Texas Christian University

Responsible Conduct of Research

TRAINING HANDBOOK

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Chapter 1: Ethics in Research

Conflict of Interest:

A conflict of interest (COI) is any circumstance where personal, professional, financial, or other private interests of a person or institution compromise or potentially compromise your professional judgment.

HISTORY:

In 1995, the U.S. government began regulating financial conflicts of interest in federally sponsored research, through the Health and Human Services and Public Health Service (PHS) offices. These regulations spelled out responsibilities between institutions receiving PHS research funding and the research investigators.

DEFINITIONS:

Investigator: Project director or principal investigator and any other person who is responsible for the design, conduct or reporting of research funded by the PHS (collaborators, consultants, post-doctoral fellows, and graduate students).

While non-financial factors affecting professional judgment are important, we focus on the potential for the financial interests of investigators to affect the design, conduct, or reporting of their research. This may include the receipt of personal compensation for consulting activity, the ownership of equity in publicly or privately held businesses, and the receipt of income from intellectual property rights held by the researcher.

The cornerstone of managing conflicts of interest is transparency,
which begins with the investigator's disclosure of
significant financial interests (SFIs) to the institution.

Significant financial interest (SFI): anything of monetary value, whether or not the value is readily ascertainable, that:

- Is related to the investigator's professional responsibilities on behalf of the Institution including research, consultation, teaching, professional practice, committee memberships, and service on panels.
- Belongs to the investigator or their spouse or dependent children.

Financial conflict of interest (FCOI):

- Significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

The Bayh-Dole Act (1980)

Before 1980, the federal government retained the rights to the research and discoveries of the investigators it funded. Many companies were having difficulty obtaining licenses to manufacture and market their discoveries. In response to this, the U.S. Congress passed the Bayh-Dole Act in 1980.

The Bayh-Dole Act permits recipients of federal funds to obtain the title to the inventions they develop under their federally funded projects and to transfer the technology to the private sector. The Act allows academic researchers to take an active role in the private applications of their research. It also enables universities to benefit from the shared royalties.

Critics suggest that there is a downside to academic-industry partnerships. They argue that financial arrangements with sponsors can have effects on publication practices and even on the assignment of students or trainees to work on projects from which the researcher is likely to benefit financially.

POLICY:

Reporting, managing and publicizing information on FCOIs and SFIs: The Department of Health and Human Services (HHS) issued a final rule on FCOI in 2011. Beginning August 24, 2012, institutions applying for or receiving PHS funding must be compliant with the new rule.

Individual institutions may choose to apply the standards of the revised regulations to all research, regardless of whether there is PHS support. They now have to take on these additional responsibilities with respect to conflicts of interest in PHS-funded research:

- Maintaining an up-to-date, written, enforced policy on financial conflicts of interest and make such policy available via a publicly accessible Web site
- Designating an institutional official(s) to solicit and review disclosures of significant financial interests from each investigator who is participating in the PHS-funded research
- Providing guidelines for the designated institutional official(s) to determine whether an investigator's significant financial interest is related to PHS-funded research and whether it is a financial conflict of interest
- Taking any actions necessary to manage financial conflicts of interest. Management of an identified financial conflict of interest requires development and implementation of a management plan and, if necessary, a retrospective review and mitigation report

Strategies for Managing Conflict of Interest

Since the cornerstone of managing conflicts of interest is transparency, that begins with a disclosure of SFIs to the institution by the investigator. When an institution confirms a financial conflict of interest (FCOI) in PHS-funded research, a management plan must be developed and implemented. This plan may simply consist of a disclosure in presentations and manuscripts, or it may include measures such as removing the conflicted individual from primary oversight of the research, or alternatively, reducing or eliminating the financial interest. When reporting FCOIs to the PHS awarding components, institutions must report the investigator's agreement to comply with a management plan. In accordance with the Final Rule, an institution's management plan must describe:

- The role and duties of the conflicted investigator in the research project
- Conditions of the management plan
- How the management plan is designed to safeguard objectivity in the research project
- Confirmation of the investigator's agreement to the management plan
- How the management plan will be monitored to ensure investigator compliance

Depending on the seriousness of the conflict, other management strategies could include:

- Modifying the research plan

- Monitoring of research by independent reviewers
- Reducing the amount of the financial interest
- Stopping relationships that create conflicts
- Disqualification of the researcher from part of or the entire research project

The institution must update the funding agency on the status of the FCOI and any changes to the management plan annually.

Nature of Institutional Conflicts of Interest

Institutional Conflicts of Interest (COI) can occur at many levels in an organization; they can even involve the institution itself. For example, a tobacco company which intends to sponsor a study examining nicotine addiction could put an institution in conflict about accepting the company's funding. Likewise, an institution may be conflicted about accepting a grant that examines topics which contradict the fundamental beliefs of those at the institution. An institution may have a conflict with one of its researchers accepting funding from groups that support eugenics or other controversial topics.

Different Types of COI

Academic conflict of interest could occur if an individual interferes with the peer review process in the hope of achieving some type of intangible personal gain.

Conflicts of commitment (also called conflicts of effort, conflicts of obligation) occur when the time spent on outside activities competes with the time expected by the primary employer to be spent on teaching, research, or service. University policies typically allow no more than 20% of a faculty member's effort, or one day a week, to be devoted to outside activities.

Conflict of conscience occurs when personal beliefs influence objectivity in research. Researchers, for example, may have a particular moral view which affects their ability to evaluate research relating to the development of nuclear weapons.

SFI Threshold for Disclosure According to Final Rule

Each investigator who is planning to participate in PHS-funded research must disclose the following SFIs to the institution no later than the time of applying for funding:

- Income in excess of $5,000 from a publicly traded entity (a company whose stock is available for purchase by the general public) *during the past twelve months*
- Stock valued in excess of $5,000 at the time of disclosure in a publicly traded entity
- A combination of the above two items (stock and income) that exceeds $5,000
- Any amount of equity (stock, stock options, or other ownership interest) in a non-publicly traded entity (such as a start-up company)
- Compensation that exceeds $5,000 from a non-publicly traded entity *in the past twelve months*
- Income related to intellectual property rights paid by any source other than the investigator's current institution
- Any reimbursed or sponsored travel paid by an entity, including non-profit organizations, but excluding travel sponsored by or reimbursed by a government agency, a U.S. institution of higher education or a research institute affiliated with a U.S. institution of higher education, a medical center, or an academic teaching hospital

The specific details that must be disclosed are:

- The name of entity sponsoring the travel and purpose, destination, and duration of the travel
- Any other interests required under the institution's policy
- With respect to the provisions outlined in the federal regulations, institutions may have more, but not less, stringent policies
- Investigators must review their institution's conflict of interest policies to make sure that they disclose the information that is specifically required by those policies

Chapter 2: Authorship

Authorship of a publication is key for both receiving credit for one's work and for taking responsibility for the reliability of that work. Some of the most intense disputes in the history of publication have turned on the question of priority or who published first. This illustrates the extraordinary power of authorship in terms of establishing social status.

Appointment, promotion, tenure, status and more are based on: (1) whether one's name is on an article or articles, (2) how many articles have been authored or co-authored, (3) whether one is a lead author and, more recently, (4) whether anyone else has paid attention to it. With such social and economic rewards, it is no wonder that deceptive authorship practices are arguably the greatest source of corruption in the sciences and are becoming a more notable problem in the humanities.

Authorship Practices: Criteria for Earning Authorship

The Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (2010) from the International Committee of Medical Journal Editors (**ICMJE**) provides a suite of standards for publication and authorship. Guidelines are included for preparing and submitting manuscripts, publishing and editorial issues, and ethical considerations in the conduct and reporting of research. Because authorship issues have been so prominent in the field of scientific publication, fairly extensive guidelines are included on authorship, contributorship, and conflicts of interest in publication. Although these issues are not as prominent in the humanities, it is likely that with the recently increased ease of collaboration and sharing of resources, these issues will become more prevalent, and these guidelines may be instructive for scholars in many fields. In addition:

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

• When a large, multi-center group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship defined above.
• Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship.
• All persons designated as authors should qualify for authorship, and all those who qualify should be listed.
• Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Determining the order of authors on a publication can be a source of much conflict. Part of the reason is that in many disciplines, the first author is, and often should be, regarded as the most important one assuming that it is the person who made the most significant contribution to the project.

How should the order of authors be determined? There is little official guidance from professional journals on the issue but the ICMJE states that: "The group should jointly make decisions about contributors/authors before submitting the manuscript for publication. The corresponding author/guarantor should be prepared to explain the presence and order of these individuals."

Determining the order of authors should involve a process. Research team members should start a discussion about the issue at an early stage of a project.

Authorship is one of the three principal ways in which credit is assigned for a research contribution. The others are **citation** (of a researcher's previously authored work) and **acknowledgment** (of some contribution to the present research).

Professional societies have offered some guidance on the issue of citation practices. Since 1985, the American Chemical Society (ACS) has since 1985 issued several versions of its **Ethical Guidelines to Publication of Chemical Research** to guide those involved in editing, authoring or reviewing for any of its numerous publications. In the most recent revision, the ACS Guidelines include as the ninth of the twelve obligations listed for authors: “An author should identify the source of all information quoted or offered, except what is common knowledge.

Information obtained privately, as in conversation, correspondence, or in discussion with third parties, should not be used without explicit permission from the researcher with whom the information originated. Information obtained in the course of confidential services, such as refereeing manuscripts or grant applications, should be treated similarly."

Authorship makes one accountable for the work. Unless an author's contribution is explicitly stated to have been limited to a certain area, such as "Jane Smith contributed the statistical analysis for this work," the default expectation is that the author is responsible for the entire work.

The Institute for Electrical and Electronic Engineering's (**IEEE**) **Publication Guidelines** is somewhat similar to the ICMJE's **Uniform Requirements for Manuscripts Submitted to Biomedical Journals** in that they both give three criteria to be necessary for authorship, but they differ as to the content of the second criterion. The IEEE version includes reviewing (as well as drafting and revising) an article a criterion for authorship.

The IEEE affirms that authorship credit must be reserved for individuals who have met all of the following conditions. Authors must have:

1. Made a significant intellectual contribution to the theoretical development, system or experimental design, prototype development, and/or the analysis and interpretation of data associated with the work contained in the manuscript

2. Contributed to drafting the article or reviewing and/or revising it for intellectual content

3. Approved the final version of the manuscript as accepted for publication, including references

Types of Authors

Those included in the author list are all presumed to have fulfilled the obligations of authorship and are prepared to take responsibility for the article or other publication, either the portion for which they have explicitly identified as their work, or, in the absence of such a specification, the entire work.

Lead author - The lead author is the author who is principally responsible for the work, the one who made the greatest intellectual contribution. The lead author generally takes responsibility for the whole research report, even if some other coauthors explicitly state that they take responsibility for only some aspect of it.

Submitting author - This is a designation for the author who submits the manuscript for publication and usually is the author who deals with the journal and its editors from that point forward, and frequently becomes the corresponding author. This author has a special responsibility to see that all the authors are appropriate as authors and must ensure that all have read and approved the final version of the work. If there are special publication requirements, such as the requirement by some journals that all authors sign a form saying that they have read and approve the final version, the submitting author sees that those are met. The submitting author is often the lead author or the leader of the research team, but need not be. For example, if a senior investigator were publishing an article with one of her trainees, the senior investigator might submit the article, because she knows more about dealing with journals or the specific journal in question. On the other hand, the senior investigator might ask the trainee to handle the submission (to give the trainee experience) even if the senior investigator were the lead author as well as the team leader.

Corresponding author - The corresponding author is the person whom interested individuals should contact about the article after it is published. The corresponding author will typically be the author who receives the bulk of the reprints of the authored article, because that person will answer requests for reprints. The corresponding author may be designated by the other authors simply because that person has the most predictable mailing address (for instance, if all of the other authors are changing institutions in the coming year). In a few fields, the corresponding author is assumed to be the leader of the research team.

First author - This term is most frequently used to mean the lead author because in many fields it is customary to indicate the lead author by placing that person's name first in the author list. It is not surprising that in many fields, the first position in the author list is reserved for the lead author. Often, the article will then become known by the name of the first name in the author list. There are exceptions, however.

NOTE: Not all fields have adopted the first author convention. Another very common way of ordering the authors is alphabetically (by last or family name). If the author list is extremely long, alphabetical listing may be the only practical way of handling the ordering of authors. If the ordering is alphabetical, it signifies nothing about the relative contributions. Therefore, the term "first author" does not always carry implications for differential credit among the coauthors.

Some journals or fields that take author position to signify contribution (and typically publish articles with a small number of authors) fine tune the signification of contribution even further: if an article has two authors, those authors may publish the article either with the first author's name beside the second's (to indicate equal contribution) or with the first's above the second (to indicate that the first author is the lead author).

Last author - As with the first author position, the last author position may signify nothing more than position in the alphabetical order.

NOTE: In some fields in which the author order does indicate contribution, the last author position simply means the author who made the least important contribution.

In other fields in which the order of the authors indicates contribution, especially fields that have been strongly influenced by medical research traditions, the last author position is reserved for the leader of the research team that carried out the research.

The team leader need not be the lead author; another member of the team may have made the greatest contribution to this piece of research. The leader of the research team will typically be the person who planned the research program of which this research is a part and so may have the most comprehensive vision of where this research. The term last author, like first author, can be unclear as to its credit implications.

Senior author - This term, too, is ambiguous and is sometimes used to indicate the lead author and sometime only the most senior (by rank, job title, or reputation within the field) author.

Although the seniority and hence power of coauthors does seem relevant to possession of a responsibility, there is no consensus even within specific fields or disciplines about how to assess the responsibility of coauthors for misconduct committed by a colleague.

Research Collaboration Between a Supervisor and a Trainee

Credit issues between research supervisors and their trainees (graduate students and post-docs) must be handled a bit differently from credit between two senior investigators, because trainees are partially dependent on their supervisors for an understanding of:

- How to judge the importance of various contributions to research
- What constitutes fairness in crediting research contributions
- How such crediting is done in their field

A conversation about authorship at the beginning of collaboration between peers will be very different from a trainee's inquiry into a supervisor's criteria for deciding authorship, differential credit among authors, and decisions about when a trainee presents a conference paper. Supervisors bear a responsibility for educating their trainees in the principles, rules and criteria used in judging whether research conduct is being done responsibly and whether credit allocation is fair. Supervisors need to explain their practices and the values underlying them to their supervisees, especially if their trainees are to have respect for and confidence in standards of fairness. Telling trainees only after the fact that they have violated some standard is a poor substitute for preparing them for their professional responsibilities in advance.

Resolving Conflicts

Conflicts and misunderstandings about authorship may arise within laboratories or research groups. These will be reduced if trainees and supervisors will have a dialogue about credit and the supervisor's crediting practices early in the relationship. Trainees should know that research supervisors typically have many potentially competing responsibilities. These include:

- Responsibilities for advance of knowledge in their field
- Responsibilities for the education of their trainees
- Responsibilities for the wise and appropriate use of grant funding
- Responsibilities to their institutions and for various work assigned to them
- Responsibilities to their collaborators and to researchers in their field

It is a lot to juggle. If you seem not to be receiving appropriate credit for a research contribution, it is wise to begin the discussion by asking your supervisor about the significance of your contribution, rather than either assume that your contribution was worthless or that you are being treated unfairly.

Authorship Abuse and Financial Interest Disclosure

Increasingly, journals require authors to disclose any significant financial interest that might affect the integrity of the manuscript. At present the threshold for significance is usually an interest greater than $10,000 or a 5% equity interest (i.e., ownership), of a company or the stock of a company. The National Institutes of Health (NIH), however, has recently lowered its threshold for a significant financial interest to $5,000. Several engineering and scientific societies, including the American Society of Civil Engineers (ACSE), require further disclosure. They require authors to state whether they have in the preceding three years had any employment relationship, paid consulting, expert testimony work, received honoraria, or held membership on advisory boards or committees of an entity that has a financial or other interest in the results of the manuscript. Disclosure enables the editor and the readers to judge whether the research article is biased because of the authors' interests.

Here are some of the ways that authorship can be abused:

- **Authorship by authority** - While it is usually assumed that one's status as an authority is established by credible contributions to the scholarly literature, it has become quite common to see a backwards process in which powerful individuals use their authority to become authors - without doing work related to the article's content. Sometimes department chairs or other supervisors require or permit their names to be placed on documents emanating from the unit. The most common "justification" for this deception is that the person in authority either paid for the work described in the article, wrote the grant that paid for the work, provided institutional resources, or in some other way was responsible for the work. But these justifications are inadequate. It is deceptive to include anyone as a co-author if they did not do work directly related to the project described in the article.

- **Gift, courtesy or honorary authorship** - What is usually behind this type of deception is the idea that it is collegial to distribute authorship credit to especially prestigious or socially "useful" colleagues (who then graciously and humbly accept the kind offer). The problem here is still that the beneficiaries of these courtesies did not do the relevant work. Sometimes one scholar says to another, "I'll put your name on my article if you put my name on yours." This type of abuse might occur before a promotion or tenure meeting for example. In other contexts, a student or research assistant (or spouse working in the same field or research group) might be rewarded with authorship; but this, too, is inappropriate if the individual's contributions were not adequate to justify legitimate co-authorship.
- **Political authorship** - Many scholars have heard of a case where a particular professor has to be "put on the paper for political reasons." This is related both to authorship by authority and courtesy authorship. The idea behind it seems to be that certain (important) colleagues will be angry, hurt or disappointed if they are not included as co-authors, or that including a particular individual in the author list will open doors to publication or notoriety. Nonetheless, authorship is only appropriate for those who made significant contributions to the work.
- **Ghost Authors** - An unacceptable category of author is the so-called "ghost author". This refers to claiming authorship for something that another person (the "ghost writer") has written. Although it can be acceptable to receive extensive editorial help that improves the writing of one's article, the accountability requirement also makes ghost authorship an unethical practice. One abuse that the prohibition of "ghost authorship" is intended to prevent is that of a company paying researchers to publish an article reporting research favorable to the company's interests and yet the names of those researchers do not appear on the article.

There are other deceptive authorship and publication practices. These include publishing the same, or similar, paper more than once. According to the American Chemical Society (ACS):

- Authors should not engage in **self-plagiarism** (also known as duplicate publication) - unacceptably close replication of the author's own previously published text or results without acknowledgement of the source.

- There can be some appropriate justifications for what the International Committee of Medical Journal Editors (ICMJE) calls **acceptable secondary publication**, but it usually requires some sort of disclosure in print and permission from the relevant journal editors. It should be emphasized that not only must such redundancy be disclosed in published articles, it should also be disclosed or labeled in one's CV.

Acknowledgments Section

Contributions to the reported research that are not sufficiently significant to qualify a person to join the authors in writing up the research and are not written up in a published or otherwise citable source should be recognized in the acknowledgements, according to the International Committee of Medical Journal Editors (ICMJE) guidelines. Presentations often acknowledge such contributions with a slide containing the names of all contributors and the nature of their contributions. Data collection by itself does not qualify someone for authorship even though it is an essential task. This can cause problems in cases where trainees believe they should be included as authors when their role has been limited to data collection. A potential solution is to include trainees in the intellectual life of the project so that they participate in design of the work, drafting of the article, *and* final approval of the manuscript. This approach would not only ensure that their authorship is deserved, it can also produce a more comprehensive education and training experience.

The American Physical Society (APS) states: "Proper acknowledgement of the work of others used in a research project must always be given." Yet the act of acknowledging someone in a publication, or presentation, can raise ethical issues. This is in part because the motivation behind acknowledging a prominent researcher might be to improve one's own reputation. It is not always clear what kind of contribution warrants an acknowledgment; this decision involves judgment and critical thinking. But asking for permission from the acknowledged person is one way to try to reduce the chance of deception. One might be reluctant to refuse to be acknowledged when asked for permission, but this can contribute to an act of deception if it is not appropriate to connect one's name to the project.

Acknowledgement of someone's contribution does not make the person cited accountable for the work in which the person was acknowledged beyond the specific contribution for which

the person is acknowledged. The ethical guidelines of some engineering and scientific societies require permission for acknowledgement for publications in their journals. Even when they do not, it is prudent and considerate to at least inform and perhaps obtain the permission of anyone acknowledged prior to publication of the manuscript. It is conceivable that the researcher may, for a variety of reasons, not want to be publicly associated with the contribution.

Chapter 3: Peer Review

Peer Review

All major U.S. funding agencies require peer review (PR) of grant applications, and most scientific journals require it for submitted manuscripts. Journal editors rely on the expert opinions of knowledgeable researchers to ensure the quality of papers that they publish. Professional advancement is often based on the ability to get articles published in high quality, peer reviewed journals.

An international survey of over 3,000 academics in science and humanities disciplines reported that 93% felt that peer review was necessary, and 90% said that the process improved the quality of published papers:

http://www.publishingresearch.net/documents/PeerReviewFullPRCReport-final.pdf

Peer Review Process and the Responsibilities of the Peer Reviewer

After a manuscript is submitted to a journal, an editor typically sends it to members of the journal's advisory board or to external reviewers who have expertise in the subject of the article. Peer reviewers are typically expected to provide the editor with a document that describes:

- The value and the originality of the work
- Problems with the methodology or approach
- Problems with how the research has been explained (for example, whether the writing style is understandable for the intended audience)
- Whether appropriate credit has been given to others

Peer reviewers are supposed to provide insight into many different aspects of the manuscript, including whether it places the research in an appropriate perspective, addresses clearly the problem of the research, and provides adequate and fair credit to others in the field. Reviewers also should comment on the originality of the work and whether the research design is adequate to support the conclusions. It is also helpful if reviewers provide feedback on the quality of the

writing, including its style and structure. In general, the editor considers the comments from one or more reviewers and then makes a determination as to whether the paper should be accepted as is, accepted with revisions, or rejected.

Peer review of grant applications works somewhat differently. For example, when researchers submit a grant application to a federal funding agency, the agency will form a committee, often with external reviewers, that evaluates the quality of the application. The various federal agencies differ in how they operate with regard to funded research projects, including how they decide which projects to fund, when they monitor projects, and how they evaluate projects prior to publication.

Differences Between Single-blind Reviews and Double-blind Reviews

Some journals use a **double-blind** review process; in other words, neither the author nor the reviewer knows the other person's identity. In **single-blind** review (common in the sciences), the author's identity usually is known by the reviewer, but the reviewer's identity is not known by the author.

Peer Review Process for Grant Applications

The National Institutes of Health (NIH) uses a two level review process for grant applications:

http://grants.nih.gov/grants/peer_review_process.htm

The first level of review is conducted by a committee whose members have expertise in the subject of the applications. The second level of review is conducted by an advisory council that is made up of researchers not affiliated with the initial committee and lay members of the general public, including patient-group advocates.

The National Science Foundation (NSF) evaluates grant proposals using two main criteria - intellectual merit and broader impacts:

http://www.nsf.gov/pubs/policydocs/pappguide/nsf11001/gpg_3.jsp#IIIA1

Issues that reviewers are likely to consider include:

- Qualifications of the proposing researchers
- Extent to which the project is creative and original
- How the work will advance discovery, promote teaching, and benefit society

Proposals received by the NSF are reviewed by an NSF program officer and usually a group of external reviewers who are experts in the field of the proposal. The findings of the external reviewers help to inform the program officer's recommendations. These recommendations are reviewed further by NSF senior staff.

Approved NSF grants, which generally run from one to five years, are reviewed annually by outside experts to assess their progress.

Conflict of Interest Relating to the Peer Review Process / Ethics and Peer Review

Peer reviewers play important roles in the publication process, and ultimately have an impact on authors, publishers, and the potential audience for the published work. Peer reviewers must uphold ethical standards in order to maintain the integrity of the review process.

Confidentiality - When submitting manuscripts for publication, authors trust peer reviewers to maintain confidentiality. Manuscripts under review should not be distributed to others unless permission has been granted by the editor. Outside of completing the review, reviewers should not make use of the information gained from a reviewed manuscript.

Constructive critique - According to the Council of Science Editors (CSE): "Reviewer comments should acknowledge positive aspects of the material under review, identify negative aspects constructively, and indicate the improvements needed."

Competence - Reviewers do not necessarily have to be an expert with regard to every facet of a manuscript, but they need to inform the journal of the situation so that the editor can make an informed decision about selecting reviewers.

Impartiality and integrity - Potential reviewers should honestly evaluate their own ability to be impartial. A reviewer's comments should be based on an objective and fair consideration of a manuscript. A review must be based on the manuscript's merits.

Disclosure of conflict of interest - According to the American Physical Society (APS): "Reviewers should disclose conflicts of interest resulting from direct competitive, collaborative, or other relationships with any of the authors, and avoid cases in which such conflicts preclude an objective evaluation."

http://www.aps.org/policy/statements/02_2.cfm#supplementary_guidelines1

Reviewers must disclose conflicts of interest that could potentially compromise their ability to evaluate a manuscript honestly and objectively. In some circumstances, it would be appropriate for reviewers to decline to review a manuscript because of a conflict of interest. Reviewers should refer to the journal's policies on conflicts of interest in order to determine which specific information needs to be disclosed.

Resolving Problems with a Review

If authors believe that a manuscript has been rejected unfairly, they can contact the journal editor and discuss the relevant concerns. There are appeals in the grant application process as well. For example, if someone has evidence that their work has been appropriated during the peer review process, then the author or grant applicant could seek legal advice and perhaps contact the institution where the peer reviewer works. The institution will have an office that will deal with the alleged misconduct. Contacting the granting agency or the journal might be appropriate as well.

Conclusion

Reviewing the manuscripts and grant applications of others is a vital activity for research communities. Peer reviewers need to be aware of their responsibilities to editors, authors, and

ultimately readers. Maintaining the integrity of the peer review process is essential in order for it to be effective.

Chapter 4: Research Misconduct and Data Management

Research Misconduct

For the vast majority of people engaged in research, doing it carefully and properly is a fundamental principle. Integrity is vital if the work of researchers is to have credibility. Integrity is also necessary in order for much of research to *continue*, since in many fields scholarship is based on prior research, and advances hinge on the quality and reliability of previous work. It can be challenging, however, while developing a research career in a given field, to know the expectations for the responsible conduct of research.

The U.S. Office of Science and Technology Policy (OSTP) defines research misconduct as: "Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results."

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

Research misconduct does not include honest error or differences of opinion.

The First Amendment to the U.S. Constitution protects the freedom of speech of someone who reports an allegation of misconduct. Also, the False Claims Act of 1986 protects whistle-blowers. The act awards a whistle-blower 15% to 30% of the resulting settlement in a case of misconduct. The act also provides for remedies if it can be shown that a whistle-blower suffered a discriminatory action in retaliation for the allegation brought under the legislation.

Even with regulations and rules in place, how should a whistle-blower proceed with an allegation?

Michael Kalichman, of the University of California, San Diego, provides some guidelines for those who report allegations of misconduct:

Documentation - When making an allegation of misconduct, clear documentation of who did what, and when they did it, will provide the best chance for a fair and timely resolution of the allegation.

Rules and procedures - Even though the federal government has requirements about how institutions should handle misconduct, institutions have some leeway in how they apply the regulations. Involved parties should review institutional procedures on the issue. A whistle-blower needs to know who should be apprised of the allegation, what constitutes evidence for or against an allegation, how the evidence should be obtained, who will review the allegation, what the whistle-blower's role will be, and how much time the process is expected to take.

Perspective - New researchers should seek guidance before making allegations of misconduct. What might appear to be a serious action could be a misunderstanding. It might be appropriate to talk to peers, senior researchers on a team, an ombudsperson, or the individual in question.

Dispute resolution - Some allegations of research misconduct might be resolved through other means, such as conflict resolution. This involves dealing with a problem as soon as possible; striving for an agreement rather than disagreement; emphasizing the problem, not the people involved; and using a third party, such as an ombudsperson, to clarify issues if necessary.

Motivation of a whistle-blower - Whistle-blowers should be aware that they may suffer retribution for their actions and that institutions are responsible for a misconduct inquiry and investigation. They should also distinguish between facts and speculation and not guess at the motives of others. Whistle-blowers should ask questions rather than draw conclusions.

According to the **Federal Research Misconduct Policy, published by the Office of Science and Technology Policy (OSTP):** "Federal agencies have ultimate oversight authority for Federally funded research, but research institutions bear primary responsibility for the

prevention and detection of research misconduct and for the inquiry, investigation, and adjudication of research misconduct alleged to have occurred in association with their own institution."

To determine whether misconduct has occurred, the action must have been committed intentionally or knowingly or in reckless disregard of known practices. The allegation must be proved by **a preponderance of the evidence**, which means determining whether the claim or fact is more likely to be true than not true. Government agencies typically rely on institutions to make the initial response to allegations of misconduct.

Inquiry is the assessment of whether the allegation has substance and whether an investigation is warranted. **Investigation** is the formal development of the factual record and the examination of the record leading to dismissal of a case or to a recommendation for a finding of research misconduct or to other remedies. During the **adjudication** phase, recommendations are reviewed and corrective actions, such as sanctions, are determined.

The Public Health Service (PHS) Policies on Research Misconduct requires institutions to protect whistleblowers, witnesses and members of inquiry and investigation committees.

Data Management

Different disciplines have different notions of what constitutes data. Data can range from material created in a laboratory, such as an electrophoresis gel or a DNA sequence, to information obtained in social science research, such as a filled-out questionnaire, video and audio recordings, or photographs. Data can be astronomical measurements, microscope slides, climate patterns, cell lines, field notes, soil samples, or results of statistical analyses. Data management issues occur throughout the research lifecycle, from protocol development to the archiving or disposal of research materials at the end of a project. Researchers must be prepared to address questions that can arise at each stage.

Data protection encompasses rules about who can access information, and under what conditions - sometimes called the privacy or **confidentiality rules**. The regulations governing

security for data are based on many factors, including the nature of the data themselves. **Identity data**, such as names and social security numbers, are protected by many state laws and are the subject of several federal regulations. At the federal level, **health data** are protected by the Health Insurance Portability and Accountability Act (HIPAA), **education data** are protected by the Family Education Rights and Privacy Act (FERPA), and **financial data** are protected by the Financial Services Modernization Act (FSMA).

Many laws, regulations, and policies require that researchers obtain permission to collect and use data before a project begins. Factors that must be considered include the kind of data to be collected, the origin of the data, and the purposes for which they are collected. Researchers are always urged to make use of the expertise of their organization's compliance and legal departments in order to be certain exactly which rules apply. For example:

- Permission might be needed from an organizational committee, such as an Institutional Review Board (IRB), before data collection begins.
- Consent might be needed from the individual human subjects.
- There may be a requirement to itemize when and how data are going to be used.
- There may be a requirement to describe how data will be protected and how they will be disposed of at the end of a study.
- There may be a requirement to submit plans for data sharing with research subjects or the general public.

Research data must be stored securely both during a research project and after it ends. Reliable security policies and procedures are essential to safeguard data stored electronically or in the physical form of paper files, journals, and notebooks. Data must be protected at all times.

Information protection consists of three core elements: **confidentiality**, **integrity** and **availability**.

Data Sharing and Ownership

Data ownership generally refers both to the possession of and responsibility for information. It covers the range of rights and obligations with respect to data collection and sharing. Information

control is defined both by technical capabilities to access, create, modify, or package it, and by legal-regulatory constraints. As discussed previously, rights and obligations related to ownership of data depend on the data type in question (for example, health, education, or financial), as well as on the sources of the data. Rights and obligations also may be governed by a data-use agreement for a particular study, which sets limits on how the data are handled, including whether they can be transferred to third parties or disposed of at the end of a project.

In an **industrial research setting**, the near-universal practice is that the data collected during a research project is owned by the company - indeed, employees often are required to sign an agreement confirming their understanding of this arrangement.

Results of research performed in an **academic setting** are usually considered to be the property of the university. In essence, work performed by a faculty member or by a graduate student is usually considered "work for hire," the same as in an industrial research setting, and therefore is owned by the institution. But universities may negotiate variations on these arrangements with faculty.

There are other parties who also may assert ownership of data or the intellectual property resulting from a research project. Research projects at universities are generally funded through a grant or a contract with an outside entity. Federal law, expressed through the Bayh-Dole Act of 1980, gives universities control over data and other intellectual property that results from research that is funded by a federal agency. However, when a project is funded by private corporations or non-governmental foundations, ownership of data and intellectual property is best determined by contract before the research program begins.

Complications also arise when faculty or students perform research **outside the university setting** on their own time. Generally, this data is owned by the researcher, though it can sometimes be difficult to demonstrate that the research was undertaken on the researcher's own time and without the use of the employer's resources.

All members of a research team should review their institution's policies with respect to data ownership. **Graduate students and postdoctoral fellows** involved in research might, for example, work under the mistaken belief that they own the data collected. However, when such

persons work as employees of a university, as they typically do, they are usually considered to be "working for hire." In that case, the institution likely owns the rights to the data.

Under some kinds of federally funded research, the institution supporting the research may own the data but allow the principal investigator (PI) to act as steward of the data. The PI then takes responsibility for data collection, recording, storage, retention, and disposal. If the copyright is retained by the PI, it may be assigned to a journal when data are published.

Notebooks and Journals Data and data books developed **by undergraduates, graduates, and postdoctoral fellows** on a research project generally belong either to the grantee institution or the PI. Trainees should not assume that they will be allowed to take "their data" when they leave. Appropriate arrangements need to be made in advance to minimize misunderstandings.

The Bayh-Dole Act of 1980 allows universities to control intellectual property, such as patents, generated from federally funded research that they conduct. Universities could then exclusively license its patent to a business. Although the Act has had its share of critics, many universities have benefited from the licensing revenue that has flowed from this type of arrangement.

When researchers leave institutions where they conducted research, they usually must negotiate agreements to retain their grants and data. With industry- or privately-funded research, data can belong to the sponsor, although the right to publish the data may or may not be extended to the researchers.

Researchers should review the policies of their institutions as well as the terms of any contract signed with a funding source. It is equally important in collaborations, whether between faculty peers, students, or institution staff, that all parties should have a clear understanding of who will determine how the data will be distributed and shared (if applicable) before collection begins.

Potential Intellectual Property

Patents are grants given by the federal government to an inventor, giving the inventor or his assignees the exclusive right to commercially exploit the invention for a specific period of time.

Patents can cover, among other things, new devices, materials, designs, and processes. Patentable ideas often are created in the course of engineering or scientific research.

Copyrights relate to written work and are intended to give the author or assignee exclusive rights to sell the work. Copyrights can be applied to books, music, photographs, film, web sites, and in some cases to software. In the course of research work books, images, or software may be developed that would be subject to copyright.

Trademarks refer to symbols or logos often used by companies as part of their effort to create a "brand" for their products.

Trade secrets, like patents, cover new devices, materials, designs, and processes, but unlike patents, there is no public disclosure of the trade secret. Essentially, a trade secret is used to keep all information about an invention away from the public indefinitely.

Federal Policy on Data Retention

There can be numerous problems with data storage that affect the integrity of data in a research project. These problems can include decay of storage media which alters or destroys data, or inadvertent or malicious alteration of data. Most troubling is alteration of data once it has been stored. Unfortunately, almost all forms of data storage are subject to alteration and the changes may be undetectable without additional safeguards. Handwritten laboratory notebooks can be altered by overwriting the recorded data. Data stored in an electronic form can be altered by persons authorized to utilize the computer where the data are stored, or by individuals who gain unauthorized access.

When data are kept on paper, it is often clear when the data have been altered since there are erasures, cross-outs, or missing pages. Of course, the use of paper media to record data is becoming less common as researchers move to electronic media for data recording and storage. Storing data on a computer makes the detective work harder; altering an electronic database may leave traces only discernible by a computer expert.

Data handling procedures should describe when, how, and who may handle data for storage, retrieval, sharing, archiving and disposal purposes.

Another important ethical issue related to data storage is the **duration of data retention**. The results of an experiment that are reported in a publication are rarely the "raw" data, but are rather graphs or tables that represent a selection of data that will be presented, including elimination of spurious data, and an interpretation of what the data mean. If the original data are discarded, then it is impossible to revisit the interpretation of an experiment or a data set and for other researchers to use the data to develop their own understanding and interpretation of them.

Many scientific and engineering journals have guidelines for how long data should be retained, ranging from "*a reasonable amount of time"* to very specific guidelines, such as ten years. Research institutions and funding agencies typically have data retention policies that specify retention periods according to type of data. Researchers should learn the policies that apply to their work and, even where no formal requirements exist, should retain complete records of experimental data for at least several years after the initial publication so that any questions that may arise when the research results are used by others can be revisited.

How long should the data be kept after a project is over? The answer usually depends on the nature of the project, including potential ongoing interest in or need for the data, as well as:

- Costs of maintaining the data over the long run
- The requirements and guidelines of the research sponsor

Under **U.S. Department of Health and Human Services (DHHS)** requirements, for example, research records must be maintained for at least three years after the last expenditure report. Other federal regulations or institutional guidelines may require that data be retained for a different period of time.

Retaining data on paper files and electronic media long past the end of a project can increase the chances of unauthorized access. Risks can increase when researchers leave the project or the institution without establishing proper data management procedures, including for secure disposal or archival storage.

Data Analysis Practices

Researchers must attend to a number of questions regarding data analysis, the most important of which is the need for the relevant skills. Researchers sometimes assume they have received sufficient training when that is not the case. Unintentional errors become likely when researchers operate beyond the frontiers of their expertise. Review of proposed protocols - particularly proposed analytic methods - is critical when researchers have any doubts about their level of expertise.

As with data selection criteria, the selection of statistical analysis methods always should precede data collection. If it is delayed until later in the research process, this may increase the risk that analytic choices will be made based on which method produces the most favorable results. In other words, it will increase the likelihood of bias. Disciplines have developed accepted practices for data analysis. If one uses an unconventional approach, it is crucial to state clearly that this is being done, explain why, and show how this new and possibly untested method of analysis is being used, as well as how it differs from other more traditional methods.

Whether statistical or non-statistical methods are used, researchers should be clear (both to themselves and to readers or reviewers) about the limitations and possible biases of their methods. Regardless of whether one studies quantitative or qualitative phenomena, researchers use a variety of tools to analyze data in order to test hypotheses, discern patterns of behavior, and ultimately answer research questions. Failure to understand or acknowledge data analysis issues can compromise the integrity of the research.

Secure Disposal of Research Data

Disposal of sensitive data requires care and technical expertise to ensure that the data cannot be retrieved or reconstructed. When disposing of magnetically recorded data stored on computer hard drives, flash drives or floppy disks, multiple-pass erasures are required. Optical media may need to be over-written or shredded. If researchers lack the required expertise and tools, appropriate technical resources from their organization should be sought or a third-party disposal contractor hired. Researchers also can contract for disposal of data stored in laboratory notebooks or paper files.

Chapter 5: Mentoring and Collaborative Research

Mentoring

Mentoring is one of the primary means for one generation of researchers to impart their knowledge to the next generations. More than textbooks and formal classes, the relatively informal dimensions of research, including the relationship between mentor and trainee, prepare the next generation of professionals. Mentoring has received increasing attention. A body of literature has emerged that discusses the mentoring process and its potential benefits and problems. Such topics as fair access to mentors and inadequate mentoring for women and minority scientists are especially important. At some institutions, guidelines and formal programs have been established to address these shortcomings.

Mentor's Responsibilities

Although the role of the research adviser or supervisor can lead to mentoring opportunities, the mentor's role is different from that of a supervisor or adviser. The essence of mentoring has been described in a report by the National Academy of Sciences as being an adviser, teacher, role model, and friend. A mentor might be a faculty adviser or another faculty member, a project leader, a fellow student, a wise friend, or simply another person with experience. A trainee in the research setting could be anyone in a junior or apprentice position, such as an undergraduate or graduate student, a postdoctoral fellow, or a junior research staff member or faculty member.

The role of the mentor is often complex and can take on many forms. A true mentor is typically someone who possesses:

- Experience with the research and challenges that trainees face
- The ability and willingness to communicate that experience
- An interest in helping another person develop into a successful professional

Qualities to look for in potential mentors include:

- Experience in areas relevant to the trainee's personal and career development
- An interest in the trainee's career

- A willingness to make the time to meet with the trainee
- An ability to provide the trainee with useful advice

Academic Advisor Versus Mentor

Even though the terms "advisor" and "mentor" are often used interchangeably, they do not necessarily mean the same thing. Mentoring includes responsibilities beyond advising. Thesis advisers are responsible for ensuring that students fulfill departmental and institutional requirements for a graduate degree and for giving advice about research directions, methods, and publication. Mentors typically provide information that is essential for professional success, such as how to obtain funding, manage a research lab or group, and use time effectively. Mentors focus more directly on a mentee's achievements, success in school, and preparation for the workforce through a non-threatening and non-judgmental one-on-one relationship. This relationship can change over time as each grows, learns and shares experiences in the mentoring relationship. It has a career and psychosocial focus for both mentor and mentee. The mentoring relationship can impact the expectations on all parts of one's life.

An advisor who is also a mentor (advisor-mentor) has the unique ability to be able to discuss the mentee's research with other senior colleagues and introduce the mentee to experts in the field. Many students prefer not to establish a mentoring relationship with their faculty advisor because of the power and authority the advisor has regarding the student's academic future. Some advisors are overburdened with committee work, teaching and research, and can offer little more than advisor support to all but one or two of their students. Occasionally personalities clash, and although the professional aspects of advising permit the faculty member and student to work together, the more personal aspects of mentoring are difficult to achieve.

A mentoring relationship should not be a passive one. The trainee must take an active role in identifying and communicating needs and expectations as a professional-in-training. And, although a mentor can provide a unique and invaluable perspective, the mentor's advice should not be accepted without reflection. Trainees should seek to continue learning about the mentoring process to optimize their own experience and to prepare to be effective mentors

themselves. Further, faculty and graduate students might consider adding mentoring as a topic for departmental seminars.

Mentoring and Research Misconduct

Because of the inherent imbalance of power between mentor and trainee, the mentor-trainee relationship can be abused in many ways. Even a less-senior mentor has a great deal of power relative to a trainee. The trainee potentially has much to gain from the mentor's support and advocacy, and fear of jeopardizing that support further imbalances the relationship. A mentor can use this power to exploit the trainee, for example, by refusing to give proper credit for the trainee's contributions or by seeking personal favors. A common complaint of trainees is that they are required to spend so much time working on the adviser's research that they have little time left for their own work.

While it is the trainee's responsibility to seek assistance, the comfort range for the student can be expanded with some assistance by the institution. Some of the questions that institutions and mentors should provide clear answers to include:

- What are the responsibilities of the advisory committee and the entire graduate program faculty for the success of graduate research training?
- Is there a difference between a research supervisor and a research mentor?
- If there is a difference, are the duties associated with mentoring optional?
- What are the responsibilities of faculty members regarding research supervision, their personal work, and other academic duties?
- Who is responsible for protecting students from poor research advisers / supervisors / mentors?

A number of so-called "boundary Issues" can arise between mentors and trainees. The boundaries between the financial and career interests of faculty members and their responsibilities to trainees are one such example. In the case of industry-funded research, it may be in the sponsor's interest to delay publication of results for an extended period of time. A faculty member must consider the consequences for any graduate student or trainee involved in such research. Trainees should be made aware of constraints on publication before choosing to

participate in the research. The mentor and the trainee must consider the possible impact of such delays on the trainee's career prospects.

Those who take advantage of or ignore trainees must be reminded that as a person in authority, they have a special obligation to foster the intellectual development and independence of the next generation of researchers. The most effective mentors typically take actions that:

- Ensure that the trainee gets the maximum appropriate credit for any joint publications
- Encourage the trainee to attend and present at national or international conferences, workshops, and symposiums
- Promote the trainee's work among colleagues
- Help the trainee create important professional networks

The guiding principle of mentoring should be protecting the interests of the trainee.

Collaborative Research

Researchers in many fields prefer to work with others in and out of their areas, in order to obtain complementary expertise, save time, or decrease expenses. Other researchers seek collaborations as a way of finding innovative approaches to solving problems. Multiple factors contribute to this increase in research collaborations. Technology, such as e-mail, allows for communication across countries and nations. Further, private and federal funding sources encourage collaborative and multidisciplinary projects. Although collaborative and multidisciplinary research is flourishing, problems can arise.

Increasingly, researchers are collaborating in small and large groups, and in many cases will work with scholars who are educated and skilled in different subjects. As the trend towards more interdisciplinary research continues, scholars must be willing to embrace new ways of thinking. However, any collaboration, whether in a field where joint effort is well established, or as part of a new investigative approach, takes special skills, time, and can create conflict.

The federal government, including the National Institutes of Health (NIH) and the National Science Foundation (NSF), supports projects that ask for researchers in different

disciplines to work together. The NIH has identified certain areas of study, such as nano-medicine and structural biology, which will involve research within and across disciplines, and, in some cases, with industry. NSF supports "cross-cutting/interdisciplinary programs" that seek new, multidisciplinary approaches in research, education, earth systems, and organizational structures. Private foundations also will fund centers at universities that bring together expertise in different areas to solve a particular problem.

The members of the collaboration should define and set clear goals:

- The leadership of the collaboration also must be defined. As multiple laboratories or groups of researchers may be involved, coordinating the effort among the collaborators requires management and communication.
- When a research project changes direction, the potential impact on the collaborators needs to be addressed. Authors might need to be added or removed.
- The researchers need to have a mechanism in place to determine when the collaboration should be concluded.

Collaborative Research and Authorship

Standards of authorship vary among disciplines, and may not be well established in some research areas. In many fields, people who have not contributed substantially to the intellectual process of the research are not included, while, in other fields, people get authorship if they participated in doing the research at any level. Determining the order of names appearing on a multi-author paper can be quite complicated and become a source of conflict.

Different disciplines have varying standards for determining authorship. The criteria for authorship among collaborators should be established at the beginning of the collaboration, so all know what to expect. But with authorship comes responsibility, so collaborators need to determine how they will deal with the differing levels of contribution from each author. In general, scientists should contribute substantially to the intellectual process of a research project before they are listed as an author. Who will write the manuscript and be responsible for collecting input from collaborators has to be established. The evolution of a project has to be considered, because if the research changes direction, someone expecting authorship might be

disappointed. Also, who will be included in the acknowledgments rather than in the byline should be addressed as early as possible in the collaboration.

It is vital to establish and maintain communication throughout a project. Once collaboration is created, then discussion about data, ideas, and personnel issues should occur. If two scholars plan to exchange data, personnel, or materials, they should carefully consider whether a formal written collaboration agreement should be established. Each institution and its researchers have to abide by certain regulations, policies, and laws. When working with human subjects, especially in fields such as clinical research, anthropology, or history, researchers must maintain the confidentiality of their subjects and be aware of participants' rights. They also need to inform one another of any conflicts of interest that they might have that relate to the project.

Dealing with authorship and credit issues in advance can help protect the rights of all collaborators to appropriate credit. In the case of potentially patentable discoveries, the timing of publication can be important. While early publication usually ensures primary credit, disclosing results early could prevent authors from being able to obtain patent protection. In addition, most institutions and grant agencies have policies regarding intellectual property and patent procedures. These can help clarify the situation, and provide a basis for discussion and decision-making.

Most universities have a Technology Transfer Office (TTO), which is responsible for identifying and patenting new inventions and copyright materials, including software. The office helps inventors develop the necessary documentation for patents and other kinds of protection. Although the university typically owns the intellectual property generated from research, the TTO works with the university and the inventor, as both may receive licensing revenues.

The TTO interacts with industry representatives to set up collaborative research agreements, to inform them of new inventions, and to negotiate license agreements. The TTO can also provide guidance regarding how researchers can protect their inventions. If results of research are made public without being protected first - with a confidentiality agreement, a material transfer agreement, or patent application - the monetary value of the invention may be substantially reduced.

Data Ownership Issues

The free exchange of information at professional meetings and in publications is crucial to academic communities. However, the data from industry-supported research can have profound financial repercussions and for intellectual property reasons, they might not be published. When academics and industry researchers work together on projects, they must agree on how data and materials will be shared. Some universities do not permit the sponsor to hinder or delay the publication of data. Other universities might be willing to forgo some freedom in exchange for funding, access to industry ideas, and opportunities to train students in commercial research endeavors.

The issue of who owns data is governed by the type and source of funds used to support the research project. NIH and NSF allow grantee institutions to own data; this has for research conducted by collaborators off-site. Institutions also have rules for the custody and retention of data.

The transfer of materials among collaborators is subject to a **Material Transfer Agreement** (MTA), developed by administration offices. An MTA might include:

- Limits on the use of the material, usually for non-commercial research purposes
- Prohibitions on the redistribution of the material
- Conditions for publication, usually with provisions that the manuscript must be seen by the donor before submission for publication
- A hold-harmless cause, meaning that the donor has no liability resulting from the use of the material
- The issue of the return of unused materials

An important consequence of terminating a collaborative relationship is the need to clarify data ownership issues beyond the relationship. For example:

- Which party or parties will be responsible for the data?
- How the data can be used for future projects?
- What restrictions are placed on data sharing?

Chapter 6: Human Subjects Research

Because of the vast array of research that either directly or indirectly involves humans, a fundamental challenge associated with human subjects research is simply defining it. The most widely accepted definitions of "human subjects" and "research" are provided within the **Common Rule**, a set of regulations to which numerous U.S. federal agencies are signatory.

According to the Common Rule, "*Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

The Common Rule defines a **human subject** as: *"*...a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information."

Policies and Regulations Governing Human Subjects Research

The current ethical and legal framework for conducting human subjects research evolved from the **Nuremberg Code**, a set of guidelines developed after the Second World War in response to the atrocities committed by Nazi researchers. Among other ethical notions, the Nuremberg Code expresses the principle that human beings must consent voluntarily to participate in research before they are enrolled.

Because of concerns that humans were being abused in research, primarily within the *U.S. Public Health Service Syphilis Study at Tuskegee* (1932-1972), the U.S. government in 1974 ratified the **National Research Act**. The National Research Act led to the drafting of the **Belmont Report,** which emphasizes the three ethical principles of **respect for persons, beneficence, and justice.**

Respect for Persons - Respect for persons refers in part to the ethical obligation to uphold autonomy, that is, the right of competent individuals to make decisions about their own lives. Respecting autonomy requires, for example, that a researcher honor the decision of a potential

subject who refuses to participate in a research protocol. Federal regulations provide guidance for researchers if they are seeking to enroll subjects with diminished autonomy, such as children (Common Rule).

Beneficence - Beneficence obligates researchers to protect and uphold the well-being of others. According to the Belmont Report, beneficence requires one to "do no harm" and "maximize possible benefits and minimize possible harms". Beneficence further means that researchers are responsible for weighing the risks of a protocol against its potential benefits. Researchers must design protocols that expose subjects to the least amount of risk possible.

Justice - Justice calls for the benefits and burdens of research to be distributed fairly. Justice might require researchers to develop a strategy for ensuring that subjects, or perhaps the population from which research subjects were drawn, receive a fair share of the benefits from the research.

Institutional Review Board

An **Institutional Review Board (IRB),** also sometimes referred to as a Ethics Review Board (ERB) or an Ethics Review Committee (ERC), seeks to ensure that only ethically and legally appropriate research involving human subjects is allowed to proceed. The primary federal agency responsible for monitoring human subjects research, the Office of Human Research Protections (OHRP), states that: "The IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated." IRBs must review human subjects research that is supported by federal funds. Many institutions require their IRBs to review all human subjects research protocols including those that are not federally supported.

In accordance with the Common Rule:

- IRBs must have at least five members; typically, most members are from scientific fields.
- At least one member of an IRB must be a non-scientist.

- At least one member must not be affiliated with the parent institution or organization other than being a member of the IRB.
- An IRB must ensure that a research protocol fulfills certain criteria before it can be approved. For example, the IRB must review the consent process to determine if it will enable potential subjects to understand the research clearly. The IRB also must assess whether researchers have developed adequate safeguards, such as providing to subjects the names of contact persons.
- Faculty, students, postdocs, and other researchers must consult with their local IRB in order to determine whether IRB review is required for their research. For example, the use of surveys to collect data about students' attitudes and behaviors might require some form of IRB review.

If a research protocol needs to undergo full review, then it requires that "a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas" (Common Rule).

After receiving IRB approval for their protocols, researchers are required to provide periodic reports about ongoing research to the IRB. Due to continuing review requirements, researchers typically need to submit reports to the IRB no less than once per year. Researchers also must be aware of federal and institutional policies governing how long research records, including originals of consent forms, must be retained after a study concludes.

Research might qualify for **expedited review** if it poses "no more than minimal risk" and falls into one of the categories recognized by the federal government for expedited review using expedited review criteria. A protocol may qualify for a review exemption if it falls into one or more of the exemption categories that are specifically delineated within the Common Rule.

Many private companies have followed suit by establishing a relationship with an IRB to guide how their human subjects research is conducted. In general, companies have been motivated to have their research reviewed by IRBs in order to comply with the Food and Drug Administration’s (FDA) requirements for approval of a drug or device application.

Consent Form

Conducting human subjects research in a respectful and responsible manner usually requires that **informed consent**, or what is often referred to as **valid consent**, has been obtained from potential subjects. Three fundamental components of informed consent are:

1. Subjects must be adequately informed about the research protocol in which they are being asked to enroll, including being notified about the potential benefits and risks that may be associated with participation.
2. The decision of each subject to enroll must be voluntary. In other words, the subject should not be unduly influenced or coerced into making a decision about participation. Undue influence or coercion includes but it is not limited to offering potential subjects an exorbitant amount of money for enrolling. It also would include pressuring a vulnerable person such as a prisoner to enroll by offering a reduced prison sentence in exchange for participation in the research protocol.
3. A subject must be competent to voice a decision about participation. The subject must be capable of understanding the information presented about the research and of appreciating the consequences of enrolling or of declining to enroll. However, in certain circumstances a non-competent individual, such as a child, could participate if that individual's parent or legally authorized representative gives permission.

Obtaining consent usually, but not always, occurs through a process whereby potential subjects are asked to review and sign a consent form before the research begins. The issues that researchers should address during the consent process include:

- The purpose of the research
- Possible benefits and risks associated with the research
- Available alternatives
- The rights of the research subject, including the freedom to discontinue participation at any time
- How the subject's privacy and confidentiality will be protected
- Whether there is compensation for participating
- Who the subjects can contact if they have questions or concerns about the research

A subject's consent is not valid if, for example, the researcher fails to describe adequately the risks associated with participation or if a consent form is overly technical and confusing. Because subjects in research may be vulnerable to harm, it is of the utmost importance that researchers explain the research clearly and thoroughly before a consent form is signed. It can be difficult to determine whether an activity constitutes human subjects research, such as monitoring the behavior of users on social networking websites, and if so, whether a formal process for obtaining consent is necessary. In general, if the research involves human beings and can pose some non-trivial risk, it is highly likely that consent is required. It is critically important that researchers consult with an IRB to determine if and how regulations for human subjects research, including those pertaining to informed consent, apply to their work.

Conclusion

Merely complying with the law does not necessarily satisfy all of a researcher's professional obligations when conducting research with human beings. Researchers must always keep in mind that their foremost responsibility when conducting human subjects research is to the volunteering participants. The failure of researchers to protect their subjects not only risks harm to those individuals and to society, but it can also profoundly erode the public's trust in research communities.

Chapter 7: Animal Subjects Research

One of the primary ethical concerns regarding the use of animals in research is the degree of suffering that research procedures can inflict on the animals. Some people argue that animals should not be exploited for any reason, but others suggest that animal research should be permitted for the good of society as long as it is conducted humanely and with integrity. A strong consensus exists that animal research must be subject to ethical guidelines, laws, and regulations.

The notion that animals have rights is not universally embraced. Noted physiologist and physician **Marshall Hall** (1790-1857) contributed one of the earliest publications regarding the treatment of animals in the context of research.

He outlined five principles that should govern the use of animals in experimentation, arguing that animal experimentation is ethical only if:

- Alternative approaches are not available.
- The experiment has a clearly stated objective.
- The work should not be unduly repetitious.
- The researchers are committed to minimizing pain and suffering.
- The results of the studies are published in a clear and concise manner.

In 1959, **William Russell** and **Rex Burch** published their landmark work, **The Principles of Humane Experimental Technique**, which described key ethical guidelines for research with animals. Russell and Burch describe not only the pain and distress inflicted on animal research subjects, but also how the suffering caused by procedures in animal research could be diminished or removed through **Reduction**, **Replacement**, and **Refinement**, often referred to as The 3Rs.

According to Russell and Burch:

Reduction means reduction in the numbers of animals used to obtain information of given amount and precision.

Replacement means the substitution for conscious living higher animals [with] insentient material. The objective is to replace animals in a research protocol with non-living or non-vertebrate models whenever possible.

Refinement means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used. Some examples of refinement are:

- Improvement of a surgical technique that results in fewer model failures would reduce the number of animals needed for statistical validity
- Modification of research procedures to be less painful or stressful to subjects
- Use of an improved pain-control strategy

Regulations Governing Animal Research

Congress gave the U.S. Department of Agriculture (USDA) broad authority to regulate animal research when it passed the Animal Welfare Act (AWA) in 1966. The USDA then established the AWA regulations to enforce the Act. The AWA, which has been amended several times since 1966, instructs the Secretary of the USDA to regulate any institution that:

- Uses live animals in research, tests, or experiments, and
- Purchases or transports live animals in (interstate) commerce, or
- Receives funds under a grant, award, loan, or contract from a department, agency, or instrumentality of the United States for the purpose of carrying out research, tests, or experiments

The USDA specifically excludes birds as well as rats and mice purposely bred for use in research. In 1985, the U.S. Congress passed the Health Research Extension Act that directed the Public Health Service (PHS) to develop specific guidelines for animal research.

The Office of Laboratory Animal Welfare (OLAW) is responsible for monitoring institutional compliance with PHS policy and guidelines. OLAW relies primarily on the following two documents for judging compliance:

- The PHS Policy on Humane Care and Use of Laboratory Animals
  http://grants.nih.gov/grants/olaw/references/phspol.htm
- The Guide for the Care and Use of Laboratory Animals (often referred to as *The Guide*).
  http://www.nap.edu/catalog.php?record_id=12910

The Institutional Animal Care and Use Committee

The Institutional Animal Care and Use Committee (IACUC) is responsible for providing independent oversight to all activities that involve vertebrate animals at a federally-funded institution. The role of the Institutional Official (IO) may be delegated to a member of the senior administration who has the authority to allocate the resources needed to ensure the overall effectiveness of the organization's animal care and use program. The IO bears ultimate responsibility for the program and is responsible for resource planning and ensuring alignment of the animal program goals with the organization's mission.

The USDA AWA regulations and PHS Policy define the role and responsibilities of the IACUC.

The responsibilities of an IACUC include:

- Assuring that the institution and its employees remain in compliance with all federal policies and regulations relating to animal research
- Defining and implementing institutional policies regarding the laboratory animal care program
- Reviewing and approving all research, teaching, and testing activities that use vertebrate animals
- The semi-annual inspection of all facilities where animals are housed and used in research, teaching, and testing
- The semi-annual review of the entire animal care and use program at the institution. This includes review of the quality of the veterinary care program, the lab animal training programs, the occupational health and safety program, and the IACUC itself
- Identifying and investigating instances of noncompliance
- Providing a semi-annual report to the IO on the status of the institution's animal care and use program
- Maintaining records associated with the review of animal care and use activities, including the minutes from the IACUC meetings, for at least three years after the conclusion of a project

Beginning Any Work Involving Research Animals

Getting Started

The USDA AWA regulations and PHS policy both describe many responsibilities of the investigator and research team. Researchers are required to design protocols that offer relevance or value. In an animal use protocol, animal researchers are required to describe the following:

- The rationale and purpose for the use of animals
- The justification of the species and number of animals requested. Whenever possible, the number of animals requested should be justified statistically
- The availability or appropriateness of alternatives, such as less-invasive procedures, using other species, cell or tissue cultures, or computer simulations

The Lay Summary

The lay summary should summarize the proposed study in terms that will allow a person without a science background to understand what the researchers hope to accomplish. The summary should include an explanation of:

- The purpose
- The experimental approach
- What happens to the animals when the research concludes
- The significance of the research

An IACUC will likely require the researchers to rework the protocol if they fail to address these issues in language that a layperson would understand.

Personnel Training and Experience

The USDA AWA regulations require that all those who use in animals in research, testing, and teaching complete basic training in the human care and use of animals in a research environment.

The PHS Policy also delineates what relevant training programs should include. Researchers must demonstrate that they have sufficient experience with the animal model chosen and with the procedures proposed. Researchers who lack experience in the procedures of choice must receive training from the veterinary staff or from other experts in the field. It is the PI's responsibility to ensure that the research staff is adequately trained. The IACUC will review the qualifications of the research team prior to approval of the animal protocol.

Many institutions require the research protocol to describe the potential for and severity of the pain, distress, and discomfort that the animals will experience during the proposed research procedures. It is common to use the "BCDE" pain category system described by the USDA.

The USDA AWA regulations stipulate that the number of regulated research animals used by an institution must be reported annually to the USDA. The animals must be placed, by species, into one of the four USDA pain/distress categories.

If alternatives exist to the use of a painful procedure, the PI is required to explain why the alternatives are not appropriate for the proposed study. If no alternatives are known, that must be stated as well. The research team also is required to provide details of the literature search used to attest to the lack of appropriate alternatives to the potentially painful, distressful, or discomforting procedures.

Attending Veterinarian

- The attending veterinarian (AV) is responsible for the health and medical treatment of all animals at the institution's facilities and is the ultimate authority regarding the medical condition of the animals. To carry out this responsibility, the veterinarian must have access to all animals at all times.
- The AV may intervene immediately in any animal-related procedure and has the authority to halt the procedure. This may occur if the procedures are being conducted incorrectly or if an animal is experiencing undo pain and distress.

The Veterinary Consultation

The USDA AWA Regulations stipulate that if procedures on animals are proposed that may cause more than momentary or slight pain or distress, the principal investigator (PI) must consult with the AV or the AV designate (a veterinarian with training or experience in laboratory animal medicine) in the planning of those procedures. Many institutions require a veterinary consultation during the planning stages for all projects involving animals.

Procedure to be performed prior to implementing any significant change in the use of animals:

The Institutional Animal Care and Use Committee (IACUC) must review and approve significant changes to the procedures described in approved animal research protocols prior to implementation of such changes. Significant changes to protocols include but are not be limited to:

- Changing or adding a species
- Increasing the number of animals used
- Increasing the number of procedures performed on individual animals
- Changing procedures that would result in an increase in the pain category level
- Changing the scope of the project such as adding a new procedure
- Sharing tissues with another researcher
- Changing the anesthesia strategy
- Changing the euthanasia strategy

Performing unapproved procedures is prohibited by the IACUC and federal regulations. The use of an unapproved procedure can result in suspension of the protocol until the incident of noncompliance has been investigated and a corrective action plan has been approved and initiated.

Euthanasia

At the end of the study the animal subjects may need to be euthanized. The research team must ensure that this is done in the most humane way possible that is also consistent with the endpoints and goals of the study. An improper euthanasia method or technique can cause pain and suffering. Thus, research team must be trained to properly and humanely perform euthanasia. The euthanasia strategy and method should be discussed during the veterinary consultation prior to start of the study. PHS Policy and *the Guide* state that the means of euthanasia should be consistent with the recommendations of the American Veterinary Medical Association (AVMA).

Incidents of noncompliance with federal regulations must be reported to OLAW by the IACUC with a full explanation of the circumstances and actions taken to prevent recurrence.

Reporting Misuse, Mistreatment, or Noncompliance

Misuse or mistreatment of animals or the use of procedures that do not comply with federal regulations or guidelines must be reported immediately to any of the following:

- The AV or a member of the veterinary staff
- The IACUC Chair
- A member of the IACUC staff
- A mentor
- The IO
- The university ombudsperson

When an allegation of mistreatment, misuse, or noncompliance is received, the USDA AWA regulations and PHS Policy require the IACUC to review and if warranted, investigate the allegations.

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