to fair compensation.[68]

Future rights under pre-existing agreements [edit]

It is commonplace in copyright licensing to license not only new uses which may be developed but also works which are not yet created. However, local law may not always recognise that the wording in licensing agreements does cover new uses permitted by subsequently developed technology.[44] Whether a license covers future, as yet unknown, technological developments is subject to frequent disputes. Litigation over the use of a licensed copyrighted work in a medium unknown when the license was agreed is common.[56]



Newspaper advert: "United States and Foreign Copyright. Patents and Trade-Marks A Copyright will protect you from Pirates. And make you a fortune."

Enforcement [edit]

Copyrights are generally enforced by the holder in a civil law court, but there are also criminal infringement statutes in some jurisdictions. While central registries are kept in some countries, which aid in proving claims of ownership, registering does not necessarily prove ownership, nor does the fact of copying (even without permission) necessarily prove that copyright was infringed. Criminal sanctions are generally aimed at serious counterfeiting activity, but are now becoming more commonplace as copyright collectives such as the RIAA are increasingly targeting the file sharing domestic Internet user. (See: File sharing and the law)[*citation needed*]

Infringement [edit]

Main article: Copyright infringement

Copyright infringement, or copyright violation, is the unauthorized use of works covered by copyright law, in a way that violates one of the copyright owner's exclusive rights, such as the right to reproduce or perform the copyrighted work, or to make derivative works.[*citation needed*]

For electronic and audio-visual media under copyright, unauthorized

An unskippable anti-piracy film included on movie DVDs equates copyright infringement with theft.

reproduction and distribution is also commonly referred to as piracy. An early reference to piracy in the context of copyright infringement was made by Daniel Defoe in 1703 when he said of his novel *The True-Born Englishman* "Had I wrote it for the gain of the press, I should have been concerned at its being printed again and again by PIRATES, as they call them, and PARAGRAPHMEN: but if they do justice, and print it true, according to the copy, they are welcome to sell it for a penny, if they please: the pence, indeed, is the end of their works.".[69] The practice of labeling the act of infringement as "piracy" predates statutory copyright law. Prior to the Statute of Anne 1709, the Stationers' Company of London in 1557 received a Royal Charter giving the company a monopoly on publication and tasking it with enforcing the charter. Those who violated the charter were labeled pirates as early as 1603.[70]

Orphan works [edit]

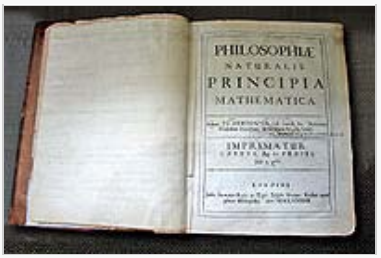
Main article: Orphan works

An orphan work is a work under copyright protection whose copyright owner is difficult or impossible to contact. The creator may be unknown, or where the creator is known it is unknown who represents them.[71]

Public domain [edit]

Main article: Public domain

Works are in the public domain if their kind is not covered by intellectual property rights or if the intellectual property rights have expired,[72] have been forfeited, or have never been claimed.[73] Examples include the English language, the formulae of Newtonian physics, as well as the works of Shakespeare and the patents over powered flight.[72]



Newton's own copy of his *Principia*, with hand-written corrections for the second edition

Copyright as property right [edit]

Copyright as a property law was initially conceived of as a "chose in action", that is an intangible property, as opposed to tangible property.[74] In the case of tangible property the property rights are bundled with the ownership of the property, and property rights are transferred once the property is sold. In contrast copyright law detaches the exclusive rights granted under property law to the copyright owner from ownership of the good which is regarded as a reproduction. Hence the purchase of a book buys ownership of the book as a good, but not the underlying copyright in the book's content. If a derivative work based on the content of the book is made, permission needs to be sought from the copyright owner, not all owners of a copy of the book.[75]

The Statute of Anne specifically referred to copyright in terms of literary property that is limited in time. Many contemporaries did not believe that the statute was concerned with property "in the strict sense of the word" and the question of whether copyright is property right dates back to the Battle of the Booksellers. In 1773 Lord Gardenston commented in Hinton v. Donaldson that "the ordinary subjects of property are well known, and easily conceived... But property, when applied to ideas, or literary and intellectual compositions, is perfectly new and surprising..."[76]

It was in the 19th century that the term *intellectual property* began to be used as an umbrella term for patents, copyright and other laws.[77][78] The expansion of copyright and copyright term are mirrored in the rhetoric that has been employed in referring to copyright. Courts, when strengthening copyright, have characterised it as a type of property. Companies have strongly emphasised copyright as property, with leaders in the music and movie industries seeking to "protect private property from being pillaged" and making forceful assertions that copyright is absolute property right.[79] With reference to the expanding scope of copyright, one commentator noted that "We have gone from a regime where a tiny part of creative content was controlled to a regime where most of the most useful and valuable creative content is controlled for every significant use."[36] According to Graham Dutfield and Uma Suthersanen copyright is now a "class of intangible business assets", mostly owned by companies who function as "investor, employer, distributor and marketer". While copyright was conceived as personal property awarded to creators, creators now rarely own the rights in their works.[80]

Copyright and authors [edit]

Copyright law emerged in 18th Century Europe in relation to printed books and a new notion of *authorship*. In the European Renaissance and Neoclassical period the writer was regarded as an instrument, not as an independent creator. The writer was seen as using external sources to create a work of inspiration. In the 18th Century a changing concept of *genius* located the source of inspiration within the writer, whose special talents and giftedness was the basis for creating works of inspiration and uniqueness. The concept of the *author* as original creator and owner of their work emerged partly from the new concept of *property rights* and John Locke's theory that individuals were "owners of themselves". According to Locke individuals invested their labour into natural goods, and so creating property. Authors were argued to be the owners of their work because they had invested their labour in creating it.[81] According to Patterson and Livingston there remains confusion about the nature of copyright ever since Donaldson v Beckett, a case heard in 1774 by the British House of Lords about whether copyright is the natural law right of the author or the statutory grant of a limited monopoly. One theory holds that copyright's origin occurs at the creation of a work, the other that its origin exists only through the copyright statute.[82]

Copyright and competition law [edit]

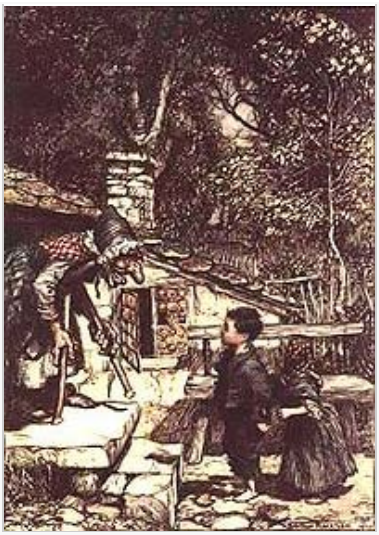
Copyright is typically thought of as a limited, legally sanctioned monopoly.[44] Because of this, copyright licensing may sometimes interfere too much in free and competitive markets.[45] These concerns are governed by legal doctrines such as competition law in the European Union, anti-trust law in the United States, and anti-monopoly law in Russia and Japan.[45] Competition issues may arise when the licensing party unfairly leverages market power, engages in price discrimination through its licensing terms, or otherwise uses a licensing agreement in a discriminatory or unfair manner.[44][45] Attempts to extend the copyright term granted by law – for example, by collecting royalties for use of the work after its copyright term has expired and it has passed into the public domain – raise such competition concerns.[44]

In April 1995, the US published "Antitrust Guidelines for the licensing of Intellectual Property" which apply to patents, copyright, and trade secrets. In January 1996, the European Union published Commission Regulation No.240/96 which applies to patents, copyright, and other intellectual property rights, especially regarding licenses. The guidelines apply *mutatis mutandis* to the extent possible.[46]

The interplay of copyright law and competition law is increasingly important in the digital world, as most countries laws allow private contracts to over-ride copyright law. Given that copyright law creates a legally sanctioned monopoly, balanced by "limitations and exceptions" that allow access without the permission of the copyright holder the over-riding of copyright law by private contracts can create monopoly activity. Well known limitations and exceptions include fair dealing in the UK and Canada, as well as the fair use doctrine in the US. The undermining of copyright law, and in particular limitations and exceptions to copyright by contract law is an issue frequently raised by libraries, and library groups such as International Federation of Library Associations and Institutions. As a result of this, this issue is increasingly being looked at and discussed at a national governmental level e.g UK [47] as well as international level such as WIPO - as part of the Development Agenda.

Copyright and traditional knowledge [edit]

Traditional knowledge includes pre-existing, underlying traditional culture, or folklore, and literary and artistic works created by current generations of society which are based on or derived from pre-existing traditional culture or folklore. Traditional culture and folklore tends to be trans-generational, old and collectively "owned" by groups or communities. Often traditional culture and folklore is of anonymous origin and expressions of this pre-existing traditional culture is generally not protected by current intellectual property laws and is treated as being in the public domain.[83] In contrast contemporary literary and artistic works based upon, derived from or inspired by traditional culture or folklore may incorporate new elements or expressions. Hence these works may be



Hansel and Gretel is a fairy tale of Germanic origin, recorded by the Brothers Grimm in 1812. The tale has been adapted to various media, most notably the opera *Hänsel und Gretel* (1893) by Engelbert Humperdinck and a stop-motion animated feature film based on the opera. Artwork by Arthur Rackham, 1909

"new" works with a living and identifiable creator, or creators. Such contemporary works may include a new interpretation, arrangement, adaptation or collection of pre-existing cultural heritage that is in the public domain. Traditional culture or folklore may also be "repackaged" in digital formats, or restoration and colorization. Contemporary and tradition based expressions and works of traditional culture are generally protected under existing copyright law, a form of intellectual property law, as they are sufficiently original to be regarded as "new" upon publication. Once the intellectual property rights afforded to these new works of traditional knowledge expire, they fall into the public domain.[84]

The public domain, as defined in the context of intellectual property rights, is not a concept recognised by indigenous peoples. As much of traditional knowledge has never been protected under intellectual property rights, they can not be said to have entered any public domain. On this point the Tulalip Tribes of Washington state, United States, has commented that "...open sharing does not automatically confer a right to use the knowledge (of indigenous people)... traditional cultural expressions are not in the public domain because indigenous peoples have failed to take the steps necessary to protect the knowledge in the Western intellectual property system, but from a failure of governments and citizens to recognise and respect the customary laws regulating their use".[84]

Copyright and economic development [edit]

According to historian Eckhard Höffner the 1710 introduction of copyright law in England and later in France acted as a barrier to economic progress for over a century, while Germany prospered in the same time frame due to the lack of copyright laws. Höffner argues that copyright laws allowed British publishers to print books in limited quantities for high prices.[85][86]

See also [edit]

- Adelphi Charter
- Philosophy of copyright
- Copyfraud
- Copying
- Copyright education
- Copyright for Creativity
- Copyright in architecture
- Copyright infringement
- Copyright infringement of software
- Copyright on the content of patents
- Copyright on typefaces
- Copyright on religious works
- Digital rights management
- Digital watermarking
- Entertainment law
- Fair use
- Freedom of panorama
- List of copyright treaty membership
- Limitations and Exceptions
- List of copyright acts
- List of copyright case law
- List of countries' copyright length
- Model release
- Moral rights (copyright law)
- Paracopyright
- Photography and the law
- Pirate Party
- Private copying levy
- Production music
- Public domain

Philosophy portal

Law portal

- Fair Dealing
- File sharing and the law
- UK government policy on illegal file sharing
- File Sharing in Europe
- Reproduction fees
- Related rights
- Rent-seeking
- Software copyright
- Threshold pledge system
- Font copyright laws, Font Copyright Laws

Treaties and International Agreements [edit]

- Berne Convention for the Protection of Literary and Artistic Works of 1886
- Universal Copyright Convention of 1952
- Rome Convention of 1961
- The WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), of 1994
- WIPO Copyright Treaty of 1996
- WIPO Performances and Phonograms Treaty of 1996

Sui generis [edit]

- Alternative Compensation System
- Anti-copyright
- Copyleft
- Copynorm
- Copyright aspects of downloading and streaming
- Copyright aspects of hyperlinking and framing
- Copyright-free
- Creative Commons
- Creative Commons Licenses
- Creative Commons jurisdiction ports
- Crypto-anarchism
- Database right
- Digital freedom
- *Free Culture: How Big Media Uses Technology and the Law to Lock Down Culture and Control Creativity* by Lawrence Lessig
- Opposition to copyright
- Permission culture — neologism by Lawrence Lessig.
- *The Uneasy Case for Copyright: A Study of Copyright in Books, Photocopies, and Computer Programs* by Stephen Breyer.
- *Good Copy Bad Copy* (documentary)

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External links [edit]

- Copyright at the Open Directory Project
- Collection of laws for electronic access from WIPO - intellectual property laws of many countries
- Copyright from *UCB Libraries GovPubs*
- About Copyright at the UK Intellectual Property Office
- A Bibliography on the Origins of Copyright and Droit d'Auteur
- 6.912 Introduction to Copyright Law taught by Keith Winstein, MIT OpenCourseWare January IAP 2006

Wikisource has the text of the 1911 Encyclopædia Britannica article ***Copyright***.

Wikisource has original text related to this article: ***Copyright law***

Wikimedia Commons has media related to: ***Copyright***

Categories: Copyright law | Intellectual property law | Library and information science | Monopoly (economics) | Metadata | Data management | Public records

HANDBOOK FOR FACULTY AND ACADEMIC ADMINISTRATORS
Revised 2009

A SELECTION OF POLICIES AND PROCEDURES OF THE UNIVERSITY OF PENNSYLVANIA

Table of Contents

III.D. Policy Relating to Copyrights and Commitment of Effort for Faculty

(Source: *1977 Research Investigator's Handbook; revised, 1978; revised, Resolution of the Trustees, February 16, 2001 and Offices of the Provost and Faculty Senate, Almanac, February 27, 2001*)

1. Policy Statement on Copyrights

The Trustees of the University of Pennsylvania, subject to the exceptions declared in Sections 1.A., 1.B. and 1.C. affirm the academic custom that creators of intellectual property own the copyright to works resulting from their research, teaching and writing and have the individual right to apply for; own all right, title and interest to enforce, profit by and transfer to other parties, such as publishers, copyrights in their works under the laws of the United States and other jurisdictions. Computer software and courseware (the tools and technologies used to present courses), to the extent not protected by patent law, are governed by this policy. With respect to works such as journal articles and other similar publications, when an author transfers an interest in these copyrightable works, the author should use reasonable efforts to secure for the University the right to reproduce such works, royalty free, for all traditional, customary or reasonable academic uses. With respect to computer software and courseware, the University shall enjoy a permanent, non-exclusive, royalty free license to make all traditional, customary or reasonable academic uses of these works**.**

A. Sponsored Research. Exceptions to this custom may arise when works are made under government-sponsored research, industry-sponsored research, and certain grants in which the University assumes specific obligations with respect to a copyrightable work resulting from a given sponsored program. To the extent necessary, where the sponsored program agreement provides that the sponsor will acquire rights to copyrightable works produced under the program, the University will own all right, title and interest to the copyrightable works created under such sponsored programs.

A.1. In accordance with such obligations, the University will use reasonable efforts to secure an acknowledgment from the authors of the copyrightable work prior to the commencement of the sponsored program. Authors who are also principal investigators and have responsibility for other authors will use reasonable efforts to secure acknowledgment from said authors prior to the commencement of the sponsored program.

A.2. The University shall negotiate a license with the sponsor in accordance with applicable provisions of the sponsored research agreement. Net revenues realized from said sponsored research agreements will be distributed in accordance with the procedures for the distribution of patent royalties described in Section 2.3 of the Patent and Tangible Research Property Policies and Procedures, except that the 30 percent research foundation share will be maintained as a copyright fund share. The copyright ; fund will be

administered by the Office of the Provost to support the development of pedagogical innovation. When negotiating sponsored research agreements, to the extent that University ownership is not necessary to fulfill its obligations to a sponsor the University shall, whenever practicable, make reasonable efforts to protect the ownership rights of the authors.

B. Works Made for Hire. Exceptions to this custom also arise when authors create works considered to be "works made for hire." Such works are the property of the University. For purposes of this policy, "works for hire" are those works that are prepared by the author pursuant to the express direction of a supervisor, prepared pursuant to the specific provisions incorporated within a position description, or prepared in the performance of any administrative duty. Works created by authors in the course of their instructional or research activities shall not be considered "works made for hire."

B.1. Prior to the preparation of the "work made for hire," the University may request, and if so the authors shall provide, an assignment or other declaration of the University's ownership of that work. Authors who are also principal investigators and have responsibility for other authors will secure assignments from said authors prior to the preparation of a "work made for hire." Failure to secure assignment does not negate the University's ownership of the work. In the event of subsequent disagreement over ownership of a "work made for hire," the case shall be referred to the committee noted in 4.B.

B.2. Net revenues realized from the commercialization of "works made for hire" will be distributed as in.A.2.

B.3. The University will have the authority to waive the "work for hire" claim where it judges that doing so is in the interest of the University.

C. Exceptions to this policy arise when the faculty create works that make substantial use of the services of University non-faculty employees or University resources. When such support is provided the works produced shall belong to the University unless there is explicit agreement otherwise. The faculty member(s) and the units providing such support shall agree in writing on the ownership of such works prior to the provision of the support. Notwithstanding the above, the faculty member(s) may subsequently petition the University to waive its ownership. The determining official for this action is the Provost, or at the Provost's designation, the dean of the school in which the faculty member has his/her (their) primary appointment(s); or the Provost in the case where a dean is the creator. In the event of subsequent disagreement over the use of University resources in the creation of a work, the case shall be referred to the committee noted in 4.B.

C.1. The reference to "substantial use of the services of University non-faculty employees or University resources" means the use of University funds, facilities, equipment, or other resources significantly in excess of the norm for

educational and research purposes in the department or school in which the creator(s) hold his or her (their) primary appointment(s). Academic year salary, office, usual library resources, usual secretarial and administrative staff resources or usual computer equipment, among other things, are not regarded as constituting "substantial use of services of University non-faculty employees or University resources." Any question about what constitutes substantial resources should be referred to the committee noted in 4.B.

C.2. Net revenues realized from the commercialization of such works will be distributed as in A.2.

D. A given intellectual property may be protected in some cases inclusively by United States patent, copyright and trademark laws, and in some cases by only one or two such intellectual property laws, with each body of law protecting a different feature of the given intellectual property. Consequently, definitions in the Patent and Tangible Research Property Policies and Procedures and the Copyright Policy and Procedures will at times overlap. When a single license agreement incorporates more than one type of intellectual property protection, prior to the execution of said license agreement, a written agreement shall be executed by the University and the authors stipulating which University intellectual property policy is applicable.

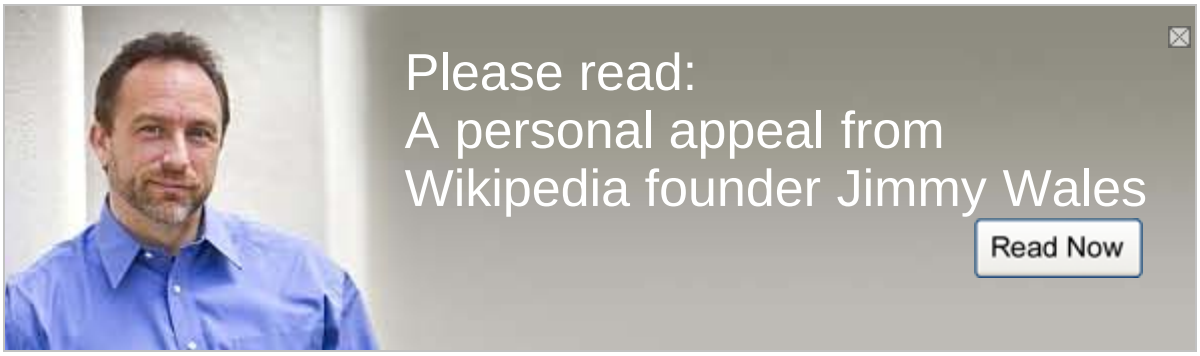
2. Commitment of Effort *(See also Conflict of Interest Policy, II.E.10)*.

A full-time faculty member's primary commitment in teaching and research is to the University of Pennsylvania. Any substantial teaching carried out in another setting, regardless of medium, for which students receive academic credit, must receive prior approval of the faculty member's dean. Any teaching, research or other activity in which the faculty member's department or school is actively engaged will presumptively claim the faculty member's primary effort, and carrying out these activities in another setting will also require a specific release from such commitment by the dean. The dean and faculty of each school should decide upon those academic activities (currently engaged in or reasonably likely to be engaged in by the school in the foreseeable future) other than teaching and research that are subject to the above restrictions.

3. Audio-Visual Works

Any videotapes or other recordings of classes or courses intended for students at the University of Pennsylvania belong to the University and may not be further distributed without permission from the appropriate school dean. Such audio-visual works may not be used commercially without the permission of everyone who appears in the final program.

A. This policy is not intended to apply to audio-visual works or recordings that have a specific short term use such as videotapes of lectures by job candidates, audio-visual works used to provide an alternative lecture when students may miss



Patent

From Wikipedia, the free encyclopedia

For other uses, see Patent (disambiguation).

A **patent** (pronounced /ˈpætənt/ or /ˈpeɪtənt/) is a set of exclusive rights granted by a state (national government) to an inventor or their assignee for a limited period of time in exchange for a public disclosure of an invention.

The procedure for granting patents, the requirements placed on the patentee, and the extent of the exclusive rights vary widely between countries according to national laws and international agreements. Typically, however, a patent application must include one or more claims defining the invention which must be new, non-obvious, and useful or industrially applicable. In many countries, certain subject areas are excluded from patents, such as business methods and mental acts. The exclusive right granted to a patentee in most countries is the right to prevent others from making, using, selling, or distributing the patented invention without permission.[1]

Under the World Trade Organization's (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights, patents should be available in WTO member states for any inventions, in all fields of technology,[2] and the term of protection available should be the minimum twenty years.[3] Different types of patents may have varying patent terms (i.e., durations).

Contents [hide]

Intellectual property law

Primary rights

Copyright • Authors' rights • Related rights • Moral rights • Industrial design right • **Patent** • Utility model • **Trademark** • Geographical indication • **Trade secret**

Sui generis rights

Database right • Mask work • Plant breeders' rights • Supplementary protection certificate • Indigenous intellectual property

Related topics

Criticism • Orphan works • Public domain • more

Lietuvių
Magyar
Bahasa Melayu
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Polski
Português
Română
Русский
Simple English
Slovenčina
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Srpskohrvatski / Српскохрватски
Suomi
Svenska
Tagalog
Türkçe
Українська
Tiếng Việt
中文

U.S patent

Definition [edit]

The term *patent* usually refers to a right granted to anyone who invents or discovers any new and useful process, machine, article of manufacture, or composition of matter, or any new and useful improvement thereof. The additional qualification *utility patent* is used in the United States to distinguish it from other types of patents (e.g. design patents) but should not be confused with utility models granted by other countries. Examples of particular species of patents for inventions include biological patents, business method patents, chemical patents and software patents.

Some other types of intellectual property rights are referred to as *patents* in some jurisdictions: industrial design rights are called *design patents* in some jurisdictions (they protect the visual design of objects that are not purely utilitarian), plant breeders' rights are sometimes called *plant patents*, and utility models or *Gebrauchsmuster* are sometimes called *petty patents* or *innovation patents*. This article relates primarily to the patent for an invention, although so-called petty patents and utility models may also be granted for inventions.

Certain grants made by the monarch in pursuance of the royal prerogative were sometimes called *letters patent*, which was a government notice to the public of a grant of an exclusive right to ownership and possession. These were often grants of a patent-like monopoly and predate the modern origins of the patent system. For other uses of the term *patent* see notably land patents, which were land grants by early state governments in the USA, and printing patent, a precursor of modern copyright. These meanings reflect the original meaning of *letters patent* that had a broader scope than current usage.

Etymology [edit]

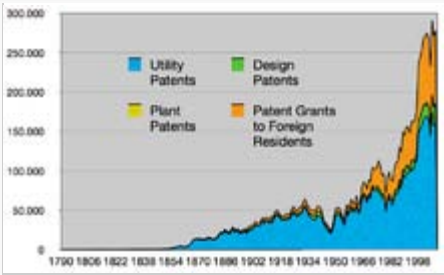
The word *patent* originates from the Latin *patere*, which means "to lay open" (i.e., to make available for public inspection), and more directly as a shortened version of the term *letters patent*, which originally denoted an open for public reading royal decree granting exclusive rights to a person.

History [edit]

Main article: History of patent law

In 500 BC, in the Greek city of Sybaris (located in what is now southern Italy),

Patents in force in 2000



U.S. Patents granted, 1790–2008.[4]

"encouragement was held out to all who should discover any new refinement in luxury, the profits arising from which were secured to the inventor by patent for the space of a year."[5]

The Florentine architect Filippo Brunelleschi received a three-year patent for a barge with hoisting gear, that carried marble along the Arno River in 1421.[6] In 1449, King Henry VI granted the first patent with a license of 20 years to John of Utynam for introducing the making of colored glass to England.[7]

Patents in the modern sense originated in 1474, when the Republic of Venice enacted a decree that new and inventive devices, once put into practice, had to be communicated to the Republic to obtain the right to prevent others from using them.[8]

England followed with the Statute of Monopolies in 1623 under King James I, which declared that patents could only be granted for "projects of new invention." During the reign of Queen Anne (1702–14), the lawyers of the English Court developed the requirement that a written description of the invention must be submitted.[9] The patent system in many other countries, including Australia, is based on British law and can be traced back to the Statute of Monopolies.[*citation needed*]

In France, patents were granted by the monarchy and by other institutions like the "Maison du Roi".[*citation needed*] The Academy examined novelty.[10] Examinations were generally done in secret with no requirement to publish a description of the invention. Actual use of the invention was deemed adequate disclosure to the public.[11] The modern French patent system was created during the Revolution in 1791. Patents were granted without examination since inventor's right was considered as a natural one [12]

In the United States, during the so-called colonial period and Articles of Confederation years (1778–89), several states adopted patent systems of their own. The first Congress adopted a Patent Act, in 1790, and the first patent was issued under this Act on July 31, 1790 (to Samuel Hopkins of Vermont for a potash production technique).

Law [edit]

Effects [edit]

A patent is not a right to practice or use the invention.[13] Rather, a patent provides the right to *exclude others*[13] from making, using, selling, offering for sale, or importing the patented invention for the term of the patent, which is usually 20 years from the filing date[3] subject to the payment of maintenance fees. A patent is, in effect, a limited property right that the government offers to inventors in exchange for their agreement to share the details of their inventions with the public. Like any other property right, it may be sold, licensed, mortgaged, assigned or transferred, given away, or simply abandoned.

The rights conveyed by a patent vary country-by-country. For

Patent law
(patents for inventions)

Overviews

Patents · History
Economics · Criticism

Processes

Application · Prosecution

example, in the United States, a patent covers research, except "purely philosophical" inquiry. A U.S. patent is infringed by any "making" of the invention, even a making that goes toward development of a new invention—which may itself become subject of a patent.

A patent being an exclusionary right does not, however, necessarily give the owner of the patent the right to exploit the patent. For example, many inventions are improvements of prior inventions that may still be covered by someone else's patent.[13] If an inventor takes an existing, patented mouse trap design, adds a new feature to make an improved mouse trap, and obtains a patent on the improvement, he or she can only legally build his or her improved mouse trap with permission from the patent holder of the original mouse trap, assuming the original patent is still in force. On the other hand, the owner of the improved mouse trap can exclude the original patent owner from using the improvement.

Some countries have "working provisions" that require the invention be exploited in the jurisdiction it covers. Consequences of not working an invention vary from one country to another, ranging from revocation of the patent rights to the awarding of a compulsory license awarded by the courts to a party wishing to exploit a patented invention. The patentee has the opportunity to challenge the revocation or license, but is usually required to provide evidence that the reasonable requirements of the public have been met by the working of invention.

Licensing · Infringement

Patentability

Patentable subject matter
Novelty · Utility
Inventive step and non-obviousness
Industrial applicability
Person skilled in the art
Prior art · Inventorship

Additional requirements

Sufficiency of disclosure
Unity of invention

By region / country

Europe
Japan
United States

Subject-matter

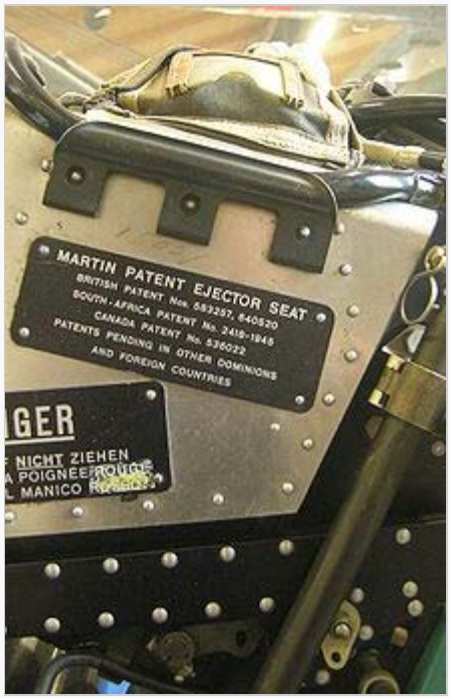
Biological patent · Gene patent
Business method · Tax patent
Chemical patent · Software patent

Category
List of concepts

v • d • e

Enforcement [edit]

Patents can generally only be enforced through civil lawsuits (for example, for a U.S. patent, by an action for patent infringement in a United States federal court), although some countries (such as France and Austria) have criminal penalties for wanton infringement.[14] Typically, the patent owner will seek monetary compensation for past infringement, and will seek an injunction prohibiting the defendant from engaging in future acts of infringement. To prove infringement, the patent owner must establish that the accused infringer practices all the requirements of at least one of the claims of the patent. (In many jurisdictions the scope of the patent may not be limited to what is literally stated in the claims, for example due to the "doctrine of equivalents").



The plate of the Martin ejector seat of the military aircraft, stating that the design is covered by multiple patents in Britain, South Africa, Canada and "others". Dübendorf Museum of Military Aviation.

An important limitation on the ability of a patent owner to successfully assert the patent in civil litigation is the accused infringer's right to challenge the validity of that patent. Civil courts hearing patent cases can and often do declare patents not valid. A patent can be found invalid on grounds that are set out in the relevant patent legislation that vary between countries. Often, the grounds are a subset of requirements for patentability in the relevant country. Although an infringer is generally free to rely on any available ground of invalidity (such as a prior

publication, for example), some countries have sanctions to prevent the same validity questions being relitigated. An example is the UK Certificate of contested validity.

The vast majority of patent rights, however, are not determined through litigation, but are resolved privately through patent licensing.[*clarification needed*] Patent licensing agreements are effectively contracts in which the patent owner (the licensor) agrees to forgo their right to sue the licensee for infringement of the licensor's patent rights, usually in return for a royalty or other compensation. It is common for companies engaged in complex technical fields to enter into dozens of license agreements associated with the production of a single product. Moreover, it is equally common for competitors in such fields to license patents to each other under cross-licensing agreements in order to share the benefits of using each other's patented inventions.

Ownership [edit]

In most countries, both natural persons and corporate entities may apply for a patent. In the United States, however, only the inventor(s) may apply for a patent although it may be assigned to a corporate entity subsequently[15] and inventors may be required to assign inventions to their employers under a contract of employment. In most European countries, ownership of an invention may pass from the inventor to their employer by rule of law if the invention was made in the course of the inventor's normal or specifically assigned employment duties, where an invention might reasonably be expected to result from carrying out those duties, or if the inventor had a special obligation to further the interests of the employer's company.[16]

The inventors, their successors or their assignees become the proprietors of the patent when and if it is granted. If a patent is granted to more than one proprietor, the laws of the country in question and any agreement between the proprietors may affect the extent to which each proprietor can exploit the patent. For example, in some countries, each proprietor may freely license or assign their rights in the patent to another person while the law in other countries prohibits such actions without the permission of the other proprietor(s).

The ability to assign ownership rights increases the liquidity of a patent as property. Inventors can obtain patents and then sell them to third parties.[17] The third parties then own the patents and have the same rights to prevent others from exploiting the claimed inventions, as if they had originally made the inventions themselves.

Governing laws [edit]

The grant and enforcement of patents are governed by national laws, and also by international treaties, where those treaties have been given effect in national laws. Patents are, therefore, territorial in nature.

Commonly, a nation forms a patent office with responsibility for operating that nation's patent system, within the relevant patent laws. The patent office generally has responsibility for the grant of patents, with infringement being the remit of national courts.

There is a trend towards global harmonization of patent laws, with the World Trade Organization (WTO) being particularly active in this area. The TRIPs Agreement has been largely successful in providing a forum for nations to agree on an aligned set of patent laws. Conformity with the TRIPs agreement is a requirement of admission to the WTO and so compliance is seen by many nations as important. This has also led to many developing nations, which may historically have developed different laws to aid their development, enforcing patents laws in line with global practice.

A key international convention relating to patents is the Paris Convention for the Protection of Industrial Property, initially signed in 1883. The Paris Convention sets out a range of basic rules relating to patents, and although the convention does not have direct legal effect in all national jurisdictions, the principles of the convention are incorporated into all notable current patent systems. The most significant aspect of the convention is the provision of the right to claim priority: filing an

application in any one member state of the Paris Convention preserves the right for one year to file in any other member state, and receive the benefit of the original filing date. Because the right to a patent is intensely date-driven, this right is fundamental to modern patent usage.

The authority for patent statutes in different countries varies. In the UK, substantive patent law is contained in the Patents Act 1977 as amended.[18] In the United States, the Constitution empowers Congress to make laws to "promote the Progress of Science and useful Arts..." The laws Congress passed are codified in Title 35 of the United States Code and created the United States Patent and Trademark Office.

In addition, there are international treaty procedures, such as the procedures under the European Patent Convention (EPC) [administered by the European Patent Organisation (EPOrg)], and the Patent Cooperation Treaty (PCT) (administered by WIPO and covering more than 140 countries), that centralize some portion of the filing and examination procedure. Similar arrangements exist among the member states of ARIPO and OAPI, the analogous treaties among African countries, and the nine CIS member states that have formed the Eurasian Patent Organization.

Application and prosecution [edit]

Main articles: Patent application and Patent prosecution

A patent is requested by filing a written application at the relevant patent office. The person or company filing the application is referred to as "the applicant". The applicant may be the inventor or its assignee. The application contains a description of how to make and use the invention that must provide sufficient detail for a person skilled in the art (i.e., the relevant area of technology) to make and use the invention. In some countries there are requirements for providing specific information such as the usefulness of the invention, the best mode of performing the invention known to the inventor, or the technical problem or problems solved by the invention. Drawings illustrating the invention may also be provided.

The application also includes one or more claims, although it is not always a requirement to submit these when first filing the application. The claims set out what the applicant is seeking to protect in that they define what the patent owner has a right to exclude others from making, using, or selling, as the case may be. In other words, the claims define what a patent covers or the "scope of protection".

After filing, an application is often referred to as "patent pending". While this term does not confer legal protection, and a patent cannot be enforced until granted, it serves to provide warning to potential infringers that if the patent is issued, they may be liable for damages.[19][20][21]

For a patent to be granted, that is to take legal effect in a particular country, the patent application must meet the patentability requirements of that country. Most patent offices examine the application for compliance with these requirements. If the application does not comply, objections are communicated to the applicant or their patent agent or attorney and one or more opportunities to respond to the objections to bring the application into compliance are usually provided.

Once granted the patent is subject in most countries to renewal fees to keep the patent in force. These fees are generally payable on a yearly basis, although the US is a notable exception. Some countries or regional patent offices (e.g. the European Patent Office) also require annual renewal fees to be paid for a patent application before it is granted.

Economics [edit]

For more details on this topic, see Economics and patents.

Rationale [edit]

There are four primary incentives embodied in the patent system: to invent in the first place; to disclose the invention once made; to invest the sums necessary to experiment, produce and market

the invention; and to design around and improve upon earlier patents.[22]

1. Patents provide incentives for economically efficient research and development (R&D). A study conducted annually by the IPTS shows that the 2,000 largest global companies invested more than 430 billion euros in 2008[23] in their R&D departments. If the investments can be considered as inputs of R&D, patents are the outputs. Based on these groups, a project named Corporate Invention Board, had measured and analyzed the patent portfolios to produce an original picture[24] of their technological profiles. Without patents, R&D spending would be significantly less or eliminated altogether, limiting the possibility of technological advances or breakthroughs.[*citation needed*]Corporations would be much more conservative about the R&D investments they made, as third parties would be free to exploit any developments. This second justification is closely related to the basic ideas underlying traditional property rights.[22][*specify*]
2. In accordance with the original definition of the term "patent," patents facilitate and encourage disclosure of innovations into the public domain for the common good. If inventors did not have the legal protection of patents, in many cases, they would prefer or tend to keep their inventions secret. Awarding patents generally makes the details of new technology publicly available, for exploitation by anyone after the patent expires, or for further improvement by other inventors. Furthermore, when a patent's term has expired, the public record ensures that the patentee's idea is not lost to humanity.[22][*specify*]
3. In many industries (especially those with high fixed costs and either low marginal costs or low reverse engineering costs — computer processors, software, and pharmaceuticals for example), once an invention exists, the cost of commercialization (testing, tooling up a factory, developing a market, etc.) is far more than the initial conception cost. (For example, the internal "rule of thumb" at several computer companies in the 1980s was that post-R&D costs were 7-to-1). Unless there is some way to prevent copies from competing at the marginal cost of production, companies will not make that productization investment.[22][*not in citation given*]

One effect of modern patent usage is that a small-time inventor can use the exclusive right status to become a licensor. This allows the inventor to accumulate capital from licensing the invention and may allow innovation to occur because he or she may choose to not manage a manufacturing buildup for the invention. Thus the inventor's time and energy can be spent on pure innovation, allowing others to concentrate on manufacturability.[25]

Costs [edit]

Some of the costs to society associated with the granting of a patent are: the immediate costs associated with preparing the patent; patent office work; legal costs associated with prosecuting alleged infringements; business costs associated with those legal actions; increasing the cost of determining whether a method is covered by an existing patent, and reduced certainty in the result; restrictions on the use of the patented method (particularly in cases where the method is redeveloped independently).

The costs of preparing and filing a patent application, prosecuting it until grant and maintaining the patent vary from one jurisdiction to another, and may also be dependent upon the type and complexity of the invention, and on the type of patent.

The European Patent Office estimated in 2005 that the average cost of obtaining a European patent (via a Euro-direct application, i.e. not based on a PCT application) and maintaining the patent for a 10 year term was around 32 000 Euro.[26] Since the London Agreement entered into force on May 1, 2008, this estimation is however no longer up-to-date, since fewer translations are required.

In the United States, direct legal costs of patent litigation are on average in the order of a million dollars per case, not including associated business costs, based on an American Intellectual Property Law Association (AIPLA) survey of patent lawyers (2005), and court documents for a sample of 89

court cases where one side was ordered to pay the other side's legal fees.[27]

Criticism [edit]

Main article: Criticism of patents

Patents have been criticized both in principle and in implementation.

In principle, patents have been criticized as a restraint of trade, for conferring a negative right upon a patent owner, permitting them to exclude competitors from using or exploiting the invention, even if the competitor subsequently develops the same invention independently. This may be subsequent to the date of invention, or to the priority date, depending upon the relevant patent law (see First to file and first to invent).[28]

As state-granted monopolies, patents have been criticized as inconsistent with free trade. On that basis, in 1869 the Netherlands abolished patents, and did not reintroduce them until 1912.[29]

In implementation, patents have been criticized for being granted on already-known inventions. In 1938, R. Buckminster Fuller wrote of the patent application process in the United States:[30]

> At present, the files, are so extraordinarily complex and the items so multitudinous that a veritable army of governmental servants is required to attend them and sort them into some order of distinguishable categories to which reference may be made when corresponding with patent applicants for the purposes of examiner citation of "prior art" disclosure. This complexity makes it inevitable that the human-equation involved in government servants relative to carelessness or mechanical limitations should occasion the granting of multitudes of "probably" invalid patent claims.

Patents may hinder innovation as well in the case of "troll" entities. A holding company, pejoratively known as a "patent troll", owns a portfolio of patents, and sues others for infringement of these patents while doing little to develop the technology itself.[31] Other commentators suggest that patent trolls are not bad for the patent system at all but instead realign market participant incentives, make patents more liquid, and clear the patent market.[32]

Another theoretical problem with patent rights was proposed by law professors Michael Heller and Rebecca Sue Eisenberg. Based on Heller's theory of the tragedy of the anticommons, the authors argued that intellectual property rights may become so fragmented that, effectively, no one can take advantage of them as to do so would require an agreement between the owners of all of the fragments.[33]

Pharmaceutical patents prevent generic alternatives to enter the market until the patents expire, and thus maintains high prices for medication.[34] This can have significant effects in the developing world, as those who are most in need of basic essential medicines are unable to afford such high priced pharmaceuticals.[35] Critics also question the rationale that exclusive patent rights and the resulting high prices are required for pharmaceutical companies to recoup the large investments needed for research and development.[34] One study concluded that marketing expenditures for new drugs often doubled the amount that was allocated for research and development.[36] Other articles shed light on the problems of today's medical research. It sets wrong priorities in research and pricing, and pushes the state-run healthcare systems even of rich nations to their limits.[37]

In one response to these criticisms, one review concluded that less than 5 percent of medicines on the World Health Organization's list of essential drugs are under patent.[38] Also, the pharmaceutical industry has contributed US$2 billion for healthcare in developing countries, providing HIV/AIDS drugs at lower cost or even free of charge in certain countries, and has used differential pricing and parallel imports to provide medication to the poor.[38] Other groups are investigating how social inclusion and equitable distribution of research and development findings can be obtained within the existing [38]

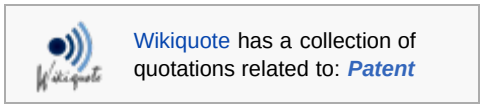
intellectual property framework, although these efforts have received less exposure.

Brazil filed a proposal in 2010 with the WIPO Standing Committee on the Law of Patents about the imbalance of rights between IP title holders and the society as a whole with emphasis on the imbalance of benefits from strong IP rights between the few developed countries and the majority of member states.[39] Such imbalance is also recognized between freedom rights and exclusion rights by the computing profession[40].

Concerns of a similar order have also been documented elsewhere, showing that public campaigns have had a concern for "preventing the over-reach" of IP protection including patent protection, and "to retain a public balance in property rights" of this kind.[41] The same source also noted the shift that had taken place away from the historical classification of such rights as "grants of privilege", towards referring to them in terms of property and rights; a change that encouraged a change of view of the relation of sovereign governments towards them, away from something that the government "may grant" towards a "duty to uphold them".[41]

See also [edit]

- List of patent legal concepts
- List of patent related topics
- List of people associated with patent law
- Category:Patent law



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12. ^ Gabriel Galvez-Behar, *La République des inventeurs. Propriété et organisation de l'innovation en France, 1791-1922*, Presses universitaires de Rennes, 2008, ISBN 2-7535-0695-7, 9782753506954.
13. ^ a b c "A patent is not the grant of a right to make or use or sell. It does not, directly or indirectly, imply any such right. It grants only the right to exclude others. The supposition that a right to make is created by the patent grant is obviously inconsistent with the established distinctions between generic and specific patents, and with the well-known fact that a very considerable portion of the patents granted are in a field covered by a former relatively generic or basic patent, are tributary to such earlier patent, and

cannot be practiced unless by license thereunder." - *Herman v. Youngstown Car Mfg. Co.*, 191 F. 579, 584-85, 112 CCA 185 (6th Cir. 1911)

14. ^ DLA Piper Rudnick Gray Cary (2005) *Patent Litigation across Europe*, handout available as per CeCollect.com.
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16. ^ See Section 39 of the UK Patents Act as an example. The laws across Europe vary from country to country but are generally harmonised
17. ^ Article 28.2 TRIPs: "*Patent owners shall also have the right to assign, or transfer by succession, the patent and to conclude licensing contracts.*".
18. ^ United Kingdom law requiring no explicit authority due to the Supremacy of Parliament.
19. ^ IP Australia website, *What does 'patent pending' mean?*, Consulted on August 5, 2009.
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24. ^ Technological profiles for global companies by analysing their patent portfolios
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37. ^ [D+C article 11/2010: Misguided research http://www.inwent.org/ez/articles/182681/index.en.shtml]
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39. ^ WIPO, SCP/14/7, Proposal from Brazil, Standing Committee on the Law of Patents, Fourteenth Session, January 20, 2010.
40. ^ Kiesewetter-Köbinger, Swen (2010). "Programmers' Capital". *Computer* **43** (2): 108, 106–107. doi:10.1109/MC.2010.47.
41. ^ [a] [b] Susan K Sell (2003), *Private Power, Public Law: The Globalization of Intellectual Property Rights*, Cambridge, 2003 (Cambridge University Press: Cambridge Studies in International Relations: 88); quoted from page 179, see also page 5.

External links [edit]

- Directory of Intellectual Property Offices, maintained by World Intellectual Property Organization (WIPO)
- Useful links, "*Your guide to intellectual property information and services on the internet.*", maintained by the European Patent Office
- OECD Patent statistics

Look up ***patent*** in Wiktionary, the free dictionary.

Categories: Intellectual property law | Patent law | Monopoly (economics) | Public records

*N*ote: The following information is meant to supplement, not supercede, the *Patent and Tangible Research Property Policies and Procedures of the University of Pennsylvania*

Roles, Responsibilities, and Expectations in Technology Commercialization at Penn

The University of Pennsylvania Center for Technology Transfer (CTT) obtains and manages patents, copyrights, and trademarks derived from the University's academic research enterprise. CTT creates relationships with industry to develop, protect, transfer and commercialize intellectual property resulting from the University's research. Drawing on the University's long tradition of innovation and service, CTT's mission is to:

- facilitate the commercialization of university discoveries for the public good;
- reward faculty and students for their commercializable discoveries;
- forge closer ties to industry;
- promote economic growth in the region and Commonwealth; and
- generate income for education and research.

It is the policy of the University that faculty inventors assign to the University all right, title and interest to their inventions and materials and partner fully with the University in the preparation and prosecution of patents related to these inventions. In return for such disclosure, assignment, and cooperation, the University commits resources to patent and license those inventions which are protectible and commercializable, and shares net income from licensing with the inventors and their laboratories, departments, and schools according to the University's Patent Policy as detailed below. CTT and the faculty work together to assure the success of the process.

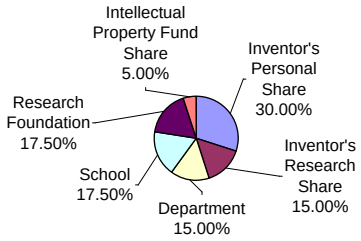
Who owns the invention?

Most universities, including Penn, require faculty members, graduate students, staff, employees, visiting professors, and the like, to assign inventions to the institution if the invention falls into any one of the following categories: (i) the invention relates to that individual's employment responsibility, or (ii) the invention results from an activity performed on Penn time and/or using Penn facilities or resources, or (iii) the activity leading to the invention was supported by a grant or contract to the University of Pennsylvania.

Who owns the patent?

The University owns the patent and, in return, provides professional services to prosecute the patent and license it, without charge to the inventor.

If the technology is licensed and successfully commercialized, how are royalties divided?
In return for the assignment of the intellectual property, Penn shares net income/royalties from licensing in accordance with the patent policy of the University:



What are the responsibilities and prerogatives of the Faculty inventor and of the CTT staff?
The technology transfer process requires the active partnership of the faculty inventor and the CTT staff. Each partner brings unique assets to the relationship. The respective roles of both partners are presented in the accompanying table, which provides a step-by-step list of activities on the path from disclosure to licensure. It is important to recognize that each partner has certain prerogatives and responsibilities and that the success of the undertaking depends upon the good faith and active cooperation of the partners.

CTT

Responsibilities include: (i) managing the expectations of faculty inventors by providing the principal investigator with a summary of the prerogatives and responsibilities of each partner; (ii) exercising due diligence in evaluating each technology for protectibility and commercial potential; (iii) keeping the principal investigator fully informed of the status of evaluation, patenting and licensing activities; and (iv) maintaining momentum throughout the process.

Prerogatives include: (i) selecting technology disclosures for patenting and licensing; (ii) determining the strategies for patenting and selecting and instructing patent attorneys; (iii) developing strategies for commercialization; (iv) determining the optimal approach for commercialization; and (v) negotiating and executing the license agreement.

Faculty

Responsibilities include: (i) filing complete technology disclosures covered by the Patent Policy; (ii) assigning to the University all right, title and interest in the technology; (iii) being available for consultation with CTT as needed; (iv) participating in discussions with patent attorneys, potential licensees, and others involved on the pathway to licensure as requested by CTT; and (v) acceptance of the prerogatives of the CTT staff in the patenting and licensure process.

Prerogatives include: (i) academic freedom to publish; and (ii) the right to decide whether or not to participate in a startup company, if this option is recommended by CTT staff.

The CTT website has a "CTT Patent Primer" that provides a useful introduction to many of the issues involved in patenting and licensure. The Primer and the Penn Patent Policy can both be found at "http:www.upenn.edu/ctt".

Faculty Consulting

Consulting relationships with a company can enrich and add perspective to academic research and teaching while allowing faculty to work on real world problems. Consulting relationships must ethically balance the consultant's primary responsibility to the University with his or her responsibility to the company. The circumstances of the consultation and those surrounding any resulting invention will determine if the faculty member is obligated to assign the invention to Penn. If it is determined that the invention should be assigned to Penn, it will be made available for license by the University to the company under favorable terms.

Faculty members are strongly advised to submit proposed consultation agreements to CTT prior to signing. CTT will review agreements to assure compliance with University policies and advise on the intellectual property aspects of the agreement.

Return to Inventor (RTI)

If CTT chooses not to pursue a technology, the faculty member has the prerogative to ask for the invention to be returned. There is a specific procedure for this event which is available on CTT's website under Information for Faculty.

RESPONSIBILITIES OF CTT STAFF AND FACULTY INVENTORS		
Activity	**Responsibility**	
	CTT staff	**Faculty**
Identify research program likely to produce results of commercial interest	**X**	**X**
Disclose research results to CTT		**X**
Faculty-CTT dialogue about disclosure	**X**	**X**
Assess disclosure for commercial potential and patentibility	**X**	
Provide feedback to PI about assessment	**X**	
Select and pay patent counsel to prepare and file patent application	**X**	
Assist counsel with patent prosecution	**X**	**X**
Sign documents required for patenting		**X**
Provide copies of references and supporting materials		**X**
Prepare non-confidential information	**X**	**X**
Market technology	**X**	**X**
Negotiate Option/License Agreement	**X**	
Provide feedback to faculty on status of licensing	**X**	
Sign deal acknowledgement form		**X**
Sign license	**X**	
Fulfill Penn COI reporting obligations		**X**
Facilitate "transfer" of technology from Penn to licensee	**X**	**X**
Monitor license agreement, pay ongoing patent maintenance fees, and distribute net income in accordance with Penn Patent Policy	**X**	

RESPONSIBLE CONDUCT OF BIOMEDICAL RESEARCH:

A Handbook for Biomedical Graduate Studies Students

Fourth Edition

BIOMEDICAL GRADUATE STUDIES PROGRAM
UNIVERSITY of PENNSYLVANIA

PREFACE TO THE FOURTH EDITION

Scientists agree that a trainee in biomedical research should be taught to maintain the highest standards of scientific integrity and ethical behavior in all phases of the conduct of research. Scientists and trainees should also be aware of the potential for subjectivity, unconscious bias and conflicts of interest that accompany the collection and treatment of data, the attribution of responsibility and credit, the mentoring of students and fellows, and the use of human and animal subjects for research. Scientific data collected and reported with the greatest care and ethical considerations may yet contain unrecognized errors due to the limitations of knowledge or technology. The requirement for high standards of scientific integrity and ethical behavior is important for a number of reasons. Scientists must be able to trust one another's work, since advances in science rely on the integrity of the research record. Furthermore, most research is carried out using public funds and thus the public should have confidence that this is money well-spent.

The goal of BGS's training in Responsible Conduct of Research (RCR) is to make graduate students aware of the rules, regulations and guidelines governing research and to minimize the potential problems associated with carrying out research. While these problems cannot be totally eliminated, they should be recognized, openly acknowledged and constructively addressed by discussions among scientists and with trainees. The incidence and consequences of misconduct can be sharply reduced by both good habits of research and by an increased understanding of what constitutes accepted responsible conduct. Education of this nature is the major goal of the RCR training program at the University of Pennsylvania.

The fourth edition of the handbook on RCR has been modified considerably, and is intended as a companion to the excellent publication, *ON BEING A SCIENTIST: third edition* (National Academy Press, Washington, DC 2009) and *Teaching the Responsible Conduct of Research Through a Case Study Approach (*a handbook prepared by the Association of American Medical Colleges, Korenman and Shipp, eds., 1994). These documents utilize a case study approach to initiate discussions of relevant issues in the conduct and training of biomedical research. The revised handbook includes additional material unique to the training of young investigators, provides practical information on the guidelines and procedures regarding alleged misconduct at the University of Pennsylvania, and includes examples of perspectives on the ethical conduct of research from the scientific community.

I would like to thank the faculty and staff of the University who assisted in editing this handbook and in developing the RCR training program. I am particularly grateful to Drs. Jane Glick and Glen Gaulton for compiling the previous three editions, to Dr. Hillary Nelson for providing material for this edition and for identifying the best available sources for RCR training and case studies and to Colleen Dunn and Judy Jackson in the BGS office for the many hours they spent executing the revised BGS RCR training and for proof-reading this document. I am also grateful to Dr. Stanley Korenman, UCLA Health System and the Association of American Medical Colleges for granting permission touse case studies and text from *Teaching the Responsible Conduct of Research through a Case Study Approach,* Korenman, S.G. and Shipp, A., eds. (AAMC, Washington, DC 1994), and to the U.S. Department of Health and Human Services, Office of Research Integrity, Nicholas Steneck, Ph.D., *ORI Introduction to the Responsible Conduct of Research (2007)* (http://ori.hhs.gov/documents/rcrintro.pdf).

Susan R. Ross, Ph.D.
University of Pennsylvania School of Medicine

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I. INTRODUCTION

The training program in Responsible Conduct of Research (RCR) has three major educational components: web-based training, program literature, and small group discussion workshops. Participation in all phases of the training program is mandatory for all graduate students in the Biomedical Graduate Studies programs.

The program is introduced through on-line RCR training available on the BGS website at http://www.med.upenn.edu/bgs/rcr.shtml. The training is designed to provide all participants with an introduction to RCR, particularly in biomedical research. The topics covered are:

A. Research Misconduct
B. Data Acquisition, Management, Sharing and Ownership
C. Mentoring
D. Collaboration
E. Conflicts of Interest
F. Publication Practices, Responsible Authorship and Peer Review
G. Human Subjects
H. Animal Welfare

All first-year graduate students must complete the introductory web-based training and pass the web-based quiz. In addition to the topic presentations, there are several RCR case studies on the web site. These are good introductions to the case study method that is the basis of RCR training for graduate students beyond the first year.

This document (RESPONSIBLE CONDUCT OF BIOMEDICAL RESEARCH: A Handbook for Biomedical Graduate Studies Students, Biomedical Graduates Studies, University of Pennsylvania, Philadelphia, PA, 2010) is the primary resource for the case study portion of the training program. It was originally written as a companion to ON BEING A SCIENTIST: A Guide to Responsible Conduct in Research, third edition (published by the National Academy Press, Washington, DC, 2009). That document is available on the web at http://www.nap.edu/catalog/12192.html. These documents utilize a case study approach to inform, stimulate discussion among and thereby educate program participants. The BGS Handbook includes a number of topics that are not included in ON BEING A SCIENTIST but that are judged to be important to the training of graduate students at the University of Pennsylvania. The BGS Handbook also includes a practical guide to acquaint students with the guidelines and procedures regarding alleged misconduct at the University of Pennsylvania and to define the appropriate sources for contact when questions arise. Copies of these booklets are available through links on the BGS web site. More detailed reference material is also available in the BGS office, 160 BRB II/III, 215-898-1030.

The final component of the training program for second, third and fourth year BGS students is topic-specific, on-line training, using the Collaborative Institutional Training Initiative (CITI), Responsible Conduct of Research Program, followed by small group discussions using a case-based study approach. Small group workshops of about 12 students are organized with two faculty preceptors each. The workshops meet for a minimum of one and one-half hours. During these workshops, students and faculty become engaged in a process of discovery together. In respect to research integrity, this includes not only learning facts, but recognizing potential ambiguities in the responsible conduct of research. The small group workshops also reveal the instructors' and students' own attitudes and prejudices, and recognition of conflicting ethical principles. This method also provides the opportunity to directly illustrate the avoidance

of misconduct through good laboratory practice. The participation of active investigators is essential in this exercise. Their involvement lends credibility to the process and may even influence the investigator's own practices.

Graduate students are expected to move through a progression of case studies that consider a specific set of topics. Second year students consider research misconduct, plagiarism, data management and lab notebooks. Third year students consider issues relating to mentoring and lab supervision, collaboration, animals and human subjects. Fourth year students discuss issues of publication practices, authorship, peer review and conflicts of interest. The cases given below are grouped accordingly, although many of the cases touch on more than one issue that may bridge topics considered in different years. Graduate students in years five and beyond have different choices for fulfilling their requirement, which may include attending University sanctioned bioethics seminars, courses or symposia sponsored by the Center for Bioethics (see http//www.bioethics.upenn.edu). Attendance at these events must be registered with the BGS office. Another option for upper level students is to co-facilitate a workshop for the second, third or fourth year students along with a faculty facilitator. This can be arranged through the BGS office.

II. A CASE STUDY APPROACH TO TRAINING OF RESPONSIBLE CONDUCT OF RESEARCH

(adapted from *Teaching the Responsible Conduct of Research Through A Case Study Approach (©1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission), Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health, and the Federal Policy on Research Misconduct*) (http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/Conduct%20Research%206-11-07.pdf)

A. Research Misconduct and Plagiarism Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records (both physical and electronic), progress reports, abstracts, theses, internal (group meetings, thesis committee meetings, etc.) and external (national/international conferences, seminars, job interviews) oral or poster presentations, internal reports, and journal articles. Fabrication is making up data or results and recording or reporting them. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit; this includes internet sources. For a detailed definition of plagiarism, see Appendix A of this document. Research misconduct does not include honest error or differences of opinion. A finding of research misconduct requires that there be a significant departure from accepted practices of the relevant research community, that the misconduct be committed intentionally, knowingly, or recklessly, and that the allegation be proven by a preponderance of evidence.

Case Studies on Research Misconduct and Plagiarism

Case #1 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Dr. Alice Charles, a mid-career scientist, was revising and updating a book chapter. This led her to review other articles on the same subject to help determine what new material to cover. During the course of her reading, she came upon a chapter in a major text by Dr. Chris Long, a departmental chair at a leading medical school, which contained long passages from her previous chapter without attribution.

Dr. Charles called Dr. Long and confronted him with her finding. At first, he vehemently denied having used any of Dr. Charles's text inappropriately. Dr. Charles then emailed Dr. Long copies of the offending passages. After some delay, Dr. Long finally responded, acknowledging that the language was indeed remarkably similar. Dr. Long noted that he had engaged younger members of his research group to write portions of the chapter because he was very busy at the time that the deadline was approaching. Furthermore, to defend himself, he pointed out that much of the original research on which her chapter was based was derived from the work of his laboratory. He admitted only to negligence in not adequately monitoring the activities of his subordinates.

Dr. Charles replied that the subordinates were not acknowledged in Dr. Long's chapter either, and that admission of plagiarism required more than an apology. She indicated her intention to report the matter to Dr. Long's Dean and the editor of the text.

Questions

1. Did Dr. Charles act appropriately? Would you have done anything differently? Considering the difference in status between herself and Dr. Long, was she taking a professional risk?
2. Did Dr. Long do anything wrong? What if he were copying his own previous writings?
3. How would you have handled this matter if you were Dr. Long and were confronted with Dr. Charles's revelations?
4. If you were Dr. Long's Dean, how would you handle Dr. Charles's letter, which contained copies of the plagiarized texts?
5. Upon hearing Dr. Charles's complaint, what would you do as editor of Dr. Long's textbook?

Case #2 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled “Teaching Research Ethics: A Workshop at Indiana University”. © 1995 by Indiana University).

Charlie West completed his doctorate in biology two years ago and is in his last year as a postdoctoral fellow in Professor Wilson’s laboratory. The last few months have been both good and bad. West and his wife were thrilled by the birth of their first child six months ago, and research has been going well. There are just a few relatively straightforward controls to be run before he and Wilson can submit a manuscript they have been preparing. In addition, West had five job interviews and was then offered a position at Heartland State University, which he has accepted.

However, his success has also caused some problems. With all the preparation and traveling for interviews plus the new responsibilities of parenting, West hasn’t had the time or energy to do very much work in the lab lately. There’s another factor as well. West promised Wilson that

he'd take care of those controls as soon as he finished interviewing but he hasn't done them yet because he's been writing a grant application. During West's second visit to Heartland, the biology department chair made it clear that West is expected to bring in external funding for the research he plans to begin at HSU in a little over a year. The chair told West, "The sooner you get a grant, the better your chances for tenure."

For his post doc, West decided to switch fields in order to learn some new techniques, but for his job he plans to return to research very close to what he did for his Ph.D. In fact, his job seminar was all based on his grad research, not the work he has done as a post doc. West has an idea for a project that everyone he has consulted agrees has great potential. He is very excited about his planned research, and is highly confident that it will be successful both with the funding agency and in the lab. The only problem seems to be getting the grant written.

Unfortunately, since this is West's first grant application, writing it is proving to be far more time-consuming than he expected. He started a couple of months ago and has written the Approach section of the Research Strategy section. All the special forms, facilities statements, biographies, supporting letters, and the budget are now done, but that still leaves the Significance and Innovation sections of the text. It seems that every time he gets set to work on the grant proposal, something goes wrong. Last week he discovered that he had forgotten the animal use forms and had to rush about getting his protocol finalized and approved. A few days ago his baby daughter was up all night with an earache. Then, just this morning, Wilson was pressing him for experimental results. "Look, Charlie," he said, "I know you've been busy, but those experiments can't wait any longer. It's been eight or ten weeks since you finished interviewing and the paper still isn't ready to submit. If we don't get moving we're going to get scooped by Joe Atkins' lab. Neither of us can afford to lose an important publication like this, especially you at this stage of your career. I want to see you at the bench tomorrow. Besides, I'm supporting you on my grant to do research in my lab, not to try to pull in money for HSU."

The NIH grant application deadline for which West has been aiming, one that could give him funding just after he arrives at HSU, is now only three days away, and it's already 10 pm. As he goes through his files, frantically pulling out relevant articles while feeling fairly sure that there is no way he can get the writing done in time, he comes across a grant proposal on a similar topic that he had helped a professor review while he was a graduate student. The professor had also pointed out that it was a model proposal — scientifically sound and extremely well-written. As he looks at the photocopy he kept, West realizes that the Significance and Innovation sections of this older grant would fill in 90% of the information he needs. He could easily write the other 10% in three days. Reasoning that grant proposals are funded mostly on the quality of the proposed work, West decides to copy and paste theSignificance and Innovation sections from the old grant, add his own Research Strategy section and update the Reference section with papers that have been published in the last two years, and be done with it. This way everyone should be happy.

Questions

1. Should West use the material this way? Why or why not?
2. Should West have kept a copy of the proposal?

Case #3 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Professor Diane Archer is a tenured member of a biology department at a major Midwestern university. She has been in the department for 15 years, and during that time she has supervised the work of 20 Ph.D. students. As part of the mentoring process, she has worked closely with her students, teaching them the ropes of writing grant proposals and on occasion inviting students to assist her in reviewing NIH grant applications.

Professor Archer is currently in her last year on an NIH study section. As she is reviewing a group of proposals, she comes upon one written by Charlie West, a former graduate student of one of her close departmental colleagues. Archer knows and remembers Charlie West because she had solicited his help two years earlier in reviewing a proposal closely related to West's own area of research. As she now reads West's proposal, Archer is impressed with the scientific soundness and fine writing style in the Significance and Innovation sections. She notes, however, the extremely terse and awkward phrasing in the Approach section. Perplexed by this shift in style, Archer retrieves from her files the grant proposal West had reviewed with her two years earlier. She is dismayed to see that West has used verbatim virtually the entire Significance and Innovation sections of the earlier proposal for his own current proposal.

Archer is torn. If she reports her discovery of West's plagiarism to the NIH, she knows she will have thrown this young scientist's otherwise promising scientific career into jeopardy. If, however, she says nothing, she will be shirking her responsibility to the NIH, as well as risking her own professional reputation, should the plagiarism be detected later. She decides to contact West directly, and confront him with her finding. She plans to advise West that what he has done constitutes plagiarism and suggest to him that he withdraw the proposal.

If West agrees, and withdraws the grant application, Archer feels she need take this incident no further.

Questions

1. Should Archer proceed with her plan to contact West? Why or why not? Is there anyone else she needs to contact?
2. Should Archer have solicited West's assistance in reviewing the grant?
3. Should Archer have kept grants that she had reviewed in her files?

Case #4 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Alan Yeager has completed a series of experiments characterizing the receptor for a new class of hormones. During the course of his work, he studied binding characteristics and hormonal responses in tissue culture and in vitro, utilizing gels to characterize the molecular weights of receptor variants. This was exciting work for a second-year graduate student doing his first project. One day, Alan's laboratory chief asked him to prepare an abstract for an upcoming meeting and a paper for publication, both to be based on the work Alan had been doing. The abstract was due in one week.

As Alan examined his accumulated data, he noted that a number of cell culture plates failed to respond to the hormonal stimulus and that there was considerable variability in the dose-response relationship. Furthermore, on reexamination, he noted that a number of his gels were not very aesthetic in appearance, yet he was sure that they demonstrated the molecular weight, agonist binding, and subunit characteristics of the receptor.

Alan mentioned his distress to Pam Alden, a fifth-year graduate student, who said, "Why don't you clean up your data? You'll never get the paper published unless you do. We always clean up the data around here." She then suggested that the four culture points failing to show a response be dropped because the cells were probably dead. She also pointed out that he might eliminate the top data point at the 45 minute interval as an outlier. She examined the gels and suggested using Adobe Photoshop™ to improve the quality of the pictures, including the duplication of one of the nicer gel lanes to replace another that turned out poorly, but showed essentially the same result. "That will greatly improve your chances of publication," she said. Alan replied, "Maybe I should repeat a few of the experiments or try to improve the culture conditions?" "No," said Pam, "If you're convinced of your results, why go through the time, expense, and uncertainty of more repetitions? You'll never complete an experiment in time for the abstract, anyhow." Somewhat dismayed, Alan thanked her and turned back to his work.

Questions

1. What do you think about Pam's comments on publication practices and her suggestions for "cleaning up" the data?
2. How should Alan go about determining which points to include and which to exclude?
3. What other course(s) of action would you recommend to Alan?
4. Pam's perception about improving the chances of publication by "cleaning up" the data is not uncommon. How might journal editors and reviewers work toward correcting this perception?

Case #5 (©ASM Press. This case is from Francis L. Macrina (2000): Scientific Integrity, 2nd edition, published by ASM Press. Appropriate permission being processed.)

Jim, a new assistant professor, is getting ready to submit his first paper since joining the faculty. He reviews one of the figures for this paper which is a photo of an ethidium bromide-stained agarose gel. The gel contains the products of polymerase chain reaction (PCR)-amplified whole cell DNA. The photo displays the predicted 3 kb DNA fragment. Jim comments that a second minor signal was also evident on the original gel. Based on its size, Jim believes that this second fragment represents a very exciting discovery, but it needs considerable additional work. This second fragment cannot be seen in the photograph because Jim discloses that he has deliberately cropped the photo to obscure the second fragment. He says he did this because he is worried that competing groups in larger, more established labs will interpret the potential of the second fragment and they will "scoop" him. He has prepared a figure legend that says: "a second minor signal of unexplained origin was present in this experiment but is not shown in the figure". But, the figure legend does not include the size of the unexplained fragment. Thus, he argues he'll be telling the truth while, at the same time, he'll be protecting himself from his competition.

Questions

1. Are Jim's actions appropriate?

2. Is he simply playing fairly in the hotly competitive arena of biomedical research, falling victim to self-deception or perpetrating scientific fraud?

B. Data Acquisition, Management, Sharing and Ownership Research data, including detailed experimental protocols, all primary data, and procedures of reduction and analysis are the essential components of scientific progress. Scientific integrity is inseparable from meticulous attention to the acquisition and maintenance of these research data.

The results of research should be carefully recorded in a form that will allow continuous access for analysis and review. Attention should be given to annotating and indexing notebooks and documenting computerized information to facilitate detailed review of data. All data, even from observations and experiments not directly leading to publication, should be treated comparably. All research data should be available to scientific collaborators and supervisors for immediate review, consistent with requirements of confidentiality. Investigators should be aware that research data are legal documents for purposes such as establishing patent rights or the veracity of published results when the data are challenged. The data are subject to subpoena by congressional committees and the courts.

Research data, including the primary experimental results, should be retained for a sufficient period to allow analysis and repetition by others of published material resulting from those data. In general, five to seven years is specified as the minimum period of retention but this may vary under different circumstances.

In most cases, such as with federally-funded research, the university owns the data, not the faculty, graduate students, postdoctoral fellows or staff who perform the research (see Appendix B). Notebooks, other research data, and supporting materials, such as unique reagents, belong to the university, and are entrusted to the laboratory in which they were developed. Departing investigators may take copies of notebooks or other data for further work if approved by the responsible principal investigator. For industry-sponsored research, data may belong to the sponsor. This is usually negotiated with by the investigator and the university with the industry sponsor prior to initiating the research.

Data management, including the decision to publish, is the responsibility of the principal investigator. After publication, the research data and any unique reagents that form the basis of that communication should promptly and completely be made available to all responsible scientists seeking further information. Exceptions may be necessary to maintain confidentiality of clinical data or if unique materials were obtained under agreements that preclude their dissemination.

Sharing of reagents/resources is an important part of the scientific enterprise and is required by federal funding agencies and most journals. Reagents/resource sharing allows other investigators to both repeat and extend studies and thereby advance research. This includes not only reagents/resources such as plasmids and novel chemical reagents, but model organisms such as transgenic mice. Similarly, genome-wide association study data funded by the federal government are required to be made publically available. For more information on these policies, see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html, NIH Guide NOT-OD-04-042 and http://grants.nih.gov/grants/gwas/.

Authors should not lose sight of the principle that a major purpose of publication is to allow repetition or extension of the research findings. The information given, its accuracy, and the

CONCLUSION

With increased public funding of biomedical research, there is an increased demand for regulation and review of the efforts of scientists and institutional administrators to prevent, detect, and correct lapses in research integrity. Significant resources are now spent investigating incidents that do not involve false data but arise from a disregard or ignorance of the obligations of students, professors, and institutes. We argue that many of these conflicts stem from inappropriate conceptions about the ownership of research, which may derive from types of scientific endeavors, such as those of inventors, that are remote from most basic biomedical research.

What is still of great importance is a recognition that truthfulness in science is essential and precious. Some scientists are dishonest, and they can inject a small amount of false data into the current body of knowledge. Yet, more substantial damage is done to the fabric of trust in science by uncertainty about what the basic obligations are. There are additional levels of financial and administrative control over scientists who are held publicly accountable in their research. The leaders and teachers in our public and private institutions may have failed to place sufficient emphasis on teaching scientific ethics or even the near-universal rules of the research community. These rules may not be obvious to all members of the broad research community, and they are not all observed in nonscientific society. Honest and accurate reporting of data, generous and accurate crediting of the sources of ideas and words, and responsible reporting of research accomplishments are not gentlemanly luxuries in science, but necessities.

III. A PRACTICAL GUIDE TO QUESTIONS OF SCIENTIFIC MISCONDUCT (see Appendix C for the University of Pennsylvania's definition of research misconduct)

A. What To Do If You Have A Question, Or Feel That You Are A Victim Of Discrimination Or Harassment, Or Suspect Unethical Behavior Or Scientific Misconduct

If a member of the research community suspects that research by a particular individual, group of individuals, or laboratory is not being conducted in accordance with the generally accepted ethical standards, the individual should make his or her concerns known to one of the following: the appropriate departmental chair, graduate group chair, the Director of Biomedical Graduate Studies, the Executive Vice Dean and Chief Scientific Officer of the School of Medicine, the Ombudsman in the Medical Center or University (see below), or the Dean of the appropriate school. This disclosure should be made with utmost discretion, confidence, and guard for the rights of the alleged transgressor and the accuser. Further actions of the accuser should then be in full accord with the stated University policy.

B. What To Do If You Are Accused of Misconduct

If a BGS student is accused of misconduct in research, that individual should promptly consult with the Director of Biomedical Graduate Studies, the Executive Vice Dean and Chief Scientific Officer of the School of Medicine or the Dean of the appropriate school for complete information about the inquiry and review process as well as the rights of the accused person. The accused person has the right to engage legal counsel at any stage, including prior to meeting with any University official or faculty member.

C. University Ombudsman *(http://www.upenn.edu/ombudsman/))*

The University of Pennsylvania's Office of the Ombudsman was established in 1971 to assist individuals to find solutions to problems that they may not have been able to resolve through normal channels.

The Office of the Ombudsman is staffed by the University Ombudsman, a tenured faculty member (part-time), and an Associate Ombudsman (full-time). It is available for all members of the University community, with the exception of unionized workers at Penn and the employees of the Hospital of the University of Pennsylvania. Students, faculty, staff, and administrators seek assistance in addressing a variety of problems: academic disputes, access to resources, conflict in the workplace, compensation equity, failure to follow university procedures, and interpersonal tensions.

In all cases, initial complaints are heard confidentially. Further action is taken only when complainants want the Office to proceed on their behalf. If a complainant wishes it, the Ombudsman will approach the person or persons complained of, discuss the nature of the complaint that has been filed, and give him or her the opportunity to respond. The Office serves as an impartial mediator. We work to find solutions that are acceptable to both the complainant and the respondent.

The office is concerned with safeguarding individual rights and promoting better channels of communication throughout the University. The Ombudsman acts independently and is not an advocate for any one individual or group. He or she is an advocate for fairness, adherence to University regulations, due process, and personal responsibility. The Office supplements, but does not replace, any existing grievance mechanisms or modes of redress. It can and does recommend changes in the existing rules and practices.

The overarching mission of the Office of the Ombudsman is to resolve issues of equity and justice at the University of Pennsylvania before the tensions of polarization escalate.

D. School of Medicine Ombudsman

The mandate for the Office of the Ombudsman in the Medical Center is to provide a confidential, disinterested forum for individuals engaged in biomedical research including students, faculty and staff, who believe that their individual rights in this arena have been abrogated or who believe that a breach in ethical conduct of research has occurred.

It is not intended that the Medical Center Ombudsman will replace his or her University counterpart. Records of the University Ombudsman show that Medical Center individuals have, in the past, utilized the University Office of the Ombudsman, and it is intended that this avenue for redress of injustices be continued. The attention of the Medical Center Ombudsman is directed specifically to issues of ethics in biomedical research community. Examples of such issues are discrimination and harassment, differences of opinion over publication or presentation of disputed data, claims of ownership of research results, disputes over priority of authorship, concerns over inappropriate use of research funds, problems arising in the use of human or animal subjects, plagiarism and data distortion or fabrication.

The primary activity of the Ombudsman is as an advisor and mediator. The Ombudsman can advise the complainant of his or her rights and duties and can recommend that individuals bring their case to the appropriate University judicial and/or sanctioning offices.

E. Policy on Accusation and Response to Allegations of Research Misconduct at the University of Pennsylvania

In July 2004 edition of the Almanac, the Provost's Council on Research published a revised statement defining the University's expectations regarding **Misconduct in Research for Nonfaculty members of the Research Community** and its policy for dealing with allegations of misconduct in research by students, postdoctoral fellows and staff (http://www.upenn.edu/almanac/volumes/v51/n01/OR-research.html). A similar policy exists for faculty. The document states that "The University relies on all members of its research community to establish and maintain the highest standards of ethical practice in academic work, including research. Misconduct in research is prohibited and represents a serious breach of both the rules of the University and the customs of scholarly communities." The main steps in the procedure are summarized below:

Preliminary Inquiry

An inquiry into an allegation of misconduct in research is initiated when a written complaint is filed with the Vice Provost for Research along with the responsible administrative entities, who determine jurisdiction. The Vice Provost then forwards the complaint, in the case of BGS students, to the Associate Dean for Biomedical Graduate Studies and the Dean of the school in which the student is performing the research. The Dean informs the respondent of the charges without identifying the complainant. The Dean and Associate Dean appoint a preliminary inquiry committee of one or more impartial individuals and notify the complainant and respondent of the names of the individuals on the preliminary inquiry committee.

The preliminary inquiry committee gathers information and determines whether the allegation warrants a formal investigation. The committee submits a written report to the Dean and Associate Dean with a copy to the Provost, the complainant, and the respondent. The report should be submitted within 30 calendar days of the receipt of the original complaint by the Dean.

If the preliminary inquiry committee finds that a formal investigation is not warranted, the Dean, in consultation with the Provost, may: (1) initiate a formal investigation despite the recommendation of the preliminary inquiry committee; (2) not initiate a formal investigation, but take such other action as the circumstances warrant; or (3) drop the matter.

If the preliminary committee finds that a formal investigation is warranted (or if the Dean and Provost decide to proceed with a formal investigation), the Dean notifies the complainant and respondent, identifies the complainant to the respondent, and initiates a formal investigation. The Provost notifies the relevant funding agencies and identifies the respondent to the agency or source.

Formal Investigation

The Dean appoints a formal investigation committee of at least two impartial individuals with sufficient expertise, one or more of whom may have served on the preliminary inquiry committee. The formal investigation committee reviews the allegations and all relevant information, conducts interviews with the respondent, complainant, and other appropriate parties, and consults with University counsel. Within 90 calendar days of the appointment of the formal investigation committee, the committee submits its final written report and documentation to the Dean, with copies to the Provost and respondent.

The respondent has an opportunity to submit a response to the Dean, Provost and Vice Provost for Research within 15 calendar days; any response is appended to the formal investigation committee's report.

Resolution
After acceptance of the report by the Dean and the Provost or the Vice Provost/designee, a copy of the report will be submitted containing the outcome of the investigation to the appropriate government agency or source funding the research, if appropriate. The entire formal investigation process should be completed within 120 calendar days of its initiation, unless documented circumstances warrant a delay.

If the formal investigation committee finds that the allegations are unfounded, the matter is dropped. The Dean and Provost have the responsibility to take an active role to repair any damage done to the reputation of the respondent or the complainant (provided the complainant acted in good faith), and to take appropriate action should they determine that the accusation was knowingly false.

If the charges are substantiated, the Dean, in consultation with the Associate Dean, imposes appropriate penalties in accordance with University procedures. In the case of a major offense, the Dean and Associate Dean determine if there is just cause for suspension or termination. If the offense is found to be less serious, the Dean and Associate Dean may impose a lesser penalty. The respondent has access to the University's grievance procedures.

If the charges are substantiated, the matter will be referred to the Associate Dean for Biomedical Graduate Studies and the Dean of the school in which the student is performing the research, to determine the appropriate University sanctions. The Provost takes the steps necessary to correct any resulting misrepresentations by notifying collaborators, professional societies, and publishers involved.

IV. APPENDIX MATERIALS

A. Defining Plagiarism

(Excerpts from: The Historical, Cultural, and Social Aspects of Plagiarism: The Implications for Scientific Misconduct Investigations, Dr. Marcel LaFollette, Center for International Science and Technology Policy, The George Washington University. Also adapted from: Avoiding plagiarism, self-plagiarism, and other questionable writing practices: A guide to ethical writing, Miguel Roig, Ph.D., 2006; http://facpub.stjohns.edu/~roigm/plagiarism/)

Like puns and jokes, the metaphors for plagiarism also roll easily off the tongue; "picking someone else's mind," "mining someone else's prose." There is a flock or ornithological metaphors: "borrowed plumes," "parroted prose," "hatching stolen eggs." Redfern points out that many of the common phrases exploit the same euphemism, i.e., "borrowing". It is, however, misleading. A plagiarist does not really "borrow." He or she may take the words, but does so with no intention of giving them back, and with every intention of permanently stealing credit. The difference in perception represented by the words chosen as substitutes for "plagiarism" -- e.g., regarding copying as a breach of etiquette (borrowing without permission) rather than as a serious crime (theft) -- in fact, reflects the differences in interpretation that characterize many plagiarism disputes involving former colleagues, co-workers, or co-authors throughout the scientific community.

There are common elements to most serious definitions: 1) the use of another's words, text, ideas, or illustrations; 2) failure to credit the original ("real") author; 3) the implication statement that the plagiarist is the author; and 4) failure to seek the original author's consent. All four elements must be present (in proportions that may differ among research fields) for plagiarism to have taken place in the context of research communication in the sciences and social sciences.

None of these elements on its own constitutes misconduct, in fact. The act of simply using another's words or ideas is not plagiarism, and it may even be encouraged. Scientists and scholars want their ideas used and their words quoted. Those uses serve as measures of intellectual influence, and underpin the rationale for citation analysis. Moreover, scientists and scholars must use one another's work, or at least they must be familiar with that work in order to avoid duplicating it or repeating common errors. Graduate students are encouraged to become familiar with the great writers and thinkers in their fields. Researchers are praised for being "creatively derivative," for moving in just the right direction, while relying on their predecessors' insights as guideposts to intellectual terra incognito. For those whose work is interdisciplinary, innovation may only come from being derivative of two (or more) fields, perhaps re-assembling insights not previously applied to the problem studied.

Finally, failing to obtain a writer's consent to use his or her words is not necessarily unethical as long as one does not attempt to obscure authorship, as long as one gives appropriate credit. It is also not illegal as long as the legal boundaries of copyright and "fair use" are observed. But if all four aspects are present -- if there is use, a failure to credit, a deliberate false identification of authorship, and no consent by the real author -- then plagiarism has occurred.

To obscure authorship is also not necessarily to commit plagiarism. Washington is full of people who earn an honest living by writing for others, who produce "works-for-hire" that are published without their names. In addition, it is acceptable practice in some circumstances (again, as in the case of a work for hire) for person A even to state or imply that A is the author, when he or she is not, if A has commissioned or sponsored the work.

Whether these conditions also pertain in the case of "corporate" works written for hire, i.e. ghost-written works, has recently come under public scrutiny. Senator Charles Grassley, the ranking Republican on the Senate Finance Committee, has written to a number of major medical schools questioning the practice of using professional writing companies to write research articles based on studies performed with NIH funding. The BGS Code of Conduct (http://www.med.upenn.edu/bgs/docs/BGS_conduct.pdf) prohibits BGS students from authorship on such articles because it states: "*Plagiarism: using the ideas, data or language of another without specific and proper acknowledgment*"; all authors must be acknowledged on publications on which BGS students are co-authors.

Students should also be aware of the concept of self-plagiarism, the verbatim re-use of one's own written work. As paraphrased from Roig, the publication of essentially the same paper in more than one journal without any indication that the paper has been published elsewhere (i.e., redundant and duplicate publication) and the practice of text recycling in papers, grant proposals and other written documents all constitute self-plagiarism issues. This practice can also result in copyright infringement. Most journals require that the authors confirm that newly submitted manuscripts have not been published elsewhere. The use of relatively short direct quotes from a published work does not usually require permission from the copyright holder as it typically falls under the "fair use" provision. While it is fair to use relatively short direct quotes from a published work, extensive quoting of published text forms a copyright infringement even if the text is properly enclosed in quotation marks or correctly paraphrased and properly cited.

Students should be aware that copyright infringement extends to theses. If one includes figures or text from published manuscripts without alteration in one's thesis, permission must be obtained from the publisher. The ability to do on-line searches for particular text makes it exceptionally easy to identify plagiarism and self-plagiarism, as well as copyright infringement.

B. Ownership of Research

Taken from: Office of Research Integrity, Nicholas Steneck, Ph.D., *ORI Introduction to the Responsible Conduct of Research (2007)* (http://ori.hhs.gov/documents/rcrintro.pdf
Research produces data. As a product, common sense might suggest that the person who conducts the research should own the product—the data. In fact, conditions imposed by funders, research institutions, and data sources may dictate otherwise.

Funders. Funders provide support for research for different reasons. Government is interested in improving the general health and welfare of society. Private companies are interested in profits, along with benefits to society. Philanthropic organizations are interested in advancing particular causes. These different interests translate into different ownership claims. Typically:

- Government gives research institutions the right to use data collected with public funds as an incentive to put research to use for the public good (see the discussion of the Bayh-Dole Act, Chapter 5).

- Private companies seek to retain the right to the commercial use of data.

- Philanthropic organizations retain or give away ownership rights depending on their interests.

Since the claims of funders can and do vary considerably, researchers must be aware of their obligations to them before they begin collecting data. With government funding, it is important to distinguish between grants and contracts. Under grants, researchers must carry out the research as planned and submit reports, but control of the data remains with the institution that received the funds (see below). Contracts require the researcher to deliver a product or service, which is then usually owned and controlled by the government. If your research is supported with government funds, make sure you know whether you are working under a grant or a contract. The difference is significant and could determine who has the right to publish and use your results.

At Penn, faculty, graduate students, postdoctoral fellows or staff performing research in a university do not own the data collected. Employees work for hire for the university, which, in most cases, owns the rights to the data. Students and postdoctoral fellows sign a participation agreement that governs Research Property (http://www.med.upenn.edu/postdoc/documents/participation.agreement.pdf). Data and data books collected by undergraduates, post-baccalaureate students, graduate students, and postdoctoral fellows on a research project belong to the grantee institution. Students may not take their data when they leave without making appropriate arrangements. Retaining copies of data is allowed with permission and is usually good practice. When faculty members leave an institution, they have to negotiate with the university to keep their grants and data.

C. Procedures Concerning Misconduct in Research for Non-Faculty Members at the University of Pennsylvania

These procedures, prepared as of May 18, 2004 are those that would apply to BGS students. The procedures for faculty can be found at http://www.upenn.edu/almanac/volumes/v51/n01/OR-research.html

Introduction

The University relies on all members of its research community to establish and maintain the highest standards of ethical practice in academic work, including research. Misconduct in research is prohibited and represents a serious breach of both the rules of the University and the customs of scholarly communities.

The following procedures are applicable to nonfaculty members of the University of Pennsylvania research community including students, postdoctoral fellows, and staff.

Research Misconduct Defined

Research misconduct is defined as fabrication, falsification, plagiarism, or other serious deviation from accepted practices in proposing, performing, or reviewing research, or in reporting research results.

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, or results, or works without giving appropriate credit.
- Serious deviation from accepted practices includes but is not limited to stealing, destroying, or damaging the research property of others with the intent to alter the research record; and directing or encouraging others to engage in fabrication, falsification or plagiarism. As defined here, it is limited to activity related to the proposing, performing, or reviewing of research, or in the reporting of research results and does not include misconduct that occurs in the research setting but that does not affect the integrity of the research record, such as misallocation of funds, sexual harassment, and discrimination, which are covered by other University policies.

The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records, both physical and electronic, progress reports, abstracts, theses, oral presentations, internal reports, and journal articles.

Some forms of misconduct, such as failure to adhere to requirements for the protection of human subjects or to ensure the welfare of laboratory animals, are governed by specific federal regulations and are subject to the oversight of established University committees. However, violations involving failure to meet these requirements may also be covered under this policy or possibly by other University policies when so determined by the responsible committees or institutional officials.

Research misconduct does not include honest error or differences of opinion.

Findings of Research Misconduct

A finding of research misconduct requires that:

- There be a significant departure from accepted practices of the relevant research community; and
- The misconduct be committed intentionally, or knowingly, or recklessly; and
- The allegation be proven by a preponderance of evidence.

Jurisdiction and Applicable Process

There are a number of University policies and procedures for responding to allegations of misconduct by students, postdoctoral fellows, or staff. This policy is intended to be invoked only in instances where research misconduct (i.e. activity related to the proposing, performing, or reviewing of research, or in the reporting of research results and which therefore may have an impact on the integrity of the research record) is involved. Questions of jurisdiction and the applicability of the appropriate University procedure will be decided by the responsible administrative entity (such as the Office for Student Conduct, Office for Postdoctoral Programs, or the Office of Human Resources), in consultation with the Vice Provost for Research. Allegations of misconduct not involving the research process or the integrity of the research record will be resolved by the disciplinary process ordinarily applicable.

1. Inquiry

1.1 Allegations of research misconduct should be directed in the first instance to the Vice Provost for Research who, along with the responsible administrative entity, will determine jurisdiction and which process is applicable to resolve the allegation. If the Vice Provost determines that this process is properly invoked, the Vice Provost will forward the complaint—which must be in writing—to the Dean of the School where the research is being performed

1.2 Upon receipt of a properly documented complaint, the Dean will inform the respondent of the nature of the charges, and will provide the respondent with a copy of these procedures. The Dean will also take steps to secure relevant documents, data and other materials.
The Dean will appoint one or more unbiased, impartial individuals with appropriate expertise who will conduct a preliminary inquiry to determine whether a full investigation is warranted.

1.3 The inquiry committee will gather information and determine whether there is sufficient, credible basis to warrant a formal investigation. The committee shall offer the respondent an opportunity to provide them with relevant information regarding the allegations. The committee will submit a written report of its assessment to the Dean and the respondent, and to the complainant where appropriate. The report should state what evidence was reviewed, summarize relevant interviews, and include the committee's recommendation. This report will ordinarily be submitted within 30 calendar days of receipt of the written complaint by the Dean.

1.4 If the report of the inquiry committee determines that a formal investigation is not warranted, the Dean may (i) drop the matter, or (ii) not initiate a formal investigation, but take such other action as the circumstances warrant, or (iii), in extraordinary circumstances, nonetheless initiate a formal investigation. The Dean will inform the concerned parties of the decision.

1.5 If the inquiry committee determines that a formal investigation is warranted, the Dean will initiate a formal investigation as provided in Section 2. The Provost (Vice Provost/designee) will inform the appropriate government agency or source funding the research, in writing, that a

formal investigation has been initiated and will identify the respondent to the agency or source (1).

2. Formal Investigation

2.1 To initiate a formal investigation, the Dean will appoint a formal investigation committee of not less than two disinterested individuals with sufficient expertise, one or more of whom may have served on the preliminary inquiry committee.

2.2 Investigation. The formal investigation committee will be provided with copies of the complaint, the report of the initial inquiry and any other materials acquired during the preliminary inquiry. The formal investigation committee will undertake a thorough examination of the allegations, including, without limitation, a review of relevant research data and proposals, publications, correspondence, and records of communication in any form. Experts within or outside the University may be consulted. The Committee shall have authority to investigate, pursue and document any related research misconduct by therespondent, even if such misconduct was not covered by the initial complaint. Whenever possible, interviews will be conducted with the complainant, as well as with others having information regarding the allegations. The Committee must allow the respondent an opportunity to be interviewed at this formal investigation stage. When being interviewed by the committee the respondent and the complainant may each be accompanied by an adviser, who may be a lawyer but who may not participate directly in the proceedings except when and as requested to do so by the committee.

2.3 Reporting the findings. Following its investigation, the formal investigation committee will prepare and provide a written report of its findings to the respondent, to the Dean, to the Provost, and, if appropriate, to the complainant. The report will describe the allegations investigated, how and from whom information was obtained, the findings and basis of the findings, and will include texts or summaries of the interviews conducted by the committee. The report will conclude with a clear statement regarding which charges have been considered and what its findings are with respect to each charge the committee considered. If the committee finds that a violation of University policy in addition to or other than research misconduct might have been committed, a description of the possible violation will be included.

The committee will indicate whether each charge considered during the course of its proceedings is unsubstantiated or substantiated by a preponderance of evidence. If the matter involves a respondent who would be subject to University sanctions for misconduct only if the evidence met a clear and convincing standard, the Committee will make an additional determination as to whether that standard has also been met (2).

The final report will ordinarily be submitted within 90 days of the appointment of the formal investigation committee. The respondent will be permitted to make a written reply to the Dean with a copy to the Provost, and Vice Provost for Research, within 15 calendar days of submission of the report. The Dean may ask the committee to respond in writing to any replies from the respondent. The Dean may also ask the complainant to respond to the report if deemed appropriate. All such responses and replies will be incorporated as appendices to the report of the formal investigation committee.

3. Disposition of Final Report and Findings

3.1 The Dean will consider the final report and replies. Upon acceptance of the report by the Dean, the Provost (Vice Provost/designee) will submit a copy of the report containing the

outcome of the investigation to the appropriate government agency or source funding the research, if such action is required by regulation or otherwise appropriate. The entire formal investigation process should be completed within 120 calendar days of its initiation, unless documented circumstances warrant a delay.

3.2 If the final report of the formal investigation committee finds the charges of research misconduct against a respondent not to be substantiated, the research misconduct proceeding is terminated and the concerned parties will be informed. A finding that a charge of research misconduct has not been substantiated shall not preclude the University from taking other appropriate action against the respondent if the respondent's behavior or actions violate another University policy or rule.

3.3 If the report of the formal investigation committee finds the charges of research misconduct against a respondent to be substantiated, the matter will then be referred to the responsible administrative entity within the University to determine the appropriate University sanctions, if any, to be imposed for the misconduct (3).

4. Other Actions and Procedures

4.1 The Dean in consultation with the Provost will, during the course of the inquiry or formal investigation, take administrative action, as appropriate to protect the welfare of animal or human subjects.

4.2 At any time during the inquiry or formal investigation, the Dean and Provost will immediately notify the relevant funding agency(ies) if public health or safety is at risk; if agency resources or interests are threatened; if research activities should be suspended; if there is reasonable indication of possible violations of civil or criminal law; if Federal action is required to protect the interests of those involved in the investigation; if the University believes the inquiry or formal investigation may be made public prematurely so that appropriate steps can be taken to safeguard evidence and protect the rights of those involved; or if the research community or public should be informed.

4.3 If the final report of the formal investigation committee finds charges have been substantiated, the Provost or Dean will take appropriate steps to correct any misrepresentations resulting from the misconduct. If, at any time during the inquiry or investigatory stages, the respondent admits to the alleged misconduct, the Dean will take the necessary steps to complete the inquiry in order to correct the scientific record. If misrepresented results have been submitted for publication, already published, or otherwise disseminated into the public domain, appropriate journals and other sponsors will be notified. In addition, collaborators, and other affected individuals, organizations, institutions, and sponsors will be informed.

4.4 Complete records of all relevant documentation on cases treated under the provisions of this policy will be preserved by the offices of the Dean and the Provost in a manner consistent with the Protocols for the University Archives and Record Center. In cases adjudicated under Section 3, records will be preserved for a minimum of ten years following completion of all proceedings. Records of cases which are dropped will be preserved for at least three years following the initial inquiry. When students are involved in these procedures, the confidentiality provisions applicable to educational records will govern the disclosure of the records.

4.5 The University may act under these procedures irrespective of possible civil or criminal claims arising out of the same or other events. The Dean, in consultation with the Provost and the general counsel, will determine whether the University will proceed against a respondent

who also faces related charges in a civil or criminal tribunal. If the University defers proceedings, it may subsequently proceed irrespective of the time provisions set forth in these procedures.

Endnotes

1. The decision to initiate a formal investigation must be reported to the Office of Research Integrity, Department of Health and Human Services, if the research has been supported by a grant from DHHS, according to DHHS regulations.
2. There is a discrepancy between University regulations, which use the standard of "clear and convincing" evidence, and regulations of the Office of Research Integrity, which use the lower standard of "preponderance of evidence." Therefore, if there is a finding of fault, the inquiry must explicitly state whether the higher University standard is met, to inform the University administrative entity which is responsible for determining possible sanctions.

3. The intent of this policy is that the appropriate administrative entity will take responsibility for determining and implementing sanctions.

For instance, if the respondent is an undergraduate student any disciplinary sanctions will be determined by the Office of Student Conduct in accordance with its amended Charter procedures dealing with research misconduct findings. In order to determine sanctions, the findings and accompanying documents should be forwarded to the Office of Student Conduct. Upon review of all findings, including all submissions by the respondent etc., the Office of Student Conduct will propose appropriate sanctions to the respondent. The respondent would then have an opportunity to accept, reject or propose alternative sanctions. If either the original sanction or an alternative sanction is accepted and agreed upon, the OSC then has primary responsibility for implementing and monitoring sanctions. If the respondent rejects the sanction, the respondent may appeal the nature and severity of the sanction only to the Disciplinary Appellate Officer within the Student Disciplinary System. If the decision of the appellate officer is to uphold the proposed sanction, the sanction will be imposed, with no further levels of review.

Likewise, if the respondent is a graduate student, postdoctoral fellow, or staff member, the responsible administrative entity would consider the information and determine sanctions.

OF RECORD

The Senate Committee on Academic Freedom and Responsibility (SCAFR) recently reviewed the proposed revisions to the Procedures Regarding Misconduct in Research *that had been drafted by a faculty committee chaired by David Manning and reviewed by the Senate Committee on the Faculty (*Almanac *May 7, 2002). SCAFR approved the document with one change. Upon SCAFR's recommendation, the Senate Executive Committee approved the following version at its meeting on April 2, 2003. These procedures become effective immediately and supersede those published in* Almanac *September 9, 1997.*

— Robert Barchi, Provost —Neal Nathanson, Vice Provost for Research

Procedures Regarding Misconduct in Research

Introduction

The University relies on its faculty to establish and maintain the highest standards of ethical practice in academic work including research. Misconduct in research is forbidden and represents a serious breach of both the rules of the University and the customs of scholarly communities.

Although instances of research misconduct are relatively rare, the University has a responsibility to detect and investigate possible misconduct and to resolve cases of possible misconduct fairly and expeditiously.

The primary responsibility for maintaining integrity in research must rest with those who perform it. In light of this responsibility, the University expects each faculty member:

a. To maintain and further the highest standards of ethical practice in research. Especially important are integrity in recording and reporting results, care in execution of research procedures, and fairness in recognition of the work of others.

b. To be responsible for the integrity of the research carried out under his or her supervision, no matter who actually performs the work or under what circumstances.

c. To accept that a claim of authorship implies a definable major contribution to the work and an acceptance of responsibility for the methods and findings of the work.

d. To keep thorough and verifiable records of research and to insure that exact copies of these records are preserved by the unit in which the work is done.

e. To report suspected research misconduct to the appropriate dean.

The University must also establish certain standards to assure a healthy environment for research. These standards include procedures for dealing with alleged research misconduct.

These procedures are applicable to members of the University of Pennsylvania standing faculty, standing faculty-clinician-educator, associated faculty, academic support staff, and emeritus faculty when acting as such.

Research Misconduct Defined

Research misconduct is defined as fabrication, falsification, plagiarism, or other serious deviation from accepted practices in proposing, performing, or reviewing research, or in reporting research results.

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, or results, or works without giving appropriate credit.
- Serious deviation from accepted practices includes but is not limited to stealing, destroying, or damaging the research property of others with the intent to alter the research record; and directing or encouraging others to engage in fabrication, falsification or plagiarism. As defined here, it is limited to activity related to the proposing, performing, or reviewing of research, or in the reporting of research results and does not include misconduct that occurs in the research setting but that does not affect the integrity of the research record, such as misallocation of funds, sexual harassment, and discrimination, which are covered by other University policies.

The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records, both physical and electronic, progress reports, abstracts, theses, oral presentations, internal reports, and journal articles.

Some forms of misconduct, such as failure to adhere to requirements for the protection of human subjects or to ensure the welfare of laboratory animals, are governed by specific federal regulations and are subject to the oversight of established University committees. However, violations involving failure to meet these requirements may also be covered under this policy or possibly by other University policies when so determined by the responsible committees or institutional officials.

Research misconduct does not include honest error or differences of opinion.

Findings of Research Misconduct

A finding of research misconduct requires that:

- There be a significant departure from accepted practices of the relevant research community; and
- The misconduct be committed intentionally, or knowingly, or recklessly; and
- The allegation be proven by a preponderance of evidence.

Procedures for Handling Alleged Research Misconduct

The following procedures recognize the need to protect the rights and reputations of all individuals, including those who are alleged to have engaged in misconduct and those who report the alleged misconduct. These procedures also recognize that ethical standards are not only an individual obligation but represent a responsibility to the institution, to scientific communities, and to the public.

All committees and parties to an inquiry or investigation have the obligation to maintain maximum confidentiality throughout the proceedings. Exceptions to this obligation are those noted for the Dean and Provost in Section 4. All persons concerned have the obligation to cooperate and furnish all requested information. If any party refuses to do so, the committees of inquiry and investigation will note this in their reports to the Dean.

Charges of misconduct must be resolved expeditiously in a fair and objective manner, protecting the rights of the person or persons against whom a complaint has been filed (the respondent), the person or persons filing the complaint (the complainant), and persons serving as informants or witnesses.

The making of knowingly false or reckless accusations regarding research misconduct violates acceptable norms of behavior for members of the University community and may result in formal charges being brought against the person making such accusations under University procedures (e.g. Procedure Governing Sanctions Taken Against Members of the Faculty).

OF RECORD

1. Preliminary Inquiry

1.1 Before filing a complaint of research misconduct, an individual is encouraged to review the matter with his or her Department Chair, Dean, and/or University Ombudsman, to seek advice from individuals he or she trusts, and through such consultation to determine whether the matter should be pursued. Inquiry into research misconduct should be initiated by written complaint filed with the Dean of the School in which the respondent has his or her primary appointment. The complainant can be any individual, whether or not affiliated with the University.To the extent possible, the complaint should be detailed, specific and accompanied by appropriate documentation. Upon receipt of the complaint, the Dean will notify the Provost. The Dean and the Provost have the responsibility to protect the position and reputation of the complainant and any informants or other witnesses, and to protect these individuals from retaliation, so long as their allegations were made in good faith. The Provost will notify the Chair of the Faculty Senate that a complaint has been filed and the nature of the complaint, but will not identify either the complainant, any informant, or the respondent, in order to preserve maximum confidentiality at this very preliminary stage of inquiry.

1.2 Upon receipt of a properly documented complaint, the Dean will inform the respondent of the nature of the charges, making every effort to avoid identifying the complainant or any informant. The Dean will outline to the respondent, and to the complainant, his or her rights and obligations by reference to this and other relevant University procedures. The Dean will take steps to secure all documents, data and other materials that appear to be relevant to the allegations. The respondent is obligated to cooperate fully in all such efforts. The materials will be copied and the copies provided to the respondent. The originals will be retained as specified in Section 4.12. Every effort will be made to minimize disruption to the respondent's research during this and subsequent phases of the inquiry subject to Sections 4.4-4.7. The Dean will also appoint a preliminary inquiry committee consisting of at least three individuals, none of whom is a member of the same department as, or a collaborator with, or has a conflict of interest with the complainant or respondent. The members of the committee should be unbiased and have appropriate backgrounds to investigate the issues being raised. They may but need not be members of the faculty of the University. Upon appointment of the preliminary inquiry committee, the Dean will notify the complainant and the respondent of the names of the committee members. The Dean will also make every effort to protect the identities of both complainant and respondent with respect to the larger community. The appointment of the preliminary inquiry committee will ordinarily be completed within two weeks of the receipt of a properly documented complaint.

1.3 The preliminary inquiry committee will gather information and determine whether the allegation warrants a formal investigation. The committee will then submit a written report of its findings to the Dean with a copy to the Provost, the complainant and the respondent. The report should state what evidence was reviewed, summarize relevant interviews and include the committee's recommendation, which will be decided by simple majority of the committee; any dissenting opinion will be noted. This report will ordinarily be submitted within 30 calendar days of receipt of the written complaint by the Dean. The respondent will be given the opportunity to make a written reply to the report of the preliminary inquiry committee within 15 calendar days following submission of the report to the Dean. Such reply will be incorporated by the Dean as an appendix to the report. The entire inquiry process should be completed within 45 calendar days of the receipt of a properly documented complaint by the Dean unless circumstances clearly warrant a delay as determined by the Dean in consultation with the Provost. In such cases the record of inquiry will detail reasons for the delay.

1.4 If the report of the preliminary inquiry committee finds that a formal investigation is not warranted, the Dean may (i) drop the matter, (ii) not initiate a formal investigation, but take such other action as the circumstances warrant, or (iii), in extraordinary circumstances, nonetheless initiate a formal investigation. The decision of the Dean will be reviewed by the Provost, who will either concur or require that it be changed. The decision and its review should be completed within 25 calendar days of the receipt by the Dean of the report (10 days following a response, if any). The Dean will inform the concerned parties of the decision. In the event that a formal investigation is not initiated, the Dean and the Provost will, as appropriate, use diligent efforts to restore the reputation of the respondent and to protect the position and reputation of the complainant unless the complaint was found not to be made in good faith. The Provost will notify the Chair of the Faculty Senate that the case has been dropped.

1.5 If no formal investigation of the respondent is conducted, sufficient documentation will be maintained for at least 3 years following the inquiry to permit a later assessment of the reasons that a formal investigation was not deemed warranted (see Section 4.12).

1.6 If the report of the preliminary inquiry committee finds that a formal investigation is warranted, or the Dean or Provost decides the matter should be pursued through a formal investigation, the Dean will initiate a formal investigation as provided in Section 2. The Provost will inform both the Senate Consultation Subcommittee and the appropriate government agency or source funding the research, in writing, that a formal investigation has been initiated and will identify the respondent to the agency or source.

2. Formal Investigation

2.1 To initiate a formal investigation, the Dean will appoint a formal investigation committee of not less than three individuals, none of whom has been a member of the preliminary inquiry committee but whose appointment will be subject to the same provisions governing appointment of the preliminary inquiry committee as described in Section 1.2. A majority of the formal investigation committee must be members of the standing faculty. One of the appointed members will be designated Chair of the committee by the Dean. The formal investigation will be initiated by the committee as soon as possible and usually within 30 calendar days after the report of the preliminary inquiry committee has been received by the Dean. The formal investigation will be divided into four phases: i) investigation and development of an initial factual record, ii) draft report of the findings, iii) hearing, if requested, and iv) final report of the findings. The Office of the General Counsel will provide guidance in procedures appropriate to the case and may have a representative present at any or all meetings of the committee. The representative will not participate directly in the proceedings except when and as requested to do so by the committee.

2.2 Investigation and development of an initial factual record. The formal investigation committee will be provided with copies of the complaint, the report of the preliminary inquiry committee and any other materials acquired by the preliminary inquiry committee during the course of its inquiry. The formal investigation committee will undertake a thorough examination of the allegations, including, without limitation, a review of all relevant research data and proposals, publications, correspondence, and records of communication in any form. Experts within or outside the University may be consulted. The formal investigation committee will also investigate any possible acts of research misconduct by the respondent that come to light during its investigation, and will include them in its findings. Whenever possible, interviews will be conducted with the complainant and respondent, as well as with others having

information regarding the allegations. Tapes will be made of all interviews and saved for reference. Summaries of the interviews will be prepared, provided to the interviewed party for comment or revision, and included as part of the investigatory file. When appearing before the committee the respondent and the complainant may each be accompanied by an adviser, who may be a lawyer but who may not participate directly in the proceedings except when and as requested to do so by the committee.The committee will not conduct formal hearings at this point. Except in unusual cases, the respondent and the complainant will not appear before the committee at the same time.

2.3 Draft report of the findings. Following development of the initial factual record, the formal investigation committee will prepare and provide a written draft report of its proposed findings to the respondent, to the complainant, and the Office of General Counsel. The report will describe the allegations investigated, how and from whom information was obtained, the proposed findings and their basis, and will include texts or summaries of the interviews conducted by the committee.

2.4 Hearing. If the respondent contests any material finding of fact made by the committee in the draft report, he or she may request a hearing before the committee. The request must be made to the committee in writing within 15 calendar days following receipt of the draft report. Any such request must specify findings the respondent asserts are erroneous, the basis for the claimed error, identify each witness the respondent may desire to examine at the hearing, and specify the purpose for calling such witness and the nature of the testimony expected. Upon receipt of such a request, the committee will promptly schedule a hearing. The committee will use reasonable efforts to secure the attendance at the hearing of any witness requested by the respondent who may have information relevant to the disputed finding of fact. The committee may also request the attendance of witnesses in addition to those requested by the respondent, in which case the respondent will be provided with a list of these witnesses at the time the request is made. At the hearing, the respondent and committee will each have an opportunity to examine each witness. The respondent may be accompanied by an advisor, who may be a lawyer but may not participate directly in the proceedings except when and as requested by the committee. The committee will have full authority to determine all matters concerning the conduct of the hearing, including the number of witnesses, the amount of time allocated for questioning each witness, and the duration of the hearing. The committee may require that it pose questions on behalf of the respondent.

2.5 Final report of the findings. Following completion of the hearing, if any, the committee will submit a written final report to the Dean with copies to the Provost, the complainant, and the respondent. This report should describe the policies and procedures under which the investigation was conducted, how and from whom information was obtained, the allegations investigated, the findings and the basis of the findings, and should include texts or summaries of the interviews and hearing, if any, conducted by the committee.The committee will state that it finds the charge(s) made by the complainant or otherwise emerging during the course of its proceedings to be unsubstantiated or substantiated by a preponderance of evidence. For each charge considered, the vote of a majority of the committee will constitute the decision of the committee. The vote will be recorded. If the vote is not unanimous, a statement of any dissenting opinion will be included in the report. If the committee finds that a violation of University policy in addition to or other than research misconduct might have been committed, a description of the possible violation will be included for consideration by the Dean under other procedures. The final report will ordinarily be submitted within 90 days of the appointment of the formal investigation committee. The respondent and complainant will each be permitted to make a written reply to the Dean with a copy to the Provost within 15 calendar days of submission of the report. The Dean will ask the committee to respond in writing to any replies from the respondent or complainant within 7 calendar days. All such responses and replies will be incorporated as appendices to the report of the formal investigation committee.

3. Adjudication

3.1 The Dean will consider the final report and replies. If the Dean in consultation with the Provost determines that there has been procedural error that is likely to have affected the committee's findings, or that any material finding is unsupported by a preponderance of evidence, the Dean will remand the matter to the committee for further proceedings. Upon acceptance of the report by the Dean, the Provost will report the outcome of the investigation to the Chair of the Faculty Senate and the appropriate government agency or source funding the research. The Provost will also provide a copy of the report to the appropriate government agency or source funding the research, as required. The entire formal investigation process should be completed within 120 calendar days of its initiation, unless circumstances clearly warrant a delay as determined by the Dean in consultation with the Provost. In such cases the reasons for a delay will be documented.

3.2 If the final report of the formal investigation committee finds the charges to be unsubstantiated, the Misconduct in Research procedure will be terminated and the concerned parties will be informed. The Dean and the Provost have the responsibility to take an active role to repair any damage done to the reputation of the respondent or the complainant (provided the complainant acted in good faith), and to take appropriate action should they determine that the accusation was knowingly or recklessly false.

3.3 If the report of the formal investigation committee finds the charges against a faculty member to be substantiated, the Dean in consultation with the Provost will take whatever actions are appropriate to the level of intent of the misconduct, the consequences of the behavior, and other aggravating and mitigating factors in accordance with University procedures and which consider the previous record of the respondent. The Dean in consultation with the Provost will determine whether there is substantial reason to believe that just cause exists for suspension or termination, and will take other steps as may be appropriate under the University's Procedure Governing Sanctions Taken Against Members of the Faculty. In any subsequent proceeding commenced under such procedure, the final report of the formal investigation and all replies and responses thereto will form part of the record and be accorded appropriate weight.

4. Other Actions and Procedures

4.1 The Dean may designate the Associate or Vice Dean if a member of the Standing Faculty to represent him or her in the administration of any case of misconduct. The Provost may similarly designate the Deputy Provost, Associate Provost for Faculty Affairs, or Vice Provost for Research if a member of the Standing Faculty to represent him or her.

4.2 If the respondent feels that any action of the Dean, preliminary inquiry committee, or formal investigation committee violates procedures set forth in this document or otherwise introduces an unfair bias into the proceedings, he or she may submit to the Dean, preliminary inquiry committee, or formal investigation committee, respectively, in writing the nature of the action and the reasons why the action may influence either the material findings of fact or the conduct of the proceedings. The complaint to the Dean or respective committee must be made promptly. If the Dean or respective committee finds that the complaint does not merit action, or if the respondent is not satisfied with the nature of any corrective action,

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the respondent may appeal to the Provost. The Provost will decide the matter and will have the authority to take corrective action. Proceedings will not be delayed during consideration of the respondent's claim by the Provost unless the Provost determines that a delay is essential for fair consideration.

4.3 Any final action taken by the Dean under Section 3.3, and any administrative action taken under Sections 4.4, 4.5, 4.6, or 4.7 may be reviewed under other established University grievance and appeal procedures to the extent such review is within the stated jurisdiction of such procedures. All other actions taken, proceedings conducted and reports prepared under this procedure are not subject to review or consideration under the Faculty Grievance Procedure.

4.4 The Dean in consultation with the Provost will, during the course of the inquiry or formal investigation, take administrative action, as appropriate to protect the welfare of animal or human subjects.

4.5 At any time during the preliminary inquiry or formal investigation, the Dean and Provost will immediately notify the relevant funding agency(ies) if public health or safety is at risk; if agency resources or interests are threatened; if research activities should be suspended; if there is reasonable indication of possible violations of civil or criminal law; if Federal action is required to protect the interests of those involved in the investigation; if the University believes the preliminary inquiry or formal investigation may be made public prematurely so that appropriate steps can be taken to safeguard evidence and protect the rights of those involved; or if the research community or public should be informed.

4.6 Subject to Section 4.5, the Dean and Provost will, during the course of the inquiry and formal investigation, take administrative action, as appropriate to protect funds for sponsored research and ensure the purpose of any external financial assistance.

4.7 The Dean in consultation with the Provost will, during the course of the inquiry and formal investigation, take administrative action, as appropriate to ensure an acceptable working environment for individuals under the direction of, or working with the respondent. The Provost and Dean will also notify individuals, programs, or institutions of allegations or developments that would necessitate immediate action in order to prevent the likelihood of substantial harm.

4.8 The Chairs of the preliminary inquiry and formal investigation committees will inform the Dean of any issues relevant to Sections 4.4, 4.5, 4.6, and 4.7 arising during the course of the proceedings.

4.9 Inadvertent failure to tape any interview under Section 2.2 will not be considered a procedural defect requiring correction.

4.10 If the final report of the formal investigation committee finds charges have been substantiated, the Provost will take appropriate steps to correct any misrepresentations resulting from the misconduct in question upon acceptance of the report by the Dean. Collaborators, and other affected individuals, organizations, or institutions will be informed. If misrepresented results have been submitted for publication, already published, or otherwise disseminated into the public domain, appropriate journals and other sponsors will be notified.

4.11 If the Dean is the complainant or respondent or in any other way has a conflict of interest or the appearance of a conflict of interest, he or she is obligated to remove him or herself from the case during the preliminary inquiry and formal investigation and to transfer to the Provost responsibility for carrying out these procedures. In carrying out the latter the Provost will assume the role specified for the Dean and the President that specified for the Provost in sections 1, 2, 3, and 4.

4.12 Complete records of all relevant documentation on cases treated under the provisions of this policy will be preserved by the offices of the Dean and the Provost in a manner consistent with the Protocols for the University Archives and Record Center. In cases adjudicated under Section 3, records will be preserved for a minimum of ten years following completion of all proceedings. Records of cases which are dropped under the provisions of sections 1.4 or 3.1 will be preserved for at least three years following the initial inquiry, but not as part of the personnel record of the respondent.

4.13 The University may act under these procedures irrespective of possible civil or criminal claims arising out of the same or other events. The Dean, with the concurrence of the Provost, after consulting with the general counsel, will determine whether the University will, in fact, proceed against a respondent who also faces related charges in a civil or criminal tribunal. If the University defers proceedings, it may subsequently proceed irrespective of the time provisions set forth in these procedures.

OF RECORD

The Provost's Council on Research reviewed and approved the proposed new policy, Procedures Regarding Misconduct in Research for Non-faculty Members of the Research Community, on May 18, 2004. This policy is similar to the faculty policy, "Procedures Regarding Misconduct in Research"*, (*Almanac*, supplement, May 6, 2003) however it closes the gap in Penn policies by providing an institutional policy to deal with alleged cases of research misconduct where the respondent is a student, staff member, or postdoctoral fellow. It also attempts to integrate its investigation with existing established misconduct processes, and to respect the prerogatives of existing administrative entities to determine institutional sanctions. These procedures become effective immediately.*

—Perry Molinoff, Vice Provost for Research

Procedures Regarding Misconduct in Research for Nonfaculty members of the Research Community

Introduction

The University relies on all members of its research community to establish and maintain the highest standards of ethical practice in academic work, including research. Misconduct in research is prohibited and represents a serious breach of both the rules of the University and the customs of scholarly communities.

The following procedures are applicable to nonfaculty members of the University of Pennsylvania research community including students, postdoctoral fellows, and staff.

Research Misconduct Defined

Research misconduct is defined as fabrication, falsification, plagiarism, or other serious deviation from accepted practices in proposing, performing, or reviewing research, or in reporting research results.

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, or results, or works without giving appropriate credit.
- Serious deviation from accepted practices includes but is not limited to stealing, destroying, or damaging the research property of others with the intent to alter the research record; and directing or encouraging others to engage in fabrication, falsification or plagiarism. As defined here, it is limited to activity related to the proposing, performing, or reviewing of research, or in the reporting of research results and does not include misconduct that occurs in the research setting but that does not affect the integrity of the research record, such as misallocation of funds, sexual harassment, and discrimination, which are covered by other University policies.

The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records, both physical and electronic, progress reports,. abstracts, theses, oral presentations, internal reports, and journal articles.

Some forms of misconduct, such as failure to adhere to requirements for the protection of human subjects or to ensure the welfare of laboratory animals, are governed by specific federal regulations and are subject to the oversight of established University committees. However, violations involving failure to meet these requirements may also be covered under this policy or possibly by other University policies when so determined by the responsible committees or institutional officials.

Research misconduct does not include honest error or differences of opinion.

Findings of Research Misconduct

A finding of research misconduct requires that:

- There be a significant departure from accepted practices of the relevant research community; and
- The misconduct be committed intentionally, or knowingly, or recklessly; and
- The allegation be proven by a preponderance of evidence.

Jurisdiction and Applicable Process

There are a number of University policies and procedures for responding to allegations of misconduct by students, postdoctoral fellows, or staff. This policy is intended to be invoked only in instances where research misconduct (i.e. activity related to the proposing, performing, or reviewing of research, or in the reporting of research results and which therefore may have an impact on the integrity of the research record) is involved. Questions of jurisdiction and the applicability of the appropriate University procedure will be decided by the responsible administrative entity (such as the Office for Student Conduct, Office for Postdoctoral Programs, or the Office of Human Resources), in consultation with the Vice Provost for Research. Allegations of misconduct not involving the research process or the integrity of the research record will be resolved by the disciplinary process ordinarily applicable.

1. Inquiry

1.1 Allegations of research misconduct should be directed in the first instance to the Vice Provost for Research who, along with the responsible administrative entity, will determine jurisdiction and which process is applicable to resolve the allegation. If the Vice Provost determines that this process is properly invoked, the Vice Provost will forward the complaint—which must be in writing—to the Dean of the School where the research is being performed

1.2 Upon receipt of a properly documented complaint, the Dean will inform the respondent of the nature of the charges, and will provide the respondent with a copy of these procedures. The Dean will also take steps to secure relevant documents, data and other materials

The Dean will appoint one or more unbiased, impartial individuals with appropriate expertise who will conduct a preliminary inquiry to determine whether a full investigation is warranted.

1.3 The inquiry committee will gather information and determine whether there is sufficient, credible basis to warrant a formal investigation. The committee shall offer the respondent an opportunity to provide them with relevant information regarding the allegations. The committee will submit a written report of its assessment to the Dean and the respondent, and to the complainant where appropriate. The report should state what evidence was reviewed, summarize relevant interviews, and include the committee's recommendation. This report will ordinarily be submitted within 30 calendar days of receipt of the written complaint by the Dean.

1.4 If the report of the inquiry committee determines that a formal investigation is not warranted, the Dean may (i) drop the matter, or (ii) not initiate a formal investigation, but take such other action as the circumstances warrant, or (iii), in extraordinary circumstances, nonetheless initiate a formal investigation. The Dean will inform the concerned parties of the decision.

1.5 If the inquiry committee determines that a formal investigation is warranted, the Dean will initiate a formal investigation as provided in Section 2. The Provost (Vice Provost/designee) will inform the appropriate government agency or source funding the research, in writing, that a formal investigation has been initiated and will identify the respondent to the agency or source (1).

2. Formal Investigation

2.1 To initiate a formal investigation, the Dean will appoint a formal investigation committee of not less than two disinterested individuals with sufficient expertise, one or more of whom may have served on the preliminary inquiry committee.

2.2 Investigation. The formal investigation committee will be provided with copies of the complaint, the report of the initial inquiry and any other materials acquired during the preliminary inquiry. The formal investigation committee will undertake a thorough examination of the allegations, including, without limitation, a review of relevant research data and proposals, publications, correspondence, and records of communication in any form. Experts within or outside the University may be consulted. The Committee shall have authority to investigate, pursue and document any related research misconduct by therespondent, even

if such misconduct was not covered by the initial complaint. Whenever possible, interviews will be conducted with the complainant, as well as with others having information regarding the allegations. The Committee must allow the respondent an opportunity to be interviewed at this formal investigation stage. When being interviewed by the committee the respondent and the complainant may each be accompanied by an adviser, who may be a lawyer but who may not participate directly in the proceedings except when and as requested to do so by the committee.

2.3 Reporting the findings. Following its investigation, the formal investigation committee will prepare and provide a written report of its findings to the respondent, to the Dean, to the Provost, and, if appropriate, to the complainant. The report will describe the allegations investigated, how and from whom information was obtained, the findings and basis of the findings, and will include texts or summaries of the interviews conducted by the committee. The report will conclude with a clear statement regarding which charges have been considered and what its findings are with respect to each charge the committee considered. If the committee finds that a violation of University policy in addition to or other than research misconduct might have been committed, a description of the possible violation will be included.

The committee will indicate whether each charge considered during the course of its proceedings is unsubstantiated or substantiated by a preponderance of evidence. If the matter involves a respondent who would be subject to University sanctions for misconduct only if the evidence met a clear and convincing standard, the Committee will make an additional determination as to whether that standard has also been met (2).

The final report will ordinarily be submitted within 90 days of the appointment of the formal investigation committee. The respondent will be permitted to make a written reply to the Dean with a copy to the Provost, and Vice Provost for Research, within 15 calendar days of submission of the report. The Dean may ask the committee to respond in writing to any replies from the respondent. The Dean may also ask the complainant to respond to the report if deemed appropriate. All such responses and replies will be incorporated as appendices to the report of the formal investigation committee.

3. Disposition of Final Report and Findings

3.1 The Dean will consider the final report and replies. Upon acceptance of the report by the Dean, the Provost (Vice Provost/designee) will submit a copy of the report containing the outcome of the investigation to the appropriate government agency or source funding the research, if such action is required by regulation or otherwise appropriate. The entire formal investigation process should be completed within 120 calendar days of its initiation, unless documented circumstances warrant a delay.

3.2 If the final report of the formal investigation committee finds the charges of research misconduct against a respondent not to be substantiated, the research misconduct proceeding is terminated and the concerned parties will be informed. A finding that a charge of research misconduct has not been substantiated shall not preclude the University from taking other appropriate action against the respondent if the respondent's behavior or actions violate another University policy or rule.

3.3 If the report of the formal investigation committee finds the charges of research misconduct against a respondent to be substantiated, the matter will then be referred to the responsible administrative entity within the University to determine the appropriate University sanctions, if any, to be imposed for the misconduct (3).

4. Other Actions and Procedures

4.1 The Dean in consultation with the Provost will, during the course of the inquiry or formal investigation, take administrative action, as appropriate to protect the welfare of animal or human subjects.

4.2 At any time during the inquiry or formal investigation, the Dean and Provost will immediately notify the relevant funding agency(ies) if public health or safety is at risk; if agency resources or interests are threatened; if research activities should be suspended; if there is reasonable indication of possible violations of civil or criminal law; if Federal action is required to protect the interests of those involved in the investigation; if the University believes the inquiry or formal investigation may be made public prematurely so that appropriate steps can be taken to safeguard evidence and protect the rights of those involved; or if the research community or public should be informed.

4.3 If the final report of the formal investigation committee finds charges have been substantiated, the Provost or Dean will take appropriate steps to correct any misrepresentations resulting from the misconduct. If, at any time during the inquiry or investigatory stages, the respondent admits to the alleged misconduct, the Dean will take
the necessary steps to complete the inquiry in order to correct the scientific record. If misrepresented results have been submitted for publication, already published, or otherwise disseminated into the public domain, appropriate journals and other sponsors will be notified. In addition, collaborators, and other affected individuals, organizations, institutions, and sponsors will be informed.

4.4 Complete records of all relevant documentation on cases treated under the provisions of this policy will be preserved by the offices of the Dean and the Provost in a manner consistent with the Protocols for the University Archives and Record Center. In cases adjudicated under Section 3, records will be preserved for a minimum of ten years following completion of all proceedings. Records of cases which are dropped will be preserved for at least three years following the initial inquiry. When students are involved in these procedures, the confidentiality provisions applicable to educational records will govern the disclosure of the records.

4.5 The University may act under these procedures irrespective of possible civil or criminal claims arising out of the same or other events. The Dean, in consultation with the Provost and the general counsel, will determine whether the University will proceed against a respondent who also faces related charges in a civil or criminal tribunal. If the University defers proceedings, it may subsequently proceed irrespective of the time provisions set forth in these procedures.

Endnotes

1. The decision to initiate a formal investigation must be reported to the Office of Research Integrity, Department of Health and Human Services, if the research has been supported by a grant from DHHS, according to DHHS regulations.

2. There is a discrepancy between University regulations, which use the standard of "clear and convincing" evidence, and regulations of the Office of Research Integrity, which use the lower standard of "preponderance of evidence". Therefore, if there is a finding of fault, the inquiry must explicitly state whether the higher University standard is met, to inform the University administrative entity which is responsible for determining possible sanctions.

3. The intent of this policy is that the appropriate administrative entity will take responsibility for determining and implementing sanctions.

For instance, if the respondent is an undergraduate student any disciplinary sanctions will be determined by the Office of Student Conduct in accordance with it's amended Charter procedures dealing with research misconduct findings. In order to determine sanctions, the findings and accompanying documents should be forwarded to the Office of Student Conduct. Upon review of all findings, including all submissions by the respondent etc., the Office of Student Conduct will propose appropriate sanctions to the respondent. The respondent would then have an opportunity to accept, reject or propose alternative sanctions. If either the original sanction or an alternative sanction is accepted and agreed upon, the OSC then has primary responsibility for implementing and monitoring sanctions. If the respondent rejects the sanction, the respondent may appeal the nature and severity of the sanction only to the Disciplinary Appellate Officer within the Student Disciplinary System. If the decision of the appellate officer is to uphold the proposed sanction, the sanction will be imposed, with no further levels of review.

Likewise, if the respondent is a graduate student, postdoctoral fellow, or staff member, the responsible administrative entity would consider the information and determine sanctions.

May 14, 1998

BIOMEDICAL GRADUATE STUDIES AUTHORSHIP POLICY

The Biomedical Advisory Committee of BGS agreed unanimously to develop a single policy on authorship for all biomedical graduate groups. This policy was devised in accordance with the Graduate Council of Faculties' *Policy on Fairness of Authorship Credit in Collaborative Faculty-Student Publications*.

Most journals in which BGS faculty and students would publish are represented in the International Committee of Medical Journal Editors (ICMJE). This committee (formerly known as the Vancouver Group) has met annually since 1978 to develop and revise its Uniform Requirements for Manuscripts Submitted to Biomedical Journals. Their Requirements form the basis of section 1 below, Qualifications for Authorship. Issues of authorship in publications by BGS students and faculty should be determined as follows:

1. Qualifications for Authorship[1] All persons designated as authors should qualify for authorship.

a. Each author should have participated sufficiently in the work to take public responsibility for the content
b. Authorship credit should be based only on substantial contributions to each of the following areas:
    1. conception and design, or analysis and interpretation of data
    2. drafting the article or revising it critically for important intellectual content
    3. final approval of the version to be published
c. Conditions 1, 2, and 3 must all be met in assignment of authorship
d. Participation solely in the acquisition of funding or the collection of data does not justify authorship
e. General supervision of the research group is not sufficient for authorship
f. Appropriate credit for the contributions of other individuals to the work described in the publication should be made as an acknowledgment
g. Any part of an article critical to its main conclusions must be the responsibility of at least one author. If that author is a student, then the faculty mentor shares the responsibility

2. The Order of Authors[2]

a. The first author is that person who contributed most to the work, including writing of the manuscript (an author is a person who writes)
b. The sequence of author listing is determined by the relative contributions to the work. In the instance that equal credit is due, this should be footnoted (by asterisk) and authors should be listed alphabetically (you may wish to note this policy on your CV)
c. Decisions about authors and the order in which their names appear should be discussed as early as possible, even at the outset
d. Decisions about authors and the order in which their names appear should be made by group consensus, and under the guidance of the lead investigator(s)

3. Other General Rules

a. The data presented in the publication must preserve full protection of patients' rights to privacy at their institution(s) as specified in Informed Consent and IRB approval documents
b. The data presented in the publication must be generated under the approval of, and in full compliance with, Animal and Human Subject codes at the authors' institution(s)
c. All authors are responsible for recognizing and disclosing financial and other conflicts of interest that might bias their work
d. Decisions of the suitability of a manuscript for a particular journal should be made by group consensus and under the guidance of the lead investigator(s)
e. All items presented in the publication must be original (inclusive of other submitted publications), unless otherwise specifically stated in the publication
f. Secondary publication of manuscripts, either in full or in part, in review form, in another language and/or in another country, is justifiable provided that the authors have received approval from the editors of both journals, that the secondary manuscript includes a footnote to this effect, and that the secondary version faithfully reflects the data and interpretations of the primary version
g. In the instance of review articles, which may include previously published and/or unpublished data, appropriate consent and acknowledgements must be made; however, generation of such data does not necessarily warrant authorship (for example, if a faculty member writes a review based on a student's published work and acknowledges the student's contributions, the student does not necessarily have the right to co-authorship).

4. When Conflicts Arise

It is recognized that even when the above guidelines are followed, conflicts of opinion may arise. The process for handling disagreements regarding authorship between students and faculty members is as follows:

a. The faculty member and student should seek mediation with the graduate group chair. If the faculty member wishes, his or her departmental chair may be included in this process as well.
b. If mediation with the graduate group chair fails to satisfy both student and faculty member, the Director of BGS should be consulted. The Director of BGS will convene a committee of three BGS standing faculty members and one BGS student for arbitration. The committee will consider the opinions of the student, the faculty member, the graduate group chair, and, if appropriate, the faculty member's department chair. However, it must be understood that the opinion of the appeals committee is not binding without the consent of the lead investigator.

Failure to adhere to these guidelines may represent a violation of University policies and consequently may be subject to judicial proceedings.

If the complaint represents a violation of the BGS Code of Academic Integrity, the investigation and adjudication of the complaint will be conducted in accordance with *the Policies Governing Biomedical Graduate Student Conduct* (9/20/96) on file in the Biomedical Graduate Studies Office and the Office of the Vice Dean, Research and Research Training at the School of Medicine.

If the complaint alleges research misconduct by a member of the faculty, the investigation and adjudication of the complaint will be conducted in accordance with the University's *Procedures Regarding Misconduct in Research*, provided in the *Handbook for Faculty and Academic Administrators*.

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[1] Based on ICMJE Requirements, Ann Intern Med. 1977;126:36-47

[2] Based on editorial by D. Riesenberg and G. Lundberg, JAMA 1990;264:1857

FAIRNESS OF AUTHORSHIP CREDIT IN COLLABORATIVE FACULTY-STUDENT PUBLICATIONS FOR PHD STUDENTS

October 8, 1998

The Graduate Council of the Faculties has unanimously approved a new policy on authorship credit in collaborative faculty-student publications. The intent of the policy is to avoid situations in which graduate students or faculty feel that their contribution to published work has not been fairly recognized. Our intent in the distribution of this policy statement to faculty and graduate students is to make authorship discussions a routine part of conversations about intellectual collaboration.

Why is a policy needed?

1. For students who intend to pursue academic and/or research careers, scholarly publications that reflect the product of their research work are essential to being considered for a job and establishing a career.

2. Faculty members are almost always directly involved in the student's scholarly work as mentors, employers, collaborators, or consultants.

3. When publications emerge from collaborative faculty-student effort, it is not always clear who should be given authorship credit, and in what order the authors' names should appear on the published work.

4. The Vice Provost, the Council of Graduate Deans and the Graduate Council of the Faculties have been made aware over the years that there is widespread uncertainty among graduate students about what constitutes fair practices for the determination of authorship. Practices vary widely between and within departments at Penn.

5. Graduate students are understandably reluctant to raise issues of authorship at the beginning of projects, and skeptical about the efficacy of raising issues once the work has been completed. Students feel that authorship credit is a difficult issue to raise, because their questioning of the arrangements can be interpreted as a challenge to the mentor on whom the student depends for intellectual and/or financial support as well as future letters of recommendation.

6. The lack of clarity concerning fairness in authorship is evident not only among graduate students. Faculty members, too, are often uncertain about fair practices. Some feel that their intellectual and written contribution to a student's published work has not been sufficiently acknowledged.

7. As part of their appropriate professional education, young scholars need to learn about how questions of joint-authorship are decided. Guidelines can facilitate discussions between students and their faculty mentors which further such learning.

Diversity of practices in different disciplines and departments

In considering the task of formulating a university-wide policy on Fairness in Authorship Credit, the Graduate Council of the Faculties is aware that different traditions of joint authorship exist in different disciplines and departments.

* In some fields, the Principal Investigator of the lab is first author of all publications.

* In some fields faculty members rarely or never receive authorship credit on student publications, no matter what their contribution to the project or the product.

* In some fields, authorship depends on intellectual leadership and actual contribution to the ideas for the project and the written product.

* In some fields, authorship rules are clear; in others they are subject to negotiation.

* In some fields, research assistants and research fellows are automatically included as authors when the outcome results from paid work. In other fields, these students are automatically excluded as authors when the outcome results from paid work.

A University-wide process for establishing authorship credit

In light of the variability, ambiguity, and uncertainty regarding faculty-student authorship of published work, there are no specific rules that can be enunciated by the Graduate Council of the Faculties that will address the situation in all departments and academic disciplines. Instead, the Graduate Council of the Faculties is mandating a set of processes within each graduate group that will clarify expectations concerning authorship for each student and faculty member.

A. Graduate Group level

Graduate groups must publish and publicize general guidelines concerning authorship and make them available to all graduate students. (Graduate Group policies are available at the end of this document.)

B. Faculty-Student level

Individual mentors should conform to the graduate group policy on authorship credit. Mentors are responsible for anticipating possible disagreements concerning authorship credit regarding specific collaborative projects and should initiate clarifying discussions before students have invested substantial time on such projects. These discussions should be reopened if relative contributions change.

C. Appeals process

No policy can prevent the occurrence of all instances of actual or perceived unfair treatment. Although inequities can occur to either faculty or graduate students, we believe that graduate students are usually more vulnerable to faculty practices and less able to take action when they feel that fairness has been violated.

In cases of disagreements about authorship the following steps should be taken:

1. Students who feel that they have been mistreated should raise the issue with their mentor and their graduate chair.

2. If the disagreement is not resolved to all participants' satisfaction, an appeal can be made to the Dean of the School, who should convene a committee of faculty and graduate students to hear the disagreement and attempt to resolve it. Cases will be decided in the context of the published norms and guidelines of the graduate group.

Authorship Policies for Individual Graduate Programs, Alphabetical List

* Accounting * American Civilization * Ancient History * Anthropology * Architecture * Art and Archaeology of the Mediterranean World * Asian and Middle Eastern Studies * Biochemistry and Molecular Biophysics * Bioengineering * Biology * Cell and Molecular Biology * Chemical Engineering * Chemistry * City and Regional Planning * Classical Studies * Communication * Comparative Literature and Literary Theory * Computer and Information Science * Demography * Earth and Environmental Science * Economics * Education * Electrical Engineering * English * Epidemiology and Biostatistics * Finance * Folklore and Folklife * Geology – See: Earth and Environmental Science * Germanic Languages and Literatures * Health Care Systems * Historic Preservation * History and Sociology of Science * History of Art * History * Immunology * International Studies * Insurance and Risk Management * Linguistics * Management * Marketing * Materials Science and Engineering * Mathematics * Mechanical Engineering and Applied Mechanics * Molecular Biology * Music * Neuroscience * Nursing * Operations Research * Operations and Information Management * Organizational Dynamics * Parasitology * Pharmacological Sciences * Philosophy * Physics and Astronomy * Political Science * Psychology * Public Policy and Management * Regional Science * Religious Studies * Romance Languages * Russian Language and Literature * Social Welfare * Sociology * South Asia Regional Studies * Statistics * Systems Engineering