RESPONSIBLE CONDUCT OF BIOMEDICAL RESEARCH:

A Handbook for Biomedical Graduate Studies Students

Fourth Edition

BIOMEDICAL GRADUATE STUDIES PROGRAM
UNIVERSITY of PENNSYLVANIA

PREFACE TO THE FOURTH EDITION

Scientists agree that a trainee in biomedical research should be taught to maintain the highest standards of scientific integrity and ethical behavior in all phases of the conduct of research. Scientists and trainees should also be aware of the potential for subjectivity, unconscious bias and conflicts of interest that accompany the collection and treatment of data, the attribution of responsibility and credit, the mentoring of students and fellows, and the use of human and animal subjects for research. Scientific data collected and reported with the greatest care and ethical considerations may yet contain unrecognized errors due to the limitations of knowledge or technology. The requirement for high standards of scientific integrity and ethical behavior is important for a number of reasons. Scientists must be able to trust one another's work, since advances in science rely on the integrity of the research record. Furthermore, most research is carried out using public funds and thus the public should have confidence that this is money well-spent.

The goal of BGS's training in Responsible Conduct of Research (RCR) is to make graduate students aware of the rules, regulations and guidelines governing research and to minimize the potential problems associated with carrying out research. While these problems cannot be totally eliminated, they should be recognized, openly acknowledged and constructively addressed by discussions among scientists and with trainees. The incidence and consequences of misconduct can be sharply reduced by both good habits of research and by an increased understanding of what constitutes accepted responsible conduct. Education of this nature is the major goal of the RCR training program at the University of Pennsylvania.

The fourth edition of the handbook on RCR has been modified considerably, and is intended as a companion to the excellent publication, *ON BEING A SCIENTIST: third edition* (National Academy Press, Washington, DC 2009) and *Teaching the Responsible Conduct of Research Through a Case Study Approach (*a handbook prepared by the Association of American Medical Colleges, Korenman and Shipp, eds., 1994). These documents utilize a case study approach to initiate discussions of relevant issues in the conduct and training of biomedical research. The revised handbook includes additional material unique to the training of young investigators, provides practical information on the guidelines and procedures regarding alleged misconduct at the University of Pennsylvania, and includes examples of perspectives on the ethical conduct of research from the scientific community.

I would like to thank the faculty and staff of the University who assisted in editing this handbook and in developing the RCR training program. I am particularly grateful to Drs. Jane Glick and Glen Gaulton for compiling the previous three editions, to Dr. Hillary Nelson for providing material for this edition and for identifying the best available sources for RCR training and case studies and to Colleen Dunn and Judy Jackson in the BGS office for the many hours they spent executing the revised BGS RCR training and for proof-reading this document. I am also grateful to Dr. Stanley Korenman, UCLA Health System and the Association of American Medical Colleges for granting permission touse case studies and text from *Teaching the Responsible Conduct of Research through a Case Study Approach,* Korenman, S.G. and Shipp, A., eds. (AAMC, Washington, DC 1994), and to the U.S. Department of Health and Human Services, Office of Research Integrity, Nicholas Steneck, Ph.D., *ORI Introduction to the Responsible Conduct of Research (2007)* (http://ori.hhs.gov/documents/rcrintro.pdf).

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I. INTRODUCTION

The training program in Responsible Conduct of Research (RCR) has three major educational components: web-based training, program literature, and small group discussion workshops. Participation in all phases of the training program is mandatory for all graduate students in the Biomedical Graduate Studies programs.

The program is introduced through on-line RCR training available on the BGS website at http://www.med.upenn.edu/bgs/rcr.shtml. The training is designed to provide all participants with an introduction to RCR, particularly in biomedical research. The topics covered are:

A. Research Misconduct
B. Data Acquisition, Management, Sharing and Ownership
C. Mentoring
D. Collaboration
E. Conflicts of Interest
F. Publication Practices, Responsible Authorship and Peer Review
G. Human Subjects
H. Animal Welfare

All first-year graduate students must complete the introductory web-based training and pass the web-based quiz. In addition to the topic presentations, there are several RCR case studies on the web site. These are good introductions to the case study method that is the basis of RCR training for graduate students beyond the first year.

This document (RESPONSIBLE CONDUCT OF BIOMEDICAL RESEARCH: A Handbook for Biomedical Graduate Studies Students, Biomedical Graduates Studies, University of Pennsylvania, Philadelphia, PA, 2010) is the primary resource for the case study portion of the training program. It was originally written as a companion to ON BEING A SCIENTIST: A Guide to Responsible Conduct in Research, third edition (published by the National Academy Press, Washington, DC, 2009). That document is available on the web at http://www.nap.edu/catalog/12192.html. These documents utilize a case study approach to inform, stimulate discussion among and thereby educate program participants. The BGS Handbook includes a number of topics that are not included in ON BEING A SCIENTIST but that are judged to be important to the training of graduate students at the University of Pennsylvania. The BGS Handbook also includes a practical guide to acquaint students with the guidelines and procedures regarding alleged misconduct at the University of Pennsylvania and to define the appropriate sources for contact when questions arise. Copies of these booklets are available through links on the BGS web site. More detailed reference material is also available in the BGS office, 160 BRB II/III, 215-898-1030.

The final component of the training program for second, third and fourth year BGS students is topic-specific, on-line training, using the Collaborative Institutional Training Initiative (CITI), Responsible Conduct of Research Program, followed by small group discussions using a case-based study approach. Small group workshops of about 12 students are organized with two faculty preceptors each. The workshops meet for a minimum of one and one-half hours. During these workshops, students and faculty become engaged in a process of discovery together. In respect to research integrity, this includes not only learning facts, but recognizing potential ambiguities in the responsible conduct of research. The small group workshops also reveal the instructors' and students' own attitudes and prejudices, and recognition of conflicting ethical principles. This method also provides the opportunity to directly illustrate the avoidance

of misconduct through good laboratory practice. The participation of active investigators is essential in this exercise. Their involvement lends credibility to the process and may even influence the investigator's own practices.

Graduate students are expected to move through a progression of case studies that consider a specific set of topics. Second year students consider research misconduct, plagiarism, data management and lab notebooks. Third year students consider issues relating to mentoring and lab supervision, collaboration, animals and human subjects. Fourth year students discuss issues of publication practices, authorship, peer review and conflicts of interest. The cases given below are grouped accordingly, although many of the cases touch on more than one issue that may bridge topics considered in different years. Graduate students in years five and beyond have different choices for fulfilling their requirement, which may include attending University sanctioned bioethics seminars, courses or symposia sponsored by the Center for Bioethics (see http//www.bioethics.upenn.edu). Attendance at these events must be registered with the BGS office. Another option for upper level students is to co-facilitate a workshop for the second, third or fourth year students along with a faculty facilitator. This can be arranged through the BGS office.

II. A CASE STUDY APPROACH TO TRAINING OF RESPONSIBLE CONDUCT OF RESEARCH

(adapted from *Teaching the Responsible Conduct of Research Through A Case Study Approach (©1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission), Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health, and the Federal Policy on Research Misconduct*) (http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/Conduct%20Research%206-11-07.pdf)

A. Research Misconduct and Plagiarism Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records (both physical and electronic), progress reports, abstracts, theses, internal (group meetings, thesis committee meetings, etc.) and external (national/international conferences, seminars, job interviews) oral or poster presentations, internal reports, and journal articles. Fabrication is making up data or results and recording or reporting them. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit; this includes internet sources. For a detailed definition of plagiarism, see Appendix A of this document. Research misconduct does not include honest error or differences of opinion. A finding of research misconduct requires that there be a significant departure from accepted practices of the relevant research community, that the misconduct be committed intentionally, knowingly, or recklessly, and that the allegation be proven by a preponderance of evidence.

Case Studies on Research Misconduct and Plagiarism

Case #1 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Dr. Alice Charles, a mid-career scientist, was revising and updating a book chapter. This led her to review other articles on the same subject to help determine what new material to cover. During the course of her reading, she came upon a chapter in a major text by Dr. Chris Long, a departmental chair at a leading medical school, which contained long passages from her previous chapter without attribution.

Dr. Charles called Dr. Long and confronted him with her finding. At first, he vehemently denied having used any of Dr. Charles's text inappropriately. Dr. Charles then emailed Dr. Long copies of the offending passages. After some delay, Dr. Long finally responded, acknowledging that the language was indeed remarkably similar. Dr. Long noted that he had engaged younger members of his research group to write portions of the chapter because he was very busy at the time that the deadline was approaching. Furthermore, to defend himself, he pointed out that much of the original research on which her chapter was based was derived from the work of his laboratory. He admitted only to negligence in not adequately monitoring the activities of his subordinates.

Dr. Charles replied that the subordinates were not acknowledged in Dr. Long's chapter either, and that admission of plagiarism required more than an apology. She indicated her intention to report the matter to Dr. Long's Dean and the editor of the text.

Questions

1. Did Dr. Charles act appropriately? Would you have done anything differently? Considering the difference in status between herself and Dr. Long, was she taking a professional risk?
2. Did Dr. Long do anything wrong? What if he were copying his own previous writings?
3. How would you have handled this matter if you were Dr. Long and were confronted with Dr. Charles's revelations?
4. If you were Dr. Long's Dean, how would you handle Dr. Charles's letter, which contained copies of the plagiarized texts?
5. Upon hearing Dr. Charles's complaint, what would you do as editor of Dr. Long's textbook?

Case #2 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled “Teaching Research Ethics: A Workshop at Indiana University”.).

Charlie West completed his doctorate in biology two years ago and is in his last year as a postdoctoral fellow in Professor Wilson’s laboratory. The last few months have been both good and bad. West and his wife were thrilled by the birth of their first child six months ago, and research has been going well. There are just a few relatively straightforward controls to be run before he and Wilson can submit a manuscript they have been preparing. In addition, West had five job interviews and was then offered a position at Heartland State University, which he has accepted.

However, his success has also caused some problems. With all the preparation and traveling for interviews plus the new responsibilities of parenting, West hasn’t had the time or energy to do very much work in the lab lately. There’s another factor as well. West promised Wilson that

he'd take care of those controls as soon as he finished interviewing but he hasn't done them yet because he's been writing a grant application. During West's second visit to Heartland, the biology department chair made it clear that West is expected to bring in external funding for the research he plans to begin at HSU in a little over a year. The chair told West, "The sooner you get a grant, the better your chances for tenure."

For his post doc, West decided to switch fields in order to learn some new techniques, but for his job he plans to return to research very close to what he did for his Ph.D. In fact, his job seminar was all based on his grad research, not the work he has done as a post doc. West has an idea for a project that everyone he has consulted agrees has great potential. He is very excited about his planned research, and is highly confident that it will be successful both with the funding agency and in the lab. The only problem seems to be getting the grant written.

Unfortunately, since this is West's first grant application, writing it is proving to be far more time-consuming than he expected. He started a couple of months ago and has written the Approach section of the Research Strategy section. All the special forms, facilities statements, biographies, supporting letters, and the budget are now done, but that still leaves the Significance and Innovation sections of the text. It seems that every time he gets set to work on the grant proposal, something goes wrong. Last week he discovered that he had forgotten the animal use forms and had to rush about getting his protocol finalized and approved. A few days ago his baby daughter was up all night with an earache. Then, just this morning, Wilson was pressing him for experimental results. "Look, Charlie," he said, "I know you've been busy, but those experiments can't wait any longer. It's been eight or ten weeks since you finished interviewing and the paper still isn't ready to submit. If we don't get moving we're going to get scooped by Joe Atkins' lab. Neither of us can afford to lose an important publication like this, especially you at this stage of your career. I want to see you at the bench tomorrow. Besides, I'm supporting you on my grant to do research in my lab, not to try to pull in money for HSU."

The NIH grant application deadline for which West has been aiming, one that could give him funding just after he arrives at HSU, is now only three days away, and it's already 10 pm. As he goes through his files, frantically pulling out relevant articles while feeling fairly sure that there is no way he can get the writing done in time, he comes across a grant proposal on a similar topic that he had helped a professor review while he was a graduate student. The professor had also pointed out that it was a model proposal — scientifically sound and extremely well-written. As he looks at the photocopy he kept, West realizes that the Significance and Innovation sections of this older grant would fill in 90% of the information he needs. He could easily write the other 10% in three days. Reasoning that grant proposals are funded mostly on the quality of the proposed work, West decides to copy and paste theSignificance and Innovation sections from the old grant, add his own Research Strategy section and update the Reference section with papers that have been published in the last two years, and be done with it. This way everyone should be happy.

Questions

1. Should West use the material this way? Why or why not?
2. Should West have kept a copy of the proposal?

Case #3 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Professor Diane Archer is a tenured member of a biology department at a major Midwestern university. She has been in the department for 15 years, and during that time she has supervised the work of 20 Ph.D. students. As part of the mentoring process, she has worked closely with her students, teaching them the ropes of writing grant proposals and on occasion inviting students to assist her in reviewing NIH grant applications.

Professor Archer is currently in her last year on an NIH study section. As she is reviewing a group of proposals, she comes upon one written by Charlie West, a former graduate student of one of her close departmental colleagues. Archer knows and remembers Charlie West because she had solicited his help two years earlier in reviewing a proposal closely related to West's own area of research. As she now reads West's proposal, Archer is impressed with the scientific soundness and fine writing style in the Significance and Innovation sections. She notes, however, the extremely terse and awkward phrasing in the Approach section. Perplexed by this shift in style, Archer retrieves from her files the grant proposal West had reviewed with her two years earlier. She is dismayed to see that West has used verbatim virtually the entire Significance and Innovation sections of the earlier proposal for his own current proposal.

Archer is torn. If she reports her discovery of West's plagiarism to the NIH, she knows she will have thrown this young scientist's otherwise promising scientific career into jeopardy. If, however, she says nothing, she will be shirking her responsibility to the NIH, as well as risking her own professional reputation, should the plagiarism be detected later. She decides to contact West directly, and confront him with her finding. She plans to advise West that what he has done constitutes plagiarism and suggest to him that he withdraw the proposal.

If West agrees, and withdraws the grant application, Archer feels she need take this incident no further.

Questions

1. Should Archer proceed with her plan to contact West? Why or why not? Is there anyone else she needs to contact?
2. Should Archer have solicited West's assistance in reviewing the grant?
3. Should Archer have kept grants that she had reviewed in her files?

Case #4 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Alan Yeager has completed a series of experiments characterizing the receptor for a new class of hormones. During the course of his work, he studied binding characteristics and hormonal responses in tissue culture and in vitro, utilizing gels to characterize the molecular weights of receptor variants. This was exciting work for a second-year graduate student doing his first project. One day, Alan's laboratory chief asked him to prepare an abstract for an upcoming meeting and a paper for publication, both to be based on the work Alan had been doing. The abstract was due in one week.

As Alan examined his accumulated data, he noted that a number of cell culture plates failed to respond to the hormonal stimulus and that there was considerable variability in the dose-response relationship. Furthermore, on reexamination, he noted that a number of his gels were not very aesthetic in appearance, yet he was sure that they demonstrated the molecular weight, agonist binding, and subunit characteristics of the receptor.

Alan mentioned his distress to Pam Alden, a fifth-year graduate student, who said, "Why don't you clean up your data? You'll never get the paper published unless you do. We always clean up the data around here." She then suggested that the four culture points failing to show a response be dropped because the cells were probably dead. She also pointed out that he might eliminate the top data point at the 45 minute interval as an outlier. She examined the gels and suggested using Adobe Photoshop™ to improve the quality of the pictures, including the duplication of one of the nicer gel lanes to replace another that turned out poorly, but showed essentially the same result. "That will greatly improve your chances of publication," she said. Alan replied, "Maybe I should repeat a few of the experiments or try to improve the culture conditions?" "No," said Pam, "If you're convinced of your results, why go through the time, expense, and uncertainty of more repetitions? You'll never complete an experiment in time for the abstract, anyhow." Somewhat dismayed, Alan thanked her and turned back to his work.

Questions

1. What do you think about Pam's comments on publication practices and her suggestions for "cleaning up" the data?
2. How should Alan go about determining which points to include and which to exclude?
3. What other course(s) of action would you recommend to Alan?
4. Pam's perception about improving the chances of publication by "cleaning up" the data is not uncommon. How might journal editors and reviewers work toward correcting this perception?

Case #5 (©ASM Press. This case is from Francis L. Macrina (2000): Scientific Integrity, 2nd edition, published by ASM Press. Appropriate permission being processed.)

Jim, a new assistant professor, is getting ready to submit his first paper since joining the faculty. He reviews one of the figures for this paper which is a photo of an ethidium bromide-stained agarose gel. The gel contains the products of polymerase chain reaction (PCR)-amplified whole cell DNA. The photo displays the predicted 3 kb DNA fragment. Jim comments that a second minor signal was also evident on the original gel. Based on its size, Jim believes that this second fragment represents a very exciting discovery, but it needs considerable additional work. This second fragment cannot be seen in the photograph because Jim discloses that he has deliberately cropped the photo to obscure the second fragment. He says he did this because he is worried that competing groups in larger, more established labs will interpret the potential of the second fragment and they will "scoop" him. He has prepared a figure legend that says: "a second minor signal of unexplained origin was present in this experiment but is not shown in the figure". But, the figure legend does not include the size of the unexplained fragment. Thus, he argues he'll be telling the truth while, at the same time, he'll be protecting himself from his competition.

Questions

1. Are Jim's actions appropriate?

2. Is he simply playing fairly in the hotly competitive arena of biomedical research, falling victim to self-deception or perpetrating scientific fraud?

B. Data Acquisition, Management, Sharing and Ownership Research data, including detailed experimental protocols, all primary data, and procedures of reduction and analysis are the essential components of scientific progress. Scientific integrity is inseparable from meticulous attention to the acquisition and maintenance of these research data.

The results of research should be carefully recorded in a form that will allow continuous access for analysis and review. Attention should be given to annotating and indexing notebooks and documenting computerized information to facilitate detailed review of data. All data, even from observations and experiments not directly leading to publication, should be treated comparably. All research data should be available to scientific collaborators and supervisors for immediate review, consistent with requirements of confidentiality. Investigators should be aware that research data are legal documents for purposes such as establishing patent rights or the veracity of published results when the data are challenged. The data are subject to subpoena by congressional committees and the courts.

Research data, including the primary experimental results, should be retained for a sufficient period to allow analysis and repetition by others of published material resulting from those data. In general, five to seven years is specified as the minimum period of retention but this may vary under different circumstances.

In most cases, such as with federally-funded research, the university owns the data, not the faculty, graduate students, postdoctoral fellows or staff who perform the research (see Appendix B). Notebooks, other research data, and supporting materials, such as unique reagents, belong to the university, and are entrusted to the laboratory in which they were developed. Departing investigators may take copies of notebooks or other data for further work if approved by the responsible principal investigator. For industry-sponsored research, data may belong to the sponsor. This is usually negotiated with by the investigator and the university with the industry sponsor prior to initiating the research.

Data management, including the decision to publish, is the responsibility of the principal investigator. After publication, the research data and any unique reagents that form the basis of that communication should promptly and completely be made available to all responsible scientists seeking further information. Exceptions may be necessary to maintain confidentiality of clinical data or if unique materials were obtained under agreements that preclude their dissemination.

Sharing of reagents/resources is an important part of the scientific enterprise and is required by federal funding agencies and most journals. Reagents/resource sharing allows other investigators to both repeat and extend studies and thereby advance research. This includes not only reagents/resources such as plasmids and novel chemical reagents, but model organisms such as transgenic mice. Similarly, genome-wide association study data funded by the federal government are required to be made publically available. For more information on these policies, see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html, NIH Guide NOT-OD-04-042 and http://grants.nih.gov/grants/gwas/.

Authors should not lose sight of the principle that a major purpose of publication is to allow repetition or extension of the research findings. The information given, its accuracy, and the

extent of detailed description should be sufficient to allow others to repeat the experiments successfully. "Any responsible scientist seeking further information is to be shown the research data promptly and completely, once the findings have been published."[1] In this sense, research data lose their privacy once the findings have been made public; NIH data are expected to be retained and available for review for a minimum of five to seven years after publication. It is a shock to learn that some scientists who are accused of falsifying data claim without much apology or explanation to have lost or deliberately discarded the notebooks or primary data. In our academic experience, ordinary scientists are exceedingly reluctant to discard notebooks, even to the point of compulsion. The obligation to produce original data upon challenge is not one that can be shrugged off by any serious scientist.

The current NIH Public Access Policy (http://publicaccess.nih.gov/policy.htm) also requires that "*all investigators funded by the NIH submit or have submitted for them to the National Library of Medicine's PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication: Provided, that the NIH shall implement the public access policy in a manner consistent with copyright law."*

For more detailed information on ownership of research and authorship, see Appendix B.

Case Studies on Data Management and Lab Notebooks

Case #6 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Jessica Banks, a postdoctoral fellow in Professor Brian Hayward's lab, is about to leave for her new job. When starting research in Hayward's lab, Banks divided her time among three projects. Then in her second year, after consultation with Hayward, she decided to continue and expand upon one of the three lines of investigation as her main project. This was also the project most closely related to Hayward's grant at the time. Later, Banks's early results were included in Hayward's grant renewal. The other two promising lines of research were left incomplete.

Banks's new job is a tenure-track position in a mid-sized Western liberal arts college. Shortly before leaving for her job, she comes into the lab to pick up her notebooks. Although her new faculty position will place a heavy emphasis on teaching, she is looking forward to continuing to do some research as well. In particular, she is eager to pick up where she left off with the two uncompleted projects she worked on before.

Professor Hayward meets Banks on her way into the lab, and their genial conversation abruptly changes when she mentions she has come to take her notebooks. Hayward exclaims, "You can't take those notebooks away — they belong to the lab!" Banks is confused. "But I did the work, and I wanted to follow up on it. I can't do that without the notebooks."

Professor Hayward is adamant. "I'm sorry, but you should understand this. This lab is a joint enterprise, and all the work you did was funded by money I brought in via grants. The notebooks don't belong to you, nor to me; they belong to the lab, and the work will be continued in this lab. I've already talked to one of the new students about working on those projects this fall." Banks, seeing her plans fall apart around her, protests, but Hayward is implacable. After a

few minutes, she stalks away, without the notebooks.

Later that afternoon, Banks gets together with her labmate Paul Larson, and during their conversation, she tells him about her run-in with Hayward. “Look,” says Larson. “Hayward has no right to deny you access to the information in the notebooks. Even if the books should remain in the lab, you did the work that generated all the data.” “I know!” says Banks. “But Hayward wouldn’t listen to that argument when I made it.” “Here’s my suggestion,” says Larson after some reflection. “Just stop by the lab and photocopy the books some time during the weekend. I happen to know Hayward will be out of town, so he’ll never know. That’s the fair thing to do: He gets to keep the notebooks in his lab, and you get a copy of the data you collected.”

Banks seems uncertain, but says she’ll think about Larson’s suggestion and decide before the weekend.

Questions

1. Should Banks photocopy the notebooks? Why or why not?
2. Can you think of another approach Jessica might take to get copies of the notebook?
3. How might this conflict have been avoided in the first place?

C. Mentoring and Respectful Workplace (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*), *Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health and The University of Pennsylvania Affirmative Action and Equal Opportunity Handbook)***:** Research training is a complex process, the central aspect of which is an extended period of research carried out under the supervision of an experienced scientific mentor. This supervised research experience represents not merely performance of tasks assigned by the supervisor, but rather a process wherein the trainee takes on an increasingly independent role in the choice of research projects, development of hypotheses and the performance of the work. Indeed, if training is to prepare a young scientist for a successful career as a research investigator, it must be geared toward providing the trainee with the aforementioned skills and experience. It is particularly critical that the mentor recognize that the trainee is not simply an additional laboratory worker.

Each trainee should have at least one designated primary scientific mentor, although particularly in newer, inter-disciplinary fields, it is becoming more common for trainees to have two mentors, each with expertise in different disciplines. It is the responsibility of mentors to provide a training environment in which the trainee has the opportunity to acquire both the conceptual and technical skills of the field. In this setting, the trainee should undertake a significant piece of research, chosen usually as the result of discussions between the mentor(s) and the trainee, which has the potential to yield new knowledge of importance in that field. The mentor has the responsibility to monitor the trainee's progress closely and to interact personally with the trainee on a regular basis in such a way as to make the training experience a meaningful one. Styles of research differ, both among fields and among investigators in a given field, so that no specific rules should be made about the number of trainees that is appropriate for a single mentor to supervise. Nonetheless, mentors should limit the number of

trainees in their laboratory to the number for whom they can provide an appropriate research experience.

There are certain specific aspects of the mentor-trainee relationship that deserve emphasis. First, mentors must be particularly diligent in avoiding the involvement of trainees in research activities that do not provide meaningful training experiences but that are designed mainly to further research or development activities in which the mentor has a potential monetary or other compelling interest. Second, training must impart to the trainee appropriate standards of scientific conduct. The mentor must convey these standards by both instruction and by example. Specific responsibilities of a mentor relate to setting standards for absolute honesty in every aspect of scientific conduct, for keeping accurate and useful lab notebooks, for establishing clear guidelines for recording and storing data, and for exercising vigilance in honest data presentation. Third, mentors have a responsibility to provide trainees with realistic, unbiased appraisals of their performance and with advice about career development opportunities.

Conversely, trainees have responsibilities to their supervisors and to their institutions. These responsibilities include adherence to the guidelines for responsible conduct of research as well as the applicable rules and programmatic constraints related to the needs of the laboratory and the University. Trainees need to meet regularly with their mentors and provide updates on the progress of their research, to keep good research records and to be good lab citizens. The same standards of professionalism and collegiality apply to trainees as to their supervisors and mentors.

Both mentors and trainees should strive to maintain a respectful workplace, free of discrimination and harassment. Discrimination and harassment are sometimes difficult to define. Some examples of discrimination and harassment are illegal, some are not. Discrimination in the laboratory setting occurs when lab members are treated differently. This may include such things as requiring different working hours, not providing equal access to computers, lab equipment, supplies, etc., favoritism, or deciding not to take you as a student. If a principal investigator decides not to take you as a thesis student because she or he simply doesn't like you, that is not illegal, but the PI cannot discriminate against you because you are a member of a “protected category”. The “protected category” list includes but is not limited to race, religion, gender, sexual orientation, or ethnic ancestries. Harassment is a specific kind of discrimination. It occurs when someone else in your workplace (this can be your PI or a lab mate) says or does something to make you feel uncomfortable or intimidated. Harassment is illegal if it is done because of your race, sex, or other “protected category”. Sexual harassment involves unwelcome sexual advances, requests for sexual favors or verbal or physical conduct of a sexual nature. It is often imposed upon a person in an unequal power relationship through the abuse of authority. Central to this concept is the use of implied reward or threat of deprivation that interferes with the academic or work effectiveness of the victim.

Regardless of legality or illegality of discrimination and harassment, the Penn community, as well as the scientific community in general, depends on trust and civility. A willingness to recognize the dignity and worth of each person is essential. Penn’s policy on harassment can be found at http://www.upenn.edu/provost/category/penn_policies.

Case Studies on Mentorship, Lab Supervision and Respectful Workplace

Case #7 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

A second year graduate student is experiencing difficulties regarding the conduct of a rotation research advisor. In this graduate division, lab rotations are of somewhat variable length, and form the theoretical basis of the first and second preliminary examinations. After six months of rotation research (a typically acceptable second rotation) the student felt prepared to take the second preliminary exam. However, the advisor disagreed and said that the student was unlikely to pass the exam. The implication was clear that the advisor would not support the student during the examination review. The student questioned the advisor's motivation from the start, having noticed that the rotation work was yielding data valuable to a pending grant review. In addition, the student was confident of being ready for the exam from discussions with other students.

Questions

1. Is this an example of misconduct, or just a rigorous advisor? How should the student handle this? With whom could she or he talk?
2. What role should the graduate faculty play in reporting or evaluating this event?

Case #8 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Part I

Bob Bailey is a fourth-year graduate student in the lab of Professor Peter Martin, and he is not very happy. His research has not been going well recently, and he attributes his troubles to the romantic relationship that Martin has established with another graduate student, Sarah Stern. Stern is also a fourth-year graduate student in Martin's lab. Both she and Bailey officially joined the lab at the end of their first year of graduate study. Unlike Bailey, Stern has consistently made excellent progress in her research.

Martin is known for running a productive, highly respected, and collegial lab. During the summer after her third year, Stern was surprised but happy to find her collegial rapport with Martin blossoming into a romantic relationship. Although they tried to be as discreet as possible, it was soon common knowledge among the other four graduate students in Martin's lab that he and Stern were "an item." By now, in December, the once-collegial atmosphere has become strained. In particular, Bob Bailey is starting to show his resentment. He is growing resentful of Stern's research success and the favoritism that he perceives Martin is showing her. Since September, the Martin lab has submitted abstracts to three meetings, and Stern is the first author on all of them. Of the grad students in the lab, Martin has offered to send only Stern to this year's three big meetings in their field. For each, Stern will be traveling and staying with Martin. Last year, Stern went to two of these meetings, and her expenses were covered by Martin's grants. Although Bailey is Stern's contemporary, he has yet to attend a scientific meeting. Bailey's jealousy and resentment are, however, balanced by genuine concern for

Stern. They have been friends since they started graduate school together (though nothing more than friends), and Bailey fears that if Stern's relationship with Martin were to end, this could jeopardize Stern's work in the lab and, in turn, her future career.

It is just before winter break. Bailey has tried to work up the nerve to talk to his friend Sarah or to confront Martin, but he doesn't think there would be any point to it. He doesn't believe either of them is thinking clearly, and he fears that bringing up his complaints and his worries would just make them angry. He is considering taking his complaints about Martin and his concerns about Stern to the department chair.

Question

1. Should Bailey bring his concerns to the department chair? Why or why not?

Part II

After break, Bailey does schedule an appointment with the chair of the department to report his complaint and concern. Bailey finds that the chairperson, David O'Donald, does not know anything about the Martin-Stern romance. O'Donald asks Bailey if he believes that Stern was pressured into this relationship with Martin, or if Stern is unhappy with the situation. When Bailey answers in the negative, O'Donald, who is on Bailey's thesis committee, shifts the topic of the conversation to Bailey's current troubles with his research. After ten minutes, Bailey leaves O'Donald's office feeling unsettled. O'Donald's parting words were, "Well, I don't think there's anything to be concerned about with Stern and Martin. They're adults. If some problem arises, let me know, and I can have a chat with Martin. In the meantime, get some work done."

Question

1. Is O'Donald correct that there's nothing to be concerned about since both the student and faculty member are adults? Should O'Donald adopt the "wait and see" approach that he proposes? Why or why not?

Case #9 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*)

Lisa is a 26-year-old postdoctoral fellow working in the laboratory of Dr. H. There are three other postdocs in the lab, all men. Her mentor Dr. H, who is forty years Lisa's senior, has an excellent reputation professionally and is extremely well liked by his colleagues. Dr. H has a charming manner and a clever, often self-effacing, sense of humor. Lisa is in general fond of Dr. H and feels lucky to have acquired a position in his lab. Dr. H does have one trait, however, that detracts from his otherwise admirable character. His repertory of humor often includes remarks about women that, in Lisa's view, border on the distasteful. Dr. H's quips make Lisa uncomfortable and, she believes, discourage her colleagues from taking her work seriously. In addition, Dr. H's humor seems to spur the other male postdocs into exchanging jokes and remarks. Nonetheless, given the reputation of the lab, Lisa decides for the time being to do her best to ignore this problem.

After Lisa has been in the lab for over a year, a national science meeting for Lisa's discipline is held. Dr. H decides that Lisa has the most to gain of all his fellows by attending. Lisa is delighted, but her fellow postdocs are clearly and understandably disappointed. One day Lisa overhears two of her male colleagues joking among themselves that Dr. H has other than scientific intentions for this meeting. Their comments also suggest that Lisa has done something inappropriate to curry favor with her mentor. Upon overhearing similar remarks on several more occasions, Lisa confronts her colleagues, who retort, "Well, there are certain advantages to being a woman, aren't there?" Lisa feels offended and angry and wishes to pursue the matter further. However, she finds the situation too embarrassing and awkward to discuss with Dr. H, and she is uncertain what repercussions such a discussion would have on her career.

Questions

1. Do Dr. H's actions create a hostile environment for women? Why or why not? Would you characterize these actions as sexual harassment? Do the actions of Lisa's fellow postdocs qualify as sexual harassment? Why or why not?
2. How might this sort of atmosphere in the laboratory be avoided? Now that the current situation exists, how might it be improved under these circumstances?
3. Should Dr. H be held accountable for the behavior of Lisa's colleagues? Why or why not?
4. Given the awkwardness of discussing the matter with Dr. H, and her affection for him otherwise, how might Lisa follow up on her concerns? What support should she have available to her?

Further Discussion

Consider a somewhat different scenario in which the postdoctoral fellow is Gene, a 26-year-old African-American male working in an all white laboratory. Rather than facing remarks and innuendo relating to his gender, Gene must deal with subtle, yet pervasive attitudes concerning people of color. When invited to attend the scientific meeting by Dr. H, he overhears remarks, and is eventually told to his face, that Dr. H is "bending over backwards" to provide opportunities for Gene simply because Gene is black and considered disadvantaged. Should Gene deal with this situation any differently than Lisa? Would the solutions proposed in answers to Question 2 above also help prevent this sort of climate in the lab?

Case #10 *(from the Sexual Harassment web site at the University of Wisconsin. Copyright © 2009. The Board of Regents of the University of Wisconsin System. http://www.oed.wisc.edu/sexualharassment/case.html)*

Two graduate students who work in the same lab are having trouble getting along in the lab. Their principal investigator interviews each of them. Both report that they used to be great friends and often went out for beer together after work. The male student asserts that the tension resulted from his rejection of the female student's sexual advances. He claims that ever since he rejected her, she has said nasty personal things to him and about him to other members of the lab, creating a hostile work environment. The female student says that the tension resulted from the male student's condescending attitude and disrespect for her work. She claims that the other student belittles her and denigrates everything she does in the lab.

Questions

Put yourself in the position of the supervisor.

1. What might happen if you do nothing?
2. What could happen if you leave it to the two students to work out?
3. What should you do next?

Case #11 *(from the Sexual Harassment web site at the University of Wisconsin. Copyright © 2009. The Board of Regents of the University of Wisconsin System. http://www.oed.wisc.edu/sexualharassment/case.html)*

A professor and a research associate in his lab attend a professional meeting out of town and have a one-night sexual encounter. Both are in long-term relationships and agree that the affair will not continue when they return to campus.

Questions

Imagine you are the professor.

1. What should you do next? Why?
2. What if word of the event spreads throughout the lab and other members of the group complain that the research associate is getting preferential treatment?
3. What if, six months later, you decide to terminate the research associate's position?

D. Collaboration Research collaborations frequently facilitate progress and generally should be encouraged. Recent interest by funding agencies in funding collaborative research is the result of the recognition that complementary skills are provided by researchers with different expertise, thereby increasing scientific progress. Additionally, the ease of electronic communication has greatly enhanced researchers' ability to carry out collaborative research within their own institution and with investigators in other institutions, including foreign collaborators. Finally, technology-transfer between academia and industry has been fostered by the Bayh-Dole act, which gave universities the right to pursue ownership of inventions made during federally-funded research in preference to the government with the intent of increasing collaboration between commercial concerns and non-profit organizations such as universities.

It is advisable that the ground rules for collaborations, including eventual authorship issues, be discussed openly among all participants from the beginning (see section E). Because of the variation in detailed practices among disciplines, no universal set of standards can easily be formulated. It is expected, however, that each research group will freely discuss and resolve questions of authorship before and during the course of a study. Further, each author should review fully material that is to be presented in public forums or submitted (originally or in revision) for publication. Each author should be willing to support the general conclusions of the study. Collaborations between scientists confer on both parties an obligation to share date and to submit data to criticism.

Prior to beginning a formal collaboration, the investigators and their affiliated institutions should also formally agree on who owns the materials generated from the collaboration, how they can be used and how to acknowledge the source of the material. Such agreements help protect the interests of all collaborators.

The involvement of graduate students in collaborations between Penn and industry is subject to restrictions. Graduate students must be guaranteed a free exchange of information. Presentation of data in talks and publications is the norm in academia and is required for graduate students to get their degrees, as well as faculty hiring and promotion. Sometimes industry vets information before publication or public presentation at meetings. BGS does not allow students to be involved in collaborative research that would hinder publication or presentation of data.

Case studies on Collaboration

Case #12 (*from University of Washington Biomedical Research Integrity Cases, from http://ori.hhs.gov/education/products/burke_washington/burke.pdf*)As a result of a paper you've just published as a graduate student, you are approached by some researchers at Swell University. You have been developing a new drug which shows some promise for patients with Parkinson's disease. The work has been supported by an NIH training grant. The researchers at Swell want to collaborate with you and foresee setting up a multi-site clinical trial.

1. What do you need to consider prior to agreeing to collaboration with the researchers from Swell?
2. How will you determine issues such as ownership, and use of data and authorship on publications?
3. You've not yet finished your research nor published your results. Rather, the researchers from Swell were at a conference at which you presented some preliminary data. Are there different considerations regarding the potential collaboration due to the research being in early stages?
4. What if you were approached by a for-profit company rather than a University?
5. What if the folks from Swell just want use of some of the compounds you've developed?

Case #13 (©ASM Press. This case is from Francis L. Macrina (2000): Scientific Integrity, 2nd edition, published by ASM Press. Appropriate permission being processed.)

Drs. Hopkins and Carpender have submitted a co-authored paper reporting on the regulation of a gene introduced by transfection into fibroblasts. The paper is returned from the editor with two very positive reviews, suggesting only minor revisions. While the paper is being revised, one of Hopkins' postdocs presents data at a lab meeting demonstrating that the results of the gene regulation experiments are dependent on the concentration of DNA used to transfect the cells. She presents data showing that if the concentration of the gene construct is increased five-fold, the previously reported regulatory effects are completely abolished. In light of these results, Hopkins argues that the paper should be withdrawn and not allowed to go to press. Carpender strongly objects to this. He argues that the results of the paper are reproducible and the interpretations of the results straightforward. He further argues that the new results may be the basis for a whole new paper, and that these data shouldn't even be mentioned in the paper. Carpender argues that the paper be published with the minor revisions suggested by the reviewers.

Question:

1. What do you think should be done?

E. Conflicts of Interest (Much of the material here was adapted from the University of Minnesota's website- http://www.research.umn.edu/ethics/curriculum/conflict_interest.html - and is used with permission). The research community is committed to conduct itself in accordance with the highest standards of integrity and ethics and in compliance with applicable state and federal laws related to conflict of interest and objectivity in research. COI are situations where two or more competing interests create the perception or the reality of an increased risk of bias or poor judgment. Because trust is one of the core ethical values of science, COI involves the abuse, actual, apparent, or potential, of the trust that people have in scientists. COI are not always inherently bad and can be expected to occur. It is how they are handled that can lead to improper, inappropriate, or bad outcomes.

DEFINITIONS

There are many areas in which a potential conflict of interest may arise. These include the following. (See Scientific Integrity by F. L. Macrina for a more detailed discussion.)

Financial conflict of interest: Although the legal definition varies from state to state, financial conflict of interest basically involves any situation in which an individual exploits his or her position for personal or financial gain. This is probably the most important type of conflict because of its visibility and the potential for damage to the reputation of the University and all concerned. A conflict of interest occurs when an academic employee or student compromises his or her professional judgment in carrying out University teaching, research, outreach, or public service activities because of an external relationship that directly or indirectly affects the financial interest of the academic employee or student, their family members, or any associated entity. An obvious example would be the ownership of, or a major interest in, a private firm by a faculty member or student who also has the decision-making responsibility in awarding a contract to that firm. Sponsorship of research by commercial firms in which the faculty member or student has a significant interest is another obvious example. However, many potential conflicts of interest can be more complex and not so clearly discernible.

Potential conflicts of interest due to financial involvements with commercial institutions may not be recognized by others unless specific information is provided. Therefore, the scientist must disclose all relevant financial relationships, including those of the scientist's immediate family, to the University, Department, Center or Division during the planning, conducting and reporting of research studies, to funding agencies before participating in peer review of applications for research support, to meeting organizers before presentation of results, to journal editors when submitting or refereeing any material for publication, and in all written communications and oral presentations.

Scientific conflict of interest: This type of conflict involves participation in journal reviews, review panels or other groups that make decisions regarding the allocation of resources or the publication of papers or someone who offers scientific testimony as an expert witness. Possible conflicts in review panels or refereeing are usually handled by excusing the person with the potential conflict. The situation with expert testimony is not so clear but the individual's background and connections should be revealed before the testimony.

Academic conflict of interest: This involves utilization of the name and/or the resources of the University for personal gain.

Conflict of commitment or effort: Most of the University rules about conflict of interest apply to faculty, and they strictly limit how much time, money, and energy that a faculty member can spend on outside interests: (http://www.hr.upenn.edu/policy/policies/005.aspx). Non-University activities that require considerable time and effort could lead to a significant decrease in the time and effort devoted to the employer, the University. The University has a policy that basically allows faculty the equivalent of one day per week for outside consulting or other professional activities. The policy requires approval in advance for activities that demand more than one day per month (on average) and reporting of all activities in which more than three days per term are spent.

BGS requires students on fellowships to devote all of their time to the educational program. Any outside jobs must be approved by BGS and must pertain to the education of the student. This is usually limited to teaching assistantships and other activities that are related to their educational goals.

Conflict of conscience: Such a conflict can arise when an individual's personal convictions (e.g., religious, ethical, or moral) are so strong that they influence the decision being made. Another type of conflict can arise for individuals working on a particular disease that affects a family member or friend. There are no widely accepted procedures for dealing with conflicts of this type.

Nepotism: In the past, the employment of two related individuals (e.g., a married couple) in the same department was not allowed by anti-nepotism rules. Now, the matter is handled by a rule that simply states such individuals cannot participate in any decisions affecting the other person.

Case Studies on Conflicts of Interest

Case #14 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Marty Brown, a plant biologist at a major research university, is investigating the potential utility of transgenic tobacco plants as "factories" for the production of foreign proteins. The potential benefit of this research to human medicine is clear. For instance, the non-plant gene that Brown is working with right now is human Factor VIII, a protein essential for blood clotting and the protein that most people with hemophilia lack.

In his current experiment, Brown has introduced a construct of the Factor VIII gene into tobacco and has 100 transgenic plants that he is studying in a developmental time course. He is following both Factor VIII production and the plants' growth to assess the effect of the foreign gene on the plants' development, and vice versa. Brown is excited about the success of his experiment thus far, and he feels that the potential uses for his findings make it imperative that he publish as soon as possible. A disease-free, inexpensive source of Human Factor VIII would be of great benefit to hemophiliacs, who run the risk of contracting disease from plasma-derived sources and who must find a way to pay about $300,000 per year for their treatment. The urgency is all the more real to Brown, whose infant son is a hemophiliac. The sooner Brown's promising results are published, the sooner other scientists will be able to follow his line of work, and the sooner his discovery can have a practical, clinical impact.

One Friday, late in January, Brown checks on the 100 transgenic tobacco plants that have now been in the greenhouse for about a month. He discovers that twelve of them are beginning to look sickly. Their leaves are drooping a bit and turning yellow on the edges. He records this in his notebook, and also notes that all of these plants are close to the door. Later, in the lab, when he checks his previous results, he finds that these twelve plants have been producing Factor VIII at a consistently higher level than the other plants. Only one other plant had Factor VIII in this range, although quite a few came close. Feeling pressed for time, Brown decides not to investigate the cause of the poorer growth of the twelve plants any further. He concludes that because they happen to be near the greenhouse door, they have been repeatedly exposed to lower temperatures than the other plants, and that this is the problem. He records this conclusion in his notebook along with the other entries.

Early the following week, Brown is working on integrating his most recent transgenic plant data into the first draft of the manuscript on which he is working. He has entitled it "Human Factor VIII Production in Transgenic Tobacco Has No Deleterious Effect on Plant Growth." When Brown comes to the data on the twelve sickly plants, he considers whether he should exclude these plants from his analysis. He thinks that doing so would be justified because of the plants' proximity to the greenhouse door. In addition, the paper would be more impressive without the uncertainty associated with the data from these plants. He weighs the relevance of the data from those twelve plants against the principle that there is nothing wrong with excluding outliers and irrelevant data. Besides, he thinks these results are too important to risk letting them get held up in the review process.

Questions

1. Should Brown leave out the data from those twelve plants? Why or why not?
2. What if it was just one plant out of 100 plants instead of 12 plants out of 100?
3. How can Brown deal with the potential conflict of interest that occurs from the fact that his infant son is a hemophiliac?

Case #15 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*)

Cynthia Walsh, M.D., an associate professor of medicine, is a prominent academic cardiologist. Her personal financial investments include significant stock holdings in three publicly traded biotechnology firms. She is approached by one of these firms to be a lead investigator in a therapeutic trial of a novel agent for preventing tissue damage from myocardial infarction (MI). This will be a randomized double-blinded, placebo-controlled clinical trial (neither patient nor physician will know whether the drug under investigation or a placebo is being used in a given patient). Dr. Walsh is quite familiar with the preliminary animal and cell biology work in the area and believes that there is an excellent chance that this new drug will result in a significant improvement in survival and reduce damage to the heart muscle. She even thinks this novel agent may reduce the risk of heart failure and irregular beats.

Dr. Walsh's group is one of the few cardiology groups fully prepared to carry out this investigation, which is why she was contacted, and a clinical fellow suited to manage the study is available. She cares for a large number of patients with MI and believes that she could enroll

numerous patients efficiently. The drug will only be available to her patients if her group participates in the trial. The company is offering $5,000 for each patient enrolled and the money would really help both her salary and the division budget. As a lead investigator, she will become much better known and will likely experience an increase in referrals if the trial succeeds.

Questions

1. Is Dr. Walsh's participation in this study appropriate? Justify your position.
2. Does Dr. Walsh have a conflict of interest? If so, what is the nature of the conflict? How could it be mitigated? Would the nature of the conflict of interest be different had she not already owned stock, but instead had been offered stock as a form of compensation for conducting the study?
3. If Dr. Walsh already believes the drug is an improvement based on the literature emanating from animal experiments, can she honestly assign patients randomly to treatment or placebo? What if she believes the drug is deleterious because of its adverse effects on the kidney late in the course of treatment?
4. What should the role of the university be in this case?
5. During study of the first few patients, it becomes apparent to Dr. Walsh that she can tell who is on the active drug because the patients get a facial flush. Might that further influence her ability to remain objective? What considerations apply in answering that question?

Case #16 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*)

Dr. Simon Goldberg is a dermatologist and a tenured faculty member at a research-intensive medical school. When not attending to his clinical and educational responsibilities, he conducts research into the mechanisms by which skin tissue heals and repairs itself. Recently, Dr. Goldberg received a contract from Vanite, a large cosmetics company whose products are sold worldwide. The U.S. Food and Drug Administration (FDA) has questioned claims the company makes concerning one of its leading products, Creme de Jouvence, which Vanite asserts can repair damage to the skin caused by aging and exposure to the sun. Vanite stands by this claim, although it is uncertain which of the many ingredients in the product actually produces the rejuvenating effect. Therefore, it would like to hire Dr. Goldberg to investigate this matter. Dr. Goldberg's findings will be used in Vanite's response to the FDA. As it is under some pressure to respond in a timely manner, Vanite would like to have the results of this study as quickly as possible. Whatever Dr. Goldberg finds, he will receive $250,000 to cover the expenses and salary associated with the project. However, if he can identify an ingredient that proves active within nine months, a company representative has assured Dr. Goldberg that Vanite will hire him again to study the safety of a new cosmetic ingredient the firm has developed.

Questions:

1. What kinds of incentives are created by the promise of future employment?
2. Assume that in order to make the deadline, Dr. Goldberg enlisted two predoctoral students to assist with the project. To recruit them for this effort, he told the students that they would gain valuable exposure and experience from their participation. What problems might be posed by this situation?

3. Vanite is clearly under pressure to support its claims and Dr. Goldberg is conscious of Vanite's desire to acquire data to help the company make its case. If you were Dr. Goldberg, what would you do to retain your objectivity in this study?
4. The FDA will scrutinize Dr. Goldberg's research findings. What impact does this independent review by a government agency have on your concerns about this contract?

Case #17 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled "Teaching Research Ethics: A Workshop at Indiana University". © 1995 by Indiana University).

Professor Widom files for a patent on a novel antisense strategy for knocking out genes. The technique is potentially applicable to the treatment a variety of genetic diseases. Rather than licensing the technology to a company, Prof. Widom has decided to create a Biotech start-up company. There are still a lot of issues to address before a drug based on this strategy will be ready to go to clinical trials, including optimizing chemical synthesis, target site specificity and drug delivery. The start-up company awarded Prof. Widom a grant of $50,000/year to fund developmental research in her own lab at the University. Prof. Widom assigns two graduate students to the project.

1. Who besides the PI should know about the relationship between the company and Prof. Widom. How much does each party need to know?
2. Is it OK for Prof. Widom to manage an NSF grant involving the same chemistry as funded by her company? If so, under what circumstances would this be OK and when would it not be OK?
3. What are some of the concerns of the graduate students assigned to this project?
4. What are some of the benefits to the graduate students assigned to this project? Benefits to the PI? Benefits to the University?
5. One day Prof. Widom receives a manuscript to review from the editor of a major journal in the antisense field. The article is written by two scientists who are employed by a company working in the same area as Prof. Widom's. In fact, the two companies will compete in the same market if they are successful in developing products. The paper reports interesting advances in drug delivery. Should Prof. Widom agree to review the paper? If so, what steps should she take before agreeing to review the paper?
6. Prof. Widom needs a certain supply (cost = $2000) and she wants to buy it from her own company, which she claims is the sole supplier. Is this allowed? Are any restrictions placed on this transaction?

F. Publication Practices, Responsible Authorship and Peer Review (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)*, Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health, and the Federal Policy on Research Misconduct*) (http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/Conduct%20Research%206-11-07.pdf)

Authorship: Authorship refers to the listing of names of participants in all communications, oral and written, of experimental results and their interpretation to scientific colleagues. Authorship is the fulfillment of the responsibility to communicate research results to the scientific community for external evaluation.

Authorship is also the primary mechanism for determining the allocation of credit for scientific advances and thus the primary basis for assessing a scientist's contributions to developing new knowledge. As such, it potentially conveys great benefit, as well as responsibility. For each individual the privilege of authorship should be based on a significant contribution to the conceptualization, design, execution, and/or interpretation of the research study, as well as a willingness to assume responsibility for the study. Individuals who do not meet these criteria but who have assisted the research by their encouragement and advice or by providing space, financial support, reagents, occasional analyses or patient material should be acknowledged in the text but not be authors.

The submitting author should be considered the primary author with the additional responsibilities of coordinating the completion and submission of the work, satisfying pertinent rules of submission, and coordinating responses of the group to inquiries or challenges. The submitting author should ensure that the contributions of all collaborators are appropriately recognized and that each author has reviewed and authorized the submission of the manuscript in its original and revised forms. The recent practice of some journals of requiring approval signatures from each author before publication is an indication of the importance of fulfilling the above.

The BGS policy on authorship can be found at www.med.upenn.edu/bgs/docs/BGS_author.pdf.

Peer Review: Peer review can be defined as expert critique of either a scientific treatise, such as an article prepared or submitted for publication, a research grant proposal, a clinical research protocol, or of an investigator's research program, as in a site visit. Peer review is an essential component of the conduct of science. Decisions on the funding of research proposals and on the publication of experimental results must be based on thorough, fair and objective evaluations by recognized experts. Therefore, although it is often difficult and time-consuming, scientists have an obligation to participate in the peer review process and in doing so they make an important contribution to science.

Peer review requires that the reviewer be expert in the subject under review. The reviewer, however, should avoid any real or perceived conflict of interest that might arise because of a direct competitive, collaborative or other close relationship with one or more of the authors of the material under review. Normally, such a conflict of interest would require a decision not to participate in the review process and to return any material unread.

The review must be objective. It should be based solely on scientific evaluation of the material under review within the context of published information and should not be influenced by scientific information that is not publicly available.

The peer review process relies on confidentiality and all material under review is privileged information. It should not be used to the benefit of the reviewer unless it previously has been made public. It should not be shared with anyone unless necessary to the review process, in which case the names of those with whom the information is shared should be made known to those managing the review process. Manuscripts and grants should not be given for review to colleagues or laboratory staff, such as graduate students or postdoctoral fellows, unless explicitly allowed by the journal/funding agency or permission is obtained by the editor or grants administrator. Material under review should not be copied and retained or used in any manner by the reviewer unless specifically permitted by the journal or reviewing organization and the

author.

This handbook is concerned with three types of peer review that researchers encounter. First, there is the peer review of research proposals, the system by which the NIH and other federal and non-federal supporters of research assess the scientific merit of grant applications. Second, journals and other publishers utilize a form of peer review to assess the quality of articles and other written works describing scientific findings. The third is peer review of individual students, fellows or faculty research programs.

Case Studies on Authorship

Case #18 *(From Macrina FL (2005): Scientific Integrity, 3rd edition, published by ASM Press. Used with permission. © ASM Press. This case was contributed by Dr. Francis L. Macrina (macrina@vcu.edu) of Virginia Commonwealth University. © 2005.)*

Dr. Colleen May is a participating neurologist in a clinical trial to assess the efficacy and toxicity of a new anticonvulsant medication. For the duration of the two-year study, each neurologist is to meet with each of his or her patients for an average of 30 minutes each month. In Dr. May's case, this amounts to an average of 20 hrs/month. During each visit, the physicians administer a variety of specialized tests, requiring judgments dependent on their experience and training in neurology. At the completion of the study, the results are to be unblinded and analyzed by the project leaders. It is anticipated that at least 2 publications will be prepared for the New England Journal of Medicine. Dr. May has just learned that she will be listed in the acknowledgements, but not as an author of the manuscript. Dr. May argues that she has provided nearly 500 hours of her expert time, far more than needed to complete a publishable study in her experimental laboratory.

Question

1. Does Dr. May have a case for authorship?

Case #19 (©ASM Press. This case is from Francis L. Macrina (2000): Scientific Integrity, 2nd edition, published by ASM Press. Appropriate permission being processed.))

A postdoc and his mentor have co-authored a paper describing their research results. This paper has appeared as a preliminary report in a copyrighted monograph. One of the figures in this paper is a computer-generated graph that describes data on a series of bacterial growth curves. The postdoc and mentor presently are preparing a major paper for submission to a peer-reviewed journal. They both agree that the growth curve data in the monograph article are crucial to the story they're telling in the present manuscript. Accordingly, they decide that this same figure must be included in their present writing. Because they are aware of potential copyright violations, they generate the exact same figure using different type face fonts and different line thicknesses for the ordinate and the abscissa. They have decided that since this is not the exact same figure which appeared in their monograph article the use of it will not constitute a copyright infringement. They also plan to indicate in their manuscript that this figure has been "adapted from" the one initially published in the monograph article.

Questions

1. Do you view what these authors are doing as copyright infringement?
2. If so, are there conditions of modification of tables or figures which would sufficiently change them in a way that avoids copyright infringement?

Case Studies on Peer Review

Case #20 (©ASM Press. This case is from Francis L. Macrina (2000): Scientific Integrity, 2nd edition, published by ASM Press. Appropriate permission being processed.)

Dr. George Adams receives a manuscript for ad hoc review from the editor of a scientific journal. George gives the manuscript to Al Nance, his senior postdoctoral fellow. He asks Al to read the manuscript and prepare some written comments critiquing it. One week later, Al provides to Dr. Adams one page of comments. Al also provides Dr. Nance with an extensive verbal critique of the paper. Dr. Adams then prepares a written review which is submitted to the editor of the scientific journal. A few weeks later, Dr. Nance learns that Al made photocopies of the entire literature citation section of the manuscript because it contained "some useful references". Dr. Nance proceeds to verbally reprimand Al, telling him that no part of a manuscript received for review should be copied.

Discussion

Comment on the behavior of both the faculty member and the postdoctoral fellow in this scenario.

Case #21 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Don is a full professor at a renowned university and has a reputation as an outstanding scientist. His work has had a number of potentially profitable practical applications, which led him to join with some venture capital partners in forming a company to commercialize his inventions. Don is also a member of a National Institutes of Health (NIH) study section. Despite the long hours, he is pleased to serve since he recognizes the importance of his contributions to the peer review system. In addition, he believes it is an excellent way of keeping absolutely current with the work done in his and related fields. He is very aware of the importance of confidentiality as reiterated in the statement read before each study section meeting.

Don just returned from reviewing a fascinating grant application from a scientist working in a closely related area of research. After evaluating the application's preliminary work report, Don came to realize that much of his own current NIH-funded and corporate research was proceeding down a blind alley. A meeting to review his research team's progress is fast approaching, and he is due at corporate headquarters tomorrow to discuss his company's research and development projects.

Questions

1. What could Don report to his research team? To his company?
2. Should Don have proceeded differently in the case of this grant review?
3. Some people may have difficulty in segregating ideas that they gain in the course of reviewing grant applications from ideas they develop on their own or glean from non confidential sources. If you were in Don's situation, how would you ensure that you did not benefit inappropriately from information or ideas acquired during the course of your duties as a study section member?
4. Policies for peer review involve both the need for expert assessment and the avoidance of breaches of confidentiality. Develop a set of rules that you believe should guide the peer assessment.

Case #22 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*)

Anne is a postdoctoral fellow working in a highly specialized area of research on prions. Her boss, Dr. R, recognizes Anne's talents and believes that she is the most promising postdoctoral fellow in his lab. Anne's contributions have included aiding Dr. R in identifying the etiology of Creutzfeldt-Jacob disease. When Dr. R is asked by a leading neurobiology journal to review an article on the pathology of Creutzfeldt-Jacob disease, he decides to involve Anne because of her skills and specialized experience. He makes a copy of the manuscript and asks Anne to write her own critical review of the piece, just as if she were the actual reviewer. This exercise, he reasons, would afford Anne a good opportunity for exposure to the process of peer review, while putting her in touch with the latest literature on her primary field of research.

Questions

1. Is Dr. R's idea a good one? Why or why not? Are there other ways for him to involve Anne in reviewing the article?
2. Dr. R's motives for having Anne participate in this manner seem well-intended. What might be some negative reasons for involving Anne in this way?
3. What concerns might Dr. R's approach pose for the author of the article? What issues are posed for the journal in which the article may appear?
4. If Anne feels uncomfortable about Dr. R's request, how might she respond?
5. Assume that rather than sharing the paper with Anne, Dr. R distributed it to the laboratory's "journal club" for discussion. What kinds of problems does this scenario pose?

Case #23 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach,* a handbook prepared by the Association of American Medical Colleges,(Korenman SG and Shipp AC, eds., 1994.)

An author submitted a paper that was rejected after two referees independently challenged the basic concepts of the reported work, and criticized the research for faulty methodology and sloppy workmanship. The editor is now asked for her opinion in the promotion of the author. The request is accompanied by reprints of other published articles and positive evaluations by other colleagues. The editor feels that her referees' opinions were valid, but she recognizes

that some of her knowledge about the author is "privileged."

Questions

1. What are the editor's responsibilities to the author? To the referees? To the department?
2. Does the number of other published articles by that author which received excellent reviews make a difference? What if the criticized paper were submitted and rejected five years ago, and the positively evaluated papers were all more recent?
3. What if the editor were to find out that the author who submitted the paper had played a role in developing the initial hypothesis, but had not had much to do with the design and execution of the experiments? Imagine that she now sees that the author is probably not directly responsible for the faulty methodology and sloppy workmanship, but that she has become concerned about the scientist's willingness to be listed as an author on the paper given how little he was involved in conducting the experiment. What should she do now?

G. Human Subjects Research Research involving humans entails a rigorous responsibility for the well-being of the research subjects, as well as a delicacy and sensitivity not required when working strictly with test tubes and reagents. Patients make an important contribution to science and society by participating in research protocols. This commitment must invite in return the utmost in respect and diligence from the researcher. In practice, that respect and diligence should include planning studies so that the potential benefits (to both the subject and society) outweigh the potential risks. In addition, steps must be taken to guarantee that subjects are selected equitably and that they make an informed decision about participating. This last concept is known as the principle of informed consent. Informed consent requires that patients be fully informed of the risks and benefits of the protocol and be competent to evaluate this information. Not only must consent be informed, it must also be free of coercion.

Obtaining informed consent is not always a straightforward issue. For example, the most appropriate method of obtaining informed consent may not be clear. Ensuring that patients fully understand the risks and benefits of a procedure can be a complicated matter as well, particularly where the competency of the patient is in doubt. The role of what might be termed "deferred consent," or seeking consent from next-of-kin or guardians, is also controversial.

Although there is general agreement that a patient's well-being should be paramount, the level of risk to which he or she may be subjected is less clear. Even under the best of circumstances, researchers may not be able to anticipate every eventuality of the study. Thus, although patients have been informed at the outset of possible events, unanticipated risks or benefits may arise during the course of the protocol. Researchers must inform patients of these events and make appropriate determinations about whether and how to proceed. For example, even in a double-blinded study, the experimental drug may prove so promising that its therapeutic effects break the blind. At that point, physicians must consider whether it is ethical to continue to utilize a placebo in seriously ill patients when an apparently effective agent is available.

The ethics of denying patients possibly therapeutic agents is also relevant. In this instance, the alternative is a standard therapy with modest clinical effectiveness in an ultimately fatal disease. Patients who perceive that their prospects for survival are grim may be willing to subject themselves to greater levels of risk in seeking new therapies than would normally be scientifically and ethically acceptable. It is important to consider whether scientists should

make exceptions for terminally ill patients, or whether the patient's condition represents a coercive influence. Another consideration is whether expanded access to unproved therapeutic agents jeopardizes efforts to obtain scientifically valid, generalizable data of value to society.

Case Studies on Human Subjects Research

Case # 24 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)
Dr. T is meeting with the institutional review board (IRB) at the medical center where she works. She has designed a clinical protocol to study a promising new drug for the treatment of Alzheimer's disease. She must now answer the IRB's questions concerning how the protocol will be conducted and how concerns for patient safety will be handled.

In the proposal Dr. T explained that this will be a double-blinded clinical trial in which some patients will receive a placebo and others will receive the new treatment. Based on earlier studies of the drug, Dr. T knows that patients may experience improvements in memory and other cognitive functioning, though not without risk. The drug can exacerbate hypertension in those already prone to the condition, and if doses modestly exceed clinically effective levels, severe kidney damage can result. In general, the drug seems most effective for those individuals who are in the early to middle stages of the disease. She will recruit this type of individual through Alzheimer's support groups and advertisements placed in the newspaper. Prospective patients will be interviewed to see that they fit the desired patient profile. Her interview will involve asking a series of questions designed to assess the extent of the patient's impairment and sense of orientation to the environment. Those selected to participate in the trial will be paid $300 for their time and trouble. The IRB has many questions for Dr. T.

Questions

1. How can one be certain that patients have understood the objectives, risks, and benefits of the protocol? Even patients that seem lucid and appear to understand may not retain the information provided. How might Dr. T handle this problem?
2. Assume that Dr. T intended to seek consent from relatives in situations where the patient appeared unable to provide fully informed consent. Should a relative be permitted to do this on the patient's behalf? What are the legal requirements that should guide one's consideration of this issue? What about the matter of financial compensation?
3. With the knowledge that family members desperate to see their loved ones receive effective treatment may push patient’s false hopes, how can you ensure that patients aren't being coerced into trials?
4. Society has an interest in the conduct of research on patients with Alzheimer's disease and other conditions that render patients incompetent. Discuss the balance between the protection of the rights and autonomy of the individual, and the needs of society for scientific progress.

Case #25 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)
Dr. G, a fellow in pulmonary medicine, was assigned to carry out an approved study designed by Dr. S. The study entails the use of the recombinant enzyme, DNAse, to improve pulmonary

function and to reduce the incidence of new infections in patients with cystic fibrosis. The study is double-blinded, meaning that neither he nor his patients and their families know whether the inhaler the patient received contained the active enzyme or a placebo. Experiments conducted in vitro and in small animals indicated great success for the agent, though they also pointed to some potential problems. These included development of an allergic reaction to the enzyme or to the other materials in the inhaler, and a direct and adverse chemical effect on the lung passages.

The clinical study for which Dr. G was responsible consisted of a three-month trial of enzyme or placebo, a one-month drug-free period, then a three-month trial of the other arm of the study. Forty patients were to be entered by the completion of the trial. They were to be evaluated by a lung function test and, since most of the patients were children, by a standardized questionnaire completed by a parent. The experimental drug was so effective that shortly after the trail began, Dr. G found it easy to know who was receiving active enzyme and who was receiving placebo. Even though the questionnaire filled out by the patients' parents was uniform, he discovered himself encouraging respondents to comment about the beneficial effects of the enzyme. After 20 patients were entered in the trial, one of the parents, who happened to be a scientist, said to Dr. G, "The quality of our daughter's life has greatly improved since she was entered in this protocol. Clearly, the drug is having an enormous impact that cannot be ignored and the blinding must be stopped. Won't you ask the company to terminate the experiment and make DNAse available to all patients? It will save the lives of our children."

Dr. G, empathizing with the parent, asked Dr. S about ending the protocol. Dr. S responded, "We are not only testing efficacy here; we are also testing for adverse effects that may be uncommon but quite serious. What would you think about the agent if one percent of recipients had a bout of life-threatening anaphylaxis? Furthermore, we are also going to follow the patients for a reduction of the rate of infection, hospitalization, and need for antibiotics." Dr. G responded that the statistical power of the present study (40 subjects) would not yield this data. Dr. S pointed out that the FDA required 40 cases from their institution for the efficacy study and their requirements took priority over the statistical analysis in most cases.

Questions

1. What values are in conflict in this case? How would you approach their resolution?
2. The apparent effectiveness of DNAse in cystic fibrosis seems to have ruined the blinding of subject and investigator that protects against biased reporting of efficacy. What can or should be done about that in the context of this experiment? What about in the broader context of clinical trials?
3. The FDA plays a critical role in the design of studies intended to achieve approval of a new therapeutic agent. In fact, companies negotiate in advance with the agency to ensure that, if the study is successful, the agent will be approved. Is this in the best interest of the patient, the company, and society?

Case #26 *(This case was contributed by Dr. Michael Kalichman (kalichman@ucsd.edu) of the University of California, San Diego. ©1999. Reproduced with permission)*

Dr. Jacqui is a psychiatrist interested in the molecular basis of several different anxiety disorders. Accordingly, she requested institutional approval to collect blood samples from a large population of both affected and unaffected individuals. The plan is to identify unusual genes that occur in the affected population. After receiving approval, numerous individuals, including staff and colleagues

from Dr. Jacqui's medical center, were enrolled after signing the requisite consent form. Along with many other pieces of information, the form specifically (a) notifies the volunteer that he/she will be told at the end of the study whether or not they carry the genes in question and (b) prompts the volunteer to ask any questions they might have. The blood samples are then collected. In the process of testing and refining methodology, one of Dr. Jacqui's postdocs runs a "negative control" by screening the samples for the presence of a rare gene he has recently identified in a collaborative project with another laboratory studying breast cancer. Surprisingly, this gene is detected in one of the samples. Evidence to date is that this gene carries a small, but significant, increased likelihood of developing several different forms of metastatic cancer, and an estimated 70% likelihood for developing breast cancer. If known, the individual would increase their chances for long-term survival by prophylactic mastectomy and frequent check-ups. However, these measures would only decrease, not eliminate, the risk of developing cancer. The postdoc reports these findings to Dr. Jacqui. A quick look through the records allows Dr. Jacqui to identify the carrier of this gene as a clerk working in hospital admissions. Dr. Jacqui debates whether or not to tell the clerk what has been found. After some deliberation, she decides against telling the clerk because (a) the gene does not guarantee that the clerk will get cancer and (b) the clerk's wishes about whether or not she would like this information are not known.

Question

1. Consider the roles of Dr. Jacqui, the institutional review board, the postdoc, and the clerk in this case. Given the information provided, have any of them erred by acts of commission or omission?

H. Animal Research (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* *), Guidelines for the Conduct of Research in the Intramural Research Program at the National Institutes of Health and The University of Pennsylvania Affirmative Action and Equal Opportunity Handbook)*

Research utilizing animals has contributed greatly to our understanding of nature and the pathophysiology of disease. Animal research not only plays an essential role in improving human health, but in many cases benefits the care and treatment of the animals themselves. Yet the use of animals in research is a matter of significant controversy. Animal rights groups, many of whom consider the life of an animal as morally equivalent to that of a human, eschew all animal research no matter what the apparent justification. By contrast most scientists and much of the public support animal research if it is carried out humanely and if research animals are treated well. Often, the priority that these individuals accord animal life is based on distinctions between species and their proximity to humans in the evolutionary ladder.

Finally, there is general agreement among those who advocate the use of animals in research that there must be appropriate scientific support to justify experiments using animals and the number of animals to be studied. This is accomplished at research institutions through a mechanism known as the Institutional Animal Care and Use Committee (IACUC.) The IACUC reviews proposed projects involving animals to ensure they are meeting scientific and humane standards, including those determined by NIH.

Just as with the use of human subjects, the use of animals can present difficult choices and ethical dilemmas. Some questions that scientists may face in animal research include the following:

- Is it appropriate to use an animal model if an alternative, non-living system would work, albeit less well?

- If the use of an analgesic or anesthetic would alter body chemistry in a way to compromise the data obtained, should the need for accurate data outweigh the concern for alleviating pain and suffering?

- If an animal can survive an experiment, what is one's obligation to sustain its life after the experiment is completed? Should the species of animal involved weigh into the decision (i.e., should one feel differently about preserving the life of a rat versus a chimpanzee?)

- Is repeated experimentation on a single animal justified if it means sacrificing fewer animals overall?

Case Studies on Animal Research

Case #27 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,*)

Eric is a second-year graduate student in a neuroscience program. Having just completed his course work, he must design his own project of research. His special area of interest is in studying the effects of methamphetamine and related compounds on brain activity. These compounds are commonly abused as recreational drugs and, although many are illegal, new "designer drugs," or slightly different chemical variations, are developed on a regular basis by illicit drug manufacturers.

One of his first considerations in designing his project is to find an appropriate animal model. In his review of the literature, Eric finds that cats are an adequate model because their brains are physiologically and anatomically similar to those of humans. Rhesus monkeys, however, have brains even closer to those of humans with more complex patterns of brain wave activity. His protocol would entail restraining the animal, hooking up electrodes, measuring brain wave activity both before and after administration of the drug, then sacrificing the animal to examine any physiological and anatomical changes in the brain tissue.

Eric is concerned that any sedatives, anesthetics, or analgesics administered before sacrificing the animal could possible alter the brain chemistry and consequently Eric's results. Yet, as a humane and compassionate person, he is concerned that the animals not experience any unnecessary pain or suffering.

Questions

1. Eric wishes to use the best model possible for the experiment, but hesitates to do so in this instance for a number of reasons. First, rhesus monkeys are much more expensive and less available than cats. Second, Eric feels a certain "kinship" toward primates that he does not feel toward cats. Is either of these issues appropriate considerations in selecting his animal model?
2. The initial phase of the study, restraint and brain wave monitoring, is not painful for the animal, though the animal will generally resist the limitations on its physical movement.

Nonetheless, Eric believes that not providing any pain-reducing substances at this point is entirely appropriate. He is less certain when it comes to sacrificing the animal. Are there humane ways to sacrifice the animal without providing anesthetics or analgesics? How might Eric deal with this issue?

3. Assume that for purposes of Eric's study, it is not necessary to sacrifice the animal in the end. The protocol, which then only entails restraint and attachment of electrodes and administration of the drug under study, is rather non-invasive. Is it appropriate to use the animals (either cats or monkeys) for other, unrelated experimental procedures afterward? What if the initial experiment involved a surgery from which the animal would survive? Should the availability or species of the animal weigh in this decision?

Case #28 (from *Teaching the Responsible Conduct of Research Through a Case Study Approach, Korenman, S.G., and Shipp, A. Eds,* © 1994 Association of American Medical Colleges. All rights reserved. Reproduced with permission.)

Dr. J, a senior postdoctoral fellow in veterinary medicine, was appointed to the Committee for the Protection of Animals in Research at her university. She was given the following proposal to review because of her expertise in primate biology.

A team of investigators is proposing to test an altered live virus vaccine for human immunodeficiency virus (HIV) utilizing a free-ranging chimpanzee colony. This colony was established for behavioral research studies 20 years earlier on an isolated island near Puerto Rico. Having grown dramatically since its inception, the colony requires daily food supplementation by boat, the support for which is increasingly in jeopardy. The plan is to inject one of the dominant males with HIV and to vaccinate half of the remaining animals, both males and females. All chimpanzees are to be monitored for the development of HIV virus antigens and antibodies, altered T-helper cell numbers, and symptoms. An additional protocol is being formulated that will utilize those animals that become infected for a clinical trial of new chemotherapeutic agents. Chimpanzees were selected because, like humans, they often have multiple sexual partners and are susceptible to the virus. Although the vaccine was effective in lower species, including transgenic mice, the research group felt that it was necessary to get a definitive answer under field conditions prior to introducing live retroviruses into uninfected human populations.

As principal reviewer, Dr. J must advise her colleagues as to the appropriateness of this use of animals for research purposes.

Questions

1. What legal and ethical standards should guide Dr. J in making her recommendation?
2. What are some of the troublesome issues associated with this set of experiments?
3. Does giving an animal a fatal infection constitute cruelty, especially considering the characteristics of HIV infection in humans?
4. Is it ethically appropriate to transmit intentionally a human virus in a setting that is not fully controlled?
5. If Dr. J were to respond that the study could not be carried out in chimpanzees, how might it be designed instead for human subjects?

Case #29 (This case is adapted from *Moral Reasoning in Scientific Research* developed by Muriel Bebeau, University of Minnesota., for a project entitled “Teaching Research Ethics: A Workshop at Indiana University”. © 1995 by Indiana University).

Jenny Ito is a second-year graduate student working in the biology lab of Chris Holzer. Ito has been overseeing an experiment that Holzer designed to determine whether a special anti-bacterial coating can reduce the incidence of infection associated with the use of steel surgical pins. With Holzer's help, Ito has inserted a two-inch pin into the right tibia of thirty rabbits; fifteen of the pins are standard surgical pins, and fifteen have the anti-bacterial coating. About one-quarter inch of each pin protrudes through the skin. Ito also inocculated all of the rabbits at the insertion point with 1×10^8 Staphylococcus aureus and routinely administers morphine at 5 mg/kg to alleviate any discomfort the rabbits may be experiencing because of the procedure. For almost a month, Ito has cared for the rabbits and recorded her observations, watching for any sign of distress or infection.

In her weekly meeting with Holzer, Ito reports that none of the rabbits seems to be particularly uncomfortable, and none of them shows any signs of infection. Holzer seems impatient. "If we don't get an infection, we won't learn anything. Here's what we'll do. Since it would be a shame to have put these rabbits through this, not to mention wasting all your time, without getting some results, I want you to help things along a bit. I want you to innoculate all of the rabbits with 1×10^9 Pseudomonas aeruginosa. We'll see what happens then." Ito hesitates. "The protocol specifies Staphylococcus, Dr. Holzer." Holzer brushes this off. "It's only a small change. We've been approved to run the risk of infecting these rabbits; all we're going to do is give the process a little boost." And with that Holzer walks away.

Ito knows how to do what she's been asked, but she is not sure whether she should. When she goes home that night, she mentions her dilemma to her roommate, Ruth Thompson, an English major. Thompson snorts. "Why are you so squeamish now? Go ahead and do it. In fact, if you really want to make him happy, you should put the new bacteria on just the untreated pins. That'll prove his point!"

Ito responds, "Thanks for the sarcasm. You know I can't do that; it would be bad science." "The whole thing is bad science," Thompson retorts. "Torturing bunnies like that." Ito throws up her hands in exasperation. "You're not helping me at all, Ruth! I know you don't approve of animal experimentation, but sometimes it's necessary, and I'm convinced this is one of those times. Still, Pseudomonas can cause a really nasty infection, and I hate to subject the rabbits to it, especially since it's so hard to treat. You know, they're sort of cute and I've gotten kind of fond of them over the last month. And then there's the whole question of the protocol. . . " Ito moans as she throws herself down on the couch. Thompson takes a deep breath. "Well, your boss has already told you that it falls within the realm of reasonable interpretation of the protocol. You've always got to interpret everything, you know. Besides, you always planned on some of these rabbits developing infections. What does it matter if they're infected by one bacterium or another? Hey, if it makes you feel better, look at it this way: If you don't get results, you'll just have to yank the pins from this batch and operate on a new bunch of bunnies. In the end, it would reduce the suffering if you just brewed up the new bugs and poured them on." With that, Thompson walks away, clearly disgusted by the whole procedure. Ito does not feel any surer of the proper course of action.

Question

1. Should Ito follow Holzer's suggestion? Why or why not?

CONCLUSION

With increased public funding of biomedical research, there is an increased demand for regulation and review of the efforts of scientists and institutional administrators to prevent, detect, and correct lapses in research integrity. Significant resources are now spent investigating incidents that do not involve false data but arise from a disregard or ignorance of the obligations of students, professors, and institutes. We argue that many of these conflicts stem from inappropriate conceptions about the ownership of research, which may derive from types of scientific endeavors, such as those of inventors, that are remote from most basic biomedical research.

What is still of great importance is a recognition that truthfulness in science is essential and precious. Some scientists are dishonest, and they can inject a small amount of false data into the current body of knowledge. Yet, more substantial damage is done to the fabric of trust in science by uncertainty about what the basic obligations are. There are additional levels of financial and administrative control over scientists who are held publicly accountable in their research. The leaders and teachers in our public and private institutions may have failed to place sufficient emphasis on teaching scientific ethics or even the near-universal rules of the research community. These rules may not be obvious to all members of the broad research community, and they are not all observed in nonscientific society. Honest and accurate reporting of data, generous and accurate crediting of the sources of ideas and words, and responsible reporting of research accomplishments are not gentlemanly luxuries in science, but necessities.

III. A PRACTICAL GUIDE TO QUESTIONS OF SCIENTIFIC MISCONDUCT (see Appendix C for the University of Pennsylvania's definition of research misconduct)

A. What To Do If You Have A Question, Or Feel That You Are A Victim Of Discrimination Or Harassment, Or Suspect Unethical Behavior Or Scientific Misconduct

If a member of the research community suspects that research by a particular individual, group of individuals, or laboratory is not being conducted in accordance with the generally accepted ethical standards, the individual should make his or her concerns known to one of the following: the appropriate departmental chair, graduate group chair, the Director of Biomedical Graduate Studies, the Executive Vice Dean and Chief Scientific Officer of the School of Medicine, the Ombudsman in the Medical Center or University (see below), or the Dean of the appropriate school. This disclosure should be made with utmost discretion, confidence, and guard for the rights of the alleged transgressor and the accuser. Further actions of the accuser should then be in full accord with the stated University policy.

B. What To Do If You Are Accused of Misconduct

If a BGS student is accused of misconduct in research, that individual should promptly consult with the Director of Biomedical Graduate Studies, the Executive Vice Dean and Chief Scientific Officer of the School of Medicine or the Dean of the appropriate school for complete information about the inquiry and review process as well as the rights of the accused person. The accused person has the right to engage legal counsel at any stage, including prior to meeting with any University official or faculty member.

C. University Ombudsman *(http://www.upenn.edu/ombudsman/))*

The University of Pennsylvania's Office of the Ombudsman was established in 1971 to assist individuals to find solutions to problems that they may not have been able to resolve through normal channels.

The Office of the Ombudsman is staffed by the University Ombudsman, a tenured faculty member (part-time), and an Associate Ombudsman (full-time). It is available for all members of the University community, with the exception of unionized workers at Penn and the employees of the Hospital of the University of Pennsylvania. Students, faculty, staff, and administrators seek assistance in addressing a variety of problems: academic disputes, access to resources, conflict in the workplace, compensation equity, failure to follow university procedures, and interpersonal tensions.

In all cases, initial complaints are heard confidentially. Further action is taken only when complainants want the Office to proceed on their behalf. If a complainant wishes it, the Ombudsman will approach the person or persons complained of, discuss the nature of the complaint that has been filed, and give him or her the opportunity to respond. The Office serves as an impartial mediator. We work to find solutions that are acceptable to both the complainant and the respondent.

The office is concerned with safeguarding individual rights and promoting better channels of communication throughout the University. The Ombudsman acts independently and is not an advocate for any one individual or group. He or she is an advocate for fairness, adherence to University regulations, due process, and personal responsibility. The Office supplements, but does not replace, any existing grievance mechanisms or modes of redress. It can and does recommend changes in the existing rules and practices.

The overarching mission of the Office of the Ombudsman is to resolve issues of equity and justice at the University of Pennsylvania before the tensions of polarization escalate.

D. School of Medicine Ombudsman

The mandate for the Office of the Ombudsman in the Medical Center is to provide a confidential, disinterested forum for individuals engaged in biomedical research including students, faculty and staff, who believe that their individual rights in this arena have been abrogated or who believe that a breach in ethical conduct of research has occurred.

It is not intended that the Medical Center Ombudsman will replace his or her University counterpart. Records of the University Ombudsman show that Medical Center individuals have, in the past, utilized the University Office of the Ombudsman, and it is intended that this avenue for redress of injustices be continued. The attention of the Medical Center Ombudsman is directed specifically to issues of ethics in biomedical research community. Examples of such issues are discrimination and harassment, differences of opinion over publication or presentation of disputed data, claims of ownership of research results, disputes over priority of authorship, concerns over inappropriate use of research funds, problems arising in the use of human or animal subjects, plagiarism and data distortion or fabrication.

The primary activity of the Ombudsman is as an advisor and mediator. The Ombudsman can advise the complainant of his or her rights and duties and can recommend that individuals bring their case to the appropriate University judicial and/or sanctioning offices.

E. Policy on Accusation and Response to Allegations of Research Misconduct at the University of Pennsylvania

In July 2004 edition of the Almanac, the Provost's Council on Research published a revised statement defining the University's expectations regarding **Misconduct in Research for Nonfaculty members of the Research Community** and its policy for dealing with allegations of misconduct in research by students, postdoctoral fellows and staff (http://www.upenn.edu/almanac/volumes/v51/n01/OR-research.html). A similar policy exists for faculty. The document states that "The University relies on all members of its research community to establish and maintain the highest standards of ethical practice in academic work, including research. Misconduct in research is prohibited and represents a serious breach of both the rules of the University and the customs of scholarly communities." The main steps in the procedure are summarized below:

Preliminary Inquiry

An inquiry into an allegation of misconduct in research is initiated when a written complaint is filed with the Vice Provost for Research along with the responsible administrative entities, who determine jurisdiction. The Vice Provost then forwards the complaint, in the case of BGS students, to the Associate Dean for Biomedical Graduate Studies and the Dean of the school in which the student is performing the research. The Dean informs the respondent of the charges without identifying the complainant. The Dean and Associate Dean appoint a preliminary inquiry committee of one or more impartial individuals and notify the complainant and respondent of the names of the individuals on the preliminary inquiry committee.

The preliminary inquiry committee gathers information and determines whether the allegation warrants a formal investigation. The committee submits a written report to the Dean and Associate Dean with a copy to the Provost, the complainant, and the respondent. The report should be submitted within 30 calendar days of the receipt of the original complaint by the Dean.

If the preliminary inquiry committee finds that a formal investigation is not warranted, the Dean, in consultation with the Provost, may: (1) initiate a formal investigation despite the recommendation of the preliminary inquiry committee; (2) not initiate a formal investigation, but take such other action as the circumstances warrant; or (3) drop the matter.

If the preliminary committee finds that a formal investigation is warranted (or if the Dean and Provost decide to proceed with a formal investigation), the Dean notifies the complainant and respondent, identifies the complainant to the respondent, and initiates a formal investigation. The Provost notifies the relevant funding agencies and identifies the respondent to the agency or source.

Formal Investigation

The Dean appoints a formal investigation committee of at least two impartial individuals with sufficient expertise, one or more of whom may have served on the preliminary inquiry committee. The formal investigation committee reviews the allegations and all relevant information, conducts interviews with the respondent, complainant, and other appropriate parties, and consults with University counsel. Within 90 calendar days of the appointment of the formal investigation committee, the committee submits its final written report and documentation to the Dean, with copies to the Provost and respondent.

The respondent has an opportunity to submit a response to the Dean, Provost and Vice Provost for Research within 15 calendar days; any response is appended to the formal investigation committee's report.

Resolution
After acceptance of the report by the Dean and the Provost or the Vice Provost/designee, a copy of the report will be submitted containing the outcome of the investigation to the appropriate government agency or source funding the research, if appropriate. The entire formal investigation process should be completed within 120 calendar days of its initiation, unless documented circumstances warrant a delay.

If the formal investigation committee finds that the allegations are unfounded, the matter is dropped. The Dean and Provost have the responsibility to take an active role to repair any damage done to the reputation of the respondent or the complainant (provided the complainant acted in good faith), and to take appropriate action should they determine that the accusation was knowingly false.

If the charges are substantiated, the Dean, in consultation with the Associate Dean, imposes appropriate penalties in accordance with University procedures. In the case of a major offense, the Dean and Associate Dean determine if there is just cause for suspension or termination. If the offense is found to be less serious, the Dean and Associate Dean may impose a lesser penalty. The respondent has access to the University's grievance procedures.

If the charges are substantiated, the matter will be referred to the Associate Dean for Biomedical Graduate Studies and the Dean of the school in which the student is performing the research, to determine the appropriate University sanctions. The Provost takes the steps necessary to correct any resulting misrepresentations by notifying collaborators, professional societies, and publishers involved.

IV. APPENDIX MATERIALS

A. Defining Plagiarism

(Excerpts from: The Historical, Cultural, and Social Aspects of Plagiarism: The Implications for Scientific Misconduct Investigations, Dr. Marcel LaFollette, Center for International Science and Technology Policy, The George Washington University. Also adapted from: Avoiding plagiarism, self-plagiarism, and other questionable writing practices: A guide to ethical writing, Miguel Roig, Ph.D., 2006; http://facpub.stjohns.edu/~roigm/plagiarism/)

Like puns and jokes, the metaphors for plagiarism also roll easily off the tongue; "picking someone else's mind," "mining someone else's prose." There is a flock or ornithological metaphors: "borrowed plumes," "parroted prose," "hatching stolen eggs." Redfern points out that many of the common phrases exploit the same euphemism, i.e., "borrowing". It is, however, misleading. A plagiarist does not really "borrow." He or she may take the words, but does so with no intention of giving them back, and with every intention of permanently stealing credit. The difference in perception represented by the words chosen as substitutes for "plagiarism" -- e.g., regarding copying as a breach of etiquette (borrowing without permission) rather than as a serious crime (theft) -- in fact, reflects the differences in interpretation that characterize many plagiarism disputes involving former colleagues, co-workers, or co-authors throughout the scientific community.

There are common elements to most serious definitions: 1) the use of another's words, text, ideas, or illustrations; 2) failure to credit the original ("real") author; 3) the implication statement that the plagiarist is the author; and 4) failure to seek the original author's consent. All four elements must be present (in proportions that may differ among research fields) for plagiarism to have taken place in the context of research communication in the sciences and social sciences.

None of these elements on its own constitutes misconduct, in fact. The act of simply using another's words or ideas is not plagiarism, and it may even be encouraged. Scientists and scholars want their ideas used and their words quoted. Those uses serve as measures of intellectual influence, and underpin the rationale for citation analysis. Moreover, scientists and scholars must use one another's work, or at least they must be familiar with that work in order to avoid duplicating it or repeating common errors. Graduate students are encouraged to become familiar with the great writers and thinkers in their fields. Researchers are praised for being "creatively derivative," for moving in just the right direction, while relying on their predecessors' insights as guideposts to intellectual terra incognito. For those whose work is interdisciplinary, innovation may only come from being derivative of two (or more) fields, perhaps re-assembling insights not previously applied to the problem studied.

Finally, failing to obtain a writer's consent to use his or her words is not necessarily unethical as long as one does not attempt to obscure authorship, as long as one gives appropriate credit. It is also not illegal as long as the legal boundaries of copyright and "fair use" are observed. But if all four aspects are present -- if there is use, a failure to credit, a deliberate false identification of authorship, and no consent by the real author -- then plagiarism has occurred.

To obscure authorship is also not necessarily to commit plagiarism. Washington is full of people who earn an honest living by writing for others, who produce "works-for-hire" that are published without their names. In addition, it is acceptable practice in some circumstances (again, as in the case of a work for hire) for person A even to state or imply that A is the author, when he or she is not, if A has commissioned or sponsored the work.

Whether these conditions also pertain in the case of "corporate" works written for hire, i.e. ghost-written works, has recently come under public scrutiny. Senator Charles Grassley, the ranking Republican on the Senate Finance Committee, has written to a number of major medical schools questioning the practice of using professional writing companies to write research articles based on studies performed with NIH funding. The BGS Code of Conduct (http://www.med.upenn.edu/bgs/docs/BGS_conduct.pdf) prohibits BGS students from authorship on such articles because it states: "*Plagiarism: using the ideas, data or language of another without specific and proper acknowledgment*"; all authors must be acknowledged on publications on which BGS students are co-authors.

Students should also be aware of the concept of self-plagiarism, the verbatim re-use of one's own written work. As paraphrased from Roig, the publication of essentially the same paper in more than one journal without any indication that the paper has been published elsewhere (i.e., redundant and duplicate publication) and the practice of text recycling in papers, grant proposals and other written documents all constitute self-plagiarism issues. This practice can also result in copyright infringement. Most journals require that the authors confirm that newly submitted manuscripts have not been published elsewhere. The use of relatively short direct quotes from a published work does not usually require permission from the copyright holder as it typically falls under the "fair use" provision. While it is fair to use relatively short direct quotes from a published work, extensive quoting of published text forms a copyright infringement even if the text is properly enclosed in quotation marks or correctly paraphrased and properly cited.

Students should be aware that copyright infringement extends to theses. If one includes figures or text from published manuscripts without alteration in one's thesis, permission must be obtained from the publisher. The ability to do on-line searches for particular text makes it exceptionally easy to identify plagiarism and self-plagiarism, as well as copyright infringement.

B. Ownership of Research

Taken from: Office of Research Integrity, Nicholas Steneck, Ph.D., *ORI Introduction to the Responsible Conduct of Research (2007)* (http://ori.hhs.gov/documents/rcrintro.pdf
Research produces data. As a product, common sense might suggest that the person who conducts the research should own the product—the data. In fact, conditions imposed by funders, research institutions, and data sources may dictate otherwise.

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

- Government gives research institutions the right to use data collected with public funds as an incentive to put research to use for the public good (see the discussion of the Bayh-Dole Act, Chapter 5).

- Private companies seek to retain the right to the commercial use of data.

- Philanthropic organizations retain or give away ownership rights depending on their interests.

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

At Penn, faculty, graduate students, postdoctoral fellows or staff performing research in a university do not own the data collected. Employees work for hire for the university, which, in most cases, owns the rights to the data. Students and postdoctoral fellows sign a participation agreement that governs Research Property (http://www.med.upenn.edu/postdoc/documents/participation.agreement.pdf). Data and data books collected by undergraduates, post-baccalaureate students, graduate students, and postdoctoral fellows on a research project belong to the grantee institution. Students may not take their data when they leave without making appropriate arrangements. Retaining copies of data is allowed with permission and is usually good practice. When faculty members leave an institution, they have to negotiate with the university to keep their grants and data.

C. Procedures Concerning Misconduct in Research for Non-Faculty Members at the University of Pennsylvania

These procedures, prepared as of May 18, 2004 are those that would apply to BGS students. The procedures for faculty can be found at http://www.upenn.edu/almanac/volumes/v51/n01/OR-research.html

Introduction

The University relies on all members of its research community to establish and maintain the highest standards of ethical practice in academic work, including research. Misconduct in research is prohibited and represents a serious breach of both the rules of the University and the customs of scholarly communities.

The following procedures are applicable to nonfaculty members of the University of Pennsylvania research community including students, postdoctoral fellows, and staff.

Research Misconduct Defined

Research misconduct is defined as fabrication, falsification, plagiarism, or other serious deviation from accepted practices in proposing, performing, or reviewing research, or in reporting research results.

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, or results, or works without giving appropriate credit.
- Serious deviation from accepted practices includes but is not limited to stealing, destroying, or damaging the research property of others with the intent to alter the research record; and directing or encouraging others to engage in fabrication, falsification or plagiarism. As defined here, it is limited to activity related to the proposing, performing, or reviewing of research, or in the reporting of research results and does not include misconduct that occurs in the research setting but that does not affect the integrity of the research record, such as misallocation of funds, sexual harassment, and discrimination, which are covered by other University policies.

The research record is the record of data or results that embody the facts resulting from scientific inquiry, and includes, but is not limited to, research proposals, laboratory records, both physical and electronic, progress reports, abstracts, theses, oral presentations, internal reports, and journal articles.

Some forms of misconduct, such as failure to adhere to requirements for the protection of human subjects or to ensure the welfare of laboratory animals, are governed by specific federal regulations and are subject to the oversight of established University committees. However, violations involving failure to meet these requirements may also be covered under this policy or possibly by other University policies when so determined by the responsible committees or institutional officials.

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

Findings of Research Misconduct

A finding of research misconduct requires that:

- There be a significant departure from accepted practices of the relevant research community; and
- The misconduct be committed intentionally, or knowingly, or recklessly; and
- The allegation be proven by a preponderance of evidence.

Jurisdiction and Applicable Process

There are a number of University policies and procedures for responding to allegations of misconduct by students, postdoctoral fellows, or staff. This policy is intended to be invoked only in instances where research misconduct (i.e. activity related to the proposing, performing, or reviewing of research, or in the reporting of research results and which therefore may have an impact on the integrity of the research record) is involved. Questions of jurisdiction and the applicability of the appropriate University procedure will be decided by the responsible administrative entity (such as the Office for Student Conduct, Office for Postdoctoral Programs, or the Office of Human Resources), in consultation with the Vice Provost for Research. Allegations of misconduct not involving the research process or the integrity of the research record will be resolved by the disciplinary process ordinarily applicable.

1. Inquiry

1.1 Allegations of research misconduct should be directed in the first instance to the Vice Provost for Research who, along with the responsible administrative entity, will determine jurisdiction and which process is applicable to resolve the allegation. If the Vice Provost determines that this process is properly invoked, the Vice Provost will forward the complaint—which must be in writing—to the Dean of the School where the research is being performed

1.2 Upon receipt of a properly documented complaint, the Dean will inform the respondent of the nature of the charges, and will provide the respondent with a copy of these procedures. The Dean will also take steps to secure relevant documents, data and other materials.
The Dean will appoint one or more unbiased, impartial individuals with appropriate expertise who will conduct a preliminary inquiry to determine whether a full investigation is warranted.

1.3 The inquiry committee will gather information and determine whether there is sufficient, credible basis to warrant a formal investigation. The committee shall offer the respondent an opportunity to provide them with relevant information regarding the allegations. The committee will submit a written report of its assessment to the Dean and the respondent, and to the complainant where appropriate. The report should state what evidence was reviewed, summarize relevant interviews, and include the committee's recommendation. This report will ordinarily be submitted within 30 calendar days of receipt of the written complaint by the Dean.

1.4 If the report of the inquiry committee determines that a formal investigation is not warranted, the Dean may (i) drop the matter, or (ii) not initiate a formal investigation, but take such other action as the circumstances warrant, or (iii), in extraordinary circumstances, nonetheless initiate a formal investigation. The Dean will inform the concerned parties of the decision.

1.5 If the inquiry committee determines that a formal investigation is warranted, the Dean will initiate a formal investigation as provided in Section 2. The Provost (Vice Provost/designee) will inform the appropriate government agency or source funding the research, in writing, that a

formal investigation has been initiated and will identify the respondent to the agency or source (1).

2. Formal Investigation

2.1 To initiate a formal investigation, the Dean will appoint a formal investigation committee of not less than two disinterested individuals with sufficient expertise, one or more of whom may have served on the preliminary inquiry committee.

2.2 Investigation. The formal investigation committee will be provided with copies of the complaint, the report of the initial inquiry and any other materials acquired during the preliminary inquiry. The formal investigation committee will undertake a thorough examination of the allegations, including, without limitation, a review of relevant research data and proposals, publications, correspondence, and records of communication in any form. Experts within or outside the University may be consulted. The Committee shall have authority to investigate, pursue and document any related research misconduct by therespondent, even if such misconduct was not covered by the initial complaint. Whenever possible, interviews will be conducted with the complainant, as well as with others having information regarding the allegations. The Committee must allow the respondent an opportunity to be interviewed at this formal investigation stage. When being interviewed by the committee the respondent and the complainant may each be accompanied by an adviser, who may be a lawyer but who may not participate directly in the proceedings except when and as requested to do so by the committee.

2.3 Reporting the findings. Following its investigation, the formal investigation committee will prepare and provide a written report of its findings to the respondent, to the Dean, to the Provost, and, if appropriate, to the complainant. The report will describe the allegations investigated, how and from whom information was obtained, the findings and basis of the findings, and will include texts or summaries of the interviews conducted by the committee. The report will conclude with a clear statement regarding which charges have been considered and what its findings are with respect to each charge the committee considered. If the committee finds that a violation of University policy in addition to or other than research misconduct might have been committed, a description of the possible violation will be included.

The committee will indicate whether each charge considered during the course of its proceedings is unsubstantiated or substantiated by a preponderance of evidence. If the matter involves a respondent who would be subject to University sanctions for misconduct only if the evidence met a clear and convincing standard, the Committee will make an additional determination as to whether that standard has also been met (2).

The final report will ordinarily be submitted within 90 days of the appointment of the formal investigation committee. The respondent will be permitted to make a written reply to the Dean with a copy to the Provost, and Vice Provost for Research, within 15 calendar days of submission of the report. The Dean may ask the committee to respond in writing to any replies from the respondent. The Dean may also ask the complainant to respond to the report if deemed appropriate. All such responses and replies will be incorporated as appendices to the report of the formal investigation committee.

3. Disposition of Final Report and Findings

3.1 The Dean will consider the final report and replies. Upon acceptance of the report by the Dean, the Provost (Vice Provost/designee) will submit a copy of the report containing the

outcome of the investigation to the appropriate government agency or source funding the research, if such action is required by regulation or otherwise appropriate. The entire formal investigation process should be completed within 120 calendar days of its initiation, unless documented circumstances warrant a delay.

3.2 If the final report of the formal investigation committee finds the charges of research misconduct against a respondent not to be substantiated, the research misconduct proceeding is terminated and the concerned parties will be informed. A finding that a charge of research misconduct has not been substantiated shall not preclude the University from taking other appropriate action against the respondent if the respondent's behavior or actions violate another University policy or rule.

3.3 If the report of the formal investigation committee finds the charges of research misconduct against a respondent to be substantiated, the matter will then be referred to the responsible administrative entity within the University to determine the appropriate University sanctions, if any, to be imposed for the misconduct (3).

4. Other Actions and Procedures

4.1 The Dean in consultation with the Provost will, during the course of the inquiry or formal investigation, take administrative action, as appropriate to protect the welfare of animal or human subjects.

4.2 At any time during the inquiry or formal investigation, the Dean and Provost will immediately notify the relevant funding agency(ies) if public health or safety is at risk; if agency resources or interests are threatened; if research activities should be suspended; if there is reasonable indication of possible violations of civil or criminal law; if Federal action is required to protect the interests of those involved in the investigation; if the University believes the inquiry or formal investigation may be made public prematurely so that appropriate steps can be taken to safeguard evidence and protect the rights of those involved; or if the research community or public should be informed.

4.3 If the final report of the formal investigation committee finds charges have been substantiated, the Provost or Dean will take appropriate steps to correct any misrepresentations resulting from the misconduct. If, at any time during the inquiry or investigatory stages, the respondent admits to the alleged misconduct, the Dean will take the necessary steps to complete the inquiry in order to correct the scientific record. If misrepresented results have been submitted for publication, already published, or otherwise disseminated into the public domain, appropriate journals and other sponsors will be notified. In addition, collaborators, and other affected individuals, organizations, institutions, and sponsors will be informed.

4.4 Complete records of all relevant documentation on cases treated under the provisions of this policy will be preserved by the offices of the Dean and the Provost in a manner consistent with the Protocols for the University Archives and Record Center. In cases adjudicated under Section 3, records will be preserved for a minimum of ten years following completion of all proceedings. Records of cases which are dropped will be preserved for at least three years following the initial inquiry. When students are involved in these procedures, the confidentiality provisions applicable to educational records will govern the disclosure of the records.

4.5 The University may act under these procedures irrespective of possible civil or criminal claims arising out of the same or other events. The Dean, in consultation with the Provost and the general counsel, will determine whether the University will proceed against a respondent

who also faces related charges in a civil or criminal tribunal. If the University defers proceedings, it may subsequently proceed irrespective of the time provisions set forth in these procedures.

Endnotes

1. The decision to initiate a formal investigation must be reported to the Office of Research Integrity, Department of Health and Human Services, if the research has been supported by a grant from DHHS, according to DHHS regulations.
2. There is a discrepancy between University regulations, which use the standard of "clear and convincing" evidence, and regulations of the Office of Research Integrity, which use the lower standard of "preponderance of evidence." Therefore, if there is a finding of fault, the inquiry must explicitly state whether the higher University standard is met, to inform the University administrative entity which is responsible for determining possible sanctions.

3. The intent of this policy is that the appropriate administrative entity will take responsibility for determining and implementing sanctions.

For instance, if the respondent is an undergraduate student any disciplinary sanctions will be determined by the Office of Student Conduct in accordance with its amended Charter procedures dealing with research misconduct findings. In order to determine sanctions, the findings and accompanying documents should be forwarded to the Office of Student Conduct. Upon review of all findings, including all submissions by the respondent etc., the Office of Student Conduct will propose appropriate sanctions to the respondent. The respondent would then have an opportunity to accept, reject or propose alternative sanctions. If either the original sanction or an alternative sanction is accepted and agreed upon, the OSC then has primary responsibility for implementing and monitoring sanctions. If the respondent rejects the sanction, the respondent may appeal the nature and severity of the sanction only to the Disciplinary Appellate Officer within the Student Disciplinary System. If the decision of the appellate officer is to uphold the proposed sanction, the sanction will be imposed, with no further levels of review.

Likewise, if the respondent is a graduate student, postdoctoral fellow, or staff member, the responsible administrative entity would consider the information and determine sanctions.

D. IMPORTANT CONTACTS

Dean, School of Medicine	Arthur H. Rubenstein, MBBCh 295 John Morgan/6055 215-573-2030
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Medical School Student Ombudsman	Helen C. Davies, Ph.D. 203B Johnson Pavilion/6076 215-898-8733
University Ombudsman	Joan F. Goodman, Ph.D. 113 Duhring/6063 215-898-8261
Director, Biomedical Graduate Studies Associate Dean for Graduate Education	Susan R. Ross, Ph.D. Room 313 BRBII/III/6160 215-898-9764