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| AFYA BORA CONSORTIUM GLOBAL HEALTH LEADERSHIP FELLOWSHIP PROGRAM |
| RESPONSIBLE CONDUCT OF RESEARCH |
| A Distance Learning Module |

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**AFYA BORA CONSORTIUM**

**RESPONSIBLE CONDUCT OF RESEARCH**

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**Module Instructors**

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**Guide for Fellows and Instructors**

**AFYA BORA CONSORTIUM**

**A “DISTANCE” LEARNING MODULE**

**RESPONSIBLE CONDUCT OF RESEARCH (RCR)**

**NOTE. Plagiarism disclaimer. Some of the materials in this module are revised versions of text in publicly available guidelines and policies, most of which have been published as web-based documents.**

Contents

1. Overview, competencies, and plan of work
2. RCR reference manual
3. Presentations with references, case studies, and competency questions

TOPICS FOR STUDY

1. Conflict of interest: description and management
2. Human subject research
3. Peer reviewing
4. Data management
5. Research misconduct
6. Authorship guidelines

In addition to the present document, there are two other documents that are provided as part of this module (they will be sent as separate email attachments)

* References as PDF copies of the original publications
* Reference manual

DISCLOSURE. Much of the material in this module has been taken verbatim or adapted from a variety of readily accessible public guides and publications. The major sources used were materials posted on the websites of the U.S. government, the University of Pennsylvania, and Wikipedia. Since there are differences between current practices in different countries, some of the recommendations may not apply in a given country.

**1. Overview, competencies, and plan of work**

* 1. **Overview**

The 21st Century is marked by significant advances in information and technology development. The technology development has in turn contributed to improved research methods and techniques. The century has also seen expanded research engagement and collaboration between researchers from the north and those in the south. Increases in multi-disciplinary research, cultural differences, needs and relevance have increased the need to ensure high standards of research practices now than ever before. Enhanced standards in research protects the rights of human subjects and has improved the quality of research outputs and applications.

“Responsible conduct of research” (RCR) is a term used by the U.S. government to cover a set of policies and practices that should guide the conduct of research activities. As future leaders in your respective field and as a requirement by our funders, Afya Bora Fellows are required to understand the principles of RCR and how to manage these issues. Furthermore, you will find this information useful in your future professional career, as a manager, educator, or researcher. Because we are constrained by time and resources, this material will be available to you as a “distance learning” module, and you will have to take responsibility to complete the components of the module on your own. To help organize your time, we are providing a plan of work together with a set of competencies that you should acquire from this module.

RCR – as defined by the U.S. National Institutes of Health - consists of 9 topic areas, that are listed in the 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 Fellowship.

| THE FOLLOWING TOPIC NAMES ARE COPIED FROM THE (U.S.) National Institutes of Health INSTRUCTIONS | THIS MODULE |
| --- | --- |
| 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  (an important subject beyond the scope of this module) |

**1.2 Competencies**

Many of the RCR topics are complicated, technical and have legal implications. Therefore, we do not expect Fellows to fully master all of these details. Instead, we are supplying a "reference manual" of materials that provide great details about these topics, in a digital version that can be saved on the hard drive of each Fellow's laptop. As with other reference manuals, these materials will constitute a continuous resource that Fellows can access if RCR issues arise, either during their Fellowship or thereafter. It is expected that Fellows will:

* Have sufficient understanding to be able to write short cogent answers to the case studies and reasonable brief responses to the competency questions.
* Be aware that supporting materials can be accessed on their hard drive if need arises.
* Realize that if issues arise, such as conflict of interest or authorship, they are not expected to be able to deal with these on their own. Instead, Fellows should be aware of the potential problem, and consider consulting with other members of their organization. Also, remember 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.

**1.3 Plan of work**

For each of the topic areas, we will provide a short written guide, and some short case studies. You are expected to:

* Read the guide carefully
* Write a short (no more than 1 page) response to each case study. When you have completed all of the case studies, please send them as a group (single word document with each case study numbered and your name on the document) by uploading your case studies to the canvas website.
* Read the “competency questions” that follow each section of the module, and satisfy yourself that you could answer the questions.
* Login to the canvas RCR website and complete on of the discussion questions for each topic, and respond to another fellows post as well.

There are 6 separate topics covered in this module. You should plan to complete one topic every week, and the whole module within two months, since you have two modules to complete during your first Attachment Site rotation. Each week you will be expected to post twice to a discussion forum on the RCR module website. The first post is a response to one of the discussion questions provided for the topics mentioned, and the second post will be in response on one of your colleague’s posts.

**RCR Module Important Due Dates:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Week | Dates | Topic Due | Case Study and First Discussion Post Due | Second Discussion Post Due |
| 1 | Aug 30 – Sept 5 |  |  | |
| 2 | Sept 6 - 12 | Topic 1 | Sept 7 | Sept 9 |
| 3 | Sept 13-19 | Topic 2 | Sept 14 | Sept 16 |
| 4 | Sept 20-26 | Topic 3 | Sept 21 | Sept 23 |
| 5 | Sept 27 – Oct 3 | Topic 4 | Sept 28 | Sept 30 |
| 6 | Oct 4 - 10 | Topic 5 | Oct 5 | Oct 7 |
| 7 | Oct 11-17 | Topic 6 | Oct 12 | Oct 14 |
| 8 | Oct 18-24 | Evaluations |  | |

**2. Reference manual overview**

The reference manual is provided as a separate PDF document and covers most of the 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).

Source of documents in the Reference Manual

All the 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 (U Penn), which has developed the resources for faculty and other members of its University community. The U Penn documents are presently broadly representative of established practices in research universities in the U.S. and conform to U.S. National Institutes of Health guidelines.

Are these documents "definitive"?

Fellows are encouraged to appreciate that these materials are the standards of today and they continue to evolve and change in many areas. Also, established practices vary at different universities, in different disciplines, in different countries, and are constantly revised.

Contents of the RCR Reference Manual

| TOPIC | DOCUMENT  Items in red provide basic orientation  Items in black are mainly formal policies and procedures | HEADER |
| --- | --- | --- |
| RCR GENERAL | INTRODUCTION AND TABLE OF CONTENTS | INTRO-  DUCTION-1 |
| RCR GENERAL | U.S. National Institutes of Health (NIH) Notice Number: NOT-OD-10-019 (http://www.nih.gov) Update on the Requirement for Instruction in the Responsible Conduct of Research | INTRO-  DUCTION-2 |
| RCR GENERAL | U.S. Government Printing Office, Washington, DC. Office of Research Integrity, Introduction to Responsible Conduct of Research. ISBN 979-0-16-072285-1 | INTRO-  DUCTION-3 |
| CONFLICT OF INTEREST | University of Pennsylvania. A Layman's Guide to Conflict of Interest | a-1 |
| CONFLICT OF INTEREST | University of Pennsylvania. A Reference manual for Biomedical Graduate Studies Students and Research Fellows. Conflicts of Interest: page 16 | a-2 |
| CONFLICT OF INTEREST | University of Pennsylvania. Reference manual for faculty and academic administrators. Conflict of interest policy for faculty members | a-3 |
| CONFLICT OF INTEREST | University of Pennsylvania. Policy on Outside Financial Interests | a-4 |
| CONFLICT OF INTEREST | University of Pennsylvania. Confidential Financial Disclosure Statement | a-5 |
| CONFLICT OF INTEREST | University of Pennsylvania. Financial Disclosure and Presumptively Prohibited Conflicts for Investigators Participating in Clinical Trials | a-6 |
| HUMAN SUBJECTS | University of Pennsylvania. Office of Human Research. Defining Clinical Research | b-1 |
| HUMAN SUBJECTS | University of Pennsylvania. Office of Regulatory Affairs. IRB overview, application procedures and categories of review | b-2 |
| HUMAN SUBJECTS | University of Pennsylvania. Office of Regulatory Affairs. Required Training. Training Requirements: Investigators, Research Staff, & Students Engaged in Human Research | b-3 |
| HUMAN SUBJECTS | University of Pennsylvania. Office of Human Research. Study Preparation | b-4 |
| HUMAN SUBJECTS | University of Pennsylvania. Reference manual for faculty and academic administrators. Human research protection program | b-5 |
| HUMAN SUBJECTS | University of Pennsylvania. Office of Regulatory Affairs. Institutional Review Board Standard Operating Policies | b-6 |
| PEER REVIEW | Wikipedia. Peer review, a general overview | e-1 |
| PEER REVIEW | NIH. Peer review of grant applications at the U.S. National Institutes of Health | e-2 |
| PEER REVIEW | Nature magazine, 2010; 468: 29. A discussion of peer review of manuscripts | e-3 |
| DATA | University of Pennsylvania. A Reference manual for Biomedical Graduate Studies Students and Research Fellows. Data Management and Ownership: pages 7, 37 | a-2 |
| DATA | Wikipedia. Copyright | f-1 |
| DATA | University of Pennsylvania. Reference manual for faculty and academic administrators. Policy Relating to Copyrights and Commitment of Effort for Faculty | f-2 |
| DATA | Wikipedia. Patents | f-3 |
| DATA | University of Pennsylvania. Patent and Tangible Research Property Policies and Procedures | f-4 |
| DATA | University of Pennsylvania. Roles, Responsibilities, and Expectations in Technology Commercialization at Penn | f-5 |
| MISCONDUCT | University of Pennsylvania. A Reference manual for Biomedical Graduate Studies Students and Research Fellows. Procedures Concerning Misconduct: pages 2, 32, 38 | a-2 |
| MISCONDUCT | University of Pennsylvania. Procedures Regarding Misconduct in Research for Faculty | g-1 |
| MISCONDUCT | University of Pennsylvania. Procedures Regarding Misconduct in Research for Nonfaculty members of the Research Community | g-2 |
| AUTHORSHIP | University of Pennsylvania. Biomedical authorship policy | h-1 |
| AUTHORSHIP | University of Pennsylvania. University policy. Fairness of authorship credit in collaborative publications | h-2 |

**3. Presentations with case studies, and competency and discussion questions**

Each subject area includes a short presentation that presents a concise overview, with a few case studies, and a short set of “competency” questions. As described above, for each subject area, please read the presentation. Then do the case studies by writing a short (no more than 1 single spaced page) response to each case study and posting it to the module website You will also be expected to answer one of the competency questions on the discussion forum each week, as well as responsible for adding a response on another fellows post each week.

**4. Topic 1: Conflict of interest: description and management**

**Lecture**

What is conflict of interest? Conflict of interest arises when there is a conflict between two different interests, and a decision must be made how to manage the conflict. For health professionals, COI usually involves either (1) professional commitment; (2) financial interests; or (3) professional integrity.

Many instances of COI can be “managed”, but sometimes one interest has to be abandoned. Management involves 3 elements: (a) prevention; (b) disclosure; and (c) perception. Many academic institutions have a conflict of interest policy and process to identify, review, and advice on potential conflicts of interest, and this process – when it exists – can help to manage potential conflicts. In the absence of a policy and operational procedures it becomes almost impossible to deal with conflicts of interest. These general principles may sound vague but reading the case studies carefully makes the principles much clearer.

**Professional commitment**

If a health professional is employed on a fulltime basis by an organization (University, nongovernment organization, government organization), she/he owes her/his primary professional commitment to that organization. Many organizations have policies regarding the time or effort than can be devoted to other professional activities. In some countries, one typical rule is “one day in seven”, i.e., that the employee can spend one day a week in outside professional activities. Alternatively, regulations may specify the minimum number of hours a week that the fulltime employee should spend on her/his job.

*Management strategy*

If a fulltime professional employee takes additional part time work, it is advisable for the employee to inform her/his supervisor and to discuss this external commitment in view of the policies of the organization where he/she works. Disclosure and consultation would prevent the perception that the employee is violating the work rules of her/his primary employer. The supervisor may refer the potential conflict to an institutional committee or other unit that is charged with the responsibility for adjudicating conflicts of interest.

**Financial interest**

A full-time employee of an organization has a commitment to serve the best interests of that organization and should not have financial interests that may conflict with the interests of her/his employer. For instance, if a health professional has – in addition to a fulltime position – a part time position that pays her/him on an hourly basis, she/he should not spend so much time on the part time job that it compromises the time spent discharging duties that are part of the fulltime job.

*Management strategy*

In case a fulltime employee has financial interests that she/he believes might be perceived to compromise her/his ability to discharge his job effectively or with integrity, she/he should disclose the situation to her/his supervisor, and ask for advice. The supervisor may refer the potential conflict to an institutional committee or other unit that is charged with the responsibility for adjudicating conflicts of interest.

**Professional integrity**

Professional workers are obligated to maintain a high level of integrity in the conduct of their professional duties. The potential for personal gain must not jeopardize or appear to jeopardize the integrity of their conduct, as administrators, researchers, caregivers, or educators.

With respect to research, this involves the choice of research, its design, the interpretation of results, and the reporting of results. The complete, objective, and timely dissemination of new findings through scholarly publications and professional presentations is essential for research integrity. For instance, if a research project, such as a clinical trial is financed by a pharmaceutical company, the company may want to control the disclosure of the results of the trial; or may wish to delay publication in order to submit a patent application. Such stipulations would compromise the integrity of the institutions where the research is conducted.

*Management strategy*

If a research project is to be funded under a grant or a sub contract with another institution, before accepting the grant it is important to review the terms of the grant to be sure that the researchers are free to interpret their data, reach their conclusions independently of the project sponsor. Also, the terms of the award should permit the researchers to present or publish their findings without interference from the sponsoring entity.

**Educational Mission**

Students and other trainees must be assured of an educationally appropriate training program. Training programs should be designed to give priority to the educational needs of students and research trainees. For instance, a supervisor should consider whether a project assigned to a student will be a good vehicle for training, and not just whether the project supports a program of interest to the supervisor. It is not uncommon that supervisors are tempted to put their project interests before those of their trainees and this could jeopardize the educational mission.

*Management strategies*

The supervisor should consult with the trainee about proposed projects to be sure that they will meet some of the training needs and program interests of the trainee. Also, it is good at the outset to discuss future contingencies, such as credit on presentations and publications of the project. If the trainee is supervised by a Mentoring Committee, these issues should be discussed by the whole Committee, and should provide some assurance that the trainee’s interests are being given due consideration.

**Case studies**

**Please write a short (no more than 1 single-spaced page) response for each of the following case studies. Post your responses on the Canvas website.**

**Case 1**

Dr. Y has a full-time appointment as an Assistant Professor in the Department of Surgery in the School of Medicine at a university in Sub-Saharan Africa. He works about 50 hours a week and has a hard time supporting his family on his modest salary. Apollo Healthcare, an international corporation, has just opened a new private hospital, and they are trying to expand their surgery practice since this is a major source of income. They offer Dr. Y the opportunity to become a professional associate at the new hospital, in addition to his present position. They will pay for each operation he performs (piecework) at a handsome rate. However, they require that Dr. Y will be on constant call for operations in his specialty, which is orthopedic and trauma surgery. They estimate that this will take about 25 hours a week of Dr. Y’s professional time.

* Does the offer from Apollo Healthcare involve a potential COI?
* If yes, what is the COI?
* How should Dr. Y respond?
* Can this potential COI be managed? How? Who should make that decision?

**Case 2**

Dr. X is a graduate nurse with a PhD in epidemiology and is the Associate Director for the National AIDS Control Program in Country Y in Sub-Saharan Africa. Among other responsibilities, Dr. X is a member of a committee that decides which drugs and regimens to use in the National AIDS Control Program. A major European pharmaceutical company (Global Pharma) asks Dr. X to serve as a consultant to the company to advise them on how to price their AIDS drugs in developing countries and how to most effectively deploy them in low resource settings. They offer Dr. X an annual retainer of $25,000 and will pay all expenses for 4 international trips every year, including the board meetings of the company and international AIDS meetings.

* Does the offer from Global Pharma involve a potential COI?
* If yes, what is the COI?
* How should Dr. X respond?
* Can this potential COI be managed? How? Who should make that decision?

**Case 3**

Dr. K is a physician with specialty training in Infectious Diseases, and is the Director of Clinical Research in the Institute of Medical Research, a nongovernment not-for-profit organization. The Institute for Medical Research is located in Country Z in sub-Saharan Africa, where there is a very high incidence of HIV/AIDS. Global Pharma, a large international pharmaceutical company, proposes to provide a contract to the Institute for Medical Research to do a clinical trial of their newly licensed antiretroviral drug “Antihiv” to compare its efficacy vs. Truvada, which is the current standard of treatment in Country Z. Under this proposed contract, Dr. K would be the project director, and would be reimbursed for 75% effort at $75,000, which is twice the rate of Dr. K’s fulltime salary at the Institute for Medical Research. Furthermore, if the trial is successfully completed, Global Pharma will provide a bonus of stock options to Dr. K, currently worth $100,000 on the stock market. The contract stipulates that Global Pharma will have the right to approve the plan for the clinical trial, and will own the data from the trial, with the implied prerogative to determine if, when, and how the results of the trial will be made public.

* Does the offer from Global Pharma involve a potential COI?
* If yes, what is the COI?
* How should Dr. K respond?
* Can this potential COI be managed? How? Who should make that decision?

**Case 4**

Professor Y has a PhD in microbiology and is a Professor of Microbiology at the Medical College in University W, located in a Sub-Saharan country. She has received a contract from EssentialMedicines, a large international NGO, to isolate HIV viruses from 100 patients in the HIV clinic in his Medical College. The contract specifies that these viruses will then be sequenced to classify them within HIV Clades. The viruses will also be tested for their sensitivity to 3 anti-retroviral drugs tested by EssentialMedicines. The data will belong to EssentialMedicines and they will determine whether they are published in part or in full, and whether or not they will use it in their marketing campaigns. Professor Y has 4 graduate students who need research projects for their PhD theses. The EssentialMedicines contract is the major source of equipment and supplies in Professor Y’s laboratory, so she is considering whether to ask her students to undertake various sections of his contract work in return for access to these resources.

* Does this involve a Conflict of Interest? If so, what is the conflict?
* Can the potential conflict be managed? What is a management plan
* Should Professor Y disclose the potential conflict? To whom?

**Case 5**

Dr. Q is a graduate nurse who is qualified in intensive care. She has recently taken a junior position with “Healthforall”, a nongovernment organization dedicated to promote universal primary care. Healthforall has the ability to design and operate community health centers in low resource settings in sub-Saharan Africa. Dr. Q has an offer to supplement her modest salary with part time weekend employment in a nearby medical center. She asks her supervisor if Healthforall has a conflict of interest policy, and whom he should consult about this issue. Her supervisor tells her that there is no policy at Healthforall, and that every employee makes their own decisions about such matters. Furthermore, the supervisor tells Dr. Q that she should not reveal her extramural activities and that he (the supervisor) does not want Dr. Q to ever mention the subject again.

* Does this situation involve a Conflict of Interest? If so, what is the conflict?
* Where should Dr. Q go for advice?
* How should she handle this situation?

**Competency questions**

**Read the “competency questions” that follow each section of the module, and satisfy yourself that you could answer the questions.**

1. **Name three people within your organization that can help you manage a conflict of interest.**
2. **Management of conflict of interest is said to involve three major elements: disclosure; review; and a negotiated management plan. Explain briefly, the importance of each of these three elements.**
3. **Why is perception important in managing conflicts of interest?**
4. **In your future professional position, what do you think is the most likely conflict of interest that you are likely to meet? Or have met already? And how would you (or have you) handle it?**
5. **Give three reasons why an institutional policy is important in managing conflicts of interest.**

**Discussion Questions**

Log into Moodle and answer 1 of the discussion questions posted for the week by of each week Monday. Write an additional comment on another fellows post by Thursday of each week.

**5. Topic 2: Human subject research**

**Full Disclosure**. The following materials are mainly drawn from policies in the United States. However, these policies may vary somewhat in other countries that have their own rules and regulations. Many of the following materials are “plagiarized” and modified from public guidelines available as open access on the Internet.

**Basic principles**

During the last 60 years a set of policies regarding research involving human subjects have been gradually developed and accepted as standards by many countries. Current policies are based on three essential criteria pertaining to the conduct of research:

* 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;
* JUSTICE or the obligation to distribute benefits and risks equally without prejudice to particular individuals or groups.

In the United States, most government agencies that sponsor human subject research have adopted a common set of regulations that set forth policies and their implementation. These regulations are often referred to as the “Common Rule”. The Common Rule defines both “research” and “human subjects”. Although these definitions may seem redundant and self-evident, they are important to understand since they explain why some human subject studies are exempt from review and approval.

**Research**

The Common Rule defines research as “systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge”. This means that a project or study is research if *it is conducted with the intention of drawing conclusions that have some general applicability*. The random collection of information about individuals that has no general applicability is not considered research. Also, studies that are conducted for training purposes, and which will not be used to extend generalizable knowledge, are not considered as “research” for this purpose. If the study findings are expected to be presented or published in a public forum, all activities are defined as “research”.

**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”.

“Interaction or intervention” includes questionnaires or examinations, collecting samples from the subject, as well as providing medicines, treatments, or modifying behavior. “Private” information is information where the identity of the subject is recorded or can be inferred indirectly. If either 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.

Some other countries use a broader definition of “human subjects” that includes autopsy studies.

**Implementation of policies involving human subject research (IRBs)**

The Common Rule delegates responsibility for implementation of human subject research policies to each entity where such research may be conducted, such as universities, hospitals, health professional schools, non-government organizations, or private companies. It requires that each institution use an IRB (Institutional Review Board) to oversee all human subject research. Furthermore, the Common Rule prescribes a large number of specific details about the organization and conduct of an IRB. The institution may either develop its own IRB system or can outsource this responsibility to an external commercial IRB.

Research proposals can be classified by an IRB in one of three possible categories

Exempt review

Expedited review

Full review

Usually, if the project leader believes that a proposal might qualify for either expedited or exempt review, this is stipulated when the proposal is submitted.

**Exempt review**

“Exempt” is a misleading term, since such proposals must be submitted to the IRB staff for examination and recording. Exempt research includes:

* research conducted in established or commonly accepted educational settings, such as exercises to train students how to conduct human subject research, with no intent to publish the results;
* research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if individuals are unidentifiable or this information is already publicly available;
* research conducted for purposes of marketing of products by private companies;
* research that does NOT reveal any personal information that might present any kind of risk to the subject.

Decisions about whether studies are exempt from the requirements of the Common Rule must be made by a designated professional or staff member of the IRB or an appropriate institutional official, *and not by the investigator*. Exempt proposals do not require review at a formal meeting of the full IRB and can be approved as soon as reviewed by the responsible staff or professional member of the IRB.

**Expedited review**

In general, research may be considered for *Expedited review* if it involves no more than minimal risk, does not include intentional deception, does not employ sensitive populations or topics, and includes appropriate consent procedures. Expedited review may also be used when minor changes have been made to a previously approved research project during the period (of one year or less) for which approval has already been authorized.

*Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those encountered in daily life or during the performance of routine physical or psychological examinations or tests. Keep in mind that research does not count as having "minimal risk" simply because it involves minimal physical risk or is non-invasive. There are many kinds of risk including financial risk, employment risk, criminal/civil liability, stigmatization, insurability and embarrassment. It is important to consider all of these when assessing risk.

*Sensitive populations* include children below the age of informed consent, pregnant women and their fetuses, adults not able to make decisions about informed consent, prisoners, and the like.

Research proposals that may qualify for Expedited review do not require review by the full IRB. Usually, they can be approved by a couple of members of the IRB including the Chair of the IRB. These members have the authority to approve the research, make stipulations concerning modifications, or elevate the research to a Full review, but may not disapprove the research.

**Full review**

All proposals that do not qualify for Exempted review or Expedited review must be given full review by the whole IRB. IRBs weigh many factors before approving proposals. Applications can be approved by a majority of the voting members of the IRB. Often, the IRB will request modifications of the research proposal, and may then require re-review the proposal prior to final approval. In some instances, the IRB may disapprove an application if they decide it is “fatally” flawed. Researchers cannot initiate their studies until they have received final IRB approval.

The main concerns during IRB review are to determine whether:

* risks to subjects are minimized;
* risks to subjects are reasonable in relation to anticipated benefits, if any, to the research 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;
* the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects; and
* there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Some countries do a “full review” of all studies involving human subjects, and do not permit “exempt” or “expedited” review.

**Informed consent**

Potential participants in a study are asked to sign an informed consent *document* before being enrolled in the study. The informed consent *document* provides a summary of the clinical trial (including its purpose, the treatment procedures and schedule, potential risks and benefits) and explains the rights of the human subject participants. It is designed to begin the informed consent process, which consists of conversations between the subject and the research team. The informed consent *process* should help them make educated decisions about whether to participate in a trial. As part of the process, the research team should discuss with each participant the purpose of the trial, procedures, risks and potential benefits, and the subject’s rights as a participant. Informed consent should be an ongoing, interactive process, rather than a one-time information session.

Informed consent myths and reality for human subjects

*Myth:* Informed consent is designed primarily to protect the legal interests of the research team.

*Reality:* The purpose of the process is to protect participants by providing access to information that can help them make an informed choice. It also is designed to make subjects aware of their rights as a participant.

*Myth: The* most important part of this process is signing the informed consent document. *Reality:* Actually, the heart of this process is the ongoing interaction and discussions with the research team and other medical personnel – before, during, and after the trial. The document is designed to get this conversation started.

*Myth:* Once someone signs the consent form, they have to enroll and stay enrolled in the trial.

*Reality:* That's not true. Even after signing the form, a subject is free to change her/his mind and decide not to participate. Participants also have the right to leave a clinical trial at any time for any reason, without forfeiting access to other treatment.

**Importance of knowledge gained: scientific validity and study feasibility.**

To approve a study involving human subjects, it is required to convince the reviewers that - if completed as planned – the study will make a contribution to knowledge sufficient to justify imposing the burden on the participants. This involves reviewing the scientific validity and feasibility of the project. Health professionals often do not realize that it is NOT sufficient to “do no harm” and that validity and feasibility are also assessed by the IRB.

*Scientific validity*

Scientific validity attempts to answer the following questions: Will the project contribute to the field? Will the project replicate or challenge existing findings in the literature? Is the study well designed and powered to give an answer to the questions posed?

*Feasibility*

Feasibility includes evaluation of the competence of the research team to conduct the proposed study; of the availability of enough human subjects to complete the study in a timely fashion; and of financial support for the study.

**After receiving IRB approval: Data and Safety Monitoring Board (DSMB)**

Each human subject study has to convene a Data and Safety Monitoring Board (DSMB) that has the responsibility to monitor the approved study and report periodically back to the study investigators and the IRB. In constituting DSMB, consideration should be given to include at least one local member from the institution or country where the study is being carried out. The primary responsibilities of the DSMB are to:

(1) Periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy; and

(2) Make recommendations concerning the continuation, modification, or termination of the trial. The DSMB considers study-specific data as well as relevant background knowledge about the disease, test agent, or patient population under study. During the trial, the DSMB should review cumulative study data to evaluate safety, study conduct, and scientific validity and integrity of the trial. DSMB members must be satisfied that the timeliness, completeness, and accuracy of the data submitted to them for review are sufficient for evaluation of the safety and welfare of study participants. The DSMB should also assess the performance of overall study operations and any other relevant issues, as necessary.

In some countries, approved studies are not followed by a Data Safety and Monitoring Board, and this activity may not apply to studies done by ABC Fellows.

**Operation of an IRB**

It is important to recognize that constructing and managing a well-functioning IRB is both complex and expensive.

An *effective IRB* should include at least the following components:

1. An IRB administrative staff that have been trained about the principles and practice of human subject research, with a robust database for recording, maintaining and disseminating IRB records, applications, correspondence, and other relevant materials. The IRB administrative staff members are not voting members of the IRB.
2. A group of health professionals, community representatives, and subject advocates who serve as voting members of the IRB. These members should have been thoroughly trained about IRB procedures, rules, regulations, and understand their role and responsibilities.
3. The resources to process IRB applications in a timely and efficient manner.

**Human subject training office**

In addition to an effective IRB, there should be a training and review office that serves researchers who are planning to conduct human subject research. This training office should have a staff that understands human subject research and all aspects of IRB operations. The training office has several responsibilities, including but not limited to:

1. Conducting training sessions for investigators (and their staff), who will be responsible for the planning and execution of human subject research. The unit should require that potential researchers pass a knowledge test in order to become eligible to submit an IRB application.
2. Review all proposed applications before they are submitted to the IRB, so that they can be optimized prior to review. The staff of this office should also be available to consult about any requests that the IRB may make after reviewing applications.

***IRB challenges***

Experience in conducting international studies that involve human subjects has shown that IRB review is often a major impediment. The challenges range from inadequate and competent human resources to manage an IRB office, inadequate funding and lack of autonomy because of dependence on the government and institution management for its survival. At times reviews can be very slow and may not be very “professional”. There are several reasons for this problem. (a) Many countries simply cannot afford the investment that is required to operate a highly efficient IRB. (b) There is a “scale” problem, since it is not cost effective to operate an IRB that processes only a few applications annually. (c) It is not generally recognized that an IRB cannot operate efficiently unless there is a cognate “IRB training” office that helps to prepare researchers and applications for review.

There are several possible ways to ameliorate these problems. (i) In the United States, entities that are mounting only a few human subject investigations often turn to external commercial IRBs, where they pay for reviews on a “piecework” basis, rather than attempt to operate their own IRB. (ii) Alternatively, if different entities are willing to pool their resources to create a single IRB that can process applications emanating from many different NGOs, government, and academic entities, it can be possible to create efficiencies of scale. Unfortunately, some institutions are reluctant to collaborate in this manner. Training of human resources to manage IRBs and developing sustainability strategies including financial sustainability are additional strategies for ameliorating these challenges.

It should be recognized that optimal functioning of an IRB is an ideal goal, not necessarily a reality in many situations.

**Reading**

Read “Chapter 3. The protection of human subjects”, an extract from Introduction to Responsible Conduct of Research, Office of Research Integrity, U.S. Department of Health and Human Services. (This item is provided as part of the package of References.)

This relatively short chapter is an excellent overview of human subject research.

**Case studies**

**Please write a short (no more than 1 single-spaced page) response for each of the following case studies. Post your responses on the Canvas website.**

**Case 1 (Exempt review)**

Dr. X, a public health nurse, works for an NGO in Country Y in Sub-Saharan Africa, where there is a high prevalence of HIV infection. The NGO operates a clinic in a slum area where they provide health services to a large group of commercial sex workers. The organization plans to develop a program to reduce the spread of HIV among the sex workers, and to carry out a study to determine “safe sex” practices among its clientele, in order to plan a prevention program. The study will involve completing an anonymous questionnaire about the use of male and female condoms, sexual practices, and other information relevant to the transmission risk of sexually transmitted diseases. The information will only be used for program planning purposes and is not intended for presentation or publication.

* Does this study require IRB approval? If so, at what level?
* If the Director of the NGO tells Dr. X that the study does not require IRB approval and that she should get it started, what should she respond?
* Since the NGO does not have an IRB, how should they proceed?

**Case 2 (Informed consent)**

Dr. A runs a TB clinic in sub-Saharan Africa, where there is a high prevalence of pulmonary tuberculosis, particularly among HIV-infected patients. The TB Alliance, a global NGO, is planning a multi-center efficacy trial of a new drug regimen for TB, for comparison with the “standard of care”. They have invited Dr. A’s clinic to participate in the trial and Dr. A is excited about this opportunity. The TB Alliance has developed an IRB application and informed consent form that they would like each trial site to use. The consent form is 12 pages long and full of detailed information. Only half of the patients in Dr. A’s clinic speak English and many of them are illiterate in English. Dr. A’s clinic is understaffed and he certainly does not have the personnel to read this form to each potential participant and carry on a long conversation about the form and the trial.

* What are the problems with a 12-page informed consent form?
* Would some of the other potential sites for this trial have similar problems?
* Is there a practical way to provide informed consent that meets ethical guidelines?
* Who should make that judgment?
* Should Dr. A’s clinic drop out of this trial?
* How should Dr. A handle this challenge?

**Case 3 (Seeking guidance about a study involving human subjects)**

You are a professional staff member of an NGO that has a mission to improve maternal and child health. The NGO would like to design a trial to determine the role of breast feeding upon the health of infants, in an area where practices vary between exclusive breast feeding to exclusive bottle feeding for the first 6 months of life.

* How would you design such a trial?
* What are the ethical issues involved?
* Where would you seek guidance about all of these issues?
* What role would community representatives have in these decisions?

**Case 4 (IRB management)**

Dr. M is the Dean of the School of Nursing at a prominent University in East Africa. Several of her faculty wants to discuss her initiative to expand the research activities of her School, with particular emphasis on human subject research. One problem is that her university does not have an IRB, nor does it have the resources to create and operate one. Her faculty members indicate that most of their proposed studies are collaborations with either the Ministry of Health (in the same country) and/or Northern universities, which do have IRBs that will review these studies.

* How should Dr. M handle this situation
* Do these studies have to be reviewed by an IRB within the University
* Is it ethical to delegate IRB review to an external entity? In the same country? In another country?
* Are there ways to manage this dilemma? If so, how?

**Competencies: questions**

**Read the “competency questions” that follow each section of the module, and satisfy yourself that you could answer the questions.**

1. **What are the central ethical principles that should be applied to human subject research?**
2. **Explain the differences between exempted review, expedited review, and full review.**
3. **What are the main elements in an IRB proposal?**
4. **What are the purposes of an informed consent process? And what criteria should an informed consent plan meet?**
5. **In your opinion, how should one reconcile the IRB practices used in the United States with the resources available in your country?**

**Discussion Questions**

Log into Moodle and answer 1 of the discussion questions posted for the week by of each week Monday. Write an additional comment on another fellows post by Thursday of each week.

**References**

“Chapter 3. The protection of human subjects”, an extract from Introduction to Responsible Conduct of Research, Office of Research Integrity, U.S. Department of Health and Human Services.

* A short and useful introduction to human subject research.

**6. Topic 3: Peer reviewing**

A researcher plays two different roles, as an author of grant applications or publications that are then subject to peer review; and as a peer reviewer. This section deals with the role and responsibilities of peer reviewers. Authorship is presented in a later section.

**Responsibilities of a peer reviewer**

A professional who is asked to act as a peer reviewer for either a grant application or a manuscript for publication has several responsibilities. These include:

* Conducting an unbiased review as a scientific colleague for your professional community
* Only reviewing proposals or manuscripts where you have legitimate expertise, and you can make a meaningful contribution
* Respecting confidentiality as requested by the reviewing entity
* Acting in a dispassionate way, to avoid advocating for friends and deprecating competitors; and declining reviews where you cannot be neutral or have a conflict of interest
* Avoiding exploitation of confidential information to advance the reviewer’s own research
* Returning reviews in a timely fashion (usually defined by the Journal editor)

**Review of manuscripts for a journal.** A manuscript review should cover a number of points, many of which are often requested in the review form. These include:

* Assessing the significance of the proposal or research report
* Evaluating the methods and the quality of the data; indicating if additional data are needed (within reason)
* Determining if the data justify the discussion and conclusions of the authors
* Checking if the authors or applicants have adequately cited relevant prior work of other investigators
* Indicating – if suspicious – any questions about the credibility of the data, or possible plagiarism
* Alerting the editor or program manager about any perceived possible conflict of interest if unreported

**Review of a proposal for possible funding by a sponsor.** Different sponsors have different procedures for review of applications for grants or contracts. Although there could be some slight variations between countries, the general principles are similar for most countries. The following list is revised from the procedures used by the U.S. National Institutes of Health. It represents one example of the criteria used by a funding agency. The major criteria used by the NIH are:

***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?

Reviewers should recognize that some studies justify publication because they are relevant to a particular country or region, even if the data are not particularly unique. Also, some journals are designed to serve local or regional needs, regardless of their global impact.

***Investigator(s)***

Are the project leaders, collaborators, and other researchers well suited to the project? If the applicants are Early Stage Investigators or New Investigators, who are 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, do the investigators have complementary and integrated expertise; is the 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 ofsuccess? 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?

Cultural sensitivity is an emerging concern in research involving human subjects and it has drawn the attention of ethicists. With increased the involvement of non-health professionals in human research and multi-national collaborative research, consideration of cultural sensitivity and relevance of research proposals involving human subjects in Africa are now being stressed.

**Case studies**

**Please write a short (no more than 1 single-spaced page) response for each of the following case studies. Post your responses on the Canvas website.**

**Case 1 (Conflict of interest)**

Dr. Y receives a manuscript for review. It contains data that are similar to the results of a study in which she is participating. She believes that the reported study findings are based on a smaller sample, which in her opinion does not provide sufficient evidence to provide robust conclusions. However, she knows that a request for more subjects in the study would either lead to rejection of the manuscript or delay publication of the study by at least one year.

* Is Dr. Y conflicted? If so, describe the conflict?
* Should Dr. Y decline to review the study?
* Can Dr. Y discuss this report with his colleagues?
* Can Dr. Y consult with a statistician about the power of the study?
* If Dr. Y decides to review the study, how should he disclose potential conflicts?

**Case study 2 (Confidential vs. open review)**

Different journals handle confidentiality in different ways, and there is a current dialogue in the published literature about these different options. Option 1. The authors of the manuscript are known to the reviewer but the reviewers are anonymous, and the author does not know who wrote the reviews. Option 2. The authors are requested to “anonymize” their manuscripts so that the reviewers are (in theory) blinded to the authorship, and the author is also blinded about the reviewers’ identities. Option 3. Open information, so the authors are known to the reviewers and the reviewers are identified to the authors.

* Which system would you prefer as a reviewer? As an author?
* Which system is the fairest?
* Which system would produce the most useful reviews? And lead to the best final product, whether a published manuscript or a revised research proposal?

**Competencies: questions**

**Read the “competency questions” that follow each section of the module, and satisfy yourself that you could answer the questions.**

1. **List the various elements that should be included in the review of a manuscript, and explain the importance of each one.**
2. **List the various elements that should be included in the review of a research proposal and explain the importance of each one.**
3. **From your personal experience, do you have any criticism of the peer review system or suggestions how to improve it?**

**Discussion Questions**

Log into Moodle and answer 1 of the discussion questions posted for the week by of each week Monday. Write an additional comment on another fellows post by Thursday of each week.

**References**

Pulverer B. Transparency showcases strength of peer review. Nature 2010 468: 29-31.

* An interesting short discussion of various options for peer review of manuscripts

**7. Topic 4: Data management**

The management of data involves several different issues, including data ownership, data collection, data storage and protection, and data sharing. Each of these issues is discussed below. In addition, we have added a short overview of copyright and patenting, both data-related issues.

**Data ownership**

Data ownership can be a contentious matter and is often misunderstood, particularly by junior investigators. The individuals who are directly involved in collecting the “raw” data frequently assume that they “own” it since it was generated by them. This is NOT correct. Data is usually owned by an institution and not by one or more individuals. The role of the participants in the study in ownership of the data is an interesting subject for discussion.

***What determines ownership?***

Most data are collected as part of a research study and the study is usually financed by an award, i.e. a grant, cooperative agreement, or contract. The terms of this award usually include stipulations about data ownership. In general, government or other non-for-profit funders of a research grant usually cede ownership of the data to the institution that receives the award. Typically, data collected by faculty or other employees of universities will be owned by the university. If the research is conducted by a government agency, then that agency usually owns the data. If the funder is a company, the company may stipulate that they own the data, usually generated by a research contract. However, there are no absolute rules, *so it is highly recommended that researchers determine data ownership before they embark on a study*.

***What are the implications of data ownership?***

Ownership has significant impact on how the data can be used, and who controls those decisions. Typically, if the researchers are working for a university and the university owns the data, then the researchers are free to present or publish the data at their own discretion. They are also free to patent inventions arising from the research, but usually this has to be done in collaboration with the technology transfer branch of the university (see Patents below for more information). If the research is conducted by a government agency or by an NGO, there may be bureaucratic regulations about presenting or publishing data, and the primary researchers may have to get permission or have their proposed presentations “cleared” by the agency. On the other hand, if the sponsor, such as a for-profit company, owns the data, then the company may control its presentation and publication, and they may have an exclusive right to patent any inventions arising from the research.

***Researchers need to realize that just because they collected the data, analyzed it, and prepared presentations or manuscripts, this does not automatically give them the freedom to disseminate their data*.** Therefore it is important to determine data ownership before a study is begun. If the investigation is part of a multi-center study, then the leaders of the study may have the right to control presentations and publications. Researchers at individual study sites may *not* be free to publish or present without permission from the study leadership.

Another corollary of these guidelines is that individual research personnel who are employees of a university, government agency, NGO, or other entity, should always work with the administration of their employer when arranging for grants and contracts. An investigator who makes a unilateral arrangement with a funder for a research project – and bypasses the administration of his employing entity – is committing a kind of research “misconduct” and could be terminated for such behavior.

**Data collection**

There are 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. Methods can be compromised by bias — choosing one method or set of experimental conditions so that a particular conclusion can be drawn — or sloppy technique. Although the need for appropriate methods might seem obvious, experience suggests that researchers sometimes use inadequate numbers of subjects or inappropriate statistical tests to evaluate their results. *Therefore, it is wise to discuss the proposed methods with colleagues who have the appropriate expertise and are not participants in the planned research.*

***Attention to detail***

Quality research requires attention to detail. Protocols must be properly designed and the results accurately recorded and interpreted. A failure to pay attention to detail can result in mistakes that will later have to be corrected and reported. In the case of human subject research, it may not be possible to correct errors in data collection after completion of the study.

***Authorized sources***

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

* human subjects in research
* information contained in some libraries, databases, and archives; published photographs; and information posted on some web sites
* copyrighted or patented processes or materials
* hazardous materials and biological agents

If you are not sure whether permission is needed, check before proceeding with data collection.

***Recording of data***

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 in recording data, 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, researchers are advised to keep two simple rules in mind in order to avoid problems later, should someone ask or question about the 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 altered.

**Data storage and protection**

***Protection of data from disasters***

Once collected, data must be properly stored, protected, and accessible. The information may be needed later to confirm research findings; to establish priority; or to be reanalyzed by other researchers. The responsible handling of data requires proper storage and protection from accidental damage, loss, or theft. 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 that could destroy stored data.

***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. Using random codes to identify individual subjects instead of names or social security numbers can protect private information. Whatever the method used, the researcher who collects or uses the information has the primary responsibility for its confidentiality.

***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.Some U.S. government agencies require that data be retained for 3 years following the submission of the final research report. It is difficult to predict when data collected in the past could be useful. When AIDS emerged, researchers used stored samples to pinpoint the first occurrences of HIV infections. Although the original samples may not have been stored for this purpose, nonetheless they were useful for tracking diseases years later.

Researchers should give some thought to retaining data longer than some minimum period required by specific regulations. Before throwing out notebooks, cleaning out files, or erasing your computer memory, give careful consideration to potential future uses of your data.

**Data Sharing**

It is widely agreed that research data should be shared, but deciding when and with whom to share, raises questions that are difficult to answer. Researchers are not expected to release preliminary data, which have not been carefully checked and validated. The one exception is 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 share this information with the public and other researchers before it is fully validated.

Researchers can withhold data until they have had time to establish priority for their work through publication or, in rare cases, a public announcement. Provided no agreements have been made to the contrary, keeping data confidential prior to publication is acceptable. In fact, some journals will not publish data that have already been released.

***Goals of sharing data***

Eventual release of data, preferably in a readily accessible and permanent format, such as a peer-reviewed journal, is an implicit commitment that accompanies most supported research. If none of the information is ever reported, even in the case of negative results, then the research investment was wasted. Sharing data reinforces open scientific inquiry, encourages diversity of analysis and opinion, promotes new research, and makes possible the testing of new or alternative hypotheses. It supports studies on data collection methods and measurement, facilitates the education of new researchers, and permits the creation of new datasets. Data sharing – including patenting new “inventions” - allows scientists to expedite the translation of research results into knowledge, products, and procedures to improve human health.

**Copyright or intellectual property**

Copyright is a set of exclusive rights granted to the author or creator of an original work, including the right to copy, distribute and adapt the work. Copyright now covers a wide range of works, including books, publications, maps, dramatic works, paintings, photographs, sound recordings, motion pictures and computer programs. Copyright does not protect ideas, only their expression.

In most jurisdictions, copyright arises upon creation of a work 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. The duration is usually the life of the creator plus 25-70 years (depending upon the laws of each country). Today, copyright laws have been standardized to some extent through international agreements such as the Berne Convention. Although there is considerable consistency among nations, each country has its own copyright laws and regulations.

***What does copyright mean to the holder?***

Copyright is literally, the right to copy, though "the right to control copying" is more accurate. Copyright gives the creator of a work (the copyright holder) exclusive rights to exercise control over copying and other exploitation of the works for a specific period of time. The copyright owner is also given a negative right to prevent anyone else from doing so without consent. The copyright holder can assign the copyright to another individual or business, such as a publisher, who then acquires the rights.

***How does copyright apply to a research scientist?***

If you create a power-point presentation or a poster, or write a manuscript, you are considered a “creator” of the work and you automatically – and instantly - hold copyright to that item. If you submit a manuscript to a publisher, the publisher usually requests that you assign your copyright to them, so that they are free to sell copies of the journal (containing your article) or reprints of the article. As the creator of the work, however, you retain the right to make and distribute copies (such as PDF copies or hard copies) as long as these are free. If the publisher holds the copyright they have exclusive rights to sell the article (or book). These arrangements are ordinarily covered in a copyright assignment which is a standard form provided by the publisher for your signature. Arrangements vary somewhat, so it is useful to be sure that you (and your employer) retain not-for-profit rights to the work you have created.

**Patents**

(It is unlikely that you will participate in activities that involve patents, but this section is included for your information.)

The purpose of patent laws is to encourage inventors to create new products, which –it is assumed – will benefit the public, directly or indirectly. It is expected that the ability to profit financially will create the incentive to invent, and patent laws are designed to provide inventors with the assurance that they will be remunerated for their inventions – if they are produced and sold. 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. The process for granting patents varies widely between countries according to national laws and international agreements. The following brief summary refers to practices in the United States, and will be different in other countries.

***How is a patentable invention defined****?* Typically, an invention must meet all of the following criteria to be patentable:

* new
* non-obvious
* useful or industrially applicable

The proposed invention must really be different from inventions that have already been patented. It must be “non-obvious”, in other words, something that is not apparent to the general public; and it must have the potential to be developed into a product that can be sold, since the purpose of the patent system is to commercialize technology for the public good.

In addition to products such as an automobile engine or a new antibiotic, patents can be granted for processes, such as the method to make the new antibiotic, or for computer software as well as hardware. In some cases, natural products, such as gene sequences, can be patented, as well as genetically modified plants or animals.

***How is a patent created?***

In contrast to copyright, patents are created by a carefully regulated process. Each country has its own laws governing patents and a patent office to implement those regulations. An inventor must apply to this office, and the application is rather lengthy and complex and could even include a model of the invention as well as a detailed description. In the United States, most universities have a “center for technology transfer” with expert staff. If a faculty member believes that she/he has made a discovery that could be patented as an invention, the faculty member consults with the staff of the center for technology transfer, and together they make a decision whether or not to file a patent application. In the U.S., a typical patent application is written by a patent specialist and the process costs about $25,000, so it is not trivial. Once an application is filed, the patent office usually takes 1-2 years to review the patent application and accept or reject it.

Once an “invention” is patented, it may then be licensed to a commercial company that acquires the right to develop the invention into a commercial product. The license also carries a royalty agreement, which pays the University (or other entity that holds the patent) a percent of the income from sale of the commercial product. In the U.S., Universities have patent policies, which determine how the royalties are divided between the faculty inventor and the University itself.

Creation of patents has in the recent past years been recognized in some universities in Africa. These institutions have established technology incubation and transfer centres, and have developed policies and operational procedures to guide the division of royalties between the institution and the inventor.

***How does the patent system impact a health researcher?*** Patents are only relevant if the health researcher makes a discovery that she/he believes could be patented as an invention for commercialization. In this contingency, the researcher needs to consult the administrative officials at her/his employer for advice how to proceed.

**Case studies**

**Please write a short (no more than 1 single-spaced page) response for each of the following case studies. Post your responses on the Canvas website.**

**Case study 1 (data ownership)**

Dr. M is taking a fellowship during which she has been assigned to the Ministry of Health of a country in Sub-Saharan Africa. She is part of a team that is collecting data on compliance among patients who are being treated with antiretroviral drugs for HIV infection. At the completion of her rotation in the Ministry she would like to take a copy of the records that she and other co-workers have compiled. She needs these records to write up a report of her work, which is a requirement of her fellowship. When Dr. M asks her supervisor in the Ministry for permission to make a copy of the records, the supervisor refuses on the grounds that all such records are the exclusive property of the Ministry.

* How should Dr. M handle this situation.
* Who owns these records?
* What rights does Dr. M have to make a copy of these records? .
* Does the Ministry have the right to refuse Dr. M’s request?
* Could this problem have been anticipated and prevented?

**Case study 2 (data storage and retrieval)**

Dr. A is a trainee in an NGO and is doing a survey to determine the frequency of breast and bottle feeding among a sample of women living in the Kibera section of Nairobi. He visits individual women, and records their answers on his cellphone. Each day he transfers the recent data to a laptop at the Kibera office of the NGO. One day he comes to work and the laptop is missing, presumably stolen. His data are lost.

* What should Dr. A have done to protect his data
* Considering the conditions in the NGO office in Kibera, could Dr. A have devised a practical way to back up his data?
* Is this an issue that Dr. A’s local supervisor should have discussed with him?

**Case study 3 (data dissemination)**

Dr. B is a Fellow at Makerere School of Medicine who has collected data under an IRB-approved protocol to determine the attitudes of young men in Kampala about adult circumcision and their willingness to undergo that procedure. There is an annual “research day” at Makerere University, where trainees are encouraged to present posters summarizing their research activities. Dr. B is standing by her poster when her supervisor comes by and asks her if she has requested and received permission to present these data. Dr. B says she did not realize that this was required and assumed that she had the right to present “her data” wherever she wished.

* Who “owns” Dr. B’s data?
* What “rights” does Dr. B have to present her data
* Since the poster session is for trainees at Makerere, is this a public presentation?
* What “rules” apply to such a presentation?
* The same rules that apply to a presentation at a professional meeting? Or a publication?

**Competencies: questions**

**Read the “competency questions” that follow each section of the module, and satisfy yourself that you could answer the questions.**

1. **What is the best way to protect hardcopy data from destruction and make it readily retrievable in the future?**
2. **How would you document electronic data as to the circumstances and date of collection and prevent post hoc meddling with the results?**
3. **Once a researcher has published her results, should she be required to share the raw data with other qualified investigators?**
4. **Should data belong to the researcher rather than to her/his institution?**

**Discussion Questions**

Log into Moodle and answer 1 of the discussion questions posted for the week by of each week Monday. Write an additional comment on another fellows post by Thursday of each week.

**8. Topic 5: Research misconduct**

**The following discussion is based on policies used in the United States; policies and practices may differ in other countries.**

Most individuals who conduct research intend to behave in an ethical manner. However, there are infrequent examples of investigators who consciously do unethical things, usually in order to enhance their research performance in some way or other. Furthermore, even honest research personnel need some guidance as to the limits of acceptable practice. For these reasons, the research community in many countries has devised a set of definitions of research misconduct, and a process for responding to instances where misconduct is suspected.

***What is research misconduct*?** Research misconduct is often defined as “fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results”. Fabrication is the creation of research data without any basis in actual observations. Falsification is changing reported results. Plagiarism is copying materials from other sources without permission or acknowledgement.

Plagiarism may be the most frequent problem, since it is sometimes an inadvertent use of text from a prior publication. There are commercial computer programs that will search global publications to be sure that your manuscript is “plagiarism free”.

However, there are additional types of research misconduct, which can be subsumed under the heading “significant departures from accepted ethical research practice”. One example is the failure to conform to policies regarding human subjects, such as deliberately omitting the use of an approved protocol for informed consent.

Instances of misconduct are usually reported as allegations or suspicions, leading to a formal investigation. To be considered research misconduct, an action must meet several criteria:

* represent a significant departure from accepted practices
* have been committed intentionally, or knowingly, or recklessly
* be proven by a preponderance of evidence

Certain acts that are clearly wrong, but are not unique to research, *are excluded from research misconduct*, but are subject to investigation and prosecution under other policies. These include criminal behavior, personal disputes, violations of grant management policies, discrimination or harassment, or other unacceptable behaviors.

***What is the process for evaluating alleged research misconduct?*** In the United States, most institutions have a written policy that defines research misconduct and describes a process for investigation of alleged misconduct. In many instances, an individual(s) will observe something that triggers their suspicion of misconduct, usually for a project in which they are participating. This individual, sometimes called a “whistle blower” should report her/his suspicions to an appropriate member of the administration of the organization where they are employed. At that point, the administration takes charge of an investigation that is conducted in several stages. If the administration decides that there is merit in the allegation, the final stage is usually conducted in a quasi-judicial manner, with lawyers representing both the institution and the accused individual. Because, an accused individual is considered innocent until proven guilty, every effort is made to conduct the proceedings in a confidential manner.

Should the appointed “judges” conclude that misconduct has been “proven by a preponderance of evidence”, the administration is then responsible for determining what sanctions should be instituted. These can vary from a personal reprimand to termination of employment. Also, if the misconduct is associated with research supported by an external award, the institution will report the situation to the research sponsor. The sponsor may, in turn, add additional sanctions, such as forbidding the “convicted” investigator from applying for future research awards.

**Case studies**

**Please write a short (no more than 1 single-spaced page) response for the following case studies. Post your response on the Canvas website.**

**Case study (bribery):**

Dr. X is a PhD microbiologist who is a junior investigator on a study that compares several drug regimens to treat multi-drug resistant tuberculosis. He has participated in the design of the study, has conducted all the laboratory tests involved in the study, and has written part of the manuscript dealing with the laboratory work. The senior investigator on this study is Dr. B, a Professor in the Department of Medicine and a powerful member of the faculty of Dr. X’s medical school. At the end one of the writing sessions for the study, Dr. B asks Dr. X to stay behind for a personal discussion. Dr. B tells Dr. X that if he wishes to have his name as one of the lead authors on the manuscript he will have to make a “contribution” to a “charity” that is operated by Dr. B’s wife.

Questions

* Is this a case of potential bribery?
* How should Dr. B respond?
* Should he report the situation to the Dean of the medical school, knowing that Dr. X will deny the conversation?
* Should he refuse Dr. B’s request, knowing that it may hurt his promotion within the institution?

**Competencies: questions**

**Read the “competency questions” that follow each section of the module, and satisfy yourself that you could answer the questions.**

1. **What are the criteria for an action to be considered research misconduct?**
2. **Should you be witness to an action that you suspect might be research misconduct, what should you do?**
3. **If you are in charge of a clinical trial, how would you minimize the chances of research misconduct?**
4. **If you are a junior professional staff member and a trainee, for whom you are responsible, reports to you a suspicion of research misconduct, what should you do?**

**Discussion Questions**

Log into Moodle and answer 1 of the discussion questions posted for the week by of each week Monday. Write an additional comment on another fellows post by Thursday of each week.

**9. Topic 6: Authorship guidelines**

An essential goal of most research projects is the definitive reporting of the results so that they are available to the scientific community and the public at large. If research is supported by a sponsor, an implicit obligation on the part of the funded researchers is to publish results, which is the ultimate work product expected by the sponsor. (There are some exceptions to these generalizations, however. For instance, if the sponsor owns the data and has the prerogative to decide how to treat the research results, they may decide to “suppress” presentation or publication.) It is assumed in the following discussion that one aim of the research team is the publication of the results in a scientific journal.

Because there is a separate module that deals with the preparation of scientific reports, manuscripts, and other presentations, this section focuses only on the issue of authorship.

***Who should be an author on a published report?***

Eligibility for authorship is a contentious issue and different institutions, disciplines, and journals have somewhat divergent views.

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 individuals who made more limited contributions deserve authorship credit. One of the most contentious issues is whether persons directly involved in collecting the primary data – such as laboratory technicians or research coordinators – should be included as authors or simply acknowledged in the footnotes.

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*.

Another perspective on authorship focuses on responsibilities, and requires that the list of authors include at least one investigator who can take direct responsibility for each component of the research study.

As noted above, practices for determining authors vary considerably by discipline and even between research teams. 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.***

***What are the obligations of the authors?***

It is important to understand that authorship carries responsibilities. At least one author must be able to certify to the accuracy of each part of the primary data, either because she/he collected the data or oversaw the staff members who did the data collection. Likewise, some authors must be directly responsible for digesting, collating, analyzing the data and doing any statistical tests or interpretations. Also, some authors must take responsibility for the selection and accuracy of references and for acknowledging prior relevant publications. Hopefully, all authors will have read and “signed off” on the whole manuscript.

***What determines the order of authorship?***

By general convention, certain locations on the list of authors carry special credit and responsibilities. The first place (or up to three places) are used for the workers who “spearheaded” the research project, which means that they were involved in the design and conduct of the study, and analysis of the data. The last place in the list is usually reserved for the “corresponding” or “senior” author. The senior author assumes responsibility for all aspects of a publication, including: the accuracy of the data; the names listed as authors; approval of the final draft by all authors; and handling all correspondence and responding to inquiries. The remaining authors are often listed in alphabetical order.

***Practices to be avoided***

There are a number of practices that are frowned upon, although they occur to some extent:

***Honorary authorship*.** The practice of listing undeserving authors on publications, called “honorary” authorship, is widely condemned. However, common agreement notwithstanding, honorary authorship is a significant problem in research publication. Researchers are listed because they are the chair of the department or institution, in which the research was conducted, provided funding for the research, provided reagents, or served as a mentor to the primary author. Persons in these positions can make significant contributions to a publication and may deserve recognition in the acknowledgements.

***“Salami”*** *publication* is the practice of dividing one significant piece of research into a number of small experiments (least publishable units), simply to increase the number of publications. ***Duplicate publication*** is the practice of publishing the same information a second time without acknowledging the first publication.

***Premature public statements*** of research results should – in general – be avoided. Investigators should follow standard publication practices and results should be made public only after they have been carefully reviewed and accepted by a peer-reviewed journal. 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 premature announcements are unjustified. Also, many journals will not publish an article if the results have already been publicly reported.

**Case studies**

**Please write a short (no more than 1 single-spaced page) response for each of the following case studies. Post your responses on the Canvas website.**

**Case study 1 (authorship rights)**

Ms. Y is the senior coordinator on a clinical trial of a new microbicide, with responsibility for training the other coordinators who deal directly with individual human subjects. She is responsible for accuracy of the information collected by the coordinators, and many other details that are vital to running the trial. After the trial has been completed, the lead investigators prepare a draft of a manuscript that they distribute for comments and suggestions to all the professional participants and to a few of the senior staff. Ms. Y is both surprised and angry that she is not included as an author but only given an acknowledgement along with many others who have worked on the trial.

* What should Ms. Y do?
* Does Ms. Y have a “right” to be an author? Please justify your opinion.
* In hindsight, could this problem have been avoided?

**Case study 2 (Author’s responsibilities)**

An important clinical trial about an AIDS microbicide is published in a high profile journal, reporting that this particular microbicide substantially reduces the risk of HIV infection. The paper includes self-reported data on the use of the microbicide. One of the reported findings is that there is no correlation between “compliance” (consistent use of the microbicide) and its effectiveness. After publication, there is a barrage of comments from microbicide experts that question the accuracy of the reported information on compliance.

* Are the authors of the paper responsible for the data on compliance? Which authors? All the authors?
* Are the authors responsible for the accuracy of this aspect of the study? Should they have done a better job to determine the accuracy of self-reporting?
* Should this issue have been discussed in the paper? Could it have been handled in the discussion?
* How should the authors respond when the journal editors ask them to prepare a response to several critiques that will be published in the journal?

**Case 3 (reporting prior to publication)**

Dr. Z is a nurse epidemiologist who is the lead on a trial about several new diagnostic tests for tuberculosis that are being compared for their sensitivity and specificity. She receives an invitation to present the data at a national meeting of an infectious disease society. A manuscript reporting the data has been prepared and submitted to a peer-reviewed journal, but the decision is pending and the manuscript has not yet been accepted.

* Is it proper for Dr. Z to accept the invitation and report the data
* Will the presentation jeopardize publication by the journal?
* Does Dr. Z have the right to make the presentation?
* How should Dr. Z handle this situation?

**Competencies: questions**

**Read the “competency questions” that follow each section of the module, and satisfy yourself that you could answer the questions.**

1. **List the criteria for authorship on a publication.**
2. **What kind of public presentations about a study can you make prior to publication, without jeopardizing acceptance by a peer-reviewed scientific journal?**
3. **What responsibilities does the first author have? A “middle” author? A senior author?**

**Discussion Questions**

Log into Moodle and answer 1 of the discussion questions posted for the week by of each week Monday. Write an additional comment on another fellows post by Thursday of each week.

**Appendices**

**In addition to the present document, there are two other documents that are provided as part of this module.**

1. **References**

These references are compiled into a single pdf document provided for your convenience

Chapter 3. The protection of human subjects”, an extract from Introduction to Responsible Conduct of Research, Office of Research Integrity, U.S. Department of Health and Human Services.

* A short and useful introduction to human subject research.

Pulverer B. Transparency showcases strength of peer review. Nature 2010 468: 29-31.

* An interesting short discussion of various options for peer review of manuscripts.

1. **Reference manual**

Supplied as a single pdf document