Ethical Ambiguities

For this year's research ethics case discussions, the NIH Committee on Scientific Conduct and Ethics has chosen a Commentary that appeared in Nature, *Scientists Behaving Badly*, along with letters written to Nature in response to the Commentary. In addition, we have developed five cases that illustrate some of the ethical ambiguities that underlie everyday science. An analysis of the Commentary's findings follows, for your use as a facilitator or participant. We suggest that at the end of the discussion, the group decide whether the authors were justified in concluding that "US scientists engage in a range of behaviors extending far beyond falsification, fabrication and plagiarism". We also provide a set of Bottom Lines to take home from the case discussions.

In a Commentary in Nature (1), Martinson et al. report on the results of a survey they carried out asking scientists to report on whether they had engaged in a series of behaviors. Their conclusion? - "Our findings suggest that US scientists engage in a range of behaviors extending far beyond falsification, fabrication, and plagiarism".

How bad are the sixteen "bad behaviors" identified by Martinson et al.? Members of the NIH Scientific Conduct and Ethics Committee debated the issue hotly and concluded that many of the behaviors fell into a gray zone and would be well worth discussion in the Intramural Research Program this year. Two behaviors belong to the fabrication, falsification or plagiarism definition of scientific misconduct, #1 falsifying or 'cooking' research data and #5 using another's ideas without obtaining permission or giving due credit. A third, #6 unauthorized use of confidential information in connection with one's own research, might or might not be plagiarism, depending on the situation. Two behaviors fall within the purview of IRBs because they impact clinical research, #2 ignoring major aspects of human-subject requirements and #8 circumventing certain minor aspects of human-subject requirements. The remaining eleven include five 'top behaviors' plus six other behaviors of concern. How should we think about these behaviors?

Seven of them are relevant to data management, the topic of last year's (2005) research ethics case discussions. How does one handle contradictory data from one's own research (#7 failing to present data that contradict one's own previous research)? Hopefully you are all in agreement that you rely on a critical scientific judgement based on long experience in research, since it is not uncommon for contradictory data to be obtained, either because experiments have been poorly designed or executed, or because new information changes the approach to, or interpretation of, an experiment. A similar answer applies to #15 dropping observations or data points from analyses based on a gut feeling that they were inaccurate - one can use statistical tests to determine when a result is truly an outlier, or repeat the experiment. It is difficult to know how to interpret #9 overlooking others' use of flawed data or questionable interpretation of data, since no context is provided. If the "others" are in one's own lab, the supervisor should be checking data and experiments on a regular basis and be prepared to prevent these types of 'bad behavior'. Similarly, it is the supervisor's responsibility to ensure that everyone in the lab maintains adequate experimental records, and regular review will ensure that this is happening (#16 inadequate record keeping related to research projects).

Two behaviors, #10 changing the design, methodology or results of a study in response to a funding source and #14 using inadequate or inappropriate research designs, raise issues that we frequently deal with as scientists. They are actually a normal part of scientific critique - both journal and grant reviewers constantly recommend changes in design of experiments or methodology, and a lack of response is certain to ensure rejection unless strongly justified. It is difficult to imagine anyone changing the results of their study in response to a scientific review - another 'bad behavior' that is impossible to interpret without more context. However, changing the interpretation of results based on reviewer input might be considered "wise behavior" if the reviewer has raised points you had not considered. A more serious issue is #13 withholding details of methodology or results in papers or proposals - this behavior is not acceptable and has been addressed in the online Research Ethics course http://researchethics.od.nih.gov/ and is not acceptable behavior.

Two of the bad behaviors relate to authorship issues, #11 publishing the same data or results in two or more publications and #12 inappropriately assigning authorship credit. These topics were covered in the 2002 cases on Authorship and the NIH does not consider these to be acceptable behaviors. The last two behaviors, #3 not properly disclosing involvement in firms whose products are based on one's own research and #4 relationships with students, research subjects or clients that may be interpreted as questionable, are conflict of interest issues. They are covered in the Research Ethics online course and acknowledged as inappropriate, although again the context for # 4 is not clear which may make interpretation difficult.

To facilitate discussion of these 'bad behaviors', the Committee has developed cases that deal with behaviors it considers to fall into the gray area and expect that discussion of these cases with your colleagues will enable an understanding of how to approach these kinds of behaviors. You may also find it interesting to discuss the Nature Commentary in terms of the research methods the authors employed, the amount of detail provided on their methods, and the fact that neither the questions themselves nor the introduction/instructions for the survey were published. Equally interesting are letters written in response to the Commentary (2-5).

1. Martinson, B.C., Anderson, M.S. and de Vries, R., Nature 435:737, 2005.

2. Grinnell, F., Nature 436:776, 2005.

3. Taylor, I., Nature 436:626, 2005.

4. Tait, S., Nature 437:26, 2005.

5. Bradley, S.G., ASM Newsletter 71:347, 2005.

This year's theme is ***Borrowing – Is It Plagiarism?*** We have provided three cases, all of which are applicable for all scientific staff, as well as a set of Comments and Guidelines from the Cases and four relevant attachments that include the government's definition of plagiarism (attachment 2).

Case 1 - Borrowing Results

Dr. Waverly is an NIH Principal Investigator with two postdoctoral fellows, two technicians, a graduate student and a staff scientist in his lab. The lab is investigating the role of oxidative stress in lung cancer. Five years ago the lab examined the effects of mutations in the gene LCG120 related to another disease. Pressed for time, he asks Dr. Ashby, one of the postdocs, to help him review a journal manuscript that analyzes the effects of mutations in LCG120 on the oxidative stress response in the lung. The postdoc reads the article, recommends publication following minor revisions, and provides his comments to Dr. Waverly who thanks him.

- Is it ethical for Dr. Waverly to ask the postdoc to review a manuscript for him?
- How should the postdoc respond to the request?
- Should Dr. Waverly have informed the editor and provided Dr. Ashby's name?
- Should Dr. Waverly have shared his recommendation letter to the journal with the postdoc?

Some weeks later, Dr. Waverly meets with his lab and announces that he would like to begin experiments on a possible link between LCG120, oxidative stress and the development of lung cancer. The postdoc is struck by similarities to the manuscript he reviewed.

- Is it ethical for Dr. Waverly to ask his lab to work on the role of LCG120 mutations in lung cancer?
- Should Dr. Ashby say anything?
- Should Dr. Waverly ask the manuscript authors for permission to begin this work?

The experiments are completed in three months, and the results decrease the novelty of the reviewed manuscript. Dr. Waverly drafts a manuscript to submit to a different journal. The postdoc, who is a coauthor, notices that the manuscript does not acknowledge the authors whose manuscript he reviewed for Dr. Waverly and a PubMed search does not show that this manuscript has been published. Six weeks later Dr. Waverly's manuscript is published. The authors of the original LCG120 manuscript still have not published their research.

- Has Dr. Waverly acted unethically?
- Has he violated any legal rules or guidelines?
- Is this a case of plagiarism?
- What if the original manuscript was written by a former collaborator of Dr. Waverly?
- Should Dr. Waverly share any information on the final decision by the editors with Dr. Ashby?

Case 2 - Borrowing Ideas

Dr. Bigshot is the session chair of a Gordon Conference. During the evening poster session, which takes place in the pub, he visits the poster presented by Mr. Newby, a graduate student in the laboratory of Dr. Compete. Mr. Newby is excited to meet Dr. Bigshot, as he has read his papers and is looking for a lab to do his postdoctoral fellowship. During their conversation, Mr. Newby mentions that he just did a novel bioinformatic search and identified a new protein (FabU) closely homologous to the one (BigD) that made Dr. Bigshot famous, and characterization of FabU was going to be the last part of Mr. Newby's thesis research. When Dr. Bigshot returned to his own lab, he recommended that one of his senior graduate students carry out a bioinformatic search using just the carboxy-terminal domain of BigD as Mr. Newby had done. Several months later, Mr. Newby gets an alert from the Web of Science that Dr. Bigshot, a National Academy Member, just published a characterization of FabU in PNAS, with no mention of Mr. Newby. Mr. Newby is devastated, as he is afraid that he will not be able to publish his most exciting finding.

- Gordon Conferences have no abstract book, and participants are required to sign a statement acknowledging the confidentiality of conference proceedings and discussion. Did Dr. Bigshot violate that agreement?
- Is this a case of plagiarism by Dr. Bigshot?
- Is there any recourse for Mr. Newby?
- Would the situation be different if the conversation took place in a bar at a meeting with no pledge of confidentiality?
- What if the information was included in an abstract for presentation at a meeting at which abstracts are published?

Gordon Research Conferences statement (http://www.grc.org/home.aspx)
To encourage open communication, each member of a Conference agrees that any information presented at a Gordon Research Conference, whether in a formal talk, poster session, or discussion, is a private communication from the individual making the contribution and is presented with the restriction that such information is not for public use. The recording of lectures by any means, the photography of slide or poster material, and printed reference to Gordon Research Conferences papers and discussion is prohibited. Scientific publications are not to be prepared as emanating from the Conferences. Authors are requested to omit references to the Conferences in any publication. Guests are not permitted to attend the Conference lectures and discussion sessions. Each member of a Conference acknowledges and agrees to these restrictions when registration is accepted and as a condition of being permitted to attend a Conference. Although Gordon Research Conference staff will take reasonable steps to enforce the restrictions against recording and photographing Conference presentations, each member of a Conference assumes sole responsibility for the protection and preservation of any intellectual property rights in such member's contributions to a Conference.

Case 3 - Borrowing English

Dr. X, a visiting fellow, is putting together his first paper on his studies of the PrP-Sc protein. He feels somewhat insecure about his ability to write in English, but is excited to be given the opportunity to prepare his paper. To start writing the introduction he has read several papers from his laboratory, one of which has the following introductory paragraph.

One set of neurodegenerative diseases recently linked to ER stress is caused by aberrant metabolism of the widely expressed cell surface glycoprotein PrP. These diseases can be inherited through PrP mutations or acquired via a transmissible agent composed largely of a misfolded isoform of PrP termed PrP-Sc. Exogenous PrP-Sc is capable of converting the normal cellular isoform (PrP-C) into additional PrP-Sc molecules, leading to its accumulation and generating additional transmissible agent. In the familial diseases, PrP mutations appear to cause accumulation of misfolded PrP through poorly understood mechanisms that in some cases also generate PrP-Sc. Thus, altered PrP folding, metabolism, and accumulation are the proximal causes of both familial and transmissible prion diseases. However, the downstream events that culminate in selective neuronal death in any of these diseases are unknown.

Dr. X thinks the paragraph is well written and borrows heavily in the draft he provides his mentor Dr. Z.

Some neurodegenerative diseases recently linked to ER stress have aberrant metabolism of the widely expressed cell surface glycoprotein PrP. These diseases can be inherited through PrP mutations or be acquired via a transmissible agent composed largely of a misfolded isoform of PrP termed PrP-Sc. Exogenous PrP-Sc is capable of converting the normal cellular form (PrP-C) into additional PrP-Sc molecules, leading to its accumulation and generating additional transmissible agent. In the familial diseases, PrP mutations appear to cause accumulation of misfolded PrP through poorly understood mechanisms. Thus, altered PrP folding, metabolism, and accumulation are the causes of both familial and transmissible prion diseases. However, the downstream events that lead to selective neuronal death are not known for any of these diseases.

Dr. Z reads the draft manuscript and then gives Dr. X his comments. Dr. Z thinks Dr. X should completely rewrite the introductory paragraph because it has been plagiarized.

- Do you agree that what Dr. X has done is plagiarism?
- How different do the introductions in different papers from the same laboratory need to be?
- Would it have made a difference if Dr. X had borrowed from a paper from a different laboratory?
- Could Dr. X reuse his own language in his second paper?
- Does it make a difference if text is borrowed in writing the introduction to a paper versus the results or discussion sections?
- How could Dr. X make the paragraphs acceptable?
- Dr. X plans to include a reference to the previous paper – how should he do that? Is this sufficient?
- If Dr. X. were writing a review, would the rules be different?

Comments and Guidelines from the Cases

- Manuscripts submitted for review are considered privileged information unless the data have previously been made public (open meeting, prior abstract publication).

- Material under review should not be copied and retained or used in any manner by the reviewer unless specifically permitted.

- Journal Editors require reviewers to maintain the confidentiality of the research being reviewed. If the reviewer wishes to have a postdoc help with the review, the reviewer should notify the editor and provide the postdoc's name.

- The reviewer 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.

- Be careful about how/with whom you share data. If the work can be easily reproduced and is not yet ready to publish, show restraint in what you present. The members of the Ethics Committee feel overwhelmingly that no conversation between scientists could be considered "privileged and confidential" unless one of the scientists starts the conversation by stating that what he or she is about to share is unpublished material and is not to be shared with others (see **Attachment 1**).

- Direct copying of sentences, whether from a previous paper of yours or your lab, or from someone else's paper, could be construed as plagiarism, violates the rules of journals, and is considered inappropriate by the NIH (see **Attachments 2 & 3**).

- Be aware that journals are using available technologies to detect similar word patterns (see **Attachment 4**).

Attachment 1

From The NIH Catalyst July-August 1997
Ethics Forum
Silence is not golden: making collaborations work

What is a scientific collaboration? How can one set one up and keep it going successfully? And why do they occasionally go awry?

The NIH Guidelines for the Conduct of Research (just reprinted in a revised third edition and available from your scientific director) accentuate the positive—that "research collaborations frequently facilitate progress and generally should be encouraged." And to help eliminate the negative, the Guidelines suggest setting ground rules at the start and arranging to share reagents with collaborators outside NIH through MTAs (material transfer agreements).

. . .DO NOT ASSUME

THAT LONG PERIODS OF

SILENCE INDICATE THAT

. . . ALL IS WELL. IF

YOU HAVE NOT

COMMUNICATED WITH

YOUR COLLABORATORS

FOR A YEAR, THERE

MAY NO LONGER BE A

COLLABORATION !

But the disputes that can be generated during the course of an otherwise valuable scientific collaboration—disputes revolving around not only reagent sharing but also authorship and even mentorship—are common enough that they are among the central issues the new Ombudsman/Cooperative Resolution Center pilot project was designed to handle.

So what *is* a good collaboration? The NIH Committee on Scientific Conduct and Ethics recently discussed several cases of problem-plagued collaborations and came up with what we hope are useful guidelines. First, in these days of multidisciplinary science, since almost no one is trained in all the disciplines needed to complete a study, scientific collaborations clearly make a lot of sense, both intellectually and financially. The best collaborations form between scientists with complementary expertise—for example, a molecular biologist capable of generating knock-out mice with a neuroscientist who can measure changes in the behavioral activity of those mice; or an immunologist who wants to look at the effect on T lymphocytes of engineered mutants of a virus provided by a virologist.

To work well, though, certain parameters need to be discussed and defined up front: who is going to do what and when they will do it; who will supply reagents needed for certain aspects of the study; even who will write the paper and be first author. Defining order of authorship before doing the experiments can be tricky, however, since surprise results may completely change the focus of a study and thereby dictate a change in the order. Flexibility is thus a key ingredient in any collaboration.

The cases the Ethics Committee examined have convinced us that the single most important measure in successful collaboration is keeping the lines of communication open. Communicate with your collaborators, by phone, e-mail, or even letters, frequently. Tell them what you are finding and ask what their results are. Share data as well as problems. If a collaborator outside NIH is applying for an NIH grant, or is supported by an NIH grant, the granting agency should be informed of this collaboration. You will generally be asked to prepare a letter to be submitted with such a grant application; you should ask to see the relevant parts of the application before it is submitted so that you know whether the proposal accurately represents your part of the collaboration. Although you, as an NIH employee, cannot contribute to the writing of the application, make it clear that you want to be informed when the grant is funded and when it will start. Above all, do not assume that long periods of silence indicate that your collaborator is working away and all is well. If you have not communicated with your collaborators for a year, there may no longer be a collaboration!

Bear in mind that some forms of scientific exchange do not form an appropriate basis for collaboration. The Guidelines state clearly that "individuals . . . who have assisted the research [by providing] reagents . . . should not be authors." By the same criteria, providing someone with a plasmid, or an antibody, or even a transgenic mouse, does not establish a collaboration. In line with this thinking are Public Health Service regulations that state that any reagent developed with government funds (intramurally or extramurally) must be provided to those who request it once the results have been published. Intramural scientists use MTAs when giving such reagents to colleagues at universities or other extramural sites. Such input is often acknowledged in a published study, with thanks to the suppliers of materials used in the experiments—a way to give credit without conferring authorship.

Probably the most difficult issue scientists grapple with in discussing collaborations is that of intellectual property. Is there such a thing as ownership of an idea? If there were, would anyone discuss science with anyone else? Would everyone feel that they deserved authorship or collaborator status because they had lunch with a friend, heard about new results, and suggested an interesting experiment? Conversely, are all conversations between scientists, even one-on-one, to be considered a sharing of privileged information? The members of the Ethics Committee felt overwhelmingly that no conversation between scientists could be considered "privileged and confidential" unless one of the scientists started the conversation by stating that what he or she was about to share was unpublished material and was not to be shared with others.

Many scientists believe that the constraints imposed by industry consultation and collaboration on free and open discussion of research projects are already having a deleterious effect on science. For many of us, the pleasure of doing science lies in formal and informal discussion and exchange of results and ideas with colleagues. That pleasure would be compromised or vanish entirely if each idea were fenced in as the exclusive intellectual property of one person.

Joan P. Schwartz
OIR/OD

Attachment 2

The Office of Research Integrity (ORI) has the following policy on plagiarism (http://ori.dhhs.gov/policies/plagiarism.shtml)

"As a general working definition, ORI considers plagiarism to include both the theft or misappropriation of intellectual property and the substantial unattributed textual copying of another's work. It does not include authorship or credit disputes.

The theft or misappropriation of intellectual property includes the unauthorized use of ideas or unique methods obtained by a privileged communication, such as a grant or manuscript review.

Substantial unattributed textual copying of another's work means the unattributed verbatim or nearly verbatim copying of sentences and paragraphs which materially mislead the ordinary reader regarding the contributions of the author. ORI generally does not pursue the limited use of identical or nearly-identical phrases which describe a commonly-used methodology or previous research because ORI does not consider such use as substantially misleading to the reader or of great significance.

Many allegations of plagiarism involve disputes among former collaborators who participated jointly in the development or conduct of a research project, but who subsequently went their separate ways and made independent use of the jointly developed concepts, methods, descriptive language, or other product of the joint effort. The ownership of the intellectual property in many such situations is seldom clear, and the collaborative history among the scientists often supports a presumption of implied consent to use the products of the collaboration by any of the former collaborators."

Self-Plagiarism (taken from an article by *John Dahlberg, Director, Division of Investigative Oversight, ORI*, ORI Newsletter Vol. 15, September 2007)

ORI often receives allegations of plagiarism that involve efforts by scientists to publish the same data in more than one journal article. Assuming that the duplicated figures represent the same experiment and are labeled the same, this so-called "self-plagiarism" does not meet the PHS research misconduct standard. This behavior violates the rules of journals and is considered inappropriate by the NIH.

Attachment 3

From Nature 449:658, 2007
Plagiarism? No, we're just borrowing better English

SIR — The accusations made by arXiv that my colleagues and I have plagiarized the works of others, reported in your News story 'Turkish physicists face accusations of plagiarism' (*Nature* **449,** 8; 2007) are upsetting and unfair. It's inappropriate to single out my colleagues and myself on this issue. For those of us whose mother tongue is not English, using beautiful sentences from other studies on the same subject in our introductions is not unusual. I imagine that if all articles from specialist fields of research were checked, similarities with other texts and papers would easily be found. In my case, I aimed to cite all the references from which I had sourced information, although I may have missed some of them. Borrowing sentences in the part of a paper that simply helps to better introduce the problem should not be seen as plagiarism. Even if our introductions are not entirely original, our results are — and these are the most important part of any scientific paper. In the current climate of 'publish or perish', we are under pressure to publish our findings along with an introduction that reads well enough for the paper to be published and read, so that our research will be noticed and inspire further work.

Ihsan Yilmaz
Physics Department, Çanakkale Onsekiz Mart
University, Çanakkale, Turkey

Attachment 4

From Nature 449:658, 2007
Plagiarism: text-matching program offers an answer

SIR — The removal of almost 70 papers from the arXiv server on suspicion of plagiarism is dismaying (*Nature* **449,** 8; 2007). But, in a similar way to that currently being tested by the cooperative group of publishers CrossRef ('Academic accused of living on borrowed lines' *Nature* **448,** 632–633; 2007), the search technology that led to this removal could be used to reduce future problems. Every paper submitted to arXiv could be examined by a search engine that looks for overlap or correlation with all previous arXiv submissions. If enough of a match is found, a message could be sent to the submitter, listing the work(s) in which similarities have been detected. Should the submitter wish to proceed with their submission, the program would notify the editorial board and trigger an automatic review. The submitter would also be given the chance to explain that the flagged papers were not copied or that the copying was for some reason legitimate. Such a system would address the problem of plagiarism only among papers published in arXiv, but apparently that would already be an improvement. And although plagiarists might opt to copy and translate from foreign-language journals, or simply alter wording enough to pass muster, making it more difficult will at least discourage the lazier offenders. As journals should welcome eliminating plagiarism at the preprint stage before publication, they could support the effort by giving the arXiv site search access to their own full-text databases.

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From Nature 448: 633, 2007
Copycat Trap

Plagiarists should beware. The next time they submit a paper to a journal, a red flag may pop up on the editors' screen warning them that the article's word patterns are suspiciously similar to those of a published paper. A pilot of this computer cop, called CrossCheck, was launched on 1 August by CrossRef, a group of 2,046 scholarly publishers. Commercial software of this kind has been available for some time, but until now subscription firewalls have prevented its use with online literature. CrossCheck is able to access the databases of its member publishers. Six publishers are taking part in the pilot: the Association for Computing Machinery, BMJ Publishing Group, Elsevier, the Institute of Electrical and Electronics Engineers, Taylor & Francis, and Wiley-Blackwell. Like a search engine on the web, the program computes the similarity of word strings to yield an originality score. Suspect scores are flagged-up, and it displays similar excerpts of text from different sources. But an editor will need to examine the flagged up papers to confirm plagiarism. If all goes well, the service could be available as soon as November and other software providers could request access in the future, says Geoffrey Bilder, director of strategic initiatives at CrossRef. Publishers could also get authors to test their

papers before submission, which would spread out the work and allow honest authors to check they hadn't inadvertently 'cut and paste' verbatim, says Bilder. The downside, he notes, is that the program would let hardened plagiarists play the system, by rewording detected passages. "It might just force people to become more sophisticated plagiarists."

Declan Butler

2018 Ethics Discussion Cases – Introduction to Biases

Biases related to gender, race, ethnicity, age, disabilities, sexual orientation, and other characteristics have the potential to limit the diversity of the biomedical research community. Biases can impact decisions and actions related to hiring and interviews, mentoring and training, research assignments, study designs, career advancement, recommendations, promotions, and funding. Overt biases reflected in messages and behaviors can also adversely impact the research and organizational environment, such as by creating inequities or an uncomfortable work culture.

Biases can take different forms. Explicit or conscious biases emerge from established institutional practice and policy as well as individual prejudices. Implicit or unconscious bias occurs automatically and unintentionally, escaping the conscious awareness of an individual or group, and so can be especially insidious and difficult to recognize.

This year's research ethics discussion cases are intended to increase recognition of different types of bias and the contexts in which bias can occur in the biomedical research community.

It is incumbent upon researchers at all levels to be aware of biases in themselves and in their research environment, and to be able to effectively address, manage, or eliminate them when necessary. Reducing all types of bias has been shown to increase diversity, which itself is beneficial to the biomedical research enterprise.

Approaches to minimizing biases include education, awareness (of both self and others), motivation, and accountability.

Some links related to implicit biases and diversity:

https://diversity.nih.gov/sociocultural-factors/implicit-bias
https://implicit.harvard.edu/implicit/takeatest.html

Gender Bias in Academia

Dr. Virginia Mason is an accomplished scientist at a prestigious university who has worked her way up the ranks to Assistant Professor. She has published 9 papers while on tenure track (for a career total of 40), with successful trainees and a very good reputation in her field. Her tenure review panel receives positive external letters of recommendation, with very strong support from experts in her specific field, particularly praising her as an excellent collaborator, mentor, and team player. By contrast, she received weaker positive support from leaders in related fields she had not met, who seemed concerned about the expected impact of her future research contributions.

At the same time, Dr. David Singletary, another member of the department with a fairly similar record of publications and successful trainees while on tenure track (with a career total of 25 papers), is also being considered for tenure. His external evaluation letters are generally glowing, praising him as driven, ambitious, performing high-impact research, and a future leader.

Discussion Questions

1. What scientific and personal criteria are – or should be – important for hiring for an academic position and receiving tenure?

2. How might unconscious biases enter and influence the evaluation process?

3. How important is "networking" for career success in academia, the government, or private sector? Can biases occur in networking and mentoring?

On a split vote, the tenure panel finds that the two scientists are talented and recommends that both receive tenure. The original department chair who hired both researchers and strongly supported Dr. Mason's promotion recently retired. The incoming chair wants the department to move in a new research direction different from that of the two tenure candidates, so he announces his intention to reduce the size of the department by one person to permit a future new recruitment. The next day, Dr. Mason learns that only Dr. Singletary is put forward for tenure. She requests an appointment with the chair, but his assistant makes clear that he is overbooked and about to leave for a conference in Thailand. The university Dean typically supports departmental decisions regarding tenure actions, so Dr. Mason appeals to the university President, Board of Regents, and the press, citing gender bias.

Discussion Questions

4. What factors do you feel that the President and Board should consider in this case?

5. What collateral effects might result from this case for the university and for Dr. Mason; e.g., in terms of reputation, future opportunities, recruitment, etc.

6. Would there be any differences if this scenario occurred in the NIH intramural program, and the decisions were made by a new Scientific Director?

A reporter learns that the new chair hosts a weekly poker game at his home, to which all department members are invited. Dr. Singletary often participates, but Dr. Mason does not.

Discussion Questions

7. How relevant is this fact, and what issues are involved?

8. At various points in this case, what might have been done differently to avoid or reduce problems?

9. Can the existence and consequences of biases be evaluated through external investigations?

Responsible and Equitable Mentoring of Fellows

Training and Career Goals

Dr. Anderson, a second-year postdoctoral fellow at NIH, sets up a meeting with the lab chief, Dr. Li, during which Dr. Anderson mentions some reflections regarding future career plans. Even though the experimental work has been very successful, Dr. Anderson is considering becoming a science writer instead of remaining a bench scientist. Dr. Li listens but does not comment on what Dr. Anderson is discussing. In the weeks ahead, however, Dr. Anderson finds it difficult to get time with Dr. Li to discuss their latest experimental data and to receive guidance on the manuscript. Also, two other fellows in the lab have been assigned by Dr. Li to begin new experiments extending the current findings, while Dr. Anderson is not offered participation in them.

Discussion Questions

1. Did Dr. Li respond to Dr. Anderson's revelations appropriately? What responsibilities do mentors have regarding the provision of career advice?

2. Were the subsequent events warranted? What are the immediate and long-term consequences for Drs. Anderson, Li and the lab generally?

3. What options does Dr. Anderson have in this situation? Is participation in new experiments justifiable if one is considering leaving research?

Trainee Growth and Independence

Bob is a graduate student starting his second year of NIH research in the lab of Dr. Smith, a tenure-track investigator. Bob's project involves harvesting brain tissue from a number of mouse models that took the lab a long time to generate. The project is well-defined, but many of the techniques involved are new for Bob, and challenging to master. Bob is highly motivated by the project and science in the lab, but is increasingly frustrated with how Dr. Smith is managing his project. With the rationale that the animals are in limited supply and very valuable, or that the research must move to publication as quickly as possible, Dr. Smith often instructs the more experienced lab technicians and trainees in the lab to perform critical steps of Bob's experiments. Bob is feeling increasingly demoralized and disengaged from Dr. Smith and the lab.

Discussion Questions

1. What does Bob, as a trainee, have a right to expect from his experience in the Smith lab? Do expectations vary with the trainees' skill levels?

2. What are Dr. Smith's interests at his career stage? How should he balance his professional development interests and needs with those of his trainees?

3. What steps could Dr. Smith take to increase Bob's engagement and satisfaction with his experience in the lab?

Diversity and Bias – Approach to Disabilities

Dr. Jones was recently contacted by a number of graduating PhDs who were interested in coming to her lab as postdoctoral fellows. Having just learned she would have a fellowship opening soon, she was pleased to be able to give these applicants serious consideration. Based on their training and publication record, two candidates, Dan and Frank, distinguished themselves above the rest, and Dr. Jones decided to invite them to NIH to interview and give seminars.

Arrangements for the visits proceeded smoothly, but as Dan's visit was being finalized he communicated to Dr. Jones that he uses a wheelchair. Dr. Jones was caught off guard by this news, but she quickly thought to ask what accommodations Dan might need during his visit. Having little experience with the needs of such individuals, she was relieved to establish that there were no obvious concerns or special requirements.

Dan and Frank both gave solid seminars and interacted well with the lab staff. Dr. Jones felt that either would likely be successful in the lab, which created a difficult decision for her. In the end, Dr. Jones extended the offer to Frank with the justification that his background provided slightly better preparation for the lab's research, but she remained uncertain about whether she was making the right decision, or for the right reasons. She considered herself enlightened on issues related to discrimination, and was very aware of the need to recognize biases, both unconscious and explicit.

Discussion Questions

1. At what point in the initial discussions should a trainee candidate in need of special accommodation reveal that to the PI?

2. What legitimate concerns might Dr. Jones have about Dan joining the lab?

3. Persons with disabilities are considered an underrepresented group. Are there ways in which their situation differs from that of persons who are underrepresented by virtue of race, ethnicity, etc.?

4. What options and resources are available at NIH for accommodating trainees with disabilities? For example, would Dr. Jones be able to adjust her lab layout for Dan?

Relevant NIH Resources and Policies

Guidelines for Mentoring an NIH Trainee Who is Deaf or Hard of Hearing
https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/mentoring/guidelines-mentoring_deaf_trainee.pdf

NIH Manual Chapter 2204-Reasonable Accommodations
https://policymanual.nih.gov/2204

Implicit/Unconscious Biases?

A senior investigator decides to share an article discussing a scientific analysis of racial profiling. However, contrary to her usual practice of sending out articles to the entire branch/group on a weekly basis, she only sends this article to the three minority staff members working in the lab.

1. What might have been her assumption?
2. Could there have been a good (or bad) reason for doing so?
3. How should members of her group respond?

A collaborator from an outside organization arrives to present at a meeting of 15 NIH senior investigators. Walking directly to the only minority investigator (a woman) at the conference room table, the collaborator assumes she is administrative support staff and asks if she can make enough copies of the presentation for everyone in the meeting.

1. What is the unconscious bias here?
2. Would you do something if you were one of the other senior investigators?

Should the following questions or comments posed in a neutral or friendly manner be considered innocent or implicit bias? What are the assumptions, and what would you do if you were the recipient or happened to overhear?

1. Where are you from? (Said to an Asian-American from Ohio)
2. I bet you make great tacos – can you bring that to the party?
3. How was your Chinese New Year's celebration? (asked of any Asian-American).
4. Jennifer, would you like to give us the Hispanic perspective on this?
5. We should look at all the candidates but the most important consideration is to hire the best person for the job. (What does 'best person' mean?)
6. You certainly look different from what I expected after reading your work.
7. Why can't you be like all the others here?

2020 Ethics Case #1 Study Guide – Data Access, Analysis and Reporting within a Research Group

When Dr. John Thomas (an M.D./Ph.D.) joined Dr. Rick Peterson's lab as a clinical fellow, Dr. Peterson told him about an exciting new compound they were studying that showed promise for treating schizophrenia. The lab was currently completing a Phase 1 clinical trial under the leadership of Dr. Sally Simpson, a staff clinician in Dr. Peterson's lab who served as Lead Investigator (LI) and Medically Accountable Investigator (MAI) on the study with Dr. Peterson as Principal Investigator (PI). Dr. Simpson had just gone on early maternity leave unexpectedly due to complications, and the project needed someone to take over. Dr. Peterson suggested that Dr. Thomas take over the project and start planning the Phase 2 trial because Dr. Simpson wasn't expected to return for at least six months and Dr. Peterson was eager to keep the project moving. While Dr. Thomas found the science and experimental findings very interesting, he felt uneasy about taking over the project of another investigator who would be returning to the work. Dr. Peterson told him not to worry about it because as a staff clinician, Dr. Simpson would always have projects to work on and it didn't matter if she stayed with any one study through completion because she wasn't 'ambitious in that way'.

1. How can disruptions in workflow due to unexpected absences be dealt with?
   Decision-making during a crisis can sometimes be easier when there are written agreements regarding work responsibilities during extended leave, such as Dr. Simpson's maternity leave.
2. Are there other ways Dr. Peterson could have approached this?
   The head of the lab is ultimately responsible for management of projects within the lab, but that is generally best done with input from those involved with getting the project completed. It is essential that the roles of different members in the lab, including the staff clinician, are clearly defined. Dr. Peterson might have been able to discuss coverage with Dr. Simpson before she went out but if she was unavailable to discuss it due to the suddenness of her departure, Dr. Peterson should make decisions about the project, keeping in mind the needs of the lab and the affected team members.
3. What if the Phase 1 trial had been funded by a bench-to-bedside grant (or other outside funding mechanism) obtained by Dr. Simpson? What if Dr. Simpson had served as PI on the study within Dr. Peterson's lab?
   While Staff Clinicians can apply for funding with the permission of their PI, the PI will control any funds obtained. In a respectful work environment, Dr. Peterson would acknowledge Dr. Simpson's role in obtaining funding for this project by allowing her more control over the project than she would typically have, especially if he had allowed her to serve as PI on the protocol. If it is necessary to bring in another investigator such as Dr. Thomas, Dr. Peterson should work to facilitate a cooperative arrangement between Drs. Simpson and Thomas, with clear definitions of their respective roles on the project.
4. How could Dr. Simpson handle the situation differently?
   Ideally, Dr. Simpson would formulate a plan with Dr. Peterson for coverage during her maternity leave well before the leave is expected to occur. In this situation, she left suddenly without a fully formed plan in place. She should reach out to Dr. Peterson as soon as she is able. Pregnancy and childbirth are protected under gender/sex discrimination regulations and are a qualifying medical condition under the American with Disabilities Act (ADA) that could lead to a Reasonable Accommodation (RA). Dr. Simpson may consider requesting a RA due to her medical condition, either before or after the pregnancy. She may also request job-protected leave without pay under the Family Medical Leave Act (FMLA). If she is unhappy with Dr. Peterson's handling of the issue and unable to work it out with him, she could discuss it with other trusted sources, including the laboratory chief, the Scientific Director, or the NIH Ombudsman, Civil, or Employee Assistance Program offices.

While Dr. Thomas still felt unclear about Dr. Simpson's future role on the protocol, he was excited about the opportunity to work with this compound and agreed to Dr. Peterson's plan. He learned all he could about the

compound and the Phase 1 trial and took over the day-to-day supervision of data gathering and safety monitoring, reporting back to Dr. Peterson regularly. At Dr. Peterson's suggestion, Dr. Thomas occasionally emailed Dr. Simpson about potential side effects/adverse events in the participants since she had the most experience with the compound. He then began writing up the Phase 2 protocol, which was generally very straight-forward, but after his extensive review of the preclinical data, Dr. Thomas added a novel assessment of cognitive function to the standard clinical measures of psychosis. Again at Dr. Peterson's suggestion, he sent the protocol to Dr. Simpson, who was still on leave recovering from her complicated pregnancy and caring for her premature son, for input. Dr. Simpson reviewed the protocol, raised several helpful points, and suggested that a novel assessment of mood also be included.

5. Is it appropriate for Dr. Peterson to repeatedly suggest Dr. Thomas involve Dr. Simpson in ongoing work while she is on leave? What issues should be considered in a situation like this?
   This is an issue that should be negotiated with Dr. Simpson. While it can be very helpful to continue to be kept abreast of the progress of the project and Dr. Simpson's advice on some matters could be very helpful to Dr. Thomas, care should be taken that it doesn't evolve into Dr. Simpson actually performing a significant amount of work while on leave; for example, writing sections of the new protocol rather than simply commenting on specific issues and questions. The boundary between doing uncompensated work and offering informal guidance on a project to which one expects to return can be difficult to define. Exploring options to return to work on a part-time basis including telework may be appropriate in some situations.
6. What other actions might Dr. Thomas take in this situation?
   Dr. Thomas should clarify with Dr. Peterson and with Dr. Simpson how they will work together moving forward on this protocol and who will be responsible for what. If he finds disparities in the expectations of Dr. Peterson and Dr. Simpson, he also should try to resolve these before beginning work on the project. Trainees may feel most comfortable seeking advice from their IC Training Director, laboratory/branch chief, or the NIH Office of Intramural Training and Education (OITE). If they are unable to get help from these sources, they may also contact their Scientific Director or offices of the NIH Ombudsman, NIH Civil Program, or NIH Employee Assistance Program which offer confidential help. Concerns about a workplace situation can also be reported anonymously to the Civil Program, either by phone or online. Trainees and other employees are encouraged to check the matrix of relevant NIH Workforce Resources for NIH programs that may be useful in circumstances requiring workplace flexibility, such as is discussed in this case study.

Dr. Simpson returned to the lab after about 6 months and opted for a flexible work schedule to accommodate childcare responsibilities she shared with her husband. She worked 10-hour days in the office on Mondays and Tuesdays (days her husband was responsible for childcare issues) and 20 hours flexibly the rest of the week, some of which could be unscheduled telework, in order to be available for any emergencies that might arise with her young son. Dr. Simpson told Dr. Peterson she wished to resume her work with the compound she had already spent so much time and effort developing but Dr. Peterson told her that Dr. Thomas needed to stay on that project because he was going to be applying for faculty positions and needed to demonstrate his ability to see a big project through the many phases required for developing a new treatment. Dr. Peterson also told her he thought the project needed someone who would be reliably in the office every day in order for it to continue running smoothly. He did, however, encourage her to continue to help Dr. Thomas with the protocol and told her she would be included on any publications from the project. Dr. Peterson assigned Dr. Simpson to another protocol that he felt was more suited to her irregular schedule. Dr. Simpson saw little difference in the needs of the two protocols except that her new protocol was decidedly less likely to result in high-impact results.

7. Does Dr. Simpson have a 'right' to return to the project she was working on prior to her leave?

8. Would it matter if Dr. Simpson had taken the lead on the early development of the compound?
9. What issues arise when 'ownership/leadership' of a project has changed hands?
   As PI, Dr. Peterson has the responsibility to run the lab. In addition to making sure projects move forward in a timely manner, running a lab also involves fostering an environment in which lab members feel valued for their contributions and their roles are clear. Dr. Simpson may not have a right to return to this project but since she contributed significantly to the intellectual development of the project, Dr. Peterson should recognize that contribution and foster her continued engagement in the work of the lab by allowing her continued significant participation. That might mean returning to a leadership role on this project or it might mean significant involvement as a co-investigator. NIH policies require that a person returning from extended medical leave that cannot be returned to their prior position must be returned to an equivalent position, with the same pay and same status. If Dr. Simpson is unable to work out a satisfactory arrangement with Dr. Peterson, this is also an issue she could take to the trusted sources mentioned for Questions 4 and 6.

Dr. Thomas struggled to get FDA approval for his phase II protocol. Dr. Simpson, who had extensive experience getting FDA approval for protocols, helped him navigate several rounds of queries and get the approvals from both the FDA and IRB so he could start enrolling participants. Dr. Thomas finally began enrolling participants, but recruitment was slow, and it was difficult to maintain adherence through the one-year follow-up visit, which is far longer than typical Phase 2 studies. Dr. Peterson wanted the longer follow-up because it would allow for a more clinically relevant assessment of the drug and because long follow-up phases are possible at NIH where it's part of the mission to do long-term studies that are not feasible in other settings.

In the third year of his clinical fellowship, Dr. Thomas had a motorcycle accident, badly breaking several bones and requiring an extensive leave of absence. Dr. Peterson tapped Dr. Simpson to fill in while Dr. Thomas was recuperating, which she was easily able to do since she already knew the protocol well and had covered for Dr. Thomas for 10 days when his mother unexpectedly passed away. Recruitment picked up with Dr. Simpson in charge because she had relationships with community psychiatrists who felt comfortable referring their patients knowing she was running the study. When Dr. Thomas was ready to return to work about 6 months later, Dr. Simpson again asked to stay on the project and let Dr. Thomas manage another project for the remainder of his clinical fellowship. Dr. Peterson again said that it was important for Dr. Thomas's job prospects to remain in charge of the project he had started with, while Dr. Simpson already had a stable job and didn't need this project for her CV or advancement.

10. What do you think of Dr Peterson's decision-making process regarding management of this project?
11. What assumptions is Dr. Peterson making about Dr. Simpson's career, including her future plans? Is this appropriate? Might it reflect bias?

While Dr. Peterson had previously prioritized moving the project forward when he replaced Dr. Simpson with Dr. Thomas after Dr. Simpson's early maternity leave, he is now prioritizing Dr. Thomas' career needs over moving the project forward as it is clearly running better under Dr. Simpson's leadership. He is also weighing the career needs of Dr. Simpson and Dr. Thomas differently and we are not given a clear justification for this. While post-docs and clinical fellows such as Dr. Thomas by definition have a limited time in which to show productivity and move on to a new job, staff clinicians are generally in a more stable position, although this should not imply they do not also wish to advance in their careers. Drs. Peterson and Simpson should be discussing Dr. Simpson's role in the lab and her plans for her future explicitly. Some may feel that there is disparate treatment of Drs. Simpson and Thomas that could represent a pattern of gender/sex discrimination. The PI must have a legitimate, non-discriminatory business reason for assigning work; career advancement for Dr. Thomas is not a legitimate business reason.

With the papers from his Ph.D. research and one publication from the Phase 1 data, which Dr. Peterson had allowed him to write up as first author, Dr. Thomas applied for jobs and was offered a soft money position as an Assistant Professor at a large research university. He negotiated some start-up funds but needed to apply for grant money as soon as he started. He asked Dr. Peterson to unblind the trial's treatment-arm data for participants who had completed the protocol to date (about half of the planned cohort) so he could analyze the study and use it as preliminary data for grant applications.

12. Is this an appropriate reason to unblind an ongoing protocol? Why might Dr. Peterson refuse to unblind?
    Clinical trials designed to demonstrate efficacy of a new compound must include detailed analysis plans prior to starting the trial. This is important to prevent cherry picking of results that could lead to inappropriate conclusions. Under some circumstances, especially for protocols that do not aim to demonstrate efficacy of a treatment, a protocol may include explicit provisions for interim analyses that could accommodate early exploratory analyses to allow for presentations at meetings or preliminary data for grant applications, however, such analyses cannot be used to alter the enrollment and analysis plan of the ongoing trial. If there is no provision in the protocol for interim analyses by the investigators, Dr. Peterson should refuse this request. Unblinding a trial early is often done by a DSMB to look for safety and efficacy reasons to stop a trial early but results are not shared with investigators unless action must be taken, thus mitigating the risk of compromising the integrity of the study by biasing the clinicians interacting with the participants. These analyses typically begin with unblinding participants by group without identifying the groups unless significant results warrant group identification. As Dr. Thomas is no longer working on the study, his interim analysis would not necessarily compromise the integrity of the study, but he would have to keep the results from Dr. Simpson and Dr. Peterson, himself, in order to avoid a problem. This would create its own set of difficulties since both these investigators have an intellectual stake in the study results.
13. Would the situation be any different if this protocol was a preclinical study investigating the impact of the compound in a preclinical model?
    While blinding does not always take place in preclinical studies, it can be useful for many of the same reasons as in clinical studies such as minimizing bias in assessing outcome measures. A blinded preclinical study should also specify when and for what purposes an ingoing trial can be unblinded.

Dr. Peterson agreed to unblind the completed participants, and Dr. Thomas analyzed the unblinded data quickly and began writing grants. He discovered that the compound appeared to have marginal efficacy for the primary outcome of psychotic symptoms, no effect on the cognitive functions he had hypothesized would benefit, but a strong effect on some aspects of mood that was already significant at the one-month follow-up in this initial cohort sample. The mood measures had been added at Dr. Simpson's suggestion. He formulated his next hypotheses around these mood findings and started writing up a manuscript as well, since the findings were very interesting, even if preliminary, and having a paper would help his chances of securing grant funding.

Dr. Simpson found out about Dr. Thomas's analysis and results when he sent around a manuscript with himself as first author, Dr. Peterson as senior author, and Dr. Simpson as second author. Dr. Simpson complained to Dr. Peterson that the mood assessment was her contribution to the protocol and that she had planned to present the data at a conference and serve as first author. She also thought it was premature to publish the data as a paper, since the study was ongoing and had not yet met its planned enrollment numbers. Dr. Peterson mentioned that Dr. Thomas was submitting a grant to follow up on the mood findings. Dr. Simpson was not happy, as she had planned to follow up on this hypothesis if the data looked promising.

14. Who should control use of the data in this situation?

As PI of the lab conducting the research, Dr. Peterson controls the use of the data. With multiple investigators having contributed significantly to the project, he should consider discussing data use plans with all those who have an intellectual stake in the data.

15. Is it appropriate to publish an interim analysis of an ongoing study? To include it in a grant application or present it at a conference?
    As the data are not complete, any publication should be explicitly clear about this point. In this case, the trial is likely to be used in support of an FDA indication for the drug, making it more problematic to have broken the blind for an interim analysis. In some situations, it might be acceptable to publish an interim analysis as pilot or preliminary data, but there is a risk that readers may not appropriately interpret a promising but preliminary result. Presentations at conferences, especially as posters, are expected to often be preliminary and in need of further confirmation. A conference audience and grant reviewers are generally comprised of other researchers who should be aware of the dangers of overinterpreting preliminary results while a journal audience may also include practitioners, less sophisticated in evaluating data and eager to find anything that might help their most challenging patients. It is also possible that patients in the ongoing trial may learn of the publication which might affect their willingness to continue to participate or bias their expectations, further compromising the integrity of the study. In general, publishing issues should be discussed at the start of a project, although plans may change as the project moves forward. Changes in agreed upon publishing strategies should be discussed with all stakeholders.

After two more years, the protocol completed its final one-year follow-up visit. With the assistance of the current clinical fellow, Dr. Simpson analyzed the data and found that the compound significantly improved psychotic symptoms, mood, and cognition after a year of treatment. She drafted the findings for the three outcomes, with herself as first author, Dr. Peterson as senior author, the current clinical fellow as second author, and Dr. Thomas in the middle of the author list. Dr. Thomas, now three years into his new position and struggling to secure grant funding, was upset that Dr. Simpson had included all the data in one manuscript and thought the cognitive findings warranted their own paper which he wanted to write. He complained to Dr. Peterson.

16. How should decisions about publishing and authorship be handled after a post-doc has left the lab?
    In long running projects, it can be easy to forget the important intellectual contributions of those who were involved early in the project but then moved on. However, significant intellectual contributions to the inception of a project do warrant inclusion on subsequent publications. As head of the lab, Dr. Peterson should ensure that all those who have made significant contributions are offered authorship on the papers. An authorship plan should have been in place before Dr. Thomas left and should be followed if it exists. Information about NIH authorship and publication standards can be found in the Sourcebook Conduct of Research Guidelines.
17. Is it reasonable to publish results separately in order to provide first-authorship opportunities for more study team members? What considerations should go into deciding what data get published together vs. separately?
    A manuscript should provide a complete story of a result. Many projects contain large numbers of assessments, sometimes making publication of all results in a single paper impractical. In some situations, publication of all results for a facet of the study could be reasonable, with acknowledgement that the data are part of a larger study that also included x-y-z. While this study could likely be presented coherently in a single manuscript, the realities of needing to generate publication records for individual investigators could warrant producing multiple publications addressing the psychotic, mood and cognitive results separately. It would be inappropriate, however, to publish each individual measure separately (i.e., one paper for each of two different mood assessments used, etc.).

2020 Ethics Case #2 (with Facilitator Notes) – Moving On

Dr. Pat Suarez has been a highly productive postdoc with Dr. Jones at the NIH for three years. Though excited to begin a second postdoc at the University of GreatState (UofG) in a week's time, Pat is torn. He just received data back for samples he had submitted to the NIH Sequencing Core. The data are from patients with the disease that the Jones lab studies, and the results are expected to provide insights into why some patients are unresponsive to treatment.

Pat offered to undertake the bioinformatics analysis of the data even though he was formally leaving the lab, but Dr. Jones was resistant. He gave as his reason that Pat should immerse himself in the work of his new lab, but he also had in mind that the analysis would be a good first project for the new computationally-trained postdoc scheduled to join the lab in a few days. Dr. Jones reminds Pat of all he has accomplished in three years and assures Pat that he would be co-first author on the primary publication from the project.

Though Pat highly respects Dr. Jones, he decides that Jones couldn't possibly be unhappy if he was able to rapidly analyze the sequencing data after leaving the lab (working evenings and weekends). On his way into lab on his last day, Pat stops to purchase a high capacity flash drive at his favorite computer supply store and copies the data files. He finally finishes late in the evening, grabs the three lab notebooks he's filled over the years and heads for the door.

1. Who owns the data generated by an NIH lab or research group?
2. Does Pat have the authority to take copies of the sequencing data with him? What about the lab notebooks?
3. How could this situation have been better managed by Dr. Jones?

A few days later Pat starts work in his new lab. His new PI had purchased a laptop for him, which Pat configures for use on UofG's network. He is eager to get a start on analyzing the data from the Jones lab before getting too busy with new work. When Pat gets home, he immediately loads the data from the flash drive to his new laptop and gets to work.

4. Apart from the right or wrong of taking a copy of the data, how have Pat's actions put the security of the data at risk?
5. It is not uncommon for trainees (as well as other NIH scientists) to finish up projects after leaving the NIH. For someone in Pat's situation (i.e., leaving NIH for another training position), what is the appropriate arrangement consistent with NIH data use policy?
6. What additional or different considerations would there be if Pat were leaving NIH to accept a position as independent investigator at a university? Or what if Pat were starting a job in industry?

Over the next few weeks and on his own time, Pat analyzes the sequencing data he brought from the Jones lab. He is pleased because he had been taught to use some sophisticated, home-grown bioinformatics tools in his new lab at UofG and they have proved very useful for analyzing the Jones lab data. He has found some exciting results, and when he emails his analysis to Dr. Jones he feels sure that Dr. Jones will be impressed.

But Dr. Jones is NOT happy. He tells Pat that a new computationally trained postdoc in his lab had been doing some nice analysis of the same data set with the understanding that it was HER project. And he is very concerned about Pat using software tools developed at his UofG lab. Pat is dismayed.

7. Should Dr. Jones be upset? What are his interests and obligations in this situation?

Facilitator Notes

Moving On

1. Who owns the data generated by an NIH lab or research group?

As stated in the "NIH Conduct of Research" guidelines (https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/ethical_conduct/guidelines-conduct_research.pdf) "All intramural research records remain the property of the NIH". Responsibility and stewardship of the data resides with the PI.

2. Does Pat have the authority to take copies of the sequencing data with him? What about the lab notebooks?

In a research setting, only the PI has the authority to grant departing lab members (or any outsider) access to data. It is common, however, for departing scientists to receive permission to copy or access data in order to complete projects.

Laboratory notebooks are considered part of the research record and physical volumes fairly universally remain with the laboratory when scientists depart. Again, material in lab notebooks can be copied, with PI permission.

3. How could this situation have been better managed by Dr. Jones?

When a trainee (or any scientist) leaves a research group, it is critical that there be a clear understanding of expectations related to unfinished projects. It may be necessary to have multiple conversations surrounding relevant issues, and it is good practice to put agreed-upon points in writing.

In the current case, Pat is apparently heavily invested in the sequencing project. How Jones handles the situation depends in part on expectations established at the project onset – e.g., was the plan for Pat to do the bioinformatics analysis before leaving, but unavoidable delays in the project meant he ran out of time? Or, was it never the plan that Pat would do that work?

There are lots of good reasons why Jones might prefer to keep the bioinformatics analysis in house. But he should be sensitive to Pat's attachment to the project – and to Pat's clearly high levels of competence and ambition. Jones probably would have done well to be clearer with Pat about his plans for project completion. If Pat understood that a new postdoc was going to take over the analysis, he may have been less inclined to undertake it himself.

Two mentoring tools that can be helpful for enhancing expectations and avoiding misunderstanding in a research group are the so-called laboratory "compact" and the Individual Development Plan (IDP). IDPs are a requirement for trainees in the IRP; compacts are strongly encouraged as a practice that promotes the Responsible Conduct of Research (RCR). A compact, which should first be discussed when a trainee joins a research group, is useful for establishing expectations surrounding a full range of practices and behaviors in a particular research environment. An IDP serves as a plan, agreed upon by mentor and trainee,

for the scientific and professional development activities of the trainee. Ideally an IDP is updated regularly – at least once a year.

Example compacts:
https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/ethical_conduct/lab_compact_examples.pdf

NIH IRP IDP Policy:
https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/mentoring/individual-development_plan.pdf

4. Apart from the right or wrong of taking a copy of the data, how have Pat's actions put the security of the data at risk?

Pat has violated a number of NIH policies related to data management.

i. By copying his data onto a personal flash drive he violates the policy that only Government Furnished Equipment (GFE) may be connected to the NIH network and IT equipment (https://policymanual.nih.gov/manage/chapter/view/2814).
ii. The sequencing data comes from patient samples. This raises the possibility that the data contain PII. If so, external devices (such as flash drives), must be not only GFE, but encrypted.
iii. Pat copies the data from his flash drive to a new (non-GFE) laptop connected to the UofG network, potentially making it accessible to other parties. The violation is even more egregious if the data includes PII.

5. It is not uncommon for trainees (as well as other NIH scientists) to finish up projects after leaving the NIH. For someone in Pat's situation (i.e., leaving NIH for another training position), what is the appropriate arrangement consistent with NIH data use policy?

The most appropriate arrangement depends on the particulars of the case. For a trainee who will be mostly writing and performing light analysis using commercial software for (e.g., Excel), it is often acceptable for a trainee to safely transfer needed data to a personal device. However, often a better solution, especially when the data needs to be accessed by multiple individuals, is to put the data on Box, NIH's currently approved solution for sharing data with non-NIH parties. A cloud solution may also be an option, especially if the cloud environment provides computational tools as well as data. In these cases the trainee effectively becomes a collaborator, albeit one not connected with an institution.

When an exiting trainee needs to access resources on the NIH network, Biowulf for example, or IC-based storage or NIH-licensed software, then GFE equipment is usually required. In these cases the preferred arrangement is for that individual to convert to Special Volunteer (SV) status and be allowed to take their GFE equipment with them. As a SV, the scientist has a PIV card and retains access to the NIH network. Once the planned work is complete, the equipment is returned to NIH and the SV appointment is terminated.

A complication arises when the departing individual is relocating to another country (e.g., a visiting fellow returning to his/her home country). NIH policy prohibits such individuals

from having a PIV card, meaning they cannot access the NIH network and should not have GFE. In these cases, the (current) NIH-approved solution for data sharing is to use the Box platform. (Such "solutions" can change frequently, however.)

6. What additional or different considerations would there be if Pat were leaving NIH to accept a position as independent investigator at a university and planned to continue the project with patient data collected in the Jones lab? Or, what if Pat were starting a job in industry (unrelated to his research in Jones' lab) and wanted to finish writing up his work from the Jones lab on his own time?

If Pat were leaving to establish his own research group at a university, it would be very important that he and Dr. Jones agree on exactly what project(s) he could take from the Jones lab. If he plans to continue working with human data generated in the Jones lab, it would be important that a Data Transfer Agreement (DTA) be established between the NIH (Dr. Jones' IC) and the UofG. A DTA is a "light" version of a Material Transfer Agreement (MTA), which is used when material, with or without accompanying data, is transferred. (For non-human data, a DTA is typically not necessary.) If collaborations are to continue, it is good practice to establish a formal Collaboration Agreement to insure that both parties understand their roles and responsibilities.

If Pat were leaving the NIH for a job in industry and planned to finish up the project from the Jones lab on his own time, the solutions discussed for Q5, as described above, would apply.

7. Should Dr. Jones be upset? What are his interests, obligations, and concerns in this situation?

Dr. Jones has a right to be angry, as Pat violated his trust by taking the sequencing data with him and continuing with the project when he was told not to. (Pat may not have known about the new postdoc Jones hired to do the bioinformatics anlaysis, but that shouldn't matter; Pat should have respected Jones's decision.) Pat's actions have put Dr. Jones in a very difficult position.

Dr. Jones has an obligation to support the postdoc assigned to analyze the data that Pat took with him. What is not clear from the narrative is how Pat's analysis compares to the analysis done by Jones's new postdoc. If Pat's analysis is markedly superior, Jones will be in an especially difficult position: he wants to publish the highest quality science but he doesn't want to condone Pat's poor (if well-intentioned) behavior or be accused of not supporting the postdoc whose project Pat stole.

Jones may also be concerned with the fact that Pat utilized bioinformatics tools developed in another lab. Jones may not be in a position to fully understand and vet the tools, and he could be put in an awkward position if the PI of Pat's new lab discovered that Pat had used his lab's tools in a potentially unauthorized manner. Depending on the nature of the tools and involvement of the UofG lab staff in training and helping Pat with the tools, Pat's new PI might even argue for authorship.

Introduction to the Ethics Case Study: Under Pressure

Pressure surrounds all of us in scientific settings. Depending on our respective roles within hierarchies in the laboratory, clinic, and other research groups, those pressures can come from different sources: Principal Investigators (PI) or group leaders; peers whom we compete with; journal editors and reviewers; our families and those who support us during what can be a long training/career trajectory; time itself in regards to the time limits of position appointments; and of course, ourselves. The nature of a career in research is that the output or "rewards" that we receive in the short term may not be proportional to the degree of effort we put in, which can be vexing for those whose career success is dependent on high-quality publications. Those in training positions may be particularly vulnerable to feeling pressure, even when those in supervisory roles do not consciously exert it. Trainees often feel that they must rely on positive opinions from supervisors to translate into glowing letters of recommendation that may be seen as required for successful career advancement. As a result, trainees may unduly focus on maintaining their supervisors' positive opinion of their performance, generating self-imposed pressure with potentially harmful outcomes.

The effects of being constantly surrounded by the many pressures to perform can manifest themselves in myriad ways. Comparison and competition with those in similar career stages lead to complex interpersonal dynamics in research groups. The research group leader must balance the needs and goals of all their group members along with their own position's requirements and pressures — achieving tenure, receiving continued positive scientific reviews, and maintaining one's own scientific reputation both within our institutes and in the broader scientific community. Yet, it is critical that the group leader not exert pressure on research group members resulting from unrealistic expectations inconsistent with the career goals of the research staff.

This year's case study explores the potential impact of several of these pressures in our research settings — its various sources and effects on group members, as well as the consequences when pressure is implied or direct, and when gaps in communication cause those in supervisory positions to send unclear messages about expectations. It is critical to consider this as we perform our research in a group, being aware of the competing needs and pressures of those around us as we work together on the common goal of pursuing scientific truth.

Under Pressure

As you go through the case, keep in mind that some key details are intentionally missing or left vague in order to encourage everyone to think through how the scenario might play out differently depending on some of the further case details you might want to consider.

Dr. Sam Best is a post-doctoral fellow who has worked in Dr. Taylor Jones's lab for almost 5 years. Best is now working on a project investigating how cells respond to a particular stimulant. Dr. Jones is a Tenure-Track Investigator coming up for tenure consideration within the year, who established the cell stimulation response system upon arrival at NIH, but Best later modified and perfected it. Best reported the development of the system and proof-of-principle data in two peer-reviewed publications, including one as first author. Their new research showed that the cellular response to the stimulant Invigorin was initially low but then steadily increased over time, accompanied by expression of a particular protein within a subset of the cells. Best found that adding specific chemicals inhibiting expression of that protein eliminated the cellular response. Best and Jones conclude that the protein mediates the effect and that they have uncovered a novel mechanism by which cells respond to this class of stimulants.

They draft the manuscript and send it to a high-impact journal. Dr. Jones believes their findings represent a major advance that could increase the likelihood of achieving tenure. The journal responds that while reviewers believed the work is exciting and potentially impactful, they want more direct evidence to prove the model through additional experiments, implying that the paper will be accepted if the new experimental data support the model.

1. Is publication in a 'high-impact' journal important for career success? Should it be?
2. What kind of message do reviewers send when they ask for evidence to 'prove' a model? What are the pitfalls of trying to 'prove' a hypothesis?

Meanwhile, Dr. Best is reaching the end of their NIH appointment and begins a geographically restricted job search in an effort to join their partner, who had moved for a job months earlier. Luckily, Best receives an interview invitation from Innovative Pharma, a prestigious company in the targeted area. Best also makes the short list of applicants for a position at World's Fabulous Research Institute, which provides opportunities for exciting scientific collaborations. The institute position is a dream job but requires preparing for a research proposal and an in-person interview within the next few weeks. Because the institute job is the first choice, Best delays the pharmaceutical company interview process until hearing from the research institute, even though the company position has a higher salary and is an excellent backup option.

Dr. Jones really wants to complete the reviewers' suggested experiments quickly and publish the study because it would increase the potential of achieving tenure, but Dr. Best is concerned about not being able to finish the work while applying for the institute position. Best relays these concerns to Jones and suggests that they ask Dr. Kai Ettero-Sanson, a new post-doctoral fellow that Best trained over the past year, to conduct the experiments, saying Ettero-Sanson would be eager to work on the project. However, Jones asserts that Ettero-Sanson needs more experience because the system is 'finicky' and implies that Ettero-

Sanson has lesser lab skills because of training outside the United States. Jones tells Best not to worry because even if neither position comes through, more offers will come, and compliments Best again for being "very gifted at the bench," a comment Jones has made many times. Jones adds that Best will be able to stay at NIH for an additional sixth year without a problem and that having a first-author paper in the *Journal of Fantastic Results* will greatly improve job prospects.

3. Is it fair to ask Dr. Ettero-Sanson to become involved with the project at this point? What are the advantages/disadvantages of having another researcher perform these experiments?
4. Is the advice from Dr. Jones about Dr. Best's job search reasonable? What would prompt Jones to offer this advice?
5. How should a lab handle systems that tend to be 'finicky'; i.e., a system that is reliable but requires extremely strict adherence to the protocol?
6. Do you think Dr. Jones has a bias against Dr. Ettero-Sanson? How could a bias (or the perception of one) affect lab relationships, pressure, and career development?

Dr. Best reluctantly agrees to ask the institute to postpone the in-person visit and convinces Dr. Jones to allow Dr. Ettero-Sanson to help with the experiments. It takes weeks for Best and Ettero-Sanson to finish their work, but the results are confusing and in one case, contradictory to what they predicted. Best shows the data to Jones, who concludes that the results must be incorrect and that perhaps Ettero-Sanson had misread reagent bottles or protocols. Jones suggests that Best repeat the experiments, but Best reminds Jones that the institute has been trying repeatedly to schedule the on-site interview ASAP. Jones then asks: "Do you think this institute position is a good fit for you? I say this because it is a very competitive environment, and I've found that success in places like that depend on one's ability to think broadly and develop novel and creative ideas." Dr. Best is troubled by these remarks because they imply that Best might not succeed as an independent scientist. It reminded Best of a previous comment by Dr. Jones that fellows who received PhDs from "certain types of universities" are typically better suited for non-academic positions. Best also realizes that aside from repeated compliments on technical skills, Jones has never commented on Best's potential to be a PI/group leader or suggested additional training or experience that would help with achieving a leadership position. Best is now worried about the recommendation letter that Jones had written, what had been communicated privately to professional colleagues, and whether successfully completing revisions of the paper would affect future letters.

7. Are Dr. Best's concerns legitimate? How could Dr. Best address them?
8. How might mentoring/communicating be improved in this interaction?
9. What do you think Dr. Jones meant when referring to 'certain types of places'? Do PIs/group leaders have preconceived ideas about particular schools and career paths? How do these ideas affect trainees?
10. What should take place during a conversation in which a trainee asks their PI/group leader for a letter of recommendation? What is the role of the PI/group leader in that conversation?

Dr. Best works day and night, mostly alone in the lab, repeating the experiments and finishes them faster than any of the previous experiments. This time, the data trended as expected. Dr. Jones is happy and immediately encourages Best to write up the results without Dr. Ettero-Sanson as a co-author and to resubmit the paper, commenting how this will help both of their careers. Best is relieved. While both potential job opportunities had granted interview delays, they were clear that no further delays would be acceptable.

11. Is it proper to remove Dr. Ettero-Sanson as an author? How and when should Dr. Jones have communicated how authorship on this paper would be decided?
12. Is running experiments 'day and night' appropriate in this case? What issues can arise from this behavior?

Dr. Ettero-Sanson learns of the new results and is skeptical. A meticulous experimentalist, Ettero-Sanson does not believe the new results could differ so substantially from the data obtained together with Best. After learning about the change in authorship, Ettero-Sanson tries to move on but cannot and decides to investigate further. One day, after everyone has left the lab, Ettero-Sanson looks through Dr. Best's lab notebooks and electronic files and uses the Excel data to try to replicate the results, without realizing that doing so would destroy the integrity of the spreadsheet. From the analysis, Ettero-Sanson concludes that Best ran the most recent experiment multiple times but presented only results from the three best experiments to Dr. Jones.

13. Is Dr. Ettero-Sanson justified to suspect Dr. Best's results? If so, what should Dr. Ettero-Sanson do?
14. Why is the integrity of primary data so important? How can the integrity of computer files be maintained?
15. Is it ever ok to look through a colleague's notebook and data files?
16. How should primary and analyzed data be stored?
17. Is it acceptable to present data selectively? Under what conditions, if ever, can specific data sets be removed from an analysis?

Dr. Ettero-Sanson is worried about the consequences of coming forward and questioning the experimental results, but out of great concern, speaks with Dr. Jones about the possible misconduct. Jones brushes off the concerns, saying that Ettero-Sanson must be mistaken and implies that Ettero-Sanson misunderstood Best's lab notebook and files, perhaps because of language issues. Jones begrudgingly agrees to a formal meeting to discuss the issue further but neglects to schedule one. Ignored and upset, Ettero-Sanson contacts the NIH Agency Intramural Research Integrity Officer (AIRIO). A preliminary assessment indicates that a misconduct inquiry is warranted.

18. How should Dr. Jones respond to Dr. Ettero-Sanson's concerns?
19. What type of signals is Dr. Jones sending to Dr. Ettero-Sanson by bringing up 'language issues' and by not scheduling the meeting?
20. What role does trust play in mentor-mentee relationships? How do you think the outcomes would differ if Dr. Jones trusted Dr. Ettero-Sanson more and Dr. Best less?

During the misconduct inquiry, Dr. Jones worries that rumors will spread, required external reference letters will be tainted, and the tenure committee will not recommend promotion. Jones blames Dr. Ettero-Sanson for the entire situation and begins to wonder if another lab would be a better fit. Dr. Ettero-Sanson worries that relationships within the lab are irreparably harmed. Dr. Best is extremely distressed and concerned about reputational damage. Unable to concentrate on the job proposal, Best withdraws from consideration for the institute position, but does interview with the pharmaceutical company as the inquiry progresses.

The inquiry ends and concludes that no further investigation is practical because Dr. Ettero-Sanson's handling of the original Excel file compromised its integrity. The pharmaceutical company selects a different candidate, and when Best asks for feedback, the recruiter responds that Best seemed distracted during the interview.

21. Do you see ineffective communication taking place in this case? If so, where and how might better communication from the PI/group leader to either trainee have changed the outcomes?
22. What choices could have been made differently that would have led to positive outcomes for everyone in this case?
23. Have you ever encountered or heard about any other situations related to the themes of this case study?
24. What types of services are available to the various parties involved here to get help dealing with high levels of stress?

Tell Us What You Think

The NIH Committee on Scientific Conduct and Ethics (CSCE) welcomes your voluntary, anonymous feedback on any aspect of the 2021 ethics case study. To provide feedback, please scan the QR code (a quick response code that can be read by cell phone cameras) or click the link below – each will take you to the same anonymous survey. Please provide feedback by December 31, 2021. All comments will be aggregated to generate a summary document for review. Any personal identifiers provided in the responses (e.g., names, position titles/types, etc.) will be removed prior to sharing the results outside the CSCE.

Open your cell phone camera application and focus on the QRC above, and you will be directed to Survey Monkey to leave anonymous feedback. You may choose to identify your IC and or Laboratory/Branch, if relevant to your feedback, but please do not identify any person by name or position (names will be redacted).

You may also access the survey by clicking on this URL:
https://www.surveymonkey.com/r/KQV7WRB

2023 Ethics Cases

We have prepared three cases for 2023 that deal with some important topics relating to authorship, credit, and mentoring. These include:

Case 1: Transfer of a Project and Scientific Disagreement

Case 2: Authorship or Acknowledgement of a Post-baccalaureate Trainee

Case 3: Collaboration and Outside Activities

Cases #1 and 2 may be suitable for all while case #3 is more specialized and related to CRADAs.

Since it may not be possible to cover all three cases in the allotted time, we suggest that facilitators cover the cases that meet the needs and interests of the audience.

Facilitators are encouraged to provide their audiences the information to the NIH IRP Authorship Conflict Resolution process (updated in May 2023) and other useful authorship resources, that can be found in the NIH Intramural Sourcebook (https://oir.nih.gov/sourcebook/ethical-conduct/authorship-guidelines-resources) .

Note: In these case studies we use proper names to identify characters, which do not represent real persons affiliated with NIH. The names have been randomly chosen to accurately mirror the rich diversity of the NIH intramural community. Readers are cautioned to question stereotypes they associate with names that may suggest a specific race, national origin, ethnicity, gender, or sex.

[Proceed to next page]

Case 1: Authorship, Transfer of a Project, and Scientific Disagreement

Dr. Cooper had a four-year postdoctoral fellowship in an NIH neuroscience laboratory headed by Dr. Jiang before leaving the NIH for a tenure-track research position at a university. Dr. Cooper published several first-author papers that supported a hypothesis (H1) concerning the role of the immune system in the formation of amyloid-β (Aβ) plaques in Alzheimer's disease in transgenic mice. Dr. Cooper came up with the idea for H1 while in graduate school and joined Dr. Jiang's lab as a postdoctoral fellow with the goal of testing and refining H1. Toward the end of the fellowship, Dr. Cooper began working on a project to determine whether blocking interleukin-10 causes the immune system to remove amyloid-β (Aβ) plaques from the brain. Dr. Cooper developed a protocol for the project and gathered some preliminary data that resulted in their selection for a tenure-track position at the end of the 3rd year of the fellowship. Before leaving, Dr. Cooper and Dr. Jiang agreed, by email, that Dr. Cooper would continue working on the project as an NIH Special Volunteer, would have access to NIH data, and would be the first author of a paper reporting the project's results. Dr. Jiang assigned the project to Dr. Rivas, another postdoctoral fellow. After having difficulty replicating Dr. Cooper's preliminary data, Dr. Rivas consulted with Dr. Jiang, but not Dr. Cooper, and made substantial changes to the protocol. Following these changes, the experiments proceeded smoothly. After completing data collection and analysis, Dr. Rivas wrote the first draft of a manuscript, which listed Dr. Rivas as the first author, Dr. Cooper as second author, and Dr. Jiang as last and corresponding author, with several other coauthors. Dr. Jiang sent the manuscript to Dr. Cooper, who read it carefully and became very upset because 1) Dr. Cooper is listed as second author and not first; 2) Dr. Cooper disagrees with the interpretations of the data, which undermine support for H1 and lend support to a different hypothesis proposed by Dr. Rivas; and 3) Dr. Cooper disagrees with changes to the protocol made by Dr. Rivas without consultation with Dr. Cooper and believes these may have impacted the findings.

1. **Should Dr. Rivas have consulted with Dr. Cooper before making changes to the protocol?**
2. **Who should be first author of this paper? Should Drs. Cooper and Rivas be co-first authors? What factors would you consider in making this decision?**
3. **Does Dr. Jiang's promise to name Dr. Cooper as first author carry any weight?**
4. **Should Dr. Jiang have talked to Dr. Cooper before naming Dr. Rivas as first author? Should Dr. Jiang have done anything else? Who should be listed as co-authors on a paper?**
5. **Do you have any concerns about Dr. Jiang's mentoring of Dr. Cooper? Could Dr. Jiang have done a better job of mentoring Dr. Cooper? How?**
6. **What should Dr. Cooper do to remedy a disagreement with Dr. Jiang about being placed as second, not first author on the paper?**
7. **How should the team go about resolving the dispute about interpreting the data? If they cannot resolve this issue, would it be ethical to publish the paper without naming Dr.**

Cooper as an author but mentioning Dr. Cooper in the acknowledgments? What should Dr. Cooper do if the paper is published without their consent?

8. **What are the benefits and risks of being wedded to a particular hypothesis?**

[End of case study]

Please take the survey by either clicking on the link below or scanning the QR code on your hand-held device: https://www.surveymonkey.com/r/XMH3VCF

NIH has many resources that researchers can refer to. Below are some links to guidelines related to the topics discussed in this year's ethics case studies:

Sourcebook chapter on departing scientists: https://oir.nih.gov/sourcebook/personnel/policies-recruitment-processes/departing-staff-request-remove-copies-nih-records

Sourcebook chapter on authorship resources and conflict resolution: https://oir.nih.gov/sourcebook/ethical-conduct/authorship-guidelines-resources

Sourcebook chapter on Outside Activities for FTEs and Outside Activities for non-FTE trainees: https://oir.nih.gov/sourcebook/ethical-conduct/government-ethics/guidelines-non-ftes-trainees-nih-related-activities-outside-activities

Sourcebook chapter on Publication and Abstract Clearance: https://oir.nih.gov/sourcebook/submitting-research-publications/publication-abstract-clearance

Sourcebook chapter on Foreign Interference: https://oir.nih.gov/sourcebook/personnel/policies-recruitment-processes/guide-nih-intramural-principal-investigators-navigate-international

NIH policy on CRADAs: https://www.techtransfer.nih.gov/policy/cradas

Researchers can always reach out to the NIH Office of the Ombudsman for advice on how to navigate challenging situations at work - https://ombudsman.nih.gov/

Case 2: Authorship or Acknowledgement for a Post-baccalaureate Trainee

Mx. Tegene was an NIH post-baccalaureate trainee with a BS in psychology, supervised by Dr. Murphy, an endocrinologist and clinical researcher at the NIH. Mx. Tegene spent a year at NIH before enrolling in medical school. While at NIH, Mx. Tegene assisted Dr. Murphy with a research project on medication adherence and health outcomes for patients with Type II diabetes. Other people working on the project included a pharmacy fellow, Dr. Raj, a social worker, Mx. Puig, and a research nurse. Mx. Vilensky. The project involved collecting the medical and social history of study subjects/patients, reviewing medications, collecting blood and urine samples, and administering several surveys/interviews. After a long day of interviews, Mx. Tegene was having coffee and talking with Mx. Vilensky about some ways of potentially improving medication adherence. Mx. Tegene suggested that using an interactive game on cell phones might improve medication adherence. The following week, Mx. Tegene gave a report at a lab meeting summarizing their initial findings. During the discussion period, Mx. Tegene said that it might be interesting to test whether using an interactive game on cell phones could improve medication adherence. Dr. Murphy seemed interested in this idea but not incredibly impressed. Two years after leaving the NIH, Mx. Vilensky sent Mx. Tegene a paper recently published in *The American Journal of Diabetes Management* describing the results of a study testing the efficacy of using an interactive cell phone game to promote medication adherence, which showed that playing the game increased medication adherence by 30% and glycemic control by 25%. The authors included Dr. Raj, Mx. Vilensky, Mx. Puig, and Dr. Murphy but not Mx. Tegene. Mx. Tegene was not even acknowledged in the paper. Mx. Tegene is upset after reading the paper because of not being credited for the study's original idea. Mx. Tegene contacts Dr. Murphy about this issue and demands an explanation. Dr. Murphy replies that Mx. Tegene was not acknowledged because it was not Mx. Tegene's original idea. Dr. Murphy mentions discussing this idea with other NIH colleagues before, but when pressed by Mx. Tegene, Dr. Murphy cannot remember precisely when this occurred.

1. **Should Mx. Tegene have been an author of this paper? Should Mx. Tegene be acknowledged in this paper?**
2. **How can Mx. Tegene be acknowledged at this point?**
3. **If Mx. Tegene is not acknowledged, would this be plagiarism? How would one prove plagiarism?**
4. **Should Dr. Murphy have asked Mx. Tegene to collaborate with the research team on the adherence project and possibly be an author?**
5. **Assuming that Mx. Tegene would not collect any data due to their commitment to medical school, what would Mx. Tegene need to do to qualify as an author?**
6. **If you know that an idea has been discussed by others but not published or presented formally, should you acknowledge it? How would you do this?**
7. **Should members of the research group have written down Mx. Tegene's medication adherence idea when it was discussed at the lab meeting?**

[End of case study]

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Sourcebook chapter on authorship resources and conflict resolution: https://oir.nih.gov/sourcebook/ethical-conduct/authorship-guidelines-resources

Sourcebook chapter on Outside Activities for FTEs and Outside Activities for non-FTE trainees: https://oir.nih.gov/sourcebook/ethical-conduct/government-ethics/guidelines-non-ftes-trainees-nih-related-activities-outside-activities

Sourcebook chapter on Publication and Abstract Clearance: https://oir.nih.gov/sourcebook/submitting-research-publications/publication-abstract-clearance

Sourcebook chapter on Foreign Interference: https://oir.nih.gov/sourcebook/personnel/policies-recruitment-processes/guide-nih-intramural-principal-investigators-navigate-international

NIH policy on CRADAs: https://www.techtransfer.nih.gov/policy/cradas

Researchers can always reach out to the NIH Office of the Ombudsman for advice on how to navigate challenging situations at work - https://ombudsman.nih.gov/

Case 3: Authorship, Collaboration, and Outside Activities

Dr. Johansson is a postdoctoral researcher at Cutting Edge University who is working and training at the NIH via a Special Volunteer appointment under the direction of Dr. Fathi. Dr. Fathi, Dr. Parekh, a Professor at Cutting Edge University, and researchers from BioAI, a private company, have been collaborating on developing artificial intelligence (AI)/machine learning (ML) programs that predict how respiratory viruses interact with human lung epithelial cells.

The collaboration is governed by a Cooperative Research and Development Agreement (CRADA) between NIH, Cutting Edge University, and BioAI. As part of this collaboration, Dr. Fathi agreed to have Dr. Johansson work and train at the NIH for two years. The NIH provides Dr. Johansson with training, access to facilities, equipment, expertise, and data but not stipend/salary support, which is provided by Cutting Edge University. The AI/ML programs that Dr. Johansson is working on have been developed using NIH data. Some of the software is open source, but some is under development and not yet published or shared widely. The CRADA permits the sharing of computer code between NIH, Cutting Edge University, and BioAI.

One morning, Dr. Takekazu, Dr. Fathi's Branch Chief, asks Dr. Fathi to meet in person about an urgent matter. Dr. Takekazu informs Dr. Fathi about a paper recently published online in the *Journal of Machine Learning in Biomedicine* that describes an AI/ML model for predicting how the herpes simplex virus interacts with genital cells. Dr. Johansson is the paper's first author, Dr. Parekh is the last author, Dr. Fathi is the second to last author, and 3 authors from BioAI are middle authors. Dr. Johansson's affiliation is listed as with the NIH and Cutting Edge University. The paper lists funding support from Cutting Edge University and BioAI and acknowledges NIH's support. The paper also mentions that software patents are being applied for. Dr. Takekazu further notes that: (1) there is no record of the article having gone through the NIH manuscript clearance process, and (2) no employee invention report (EIR) has been submitted to the NIH Office of Technology Transfer.

Dr. Fathi is surprised to hear this news, explaining that they were unaware of this manuscript and are now hearing about this research for the first time. Dr. Fathi is additionally dismayed at not knowing about Dr. Johansson's undisclosed work for this research, which was not part of the research plan described in the CRADA.

1. **What are some of the ethical/legal/policy concerns created by this situation?**
2. **What should the NIH/Dr. Fathi do? Should Dr. Fathi write to the journal and ask to have their name removed from the paper? Should Dr. Fathi ask the editors to withdraw the paper because computer codes were used without permission?**
3. **Can Dr. Johansson remain the first author but not list their NIH affiliation?**
4. **Should the NIH contest the patents that are being applied for?**

5. **How could this situation have been prevented? What steps would need to be taken for this type of collaboration to occur without violating ethical or legal rules or NIH policy?**
6. **Do you see any problems with Dr. Fathi's mentoring of Dr. Johansson? Should Dr. Fathi have done a better job of explaining to Dr. Johansson about the scope of the collaboration under the CRADA and what was allowable?**

[End of case study]

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2024 Annual Ethics Cases - Edited for 2025 Discussions

The Committee on Scientific Conduct and Ethics (CSCE) has prepared three cases for 2024 that deal with some important topics relating to research with human subjects and using artificial intelligence in research. These include:

Case 1: IRB Protocol Deviation
Case 2: Using AI to Write a Manuscript
Case 3: Using AI to Analyze Research Data

Since it may not be possible to cover all three cases in the allotted time, we suggest that facilitators cover the cases that meet the needs and interests of their audience.

CONTENTS

IRB Protocol Deviation (Case #1)

Fox is a research nurse at the NIH who recently started working with Bear, an MD who serves as a PI on an IRB-approved, Phase III clinical trial comparing three different FDA-approved medications for treating mild-to-moderate depression. The study has exclusion criteria pertaining to various health measures, such as blood pressure, kidney and liver function, depression score (based on two metrics), and body mass index (BMI). Participants' BMI must not be greater than 30 kg/m^2. One day, Fox was reviewing the records of new patients on the study and noticed that Bear had enrolled a patient with a BMI of 31, which is a protocol deviation. Fox asked Bear about this, but Bear shrugged and told Fox not to worry about it because, in Bear's professional judgment, the patient was healthy enough to participate in the study. Not wanting to cause any trouble, Fox tried to forget about the incident, but Bear did the same thing the following week. This time when Fox asked about the deviation, Bear became angry, grabbed Fox's wrist and told Fox to "mind your own business." During lunch at the cafeteria, Fox told Badger, another research nurse, what Bear had done. Badger responded: "You better get used to it. Bear does not tolerate people questioning a doctor's judgment."

Questions for Case #1 discussion

1. Should Fox follow the advice of Badger to "get used" to Bear's behavior?Why/Why not?

2. What are the potential consequences of not addressing the protocol deviation?

3. What resources are available to support Fox in navigating this situation?

4. Is Fox being disloyal to the research team? How does Fox balance staff loyalty with ethical responsibilities to study participants and the scientific community?

5. What steps can be taken to ensure the safety and well-being of participants enrolled in the study and ensure the validity and reliability of the data collected?

6. How might this case impact the trust and confidence of participants in clinical research at the NIH?

[End of case study #1]

Please take the survey by either clicking on the link below or scanning the QR code on your hand-held device: https://www.surveymonkey.com/r/JTDK6JN

Using AI to Write a Manuscript (Case #2)

Dr. Blue is principal investigator at the NIH who specializes in cancer genotyping. A prestigious review journal has asked Dr. Blue to write an article reviewing the current state of the field. Dr. Blue is very busy with clinical, research, and administrative responsibilities, so Dr. Blue asks Dr. Green, a postdoctoral fellow working in the lab, to write the review. Without telling Dr. Blue, Dr. Green uses an artificial intelligence (AI) tool to summarize the literature on this topic and generate references. Dr. Blue reads the review and congratulates Dr. Green on a job well done. They submit the solicited review to the journal. The article lists Drs. Blue and Green as authors but does not acknowledge the use of the AI in preparing the article. Two months after publication, an anonymous critique of the article, appearing in a post-publication peer review blog, claims that two of the citations in the article are fake. The editors of the review journal inform Dr. Blue about this and ask the authors to submit a correction. Dr. Blue meets with Dr. Green about the issue and asks how the problem occurred. Dr. Green admits to using an AI tool to help write the article and says the tool must have made the mistakes. Dr. Blue is furious at Dr. Green for using this tool without consulting with the corresponding author first. They both carefully examine the references and verify that the two references mentioned by the critic are indeed fake. They also discover that three additional references are inaccurate, three are irrelevant, and two sentences in the article are copied word-for-word from another article without quotation marks or attribution.

Questions for Case #2 discussion (with facilitator notes)

1. When Dr. Blue and Dr. Green submit their correction to the journal, should they also address the inaccurate and irrelevant references and the copied sentences and acknowledge the use of the AI tool?

2. Should they explain how the problem occurred, i.e., that the AI tool made the mistakes?

3. Should they retract the article?

4. Did they commit research misconduct, i.e., plagiarism?

5. What are the responsibilities of authors when using AI tools to review the literature?

[End of case study #2]

Please take the survey by either clicking on the link below or scanning the QR code on your hand-held device: https://www.surveymonkey.com/r/JTDK6JN

Using AI to Analyze Data (Case #3)

Dr. Falcon, a postdoc in Dr. Hawk's research group, has struggled to analyze health survey and genomic data from a longitudinal NIH intramural research study with 10,000 human participants. Dr. Falcon wonders if one might be able to use artificial intelligence (AI) tools to help analyze the data. Dr. Falcon has an account for an NIH ChatGPT platform, but this version of ChatGPT does not have the functionality needed for this data analysis, so Dr. Falcon signs up for a personal account with a commercial AI platform, HotBot1, which is able to analyze data from publicly accessible health databases that is similar to the IRP study data. Dr. Falcon uses HotBot1 to search for statistical relationships among dozens of variables from the public databases; however, Dr. Falcon soon realizes that to make significant progress, one would need to supplement the publicly available data with additional, more detailed data. Fortunately, the IRP study includes the data needed to improve the analysis and HotBot1 allows users to upload data to the platform.

Dr. Falcon de-identifies the intramural study data so it includes no names or personal identifiers and uploads them to HotBot1. After several weeks of work, Dr. Falcon has some promising results, including a genetic association that could have important public health implications. Although the analysis appears to misrepresent findings for an underrepresented minority cohort of the data, Dr. Falcon is confident that the rest of the analysis is completely reliable. Dr. Falcon shares the results of this work with Dr. Hawk at their next regularly scheduled meeting and tells Dr. Hawk how HotBot1 was used to analyze both the public and intramural datasets together. While Dr. Hawk is not very familiar with AI tools, Dr. Hawk is excited about the new findings. They quickly draft a manuscript reporting the results of their data analysis and submit it for publication clearance review in their IC.

Questions for Case #3 discussion (with facilitator notes)

1. Has Dr. Falcon done anything wrong? If so, what actions should be taken to mitigate any mistakes?

2. Were the steps that Dr. Falcon took to protect NIH data sufficient? Has Dr. Falcon committed a data breach incident that should be reported?

3. How can scientists balance the need to develop their research program quickly with their lack of formal education in emerging technologies?

4. How could HotBot1 have made an error in analyzing the underrepresented minority cohort of the population? What are the implications of using the entire dataset despite the concerns?How could this problem have been anticipated or prevented?

5. In your opinion, is Dr. Hawk appropriately overseeing the research of Dr. Falcon? Should Dr. Hawk have been informed by Dr. Falcon about embarking on this exploratory path?Should Dr. Hawk delve more deeply into the work that Dr. Falcon did using HotBot1, or is it acceptable for Dr. Hawk to trust Dr. Falcon without independently verifying any of the analyses?

6. Is it ever acceptable to use personal credentials instead of official credentials to set up an account using an NIH computer to analyze data? If so, under what circumstances?

7. More generally, what types of AI tools are permissible to use in your research?

[End of case study #3]

Please take the survey by either clicking on the link below or scanning the QR code on your hand-held device: https://www.surveymonkey.com/r/JTDK6JN

Science and Social Responsibility - Dual Use Research

Biomedical research produces many important benefits for society, but it can also lead to harmful results. Is your research potentially 'dual use'? A quick Dual Use Questionnaire (Attachment 2) will helpyou answer this question.

The term **'dual use'** refers to research that can be used to both good and bad ends and specifically to the risk that: (1) dangerous agents being studied could be stolen or diverted for malevolent purposes, or (2) results, knowledge, or techniques developed in the course of the research could be used to develop new toxins or pathogens. For example, research on bacterial resistance could be used to develop new antibiotics or to make a biological weapon. Research on human genetics could be used to develop treatments for people with genetic diseases or to discriminate against people, based on their genotypes. Among the earliest examples is the research by Fritz Haber and by Albert Einstein (Attachment 1). While scientists often have little control over how their research is applied, used, or interpreted by others, they can regulate the use of shared reagents/data/specimens through Material Transfer Agreements (MTAs) or Cooperative Research and Development Agreements (CRADAs). Most importantly, they have a responsibility to try to anticipate the possible social consequences of their research, maximize the good consequences, and minimize the bad ones. The cases developed for this year's annual Responsible Conduct of Research Training for NIH Intramural Researchers address, in different ways, the social responsibilities of biomedical researchers with respect to dual use research (cases adopted from SERCEB – see below). Dual use research is expected to be very rare.

So far, the misapplication of new biomedical knowledge has not been a significant tactic used by terrorists. But seven years after the 2001 anthrax attacks, a congressionally-ordered study concludes that there is a growing threat of biological terrorism and calls for aggressive defenses on par with those used to prevent a terrorist nuclear detonation. Referring to the fast-growing technologies in DNA synthesis, which offer new capabilities to alter the genes of existing pathogens or to synthesize them artificially, the study warns that future bioterrorists may use the new technology to make synthetic versions of lethal viruses such as Ebola or genetically modified microbes designed to resist ordinary vaccines and antibiotics.

The NIH Dual Use Committee will provide advice on such research – a questionnaire has been developed to help you determine if your research might fall into this category (Attachment 2) and you can email the committee at any time at dualuse@mail.nih.gov. They also review manuscripts ready for submission if the question on dual use is checked on the manuscript clearance form http://www1.od.nih.gov/oir/sourcebook/oversight/pub-clear-form.htm.

This year's cases deal with a topic that many scientists are unfamiliar with, 'dual use' research. We realize that not everyone will feel comfortable presenting these cases to their discussion groups and Dr. Henry Metzger has agreed that he would offer a training session for facilitators interested in that – please contact him at **hm24q@nih.gov**.

We also plan to add a section on **Frequently Asked Questions**. If you and your group have a question you were unable to answer, please send it to **jps@helix.nih.gov** and we will post it on the website along with the answer.

Case 1 – *Streptococcus pneumoniae* Membrane Pump Sequence

Dr. Ann Newby is a third year postdoc working with Dr. Peter Bigshot, a senior researcher of antimicrobial resistance in gram-positive pathogenic bacteria. Ann is studying recently isolated strains of *Streptococcus pneumoniae* that have developed antibiotic resistance and are responsible for significantly increased pneumonia morbidity and mortality. She identified a gene that she believes is responsible for the resistance, one that encodes part of a membrane-bound protein pump that removes materials from bacterial cells, and has created a variant with increased capacity that provides heightened resistance.

Ann and Peter submit a manuscript to a major bacteriology journal describing the bacterial pump gene as well as the implications of its identification for development of new therapeutic approaches. Several days later, Peter receives a call from the journal editor informing him that the paper will undergo special review due to the 'dual use nature' of Ann's research.

When Peter informs Ann of his conversation with the editor, she is understandably very worried that her manuscript may not be accepted for publication as a result of this special review. While the paper is under review, she and Peter reflect on the new dual use review policies being adopted by journals to which they regularly submit. While *S. pneumonia* is not on the **'select agent'** list, provisions of the PATRIOT Act do apply to Ann's work. Dual-use technology and research issues pertain to far more than select agents.

Do you know what laws and regulations apply to dual use research? (Attachment 3)

What is a "select agent"? (Attachment 4)

This research has clear potential public health benefits -- do the risks outweigh the benefits? Does Ann's paper pose a level of risk sufficient to prevent its publication?

How can a researcher be held responsible if someone diverts the findings for malevolent purposes?

The interested parties in this case can be identified as ranging from the scientific community as a whole, to the public, potential bioterrorists who would misuse such published information, the journal's editorial board, as well as Peter, Ann, their department, and the entire university in which they are working.

How should scientists (i.e., students, fellows, PIs), administrators, journals, institutions, review boards and the public balance the responsibilities and obligations for new knowledge, public safety, and training? Should trainees, dependent on publications for career progression, work on such projects?

Ann learned that free access to genomic and other scientific databases was being discussed by important scientific bodies, including those that fund research and influence policy. Genome databases were at the very foundation of Ann's research, which began with comparisons of bacterial and associated plasmid genomes across different strains of *S. pneumoniae* and other bacteria to look for sequences altered in resistant- versus non-resistant strains.

Should genomic data for all organisms be freely accessible? If not, is there a logical point at which the line can be drawn on what is and what is not publicly available? How would data not available to the public be accessed? How can researchers balance the need for security with the need for open, international science?
(See National Research Council report *(Executive Summary*
http://books.nap.edu/openbook.php?isbn=0309093058&page=1 **) supporting open access to genome data.)**

Case 2- Pandemic Influenza Genomic Sequence

A senior researcher at the Armed Forces Institute of Pathology (AFIP) sequenced three new genes encoding the polymerase from the 1918 Spanish influenza A virus. This strain caused a pandemic estimated to have resulted in the deaths of 50 million people worldwide. This highly important research both clarified the avian origin of this viral strain and determined the key amino acid changes which, if seen in viruses circulating today, could help identify the more pathogenic human-adapted influenza strains and aid the development of vaccines and antiviral therapies. A manuscript describing these results was submitted to *Nature*.

The Editors at *Nature* recognized the great importance of characterizing the 1918 influenza virus, but *Nature* and most other journals now expect that DNA and amino acid sequences that are described in articles will be submitted to a publicly available database in the field that gives free access to researchers from the date of publication.

What are some of the potential risks of publishing sequence data from novel pathogens?

Could the genetic sequence of the 1918 influenza strain be considered "dual-use" research, carrying the risk that it might be diverted for a harmful use?

The journal's Editor-in-Chief agrees to publish the paper along with the sequence without seeking advice from any government authority or outside advisors.

Did *Nature* overlook an important public health concern by agreeing to publish this sequence?

Nature's Editor-in-Chief felt that the benefits of publishing the sequence clearly outweighed the security and public health risk. In a parallel publication submitted to the journal *Science*, other researchers use reverse genetics to translate the AFIP sequence into a replicating virus. The investigators study the pathogenicity and immune responses to this highly pathogenic strain in infected mice. These studies reveal a number of unusual biological properties and permit the testing of antiviral therapies and vaccines in use against contemporary influenza strains.

Should the risk-benefit assessment of dual-use research differ between *Nature,* that published the sequences, and *Science,* where the studies demonstrated how the actual 1918 influenza virus could be recreated?

Following the two publications, the Department of Health and Human Services (DHHS) established an Interim Final Rule adding to the DHHS select agent list the reconstructed replication-competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments. (http://www.access.gpo.gov/nara/cfr/waisidx_07/42cfr73_07.html)

Does the Federal law change the type of research that may be done with this 1918 influenza strain?

If the rule had been in place prior to the submissions to *Nature* or *Science,* would this have affected publication decisions?

This case is based on two real articles[1] and the issue of publication was reviewed by DHHS and the National Science Advisory Board for Biosecurity (NSABB), a committee chartered by DHHS to advise the Federal government on dual-use research. In an editorial appearing in the same issue of *Science*, however, Nobel laureate and renowned molecular biologist Philip Sharp

[1] Tumpey et al. , *Science*, 310, 71 (2005); Taubenberger et al, *Nature*, 437, 889 (2005)

stated, “I firmly believe that allowing the publication of this information was the correct decision in terms of both national security and public health. It is impossible to forecast how scientific observations might stimulate others to create new treatments or procedures to control future pandemics” [2]. The debate on this particular case and on dual-use research in general will likely continue.

[2] Sharp, P.A. *Science Editorial* vol. 310, 17 (2005)

Case 3 - An Unusual Wrinkle to Translational Research

The bacterium *Clostridium botulinum* produces a toxin that is responsible for about 150 cases of food poisoning a year in the United States. However, bioterrorists could exploit several of its properties, namely that it is accessible, easy to prepare in large quantities, and would be deadly if added to the food or water supply. To counteract the effects of such an attack, Dr. Kim Janda's research team screened a library of compounds predicted to inhibit the activity of botulinum toxin to determine if they could be used therapeutically after the attack.

During the studies - work that was supported by the NIH and The Skaggs Institute for Chemical Biology - Dr. Janda's group found a small molecule scaffold that strongly *enhances* the catalytic activity through an apparent increase in binding affinity. *The compound enhanced the activity of botulinum toxin up to fourteen-fold.*

Publishing a paper that describes how to increase the potency of such a lethal toxin seems irresponsible. **Should these findings be published or should this information be suppressed?**

Dr. Janda and his colleagues reasoned as follows: Thanks to its muscle-relaxing effects, botulium toxin is used in minute doses to treat conditions such as cerebral palsy and spasmodic dysphonia, and even to iron out facial wrinkles. They concluded that "As the importance of the toxin in medicine continues to expand, adaptive immune responses to the toxin must be addressed. The discovery and optimization of small molecule activators may ultimately provide a valuable method for minimizing the dosage, thereby increasing its clinical efficacy." The work was published in J. Am. Chem. Soc. (2006) **128**: 4176.

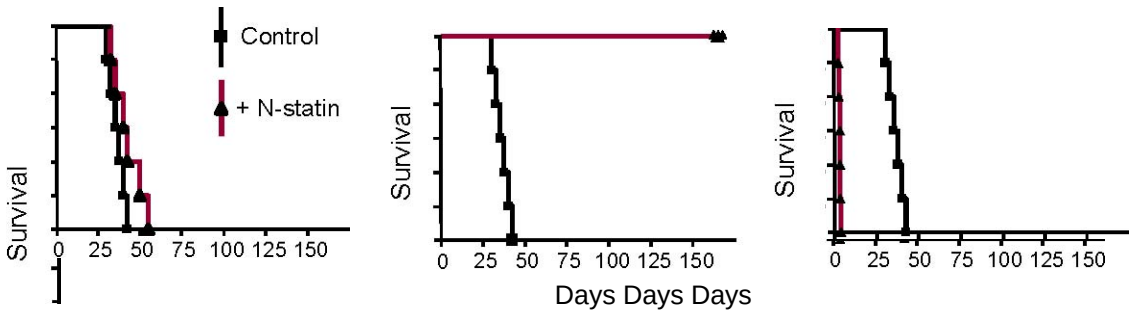
In connection with an article discussing dual use research, the publication *New Scientist* asked several experts whether they agreed with the decision to publish Janda's findings. They defended it, pointing out that in addition to the possible benefits from enhanced treatment of certain diseases, botulinum toxin is so poisonous already that bioterrorists would have little need to enhance its toxicity.

Do you agree with this reasoning?

Case 4 – Cell-matrix Interaction and Tumor Growth & Metastasis

Dr. Gray is an NIH postdoc interested in cell-matrix interaction and its role in tumor growth and metastasis. She finds that membrane protein X is over-expressed in tumor cells and thinks that it may regulate cell adhesion and invasion. She hypothesizes that the N-terminal domain would make a good dominant-negative inhibitor and discovers that expressing this domain inhibits adhesion and kills tumor cells. To produce pure protein to use as a drug to treat cancer, Dr. Gray and her colleague Dr. White develop a bacterial expression-secretion system and are able to isolate the recombinant N-terminal domain from bacterial culture medium. They are excited to find that it kills tumor cells at remarkably low concentrations (0.1 µg/ml), and they name the recombinant fragment "N-statin." They show that it does not kill normal cells until they use 20-fold higher doses.

They do the following tumor survival study using three doses of N-statin or control buffer administered to mice by intraperitoneal injection:



The lowest concentration has minimal effect, the medium dose effectively prolongs survival though the mice look lethargic for a week, and the highest dose kills the treated mice.

After repeating these experiments, the lab rushes to try to publish their exciting results in a prominent journal. They decide to publish the identification of protein X, the purification and characterization of N-statin, and only the medium-dose survival curve (center graph above). In the manuscript, they emphasize that exceptionally low doses are needed, and they decide to leave out the toxicity findings to keep the story simple because they feel that any drug – even aspirin – has side effects at very high doses. They submit the paper immediately after two days of intense writing.

Is this approach acceptable?

While Dr. Gray tries to identify how N-statin works before her fellowship ends in one month, Dr. White wonders if the new drug candidate will work if taken orally. Worried about possible toxicity, he obtains some leftover mice from a neighboring lab and puts N-statin into their drinking water. They all die immediately. Believing that you should "make lemonade if life gives you lemons," he realizes that it might make a good and very cheap rat/mouse poison, because the bacterial expression-secretion system provides an easy source of the material. He is delighted to find that putting just a single drop of the bacterial culture medium on mouse food kills all of another cage of leftover mice. For his own safety with this potent agent, he begins wearing gloves and sometimes even a lab coat – he is complimented by a secretary on his fashionable purple vinyl gloves when he returns some paperwork to the office. He also takes home a flask of bacterial medium after spinning out the cells to be tested by his brother, who runs a pest exterminator business.

What problems do you see with what he has done?

Dr. Gray has to return to her home country, and Dr. Green – the head of the lab – agrees that Dr. Gray can take the plasmids and bacteria with her to continue the work. As she is leaving the U.S. at Dulles airport, vials of these materials are found in her carry-on bag and she is detained by TSA. They ask her about if the contents are non-hazardous and whether they are valuable research materials stolen from the lab she has left.

What could have been done to avoid this problem?

Dr. Gray and Dr. Green manage to talk their way out of the problem with TSA. Dr. Gray returns home, establishes multiple collaborations, and mails her plasmid to a number of colleagues to help her determine N-statin's mechanism of action, with warnings to handle it carefully.

Is there anything wrong with this?

Meanwhile, one reviewer of the submitted paper had been so excited about this powerful new potential drug that he gave a copy of the paper to a grad student in his lab. The student quickly generates an N-statin plasmid by PCR and produces N-statin using the same bacterial expression-secretion system. While purifying the molecule without using gloves, she grabs a quick sandwich at her desk. She is found unconscious and is hospitalized in critical condition – her doctors are baffled.

What went wrong here?

Another reviewer is also impressed by the potency of the biological drug candidate, but wonders in passing whether toxicity might be a concern. The journal returns the paper to the authors for minor revisions. Dr. Green resubmits the paper after adding their toxicity data. After seeing the new results, the Editor begins to worry about the safety of this agent and tells that authors that the journal will probably have to have the paper reviewed further concerning "Dual Use" technology because of the "Patriot Act." Drs. Green, Gray, and White are quite baffled by this action.

What is the editor's concern?

Dr. White tries to continue working with N-statin, but he drops a shaker flask containing N-statin and cuts his foot because he is wearing sandals. He falls unconscious and is hospitalized. Dr. Green cleans up all the mess and puts the materials into MPW waste for disposal.

What should have been done?

Dr. Green goes to bed worried about Dr. White and dreams that he dies, and dreams further that some terrorist thanks him for providing a new tool to kill Americans. The next day, he reads more about the Patriot Act and Dual Use research and realizes that he and his colleagues might even be prosecuted and potentially sent to prison.

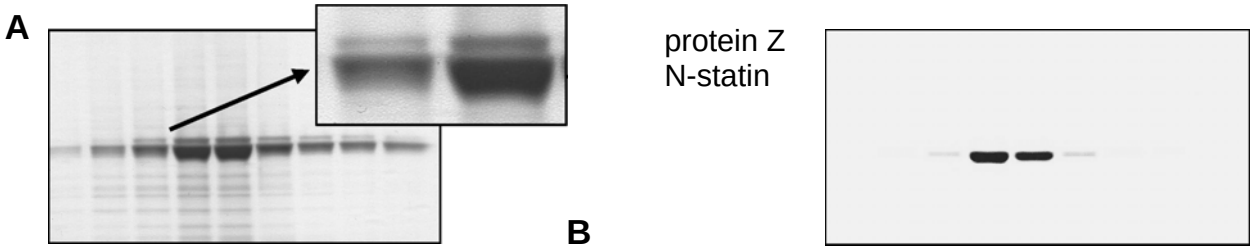
Dr. Gray begins worrying that her paper might not be accepted, that her N-statin might somehow be connected with Dr. White's coma, and that she should have been more careful about distributing her materials. And all just because she wanted to cure cancer!

After information about what has happened starts to leak out, a number of people besides friends and family members become alarmed or angry at the research team, including the Scientific and Institute Director, safety officers, Chair of the animal care and use committee, the Institute's technology transfer office, the FBI, and Department of Homeland Security.

Why did each react so negatively, and what should have been done instead?

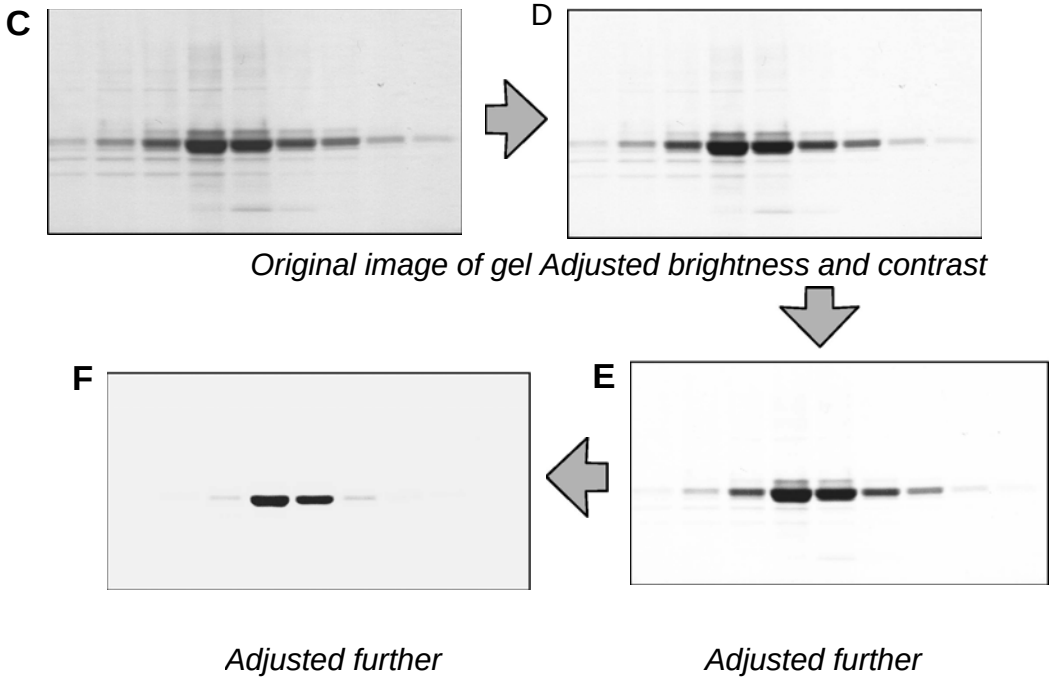
Could you have avoided these problems if N-statin was your discovery?

While the paper is still being evaluated, one of Dr. Gray's collaborators writes to say that he has discovered how N-statin becomes so potent, at least in his own lab: His own preparations contain a second "protein Z" from E. coli (upper band in panel A below) that synergizes with N-statin to kill cells. But he is puzzled because the figure from her paper shows that the same methods produce pure N-statin (panel B).



Dr. Gray sees the same protein Z band in her original gels (***C*** below). But Dr. Green had insisted that she make the gel look prettier by adjusting brightness and contrast, which he felt was "legal" because journals such as Nature allow such adjustments if not selective:

"Processing (such as changing brightness and contrast) is appropriate only when it is applied equally across the entire image and is applied equally to controls."



Was this adjustment ethically "legal"?

Besides potentially misleading readers, what was the other effect?

What should Dr. Gray and Dr. Green do about the paper under review?

Points to Consider

- Research that can be classified as dual use will be very rare but the issue of social responsibility with regards to one's research applies to everyone

- Dual research is expected to be rare but all NIH scientists should review the Dual Use Questionnaire (Attachment 2) to determine whether any research projects they are currently carrying out might fall into the dual use category. If you are not sure, contact dualuse@mail.nih.gov

- It will be preferable to determine if your research has the potential to be considered dual use when you start the project rather than at the point that you are ready to submit a manuscript for publication

- Some scientific journals have established specific policies and procedures regarding publications of this type of research

- This is an evolving policy area and the status of specific research topics may change to dual use or conversely, be removed from these lists, with time

Attachment 1

Fritz Haber and Albert Einstein

The dilemma of what the social responsibilities of scientists are for research that has moral as well as scientific implications is not a new issue. In the first half of the twentieth century, Fritz Haber, a chemist and Albert Einstein, a physicist both performed research that had potential applications beyond the initial problem they were studying. However, their views about the responsibility of the scientist with regard to other uses of his research differed greatly.

Fritz Haber determined how to fix nitrogen to produce ammonia, a necessary component of fertilizer, thereby averting a population crisis. However, ammonia is also used to produce explosives, and the ability of Germany to generate nitrogen for ammunitions prolonged World War I. Haber was not troubled by the ramifications of his research, saying that his only concern was the scientific discovery—"The interest of a wider circle has its source in the recognition that ammonia synthesis on a large scale represents a useful...way to satisfy an economic need. This practical usefulness was not the preconceived goal of my experiments". His outlook changed during World War I when Haber developed chemical warfare, becoming so involved in the process that he was on the front lines to aid with gas release. This involvement in chemical warfare almost cost him the Nobel Prize in chemistry.

Albert Einstein's famous formulation, $E = mc^2$, indicating that a large amount of energy could be released from a small amount of matter, also derived from a purely scientific question. While this knowledge was eventually used in the development of the atomic bomb, Einstein's involvement was also political, as he had become very influential in the United States. Although he was a pacifist, Einstein wrote a letter to President Roosevelt to convince him to develop an atomic bomb before Germany did. Einstein regretted writing the letter to FDR, and he subsequently worked with other scientists to prevent further use of the atomic bomb. However, he realized the significance of dual use research, noting that "The release of atomic energy has not created a new problem. It has merely made more urgent the necessity of solving an existing one."

Attachment 2

Dual Use Questionnaire

	Yes	No
1. Will an intermediate or final product of your research make a vaccine less effective or ineffective?		
2. Will the final or intermediate product of your research confer resistance to antibiotics or antivirals?		
3. Will your work enhance the virulence of a pathogen or render a non-pathogen virulent?		
4. Will the results of your work increase the transmissibility of any pathogen?		
5. Will your research result in alteration of the host range of a pathogen?		
6. Will your research result in a product or intermediate that that may prevent or interfere with diagnosis of infection or disease?		
7. Does your research enable “weaponization” of an agent or toxin?		
8. Even though your research did not involve ***any*** of the aforementioned seven criteria, and recognizing that your work product or results of your research could conceivably be misused, is there the potential for your results/product to be ***readily*** utilized to cause public harm?		

For consultation on these questions, please contact **dualuse@mail.nih.gov**

Attachment 3

RELEVANT FEDERAL LAWS

Two major U.S. federal laws relevant to life sciences research were passed by the U.S. Congress in 2001 and 2002:

1 United and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 or Patriot Act was passed after the 9/11 attacks:

- Makes it a felony to possess a type or quantity of a biological agent that cannot be justified for prophylactic, protective, or peaceful purposes.
- Makes it a federal crime for convicted felons, illegal aliens or fugitives to possess or transport biological agents or toxins, in any quantity and for any reason.
- Defines biological agents as microorganisms, or any recombinant or synthesized component thereof, capable of: causing death, disease, or other biological malfunction in a human, animal, plant or other living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment.(Public Law 107-56 2001).
- Among the biological agents referenced by the Patriot Act is a subset of Select Agents that the Centers for Disease Control or U.S. Department of Agriculture deem most likely to be used as biological weapons. A revised list of such agents went into effect in early 2003, and the rules governing their use, transfer, and registration were finalized in 2005.

2 In 2002, Congress enacted the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, also known as the Bioterrorism Preparedness Act.

- Adds new requirements for the USDA and HHS to consider when determining what should be listed as a Select Agent.
- Requires that Federal agencies must be informed of research, possession, and transport of Select Agents.
- Requires FBI background checks on anyone accessing, transporting, or receiving these agents; and
- Requires that facilities in which these agents are used and stored must be secured in specific ways.(Public Law 107-88 2002)

Attachment 4

Select Agent – a biological agent or toxin that has the potential to pose a severe threat to public health and safety

These include:

Abrin
Cercopithecine herpesvirus 1 (Herpes B virus)
Coccidioides posadasii
Conotoxins
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Ebola viruses
Lassa fever virus
Marburg virus
Monkeypox virus
Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments.
Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Saxitoxin
Shiga-like ribosome inactivating proteins
South American Haemorrhagic Fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)
Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses (Central European Tick-borne encephalitis, Far Eastern Tick-borne encephalitis [Russian Spring and Summer encephalitis, Kyasanur Forest disease, Omsk Hemorrhagic Fever])
Variola major virus (Smallpox virus) and Variola minor virus (Alastrim)
Yersinia pestis

(c) Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms:

(1) Nucleic acids that can produce infectious forms of any of the select agent viruses listed in list above

(2) Recombinant nucleic acids that encode for the functional form(s) of any of the toxins listed above if they:

(i) Can be expressed *in vivo* or *in vitro*, or

(ii) Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro.*

(3) HHS select agents and toxins listed above that have been genetically modified.

(d) HHS select agents or toxins that meet any of the following criteria are excluded from the requirements of this part:

(1) Any HHS select agent or toxin that is in its naturally occurring environment, provided the select agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.

(2) Non-viable HHS select agents or nonfunctional HHS toxins.

(3) HHS toxins under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor, if the aggregate amount does not, at any time, exceed the following amounts: 100 mg of Abrin; 100 mg of Conotoxins; 1,000 mg of Diacetoxyscirpenol; 100 mg of Ricin; 100 mg of Saxitoxin; 100 mg of Shiga-like ribosome inactivating proteins; or 100 mg of Tetrodotoxin.

(e) An attenuated strain of a HHS select agent or toxin may be excluded from the requirements of this part based upon a determination that the attenuated strain does not pose a severe threat to public health and safety.

From: Title 42--Public Health PART 73--SELECT AGENTS AND TOXINS
http://www.access.gpo.gov/nara/cfr/waisidx_07/42cfr73_07.html

Weighing the Risks and Benefits of Dual Use Research

What is Dual Use Research?

Dual use research is typically conducted for positive purposes by legitimate scientists, but it also has the potential for misuse as, for example, in the case of nuclear technology research. The dilemma is how to permit free accessibility to scientific data while minimizing national security risk. As a life science professional either working in a laboratory or overseeing a laboratory that works with materials with the potential for dual use, such as infectious agents, it is your responsibility to know the most current laws and rules. Those relevant to the research projects with which you are involved should be incorporated into your lab's rules and the decisions you make as a researcher, a research administrator, or a member of your research community.

WHAT TYPES OF RESEARCH MAY CAUSE DUAL USE CONCERNS? RECOMMENDATIONS FROM THE SCIENTIFIC COMMUNITY, 2004

The HHS Secretary chartered the National Science Advisory Board for Biosecurity (NSABB) to advise the federal government on policies related to dual use research. NSABB drew from the National Academy of Sciences' report called *Biotechnology Research in an Age of Terrorism* to develop their list of 7 research categories of concern which they recommended to the HHS Secretary in June 2007:

- **Enhance the harmful consequences of a biological agent or toxin;**
- **Disrupt the immunity or the effectiveness of an immunization without clinical and/or agricultural justification;**
- **Confer resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against a biological agent or toxin, or facilitate their ability to evade detection methodologies;**
- **Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin;**
- **Alter the host range or tropism of a biological agent or toxin;**
- **Enhance the susceptibility of a host population; or**
- **Generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent.**

In addition to making recommendations on the definition and criteria of dual use research of concern, the NSABB also made recommendations on oversight and communication strategies for the responsible conduct.

Select Agents

The National Select Agent Registry Program oversees the activities of possession of biological agents and toxins that have the potential to pose a severe threat to public, animal or plant health, or to animal or plant products. On this website you will be able to view current regulations regarding select agents, and access additional resource information, as well as download application packages and submit forms electronically http://www.selectagents.gov/index.html.

***RULES AND LAWS GOVERNING LIFE SCIENCE RESEARCH*:**

As illustrated in the figure below, there are layers of rules and governance that dictate all research practices, from decisions made on an individual level to institutional rules and finally federal and even international standards.

PUBLICATION POLICIES

The select agent regulations (42 CFR 73, 9 CFR 121, and 7 CFR 331) place no specific restrictions on the publication of select agent research findings. However, any records or information systems that could allow an individual to gain access to the select agents or toxins should be safeguarded to prevent unauthorized access, theft, loss, or release of these materials. APHIS and CDC strongly encourage entities to refrain from publishing detailed information about select agent and toxin locations, quantities on site, or researchers. APHIS and CDC consider all information provided to the Select Agent Programs in APHIS/CDC Forms 1, 2, 3, 4, and 5 to be "Sensitive but Unclassified (SBU)." Publication of SBU information could compromise the security and safety of the regulated community, public, animals, plants, and homeland security. APHIS and CDC do not release site-specific or identifying information associated with the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121) to the public.

Publication policies must be determined on a case by case basis but some journals have published guidance regarding the use of microbial information. The American Society of Microbiology (ASM), publisher of several journals[3], as the following policy statement on the "Use of Microbiological Information":

> The Council Policy Committee (CPC) of the American Society for Microbiology affirms the long-standing position of the Society that microbiologists will work for the proper and beneficent application of science and will call to the attention of the public or the appropriate authorities' misuses of microbiology or of information derived from microbiology. ASM members are obligated to discourage any use of microbiology contrary to the welfare of humankind, including the use of microbes as biological weapons. Bioterrorism violates the fundamental principles expressed in the Code of Ethics of the Society and is abhorrent to ASM and its members.
>
> ASM recognizes that there are valid concerns regarding the publication of information in scientific journals that could be put to inappropriate use as described in the CPC resolution mentioned above. Members of the ASM Publications Board will evaluate the rare manuscript that might raise such issues during the review process. However, as indicated elsewhere in these Instructions, research articles must contain sufficient detail, and material/information must be made available, to permit the work to be repeated by

[2] ASM publications include: Antimicrobial Agents and Chemotherapy, Applied and Environmental Microbiology Clinical and Vaccine Immunology, Clinical Microbiology Reviews, Eukaryotic Cell, Infection and Immunity, Journal of Bacteriology, Journal of Clinical Microbiology, Journal of Virology, Microbiology and Molecular Biology Reviews, Molecular and Cellular Biology

others. Supply of materials should be in accordance with laws and regulations governing the shipment, transfer, possession, and use of biological materials and must be for legitimate, bona fide research needs. Links to, and information regarding, these laws and regulations can be found at http://www.asm.org/.

Science and Social Responsibility

Biomedical research produces many important benefits for society but announcements and uses of those results need to be handled appropriately. Last year we focused on dual use research and this year we want to continue the theme by talking about three important issues: the potential consequences of publishing results from studies of specific human populations; how announcements of new discoveries are made to the public through the press; and how materials can/should be shared with collaborators.

Case 1 – Potential Consequences of Epidemiological Studies

In 1988, investigators from the NIH and A & T University launched a longitudinal study of a population living in an Appalachian county in the U.S. People enrolled in the study were healthy adults, aged 18-65. The population was 90% white, 4% Native American, 4% black, and 2% Asian. The goals of the study were to (1) estimate incidence of different types of cancer and (2) identify genetic and environmental factors related to cancer in this population. To promote the study and enhance recruitment efforts, the investigators collaborated with influential organizations in the community, including the public health department, a local medical clinic, the county commissioners, the local newspaper, and several churches. They formed a community advisory board that included representatives from these different organizations and was very supportive of the research project. The investigators promised to share their results with the board prior to publication.

The investigators recruited 7,500 subjects from this population of approximately 100,000 people to participate in the study. At enrollment, information about diet, smoking, work, exercise, behaviors, and various environmental exposures was recorded, and samples were taken for genetic analysis. Over the years, changes in health behaviors and outcomes (such as disease and mortality) were also recorded. Now that the study has been going for 20 years, there have been sufficient numbers of cancers for the investigators to obtain some interesting results. The population has a lower incidence of colorectal, breast, and ovarian cancer (compared to the U.S. population), but a higher incidence of prostate and testicular cancer, alcoholism, substance abuse, dementia, promiscuity, and HIV/AIDS. The researchers have also identified genetic and environmental factors associated with increased or decreased risk of some types of cancer in the population. When the investigators discuss these results with the board, the board members are pleased to learn about the cancer results, but they are disturbed to learn of the higher risk of the other outcomes, including those that are considered to reflect health behaviors that might reflect poorly on their community. The investigators assure the board that they will not mention the name or precise geographic location of the community in any publications, but the board is concerned that people will still be able to use some of the demographic and genetic information that is published to identify the community and that this will bring shame to the population and potentially affect access to health care. They ask the investigators to publish only the “less controversial” results.

How should the investigators handle this situation? Should they publish only the "less controversial" results? Does the form of the investigators' "promise" make a difference, e.g., oral vs. in writing?

Does the wording of the original consent obtained for the study affect how the investigators might handle this situation? If the purpose of the study broadened beyond the focus on cancer, what should the investigators have done at that time?

Should they publish the study after removing data that could be used to identify the population? Does it make a difference if the data might identify only the county being studied, rather than specific population groups or individual subjects? What if these data are crucial to the study?

How could this situation have been prevented? How specific should the investigators' "promise" to the community have been?

The ***Nature*** editorial (Nature 461:1174, 2009) **Mind the Spin** addresses comparable issues related to a press release on a clinical trial and is directly relevant to both this case and the next one.

Mind the spin

Scientists — and their institutions — should resist the ever-present temptation to hype their results.

The circumstances surrounding the recent announcement of results from an HIV vaccine trial in Thailand are troubling. The sponsors of the US$119-million phase III clinical trial, a consortium led by the US Army, the National Institutes of Health and the Thai government, announced on 24 September that the trial had been a success: an analysis of the data showed that the vaccine had a statistically significant effect on preventing infection.

Other scientists could not immediately assess that claim, however: the full data from the trial were not made available until 20 October, when they were presented at an AIDS vaccine conference in Paris and in an article published online the same day (S. Rerks-Ngarm *et al. N. Engl. J. Med.* doi:10.1056/nejmoa0908492; 2009). The article contained two other data analyses, not mentioned in the initial announcement, showing smaller effects that were not statistically significant (see page 1187).

The trial's sponsors defend the premature announcement on the grounds that they had promised to inform the Thai people of the results first ; 24 September is also Mahidol Day, the anniversary of the death of the king's father and a day of national observance in Thailand. The sponsors also argue that announcing the less-upbeat analyses along with the positive result would have been too complicated for the public to understand ; they wanted to quickly deliver a clear-cut message on the trial's findings. Making the full data immediately available to scientists on 24 September would also have been impossible, they add, because of the conference and journal embargoes.

To their credit, the scientists involved did emphasize in their public statements that any vaccine effect was “modest”, and that the vaccine itself was of no immediate public-health utility. At the same time, however, they hammered home the message that this was “the first time an HIV vaccine has successfully prevented HIV infection in humans” , and implied that the event was somehow historic. Such statements, together with the selective initial presentation of the data, are well outside the scientific norms for presenting the results of clinical trials. They inevitably create suspicion that the trial sponsors may have put an excessively positive spin on results that are far from clear-cut, in a trial that has long been controversial (T. V. Padma *Nature Med.* **10,** 1267; 2004) . The trial has also been six years in the works, and so there seems no particular public-health urgency to justify publication by press conference.

Fortunately, such stories are still rare in science. Witness the way scientists have behaved since the beginning of the current H1N1 flu pandemic, in which the urgent threat to health creates legitimate tensions between getting results out fast and respecting peer review. Most researchers have negotiated this tension well, through a combination of fast-track publication by journals and online pre-publication sharing of preliminary data —but not through hyping their results.

Yet the temptation for scientists and their institutions to spin their research to the media, or to go publicity-mongering, is always there. And — as illustrated by the excessive public-relations campaign surrounding Ida, a fossil presented as a missing link in human evolution (see *Nature* **459,** 484; 2009 and **461,** 1040; 2009) — too many in the media will buy into the initial hype.

Such behaviour is corrosive to the process of scholarly scientific communication. Research institutions must not allow it to become the norm.

Case 2 - Scientific Research and the Press

Ms. Newby, a graduate student, is interested in factors that control prion replication, and joins the lab of Dr. Bigshot, an expert in prions. Ms. Newby decides to artificially express the gene coding for prion protein in various mouse tissues, and investigate which ones are conducive to replicating prions upon infection. After three years of work, she finds that in this overexpression model system, some tissues (including muscle) permit prion replication, while other preclude the replication process. She and Dr. Bigshot write up these findings into a paper that is accepted by FancyJournal. A week before the paper is due to appear, Dr. Bigshot provides Ms. Newby with a draft Press Release titled “Scientists find Prions Replicating in Meat” that FancyJournal has prepared.

Ms. Newby is very excited that her first paper has generated so much interest. However, when she reads the press release, she finds that it is almost exclusively focused on one small aspect of the paper: that muscle is capable of replicating prions. Ms. Newby further discovers that the press release fails to mention that this work was done in artificially engineered mice. Moreover, the press release, and various quotes attributed to Dr. Bigshot, exaggerate the dangers of eating meat even though the new work does not provide any reason to believe muscles are a normal source of prions. Recent publicity about the Bovine Spongiform Encephalopathy (BSE) epidemic in British cattle and a resultant rise in Creutzfeld-Jakob Disease in humans, thought to be due to eating the BSE

infectious agent, a misfolded prion protein, which is present in meat, has made people around the world worried about eating beef. Ms. Newby is concerned that readers of this press release will get an inaccurate view of the paper's findings, and she brings up her concerns with Dr. Bigshot.

Dr. Bigshot dismisses her concerns; he says that the press always exaggerates findings, and that the excitement generated will be good for her career. Plus, he says he doesn't have any control over what the press chooses to write, and the actual press release does not contain any false statements.

What are your responsibilites in conveying research to the non-scientific community accurately and fairly?

What are the NIH guidelines regarding communications with the scientific and non-scientific press? Are they different if the communication is oral versus written?

Is there a difference between inaccuracies versus selective reporting and what does this example represent?

What control do authors have regarding press releases prepared by journals?

What recourse do authors have if journals or the popular press mis-represent their research? What if you were contacted by a journal to comment on someone else's new research?

You may find it useful to try a mock interview, using the suggested interview questions below:

Mock Interview between Dr. Bigshot and a writer for the Vegan Society Newsletter, an online publication:

A PI should volunteer to be Dr. Bigshot
A fellow should volunteer to be the interviewer

Two ***Nature*** editorials directly relevant to the topic of the press and scientists:

Caught on Camera, Nature 461:848, 2009

Cheerleader or Watchdog, Nature 459:1033, 2009

CASE 3: Intellectual Property – Why Use an MTA

A Material Transfer Agreement (MTA) is utilized when any proprietary material is exchanged, and when the receiving party intends to use it for his/her own research purposes. Neither rights in intellectual property nor rights for commercial purposes may be granted under this type of agreement. MTAs define the terms and conditions under which the recipients of materials, provided by either the NIH scientist or the other party, may use the materials. Included in the MTA are the requirements that the materials be used for research purposes only and that the materials cannot be used in human subjects. The purpose of a Cooperative Research and Development Agreement (CRADA) is to make Government facilities, intellectual property, and expertise available for collaborative interactions to further the development of scientific and technological knowledge into useful, marketable products.
Contact the Technology Development Coordinator
<http://ott.od.nih.gov/nih_staff/tdc.aspx> for your institute for further information.

There was a real case in the early 2000s in which use of an MTA might have reduced the problems faced by a scientist (Science, 299: 489, 2003). As reported in Science 303:1743, 2004, Dr. Thomas Butler, a professor of microbiology at Texas Tech University, captured national headlines in January 2003 after he reported that 30 vials of plague bacteria that he had originally collected in Tanzania were missing from his Texas Tech laboratory, sparking a bioterror scare and a massive investigation. The government ultimately charged Butler with 69 counts of lying to investigators, which included moving the bacteria without proper permits. He was found guilty of just three plague-related offenses, all linked to a mismarked Federal Express package containing plague samples that Butler sent back to Tanzania. In his defense, Dr. Butler said the "export of bacteria to Tanzania was done for humanitarian reasons ... so that the Tanzanians could continue their research in this area that we started together. The specimens arrived safely. No one was harmed." Judge Cummings noted that "very few cases brought before this court have the potential to impact not only science, medicine, and research, but society as a whole." Butler was sentenced to 2 years in prison for mishandling plague samples that he mailed to Africa, as well as defrauding Texas Tech University, and was required to pay back the university more than $300,000.

Case 3

Part A. Claudia is a postdoctoral fellow in Dr. Smith's lab. She has been using a vaccinia virus expressing PanCa, a novel pancarcinoma antigen, to treat tumor-bearing mice. After publishing her initial results, she received an email from Dr. Barnes, a researcher in California, who requested the virus for some experiments he was doing. She talked with Dr. Smith who agreed that this would be a good collaborative project for them.

She shipped samples of the virus to Dr. Barnes. Six months later, Claudia is shocked to learn about a press release proclaiming that Dr. Barnes is the PI of a new phase I clinical trial using vaccinia expressing PanCa.

What could Claudia or Dr. Smith have done to ensure proper use of the virus?

Should they have used an MTA to provide the samples to Dr. Barnes?

How does one balance between making reagents available, preserving NIH intellectual property rights, and protecting patients from experimental agents?

Part B. Jeffrey is a clinical fellow working with Dr. Jane. They have a clinical trial utilizing a novel vaccine. One of the endpoints of the trial was a serologic analysis for the formation of new antibodies to tumor antigens. The laboratory they had been working with had recently undergone some personnel changes and could no longer do the analysis. Dr. Jane remembered her colleague, Dr. Mann at the University of Wisconsin, who frequently did this analysis. A quick email to Dr. Mann confirmed that he would be willing to collaborate on this analysis.

Since the protocol already is IRB-approved and contains language about doing the analysis, does it need to be amended to state what laboratory is doing the analysis?

Does an MTA need to be executed?

Points to Consider

- Clinical or epidemiological studies are often carried out on very specific populations, who might be identifiable because of their uniqueness – great care is required at the start of the study to ensure that none of the results could negatively impact the study population.

- Care needs to be taken in announcing one's results through the press since there is an inherent conflict between the press's desire for an exciting announcement and the ability of patients and their families, who are generally not scientists, to evaluate whether a new scientific result is directly and immediately applicable to their disease.

- Presenting one's results in any public forum, including a seminar or a meeting or conference, can impact the ability to obtain a patent on a discovery.

- NIH intramural scientists have an obligation to make reagents or other research materials developed in the course of their work widely available for research

purposes. At the same time, they need to be cognizant of the regulations that govern such sharing, and utilize mechanisms such as a Material Transfer Agreement (MTA) or even establishment of a Cooperative Research and Development Agreement (CRADA) to protect the government's ownership of these materials.

Useful resources

Press Releases

NIH Manuscript Clearance Form – which asks if the science is newsworthy
http://www1.od.nih.gov/oir/sourcebook/oversight/pub-clear-form.htm

NIH Manual Chapter 1184 on Scientific, Technical, and Other Professional Information Presented by NIH Employees: Review, Approval, and Distribution
http://www1.od.nih.gov/oma/manualchapters/management/1184/

Woloshin S, Schwartz LM. Press releases: translating research into news. JAMA 287:2856-8, 2002.

Woloshin S, Schwartz LM, Casella SL, Kennedy AT, Larson RJ. Press releases by academic medical centers: not so academic? Ann Intern Med 150:613-8, 2009

Stamm K, Williams JW, Hitchcock NoëlP, Rubin R. Helping journalists get it right: a physician's guide to improving health care reporting. J Gen Intern Med 18:138–145, 2003.

Wilson A, Bonevski B, Jones A, Henry D. Media reporting of health interventions: signs of improvement, but major problems persist. PLoS One. 4:e4831, 2009.

Rensberger B. Science journalism: Too close for comfort. Nature 459:1055-6, 2009.

Sharing of Research Materials

NIH Guide for Sharing Resources
http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/resources.htm

Material Transfer Agreements & CRADAs
http://ott.od.nih.gov/cradas/model_agree.aspx

Model MTA
http://ott.od.nih.gov/forms_model_agreements/forms_model_agreements.aspx#MTACTA

Uniform Biological Material Transfer Agreement (“UBMTA”)
http://ott.od.nih.gov/pdfs/UBMTA_Master.pdf

Case #1 - Whistleblowers

Dr. Florence Chase was a prominent geneticist working in a well-funded Midwestern University. When one of her students, Betsy Turner, was given a few pages of one of Dr. Chase's grant applications to help her get started on a new research project, she recognized data from a previous lab publication that was identified as unpublished in the proposal. She mentioned this worry to another more advanced student in the lab, Tom Kennedy, who was already working in the area described by the grant application. Looking at the proposal, Tom noticed that there was one experiment describing his work that had never actually been done!

The students then sought advice from other scientists from outside the department who counseled them to bring their concerns to Dr. Chase and document their actions. Tom Kennedy brought his concerns to Dr. Chase who denied wrongdoing and said the data included were probably just "placeholders" she had forgotten to remove before submission. She mentioned that she would take corrective actions to inform the funding agency.

Questions

1. Did the students act appropriately in confronting Dr. Chase about the issue?

    A. What were Betsy Turner's options before going to Tom Kennedy for advice?

    B. What other options did the students have other than confronting Dr. Chase?

2. Given Dr. Chase's claim that an innocent error was made, what are the student's responsibilities to the funding agencies involved?

    A. Should the students follow-up on Dr. Chase's assurance that she would contact the funding agency? Who might they consult to make sure that she corrects the situation?

    B. What other actions might the students pursue if they are unsatisfied with Dr. Chase's response?

What are the responsibilities of the Department to protect the interests of the students in this case?

If the lab is closed because of the incident, students risk losing years of graduate work. Should a graduate program alter its criteria for granting a Ph.D. if the student's graduate advisor is proven to be guilty of misconduct?

Resources

Science Article:
http://www.sciencemag.org/content/313/5791/1222.full

ORI ruling:
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-130.html

Related content:

http://www.uwalumni.com/home/alumniandfriends/onwisconsin/owspring2008/worms.aspx

http://scienceblogs.com/ethicsandscience/2007/06/06/whistleblowing-the-communitys/

http://www.biotechniques.com/news/biotechniquesNews/biotechniques-302891.html

C.K. Gunsalus, “How to Blow the Whistle and Still Have a Career Afterwards,” *Science and Engineering Ethics*, Vol. 4 (1998), 51-64.

Case #2 - CLUES: Research Misconduct or Sloppy Science?

Professor Plum has taken on a new graduate student, Rose Scarlett, as part of an overseas exchange program. Her graduate program mandates attending their extensive training in research ethics and record keeping. She integrates easily into the lab culture, making friends, but seems very secretive, almost protective of her data. Her project is part of a collaboration with another exchange student, Grey Pu Pon, and a Research Fellow, Dr. Byrdie Peacock, who oversees the project for Professor Plum.

As the work progresses, Dr. Peacock believes the three should meet regularly to go through their data. At first, Rose brings in her results, usually in the form of finished tables or graphs, but gradually finds excuses to miss the meetings. Rose also never discusses her work with Grey. When Byrdie goes to Rose directly to go over the original data for one of her figures, Rose cannot produce the data. She claims that because the figure was finished, she deleted the original files from the lab computer associated with the image processer. Byrdie cannot find it in Rose's file on the lab's back-up server. When pressed to look at her notebook, Rose sends Byrdie the data she was unable to produce, claiming she had it on a memory stick but had forgotten about it.

Several months later, Dr. Peacock believes they have enough information and a good story to begin assembling figures and data for a manuscript. By now, Byrdie has seen several versions of a figure with Western blots that Rose had been working on. They appear similar, but have subtle differences. Rose provides yet another figure of the blots, again different from the previous versions. Byrdie insists that Rose produce her lab notebook.

Byrdie finds that experiments and data in most cases are not dated and that data sheet printouts for other assays are minimally labeled or have nothing at all by way of documentation. They are just stuffed in randomly. Of greater concern is the fact that the lanes of the original gel images for the Westerns have no labels for treatment conditions. When pressed for an explanation, Rose claims that she felt rushed to produce a final product. The last figure has been labeled directly and represents the primary data. She apologizes but maintains that the final figure she provided is the correct representation of the experiment.

Research Misconduct or Sloppy Science?

- Are there problems regarding data management, and if so, what are they?
- Who is at fault? Was there a role for Professor Plum?
- What is your opinion of Rose's explanation?
    - Is pressure-internal or in relation to a job application- ever a legitimate excuse for being sloppy?
    - What is an appropriate response to pressure?
    - Would your opinion change if Rose had had previous training in ethics and record keeping?
- How could this situation have been prevented?
- Can you show all of the primary data for each experiment you performed a year ago?
- Can your experiments be reproduced by someone else from your lab notebook?

Review the elements of a good record keeping and contents for a lab notebook
http://sourcebook.od.nih.gov/ethic-conduct/RECORDKEEPING.pdf

Case #3 - Data Management in Clinical Studies

Scene 1: Dr. Abadayo, a post-doctoral fellow in Dr. Hidalgo's section, is reviewing clinical data for the Results section of a manuscript the two are preparing. She notes that data for 60 of the 180 research participants in the study data base are not fully consistent with the primary source data in the participants' electronic medical records. Data for the remaining 120 participants are accurate. Dr. Abadayo is concerned that these discrepancies may jeopardize publication of the manuscript.

What should she do next?

Check the data again?

Review the data collection and data entry procedures with clinical staff?

Bring her concerns to Dr. Hidalgo, the principal investigator of the clinical study?

Scene 2: Dr. Abadayo presents her concerns to Dr. Hidalgo. He downplays the significance, given that two-thirds of the data are clearly correct. He suggests that Dr. Abadayo review the data collection and data entry procedures with clinical staff to identify possible sources of error.

Does the proportion of questionable data influence the seriousness of the matter and the response?

Who has responsibility for investigating this situation?

Scene 3: Dr. Abadayo finds that clinical staff used different procedures for abstracting study data from the electronic medical records and for entering it into the study data base for statistical analysis. She believes that this variability accounts for the inconsistencies that she discovered.

Do the procedures of this study reflect good clinical practice?

How can one distinguish sloppy clinical practice from research misconduct in this type of situation?

Does this distinction matter?

What steps could the investigators have taken before the start of the study to avoid this problem?

Scene 4: Dr. Hidalgo is pressing Dr. Abadayo to complete the Results section of the manuscript so that it can be submitted for publication. Dr. Abadayo is hesitant because the data discrepancies she observed make her question the validity of her initial statistical analyses.

What steps can Dr. Abadayo take to ensure the validity of the findings?

If Dr. Abadayo cannot fully resolve her doubts about the data from the 60 participants, what should she do?

Re-analyze using only data from the 120 participants whose data she is confident about?

Use all the data, reconstructing the questionable data as best she can?

Take another approach?

What role might the study Sponsor (if any) or approving IRB play in this situation?

Source: Adapted from a case in Shamoo, A., & Resnik, D. (2003). *Responsible Conduct of Research*. New York: Oxford University Press.

Case #4 – Nepotism in the Training and Research Setting

Dr. Julie Brand is a Section Chief in NCI's Intramural Research Program. Her daughter, Sally, is just finishing college and very interested in a medical career, but wants a year off to help her decide her next steps. Dr. Brand suggests that she apply for a post-bacc IRTA position at the NIH in an area of research that interests her. (Dr. Brand has post-bacc IRTA students in her own lab, and views the position as an important stepping-stone for talented students to become successful scientists.) Sally submits her application, and after two weeks mentions to her mother that the reference letters haven't arrived. In order to help Sally, Dr. Brand begins checking on the status of her application at the OITE Online Application System website, and when it is complete, she suggests a few good laboratories that Sally might focus on.

Questions

1. Is it proper for Dr. Brand as an NIH scientist to, a) encourage her daughter to pursue a biomedical career? b) review her daughter's online OITE IRTA application? (What if Brand was an A.O.?)

Sally emails several NIH P.I.s and indicates her interest in their work. However, despite initial positive replies, no offers are forthcoming. The situation leaves Sally defensive and Dr. Brand puzzled based on Sally's strong academic record and honors in science. Being a concerned parent and a scientist who knows what makes an application stand out, Brand decides to review Sally's online application and notices that one of the recommendation letters is a carelessly written draft version.

Questions

2. Why is it important that OITE applications (including reference letters) be kept confidential?

3. If Dr. Brand is contacted by an NIH colleague who is considering Sally for a post-bacc IRTA position, may Brand offer an opinion about Sally's strengths and weaknesses? May she mention anything about Sally's recommendation letters?

Over lunch one day, Dr. Brand bemoans Sally's situation to an NIH colleague she is close to, suggesting that the poor recommendation letter was an innocent mistake that could easily be corrected. Dr. Brand's friend points out that the NIH post-bacc IRTA website clearly states that access for the purpose of inspecting applications of relatives or friends is strictly forbidden. Dr. Brand is surprised to hear this, re-visits the OITE Online Application System website (appended below), and verifies that such use is indeed strictly prohibited. She resolves never to violate the rule again. In the end, however, Sally gets no offers, after which Dr. Brand approaches her NIH colleague and asks him if he would take her on in his lab.

Questions

4. Has Dr. Brand engaged in nepotism? If so, when?

5. Who is harmed by violations of nepotism policies in place on the NIH campus?

6. If you are approached by a close friend or relative seeking employment for themselves or their own children at the NIH, how should you respond?

The NIH has formulated specific guidelines for the conduct of employees in supervisory or administrative positions with respect to the employment of relatives and friends. It can be found at http://oma.od.nih.gov/manualchapters/person/2300-310-1/2300-310-1.pdf.

NIH OITE Online Application System - Terms of Use Agreement

Important: Clicking the "I accept" button below constitutes your acknowledgment that you have read and agree to follow the Terms of Use.

Warning Notice

This is a U.S. Government computer system, which may be accessed and used only for authorized Government business by authorized personnel. Unauthorized access or use of this system may subject violators to criminal, civil, and/or administrative action.

All information on this system may be intercepted, recorded, read, copied, and disclosed by and to authorized personnel for official purposes, including criminal investigations. Such information includes sensitive data encrypted to comply with confidentiality and privacy requirements.

Authorized Use

Collection of the information in this system is authorized under 42 USC 282(b)(10), 282(b)(13), 241, 242l, 284(b)(1)(C), 284(b)(1)(K), 42 CFR Part 63, and 42 CFR Part 61, Subpart A. The primary use of this information is to evaluate applicants' qualifications for research training at the NIH.

The information collected is subject to the Privacy Act, and is collected and maintained in accordance with the following Privacy Act Systems of Records Notices: 09-25-0158, "Administration Records of Applicants and Awardees of the Intramural Research Training Awards Program;" 09-25-0014, "Clinical Research: Student Records;" and 09-25-0108, "Personnel: Guest Researchers, Special Volunteers, and Scientists Emeriti."

You are responsible for safeguarding the data in this system in accordance with the above notices. For more information regarding your responsibilities, see the NIH IT Rules of Behavior, the NIH Information Technology (IT) Privacy Program, and the Secure One HHS Web site.

Examples of ***unauthorized*** access or use of this system include:

- Disclosing your login credentials to a colleague.
- Accessing the application of a relative, friend, or child of a friend for any reason. Please refer to the NIH Manual Chapter on Nepotism; 2300-310-1.
- Sharing system data, including letters of recommendation, with individuals who are not authorized personnel.
- Sending applicant data via unencrypted e-mail.
- Storing system data on portable devices such as laptops, PDAs, or USB drives.

This list is not exhaustive. If you have questions regarding authorized access or use of this system, contact OITE at 301.496.2427.

Refer any FOIA requests to the NIH Freedom of Information Act Office. You can find Privacy Awareness Training at both the NIH and HHS Web sites.

I accept | I decline

Introduction: Differentiating between Honest Discourse and Research Misconduct

(*When is it research misconduct versus honest scientific difference of opinion?*)

During just the past couple of years within the NIH Intramural Research Program, nine cases have required formal Inquiry committee examination for scientific misconduct, and four cases have already proceeded to full-scale Investigations. NIH staff engaged in this very stressful, time-consuming process included two tenured investigators, one tenure-track researcher, eight trainees, and a support staff member. Concerns raised about their research have included deliberate falsification of data, data manipulation, misrepresentation of findings, and authorship issues (which are not research misconduct). This is alarming.

Recently a finding of misconduct in the extramural community resulted in a 366-day Federal prison term for a scientist because his actions led to loss of government funds, obstruction of justice, and abuse of a position of trust. The sentenced scientist had the following explanation for his actions:

"First, I believed that because the research questions I had framed were legitimate and worthy of study, it was okay to misrepresent "minor" pieces of data to increase the odds that the grant would be awarded to UVM and the work I proposed could be done. Second, the structure at UVM created pressures which I should have, but was not able to, stand up to. Being an academic in a medical school setting, I saw my job and my laboratory as expendable if I were not able to produce. Many aspects of my laboratory, including salaries of the technicians and lab workers, depended on my ability to obtain grants for the university. I convinced myself that the responsibility I felt for these individuals, the stress associated with that responsibility, and my passion and personal ambition justified "cutting corners". Third, I cannot deny that I was also motivated by my own desire to advance as a respected scientist because I wanted to be recognized as an important contributor in a field I was committed to." Underlying this case was the issue of inappropriate data management, which was detected by one of the scientist's staff. He admitted to destruction of electronic evidence of his falsifications and fabrications, among other things.

Scientific misconduct is detrimental to all parties involved. Everyone in a lab has a responsibility to be informed and vigilant about appropriate data management to prevent instances of scientific misconduct. It is also important, however, to distinguish between misconduct, bad behavior, and honest differences in opinion.

Some of the following scenarios are based on actual misconduct cases. Choose to present 2-3 cases from 1-4 and one of the Research Reproducibility cases.

Case #1 – Handling of Images and Graphs

Case #2 – A Technically Challenging Method Collides With a Hot Topic

Case #3 – Handling of Clinical Data

Case #4 – Sources of Potential Bias and Data Sharing

Case #5 – Research Reproducibility I: Sample Composition and Reproducibility

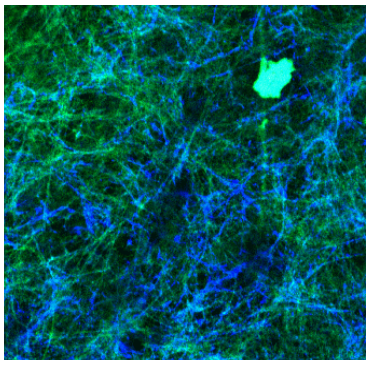
Case #6 – Research Reproducibility II: Prostate Cancer Serum Biomarker Study

Case #1 – Handling of Images and Graphs

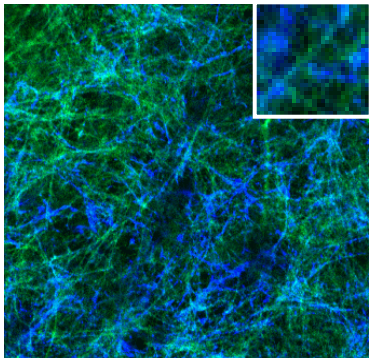
Dr. Gomez is preparing a manuscript for submission to a prominent journal and is trying to decide the best way to present her image and gel data. Other postdocs in the lab tell her that her results will have to look "clean" to be able to impress the editors and reviewers. She comes to you for advice about the following potential figures.

Imaging data

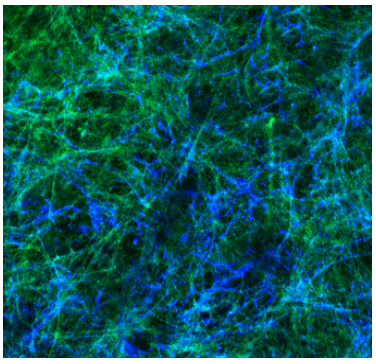
She complains that the best fluorescence images of her protein called "excitin" often have an unexplained bright blob of material that looks like junk and will be distracting to readers. She debates what to do, including covering it up with an inset, fixing the problem by masking the junk using the "clone" function in Photoshop, or by cropping the picture.



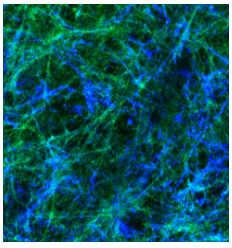
Original with "junk"



Covered up by inset



"Fixed" with Photoshop



Cropped out

What is your advice?

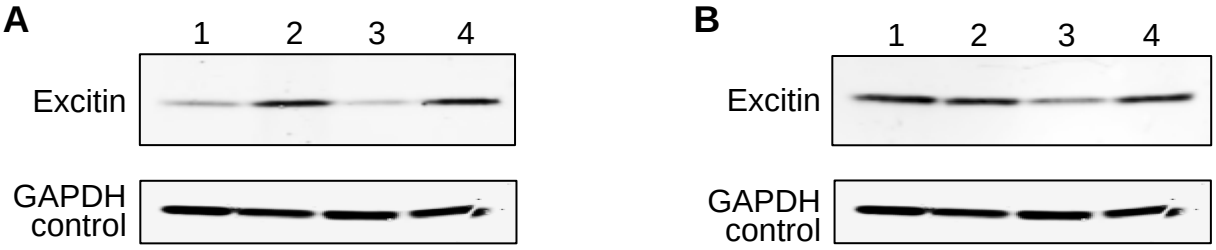
Does any approach constitute research misconduct?

What are the ethical boundaries of what data you show, and what is a "representative" image or other form of data?

Might something be missed by omitting "junk" from figures?

Gels and controls

Dr. Gomez receives the following gel images from Dr. Brown showing changes in excitin expression with different drug treatments.



Do you notice anything strange about panels A and B?

Is this permissible?

Is there any concern about showing a single part of a gel, i.e., only showing the band of interest?

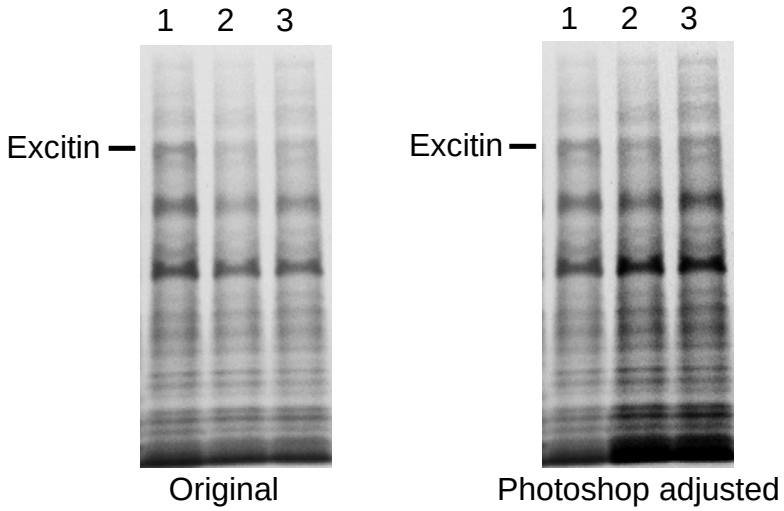
Dr. Gomez saw the same pattern of reduced excitin in lanes 1 and 3 shown in panel A in two experiments, but not in a third repeat (panel B).

Can she present just the results shown in panel A?

How should you deal with experiments that "work" sometimes but not always?

Gels – brightness/contrast

Her next question to you involves her gels, where she thinks she probably accidentally loaded less into lanes 2 and 3. Dr. Brown tells her that she should just adjust the darkness of these lanes to look equal. He says this is permissible because it is involves changing the darkness of the entire lane, not just one band.

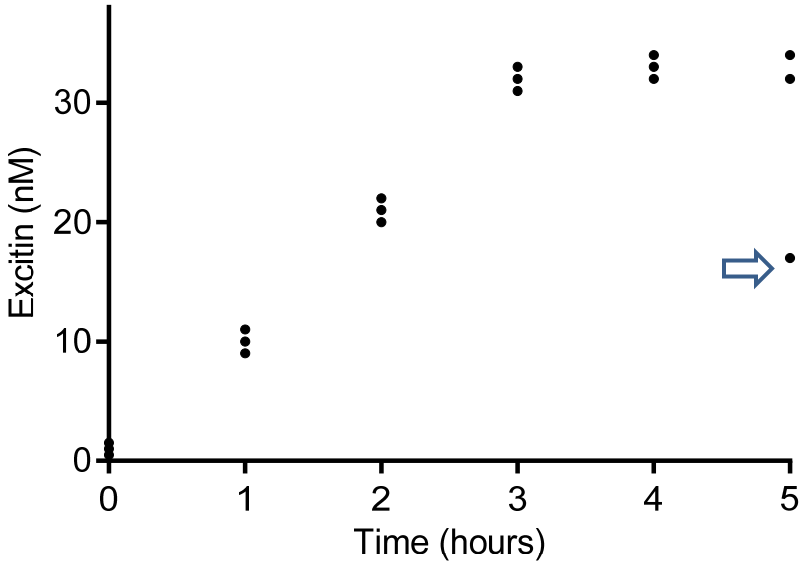


Is this change acceptable?

Why or why not?

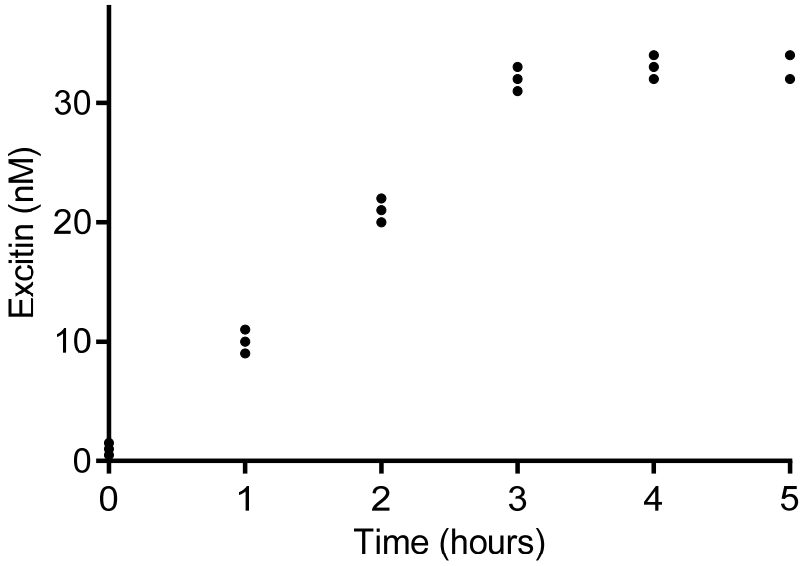
Data in graphs

Her collaborator, Dr. Blue, provides the following graph, saying that his supervisor advises that they should delete the single point that doesn't fit with the rest.



Can they omit the point because it is an obvious outlier?

What if Dr. Blue re-analyzes that specific data point with remaining sample and finds that the first analysis was in error – can he modify the figure to reflect the re-analysis?



They decide to just eliminate the outlier. Does anything else bother you about this graph?

If you were a lab colleague, what would you do?

What would you do if you were a journal editor, and a reviewer raised a concern about this figure?

Case #2 – A Technically Challenging Method Collides With a Hot Topic

(This case is based on an actual publication issue. The facts have been streamlined to highlight the ethical issues, rather than the science itself.)

"Cryo electron microscopy" or "Cryo-EM" is a method for determining macromolecular structures. The technique has been evolving for a couple of decades. Currently it is most suited for large particles such as ribosomes, proteasomes and viruses. Recent advances in sensitive electron detection, advanced computers for data collection, and application of estimates of expected structures have converged to produce a number of fascinating publications. Unfortunately, the controversial nature of some findings has touched off concern over journal peer-review practices. One recent publication of the structure of a viral surface glycoprotein complex has triggered an interesting set of articles about the method, its utilization for certain structural investigations, and the processes for data review by journal referees.

Part 1: Investigators determine the structure of the complex using cryo-EM and submit it to a journal. Peer reviewers, experts in cryo-EM, reject the paper on technical grounds. The authors then submit the same manuscript, virtually unchanged, to a second journal where – as luck would have it – one of the reviewers is the same expert who had seen the copy the first time. This time, he demands to see all of the original data before rendering his opinion. The authors supply some of the data but not all of it as he requested. Based on the information in the manuscript and the supplemental data to be published and upon the additional information provided by the authors, the reviewer again rejects the paper – this time providing extensive scientific and technical criticisms of how the authors' conclusions could be erroneous.

1. What do you think about the authors' decision to submit the same manuscript to a different journal without alteration? Should they have been required to inform the second journal that this paper had been rejected elsewhere?
2. Was the reviewer justified in requesting the complete data set? The reviewer agreed to maintain confidentiality of the data set; under these circumstances should the authors have agreed to provide the entire set?
3. Should this expert have refused to be a reviewer the second time around? Did he have an obligation to inform the editors that this paper had been submitted elsewhere?

Part 2: The authors submit the paper to journal number three, this time arranging for a selected set of reviewers. The paper is accepted and appears in print. Several experts in cryo-EM subsequently write letters to the journal that give substantial and technical criticisms of the paper and the application of the method as done by the authors. One critic [who turns out to have been the original reviewer] points out that incorrect application of appropriate controls can even allow investigators to deduce structures from the data where only random noise is actually present. In a response letter, the authors provide a detailed rebuttal to all of the criticisms and stand behind their findings.

4. What responsibilities do editors have to weigh standards of scholarship against the risk of losing out on publication of hot papers?
5. What other steps should the authors have taken in response to criticisms? Are they under any responsibility to withdraw the paper?
6. The experts did not attempt to repeat the experiments themselves. Rather, they performed re-analysis using the authors' published data. Should criticism be accompanied by attempts by peers to carry out the exact same experiments?

Part 3: Your journal club discusses all of these papers.

7. What lessons should your postdoctoral trainees learn from this series of events?
8. What obligations do authors, editors and reviewers have to ensure that adequate expertise is available when complex methodology is used and evaluated?

Case #3 – Handling of Clinical Data

Dr. Bob is a promising mid-career faculty member at Z University. His major clinical research project is a prospective, longitudinal study of changes over time in plasma levels of protein X and their association with cardiovascular disease. Previous cross-sectional studies by others suggested that protein X levels increase with age and are associated with increased risk of cardiovascular disease. A successful longitudinal study would be publishable in a high-impact journal and give a substantial boost to his achieving tenure.

Dr. Miriam, a resident at the Z University Medical School, approaches Dr. Bob for advice about a research career and he offers to let her help analyze data from the first 3 time points of his protein X study. She eagerly accepts this offer as an opportunity to gain research experience and perhaps co-authorship on a high-impact paper.

- When is it appropriate for Dr. Miriam to discuss her authorship status with Dr. Bob? Should she raise the issue now, before agreeing to analyze the data, or wait until after the results are known?

Dr. Miriam performs a statistical analysis on a spreadsheet provided by Dr. Bob, but her results are not consistent with the hypothesis Dr. Bob wrote in his grant applications as she found no association of Protein X with cardiovascular risk. When Dr. Miriam presents her analysis to Dr. Bob, he is noncommittal and suggests that she has incorrectly analyzed the data. He says he will check her work and the next week, Dr. Bob returns the spreadsheet to Dr. Miriam, explaining that he has corrected a few mistaken data entries. He asks her to redo the analysis.

- Should Dr. Miriam ask for an explanation of the data corrections? Would it make a difference if he used his home computer or his work laptop for checking her work?

When Dr. Miriam reanalyzed the data, the hypothesis was confirmed. However, she was puzzled that correction of "a few mistaken data entries" would so substantially change the outcome of the analysis. She compared the "corrected" spreadsheet with the study's case report forms and found that multiple data entries had been changed, always in the direction consistent with the hypothesis.

- Is it appropriate for Dr. Miriam to check the new spreadsheet against the case report forms (note that she did not actually participate in the trial)? Should she have just confined herself to the reanalysis given that she was not named in the trial protocol as a participant? Under what circumstances and who should have access to check a transcribed or secondary data set against the primary or source data?

When Dr. Miriam presented the data discrepancies to Dr. Bob, he blamed the apparent discrepancies on his own ineptitude with Excel and on his use of data imputed from statistical modeling, rather than actual measurements. Concerned about the situation, Dr. Miriam began secretly reviewing patient records. She found that many data entries in the spreadsheet had been changed from their original values and that some patients recorded as participating in the study did not actually exist. Based on her analysis, she began to consider lodging a formal complaint of scientific misconduct against Dr. Bob.

- Is Dr. Bob's explanation of the data discrepancies justifiable? Would it be appropriate for Dr. Miriam to independently discuss the general principles of the case with a bio-statistician for further insight?
- Is it appropriate in this context for Dr. Miriam to access patient records? Should she first have shared her concerns with someone in authority and gotten permission? Does this situation represent scientific misconduct? If so, what type of misconduct is it?
- Should Dr. Miriam have immediately lodged a formal complaint upon finding data altered?
- What other steps could she have taken before lodging a complaint? When would have been the best time to lodge a formal complaint of scientific misconduct?

Case #4 – Sources of Potential Bias and Data Sharing

Dr. Whitaker is the principal investigator for a retrospective, case-control study examining the relationship between cell phone use and three types of brain cancer (primary glioma, meningioma, or acoustic neurinoma) funded by the NIH. The study includes 1000 cases of brain cancer from the U.S., Canada, U.K., Germany, and France matched with 1000 controls from the same countries. The study asked both cases and controls to recall their cell phone use for a fifteen-year period and collected data on other risk factors, such as medical history, family cancer history, smoking, diet, and age. After analyzing the data, Dr. Whitaker found that cell phone use was associated with a 25% increased risk of brain cancer. Dr. Whitaker published his results in a top-tier epidemiology journal. One month after publication of the article, the editors of the journal informed Dr. Whitaker that they were planning on publishing a commentary critiquing the article's methodology. The editors want to give Dr. Whitaker an opportunity to respond to the letter in the same journal issue. The commentary cited a study published last year demonstrating systematic bias in recollection of cell phone use. The study showed that cases tend to overestimate their cell phone use, which would tend to bias research in favor of an association between cell phone use and brain cancer. The biasing effect increased with recollection time and was higher in European countries. The authors argued that if Dr. Whitaker's article had taken these factors into account it would have shown no significant association between cell phone use and brain cancer. The commentary was funded by the cell phone industry. The authors of the commentary contacted Dr. Whitaker and asked her to provide them with the original data from her study, so they could reanalyze it.

- How should Dr. Whitaker respond to these critiques?

- Should Dr. Whitaker provide any of the authors with original data?

- Should Dr. Whitaker have anticipated these possible critiques in developing the study design and in analyzing and interpreting the data?

- What role [if any] should the journal's original anonymous peer-reviewers play in responding to the critique? They were the ones who had approved the paper in the first place. Doesn't the journal's editorial board have a role in dealing with disputes arising from their published articles?

- If the question about the validity of the survey had been raised by scientists NOT funded by the cell-phone industry, what difference would that make to your answers to these questions?

Introduction to Enhancing Reproducibility, Cases 2014

Considerable attention has been focused on the inability of scientists and corporations to reproduce results of pre-clinical studies, especially those using animal models. Several papers[1], including a Nature Commentary by Drs. Collins and Tabak[2], expressed concern about this irreproducibility. NIH has been exploring issues affecting reproducibility and ways to improve scientific fidelity. In their Commentary, they announced that NIH will be taking the lead in developing a training module on enhancing reproducibility and transparency of research results emphasizing experimental design. This module should be ready within the year for testing. The following case studies for 2014 preview these ideas.

These case studies cover examples of specific areas of concern, which include

1. Deficiencies in reporting and bias
2. The importance of blinding and randomization
3. Defining exclusion criteria and how to handle 'outliers'
4. Determining correct sample size to reduce chance observations

[1] http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0007824
http://www.bwfund.org/newsroom/newsletter-articles/special-report-biomedical-research-are-all-results-correct
Special Report on Reproducibility
http://www.nature.com/nature/journal/v490/n7419/full/nature11556.html

[2] http://www.nature.com/news/policy-nih-plans-to-enhance-reproducibility-1.14586

Case #5 – Reproducibility I: Sample Composition and Reproducibility

Dr. Sanchez is a respected researcher who studies a fatal human neurodegenerative disease for which there is no effective treatment. He suddenly realizes that data from a cell culture model predict that a commonly prescribed cancer drug could prevent neuronal cell death. Dr. Sanchez asks his postdoc Dr. Fisher to test this hypothesis in a transgenic mouse model of the disease. Based on prior experience, they inject 6 animals with the drug and 6 animals with a vehicle control. Preliminary results are promising for these young mice: there is a 'trend' ($p=0.06$) showing 10% better neurological function in the treatment group. Based on this, Dr. Fisher injects another three animals with the drug and is happy to see that the results are now statistically significant ($p<0.05$). Although the normal phenotype was not fully rescued, they both agree that even a 10% improvement in patient function could be clinically significant, and the findings should be submitted for publication in a top-tier journal.

1. How should the animal group size and composition be determined? Is it legitimate to add more animals after the first group is analyzed? When should a study be repeated?
2. Would your opinion of the work change if you knew that the testing of neurological function was performed by the same person who injected each animal? What if the animals were assigned randomly to the control or treatment groups?
3. What if there had been 90% improvement in neurological function?

The journal sends the manuscript to two referees. Dr. Williams rates the paper highly and recommends accelerated publication because of the clinical significance. Dr. Johnson is unenthusiastic and concerned that the manuscript does not mention sample size estimates, randomization, blinding, or repeating. He also notes that the experiment used young animals, whereas the human disease occurs later in life. His review states: "To extrapolate these results to the clinical setting, the authors should replicate them, such as in a more reasonable model of the disease (i.e., in older animals.)"

Fisher and Sanchez immediately test aged mice, but to their surprise see no statistically significant effect ($p=0.35$). Nonetheless, because the initial results were so important, and because they included mechanistic in vitro experiments supporting the original hypothesis in the revised manuscript, they add a statement to the discussion: "Even though further preclinical development of the drug seems warranted, some caution may be needed because the effects in older animals are more modest (data not shown)." The journal editor is convinced by telephone of the importance of the study and accepts the article despite Dr. Johnson's remaining concerns.

1. At what point does failure to replicate an experiment become a concern?
2. How well can peer reviewing of articles address problems of reproducibility?

After publication, the article garners a great deal of attention. Several independent groups, including the company that markets the drug, try to replicate the initial finding, but all fail to show that the compound prevents neurodegeneration in animal models. A consortium of researchers asks the journal to publish a second paper refuting the study, but it declines to because the consortium "cannot present a new conceptual advance beyond negative data."

1. What mechanisms exist (or should exist) for publishing data that raise serious doubts about the validity of a published study?
2. Would having the raw data available in the original manuscript have altered the outcome?
3. Is there anything special about $p<0.05$?

<u>Useful references:</u>
Scott et al., Amyotroph Lateral Scler 2008; 9: 4-15
Simmons et al., Psychological Science 2011; 22: 1359-1366
Sullivan and Feinn, J Grad Med Educ 2012; 4: 279-282

Case #6 – Reproducibility II: Prostate Cancer Serum Biomarker Study

Dr. Simmons is an oncologist at the NIH Clinical Center whose translational research is focused on prostate cancer. In addition to seeing patients enrolled in his two active clinical trials, he has pursued studies of prostate cancer early detection biomarkers in collaboration with the mass-spectrometry (MS) laboratory of Dr. Wallace in NCI-Frederick in order to develop a screening test that performs better than the commonly used prostate-specific antigen (PSA) test. His most recent study includes a clinical series of 120 prostate cancer cases from which he has collected and stored pre-protocol fasting serum over the past 3 years. These samples were collected from the NIH Clinical Center, Howard University Medical Center and the University of Maryland Medical Center in Baltimore. Dr. Simmons brings the cancer case samples (previously aliquotted on four 30-well plates) on dry-ice with him to the monthly Wallace lab meeting, during which one of the post-doctoral fellows describes quality control (QC) and other findings from their new, highly sensitive ultra-high performance LC-MS / GC-MS metabolomic platform capable of identifying over 800 serum metabolites. After the meeting, they discuss the new study, and Wallace mentions that she has serum samples from 120 control subjects as well as additional serum QC duplicate samples ready for assay, and the set of four cancer case plates and five control subjects/QC plates are run the following week with excellent reproducibility within the duplicate serum QC samples. Multivariable analysis shows a significantly different metabolic pattern in serum from the prostate cancer cases compared to the control subjects ($P<0.0001$), with substantially higher pyruvate and acetoacetate concentrations in the cancer cases.

1. What are the implications of having only cancer case serum on some plates, with control and QC samples on other plates?

2. Was the manner in which control subjects selected appropriate? What if women were included?

3. Are there potential biases from having cancer cases enrolled in three different clinics?

Drs. Simmons and Wallace are excited by the findings, and calculate that the sensitivity and specificity for both compounds are 95-99%, which is far better than that reported for serum PSA by most investigators. They may have discovered a new prostate cancer screening test. They hurriedly draft the manuscript, obtain NCI clearance, and send the report to the New England Journal of Medicine (NEJM). Despite generally positive reviews the manuscript is returned to them for revision. The most critical comment is from Referee #1 who questions the biological plausibility of prostate tumors causing an elevation in serum pyruvate and acetoacetate, and asks that a more detailed description of sample collection, handling, and storage be added to the methods. Dr. Simmons asks his clinical fellow to track down the information from the Wallace lab and check the literature for any information relevant to their results. The fellow reports back that the serum from the control subjects were collected appropriately and frozen at -80oC in 7.5 ml aliquots immediately after their collection 5 years ago, but that they were thawed and re-aliquotted into 1 ml vials 2-3 years later. Dr. Wallace cannot find documentation in her lab regarding who re-aliquotted the samples and how it was done, or any information about the control subjects (e.g., age, gender, or fasting status). At the same time, the clinical fellow finds a recent article describing degradation of several blood metabolites following multiple thaw-refreeze cycles.

1. After discussing their data, Wallace and Simmons are unsure as to whether the sample handling and storage are responsible for the metabolite difference in their data. Is there anything they can do to address this?
2. Who should have been responsible for lab documentation of the control subjects' serum processing?
3. Having reviewed their data, Wallace and Simmons decide to withdraw their manuscript from the NEJM. What can they do to make their data and report acceptable to another journal?

Comments and Guidelines for NIH Ethics Cases 2014

- The honest and accurate presentation of scientific findings is the most important thing a scientist can do. Illustrations must provide an accurate representation of the data obtained.

- Many recent cases of scientific misconduct in both the intramural and extramural communities involve inappropriate data manipulation using programs (such as Photoshop) or inappropriate statistical analysis. As a result, journals now analyze images to detect inappropriate manipulations and often obtain separate statistical reviews of submissions.

- Changes in brightness, contrast, etc. should be applied simultaneously to all panels in a figure, including positive and negative controls. Parts of images or graphical data should not be arbitrarily modified. For digital images, the original data file must always be kept, with its original name (as recorded in a notebook); subsequent modified versions, and versions finalized for publication must be maintained as separate files.

- For safety, two copies/versions of data should be kept (e.g., original + figure version, two hard copies, hard copy + scan, computer file + backup, etc.).

- When a new technique is introduced into a laboratory, it should be validated by rigorous positive and negative controls.

- When experiments do not "work" every time, more science can often be learned by thorough trouble-shooting than by just repeating the experiment. Controls should always be part of the repeat experiments, because they will tell you something about outliers, loading differences, etc.

- Using an appropriate number of experimental animals is important both for statistical considerations and for the ethical implications of animal usage. Power calculations are required in human clinical studies and can be helpful in guiding animal experimental designs, including by having the investigator think about statistical approach ahead of time. Adding new animals or samples merely to reach an arbitrary level of statistical significance can be risky and lead to false-positive findings.

- Carefully consider and report choice of sample size, and when appropriate, the use of randomization, blinding, numbers of repeat experiments, any exclusions, and failures of replication. Many journals now require such reporting explicitly and it is good practice to gather this information before submission so it can be critically evaluated by the submitting laboratory before being even more critically reviewed by an external referee.

- Mechanisms are needed to publish data that raise serious doubts about previously published studies. It is always appropriate to have differences of opinion on data interpretation, and being wrong is not an ethical issue! However, having robust data and access to all datasets including those where data doesn't replicate is important to be able to have those discussions.

- The scientific integrity and credibility of clinical trial data depend on sound trial designs, with clearly identified primary and secondary endpoints and a description of statistical methods to be employed. This is a requirement for clinical studies under the jurisdiction of the FDA.

- Appropriate case and control subjects should be carefully selected in order to avoid potential bias, and their biospecimens (e.g., blood) should be collected, processed, stored, and assayed similarly.

- Lab notebooks should be thoroughly documented, and methods sections in manuscripts should provide detail sufficient to permit replication of the study.

- Institute/Center clearance is required for all NIH intramural manuscripts.

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Theme 16 - Research Reproducibility (2016)

Biomedical research is critically dependent on accurate and reproducible research publications. A loss of faith in the scientific literature would not only hinder further research advances and development of new clinical therapies, but it might also undermine public trust and funding. A number of recent articles have raised concerns about research reproducibility, noting that they only rarely involve research misconduct. Instead, problems encountered in replicating the work of others can have multiple causes, ranging from differences in approaches, materials, or scientific rigor, to insufficient information about methods. This case study addresses many of the potential experimental design issues, practices, and pressures that can undermine research reproducibility.

Because this important topic is both broad and provocative, with issues that could be discussed for hours, discussion leaders and participants will need to identify ways to keep the discussion on schedule. Three potential alternative approaches to this are: (a) keep discussion of the entire case concise and well-paced; (b) discuss a selected subset of the sections, labeled by Roman numerals, that are the most relevant to the particular IC and audience, and/or use only selected questions; or, (c) dedicate more than one hour to discussing this case.

The Appendix for this case provides a summary of factors that can weaken research reproducibility. It also lists web-based resources that can help strengthen this crucial foundation of modern biomedical research.

I. Drs. Smith and Garcia have independent labs in the NIH intramural program and are not familiar with each other's research. Dr. Smith's lab is studying a novel protein that they name 'tumorstatin' because they demonstrate that it is a potent inhibitor of tumor cell growth in tissue culture. Independently, Dr. Garcia's lab studies a molecule [which is only later found to be the same protein] that they call 'tumorin' because multiple experiments show that it promotes tumor growth in mice when highly expressed. Each lab feels pressure to publish quickly in a high-profile journal so lab members can obtain jobs, tenure, or grants, and each group submits their paper hastily to the same prominent journal named *High-impact*.

- Do you feel pressure to publish your research rapidly and in high-profile journals?

II. By chance, each investigator is invited by the journal to review the other's paper, not realizing that they are studying the same protein. Based on his extensive experience with animal and clinical studies, Dr. Smith harshly criticizes many perceived technical problems with the tumorin study, including missing controls, failure to randomize animals with observer blinding to avoid bias, failure to handle tissue samples sufficiently carefully in a standardized manner, and using assays now known to be unreliable. He says the paper fails to meet the guidelines from journal editors on an NIH site: http://www.nih.gov/about/reporting-preclinical-research.htm His postdoc co-reviewer criticizes both the use of an antibody in a commercial kit known to have poor specificity and the over-interpretations of microscopy images beyond theoretical limits of resolution. The Editor knows that Dr. Smith is a very tough reviewer and because the other referees were more positive, her letter to Dr. Garcia leaves the door open for resubmission if all

of the concerns can be resolved while continuing to provide exciting new findings for a "clean" complete story.

1. Under what conditions can a postdoc participate in reviewing for a journal?
2. Are all of the issues cited in their review reasonable and based on currently accepted practice?
3. Are there dangers from biased thinking in even the most careful labs to obtain the "right" answer or in trying to "prove" a hypothesis?
4. What differences in standards of research conduct exist between studies to obtain preliminary data to generate hypotheses versus testing a specific hypothesis?
5. What are pros and cons of hypothesis-driven and exploratory research that addresses a question for which any clear answer will be useful?
6. Does human clinical research have similar or additional requirements or considerations?

III. Dr. Garcia is upset by the tough review with seemingly unreasonable demands, and considers quickly submitting the paper to a specialty journal. But her two postdocs realize that their future job prospects would weaken as a result. They argue forcefully that the reviewer was unfair, and say they can quickly complete the experiments to resolve each concern to get the high-visibility publication. Although Dr. Garcia believes that the research findings are valid whether or not they agree with one's hypothesis, she gives her postdocs a free hand because she trusts them, knowing they received many hours of research ethics training. Also, getting this high-visibility publication will strengthen her site visit review next year.

1. Is there an ethical "slippery slope" when a lab tries to obtain specific results for paper acceptance?
2. How can emotional reactions to bad reviews affect subsequent decision making?
3. If only one of several reviewers raises a subtle but potentially important issue, is it acceptable to pull the paper and submit elsewhere, hoping the issue won't be raised in a fresh review?
4. Besides more specialized or less-competitive journals, what are "predatory journals"?
5. How do trainees in your group learn research ethics and best research practices?

IV. Dr. Garcia's journal review of the paper on tumorstatin from Dr. Smith's lab points out that the gels are of very low-quality, suggesting the experiments had not been repeated. She criticizes a graph reporting significance of $P < 0.05$ using an inappropriate statistical test, questions some beautiful images showing huge effects that seem too good to be true compared to the findings in a graph showing a 25% promotional effect, as well as use of only one cell line and an inhibitor with borderline specificity. Besides raising these concerns, she requests access to the primary data to check their validity. She adds that the field usually applies an independent approach to verify surprising findings. The Editor, who is a friend of Dr. Smith and would like to publish the paper, asks whether Dr. Smith can resolve the concerns that are holding up acceptance for publication, including providing primary data when practical.

1. What specific research and ethical issues are raised here, and how important or reasonable is each? For example, is it reasonable for reviewers to request access to primary data?
2. How do you draw the line between appropriate everyday conduct of science, sloppy science, and research misconduct?

3. How important are good reviewers and editors, not only for research reproducibility, but also for avoiding demands for unnecessary experiments?
4. How do personal relationships between authors, reviewers, and editors affect the peer review process?
5. How common is it for researchers to be more critical of work by others compared to their own?

V. Dr. Smith is incensed by the review and believes it came from a biased competitor. He clarifies with his lab that the experiment in question had been performed four times and worked twice, so they can state that they performed four repeats. He suggests that they find another statistical test that supports the "right" answer, and that extra data points be added as needed to achieve statistical significance. He asks his postdocs to find another cell line that gives the same results, another inhibitor, and another assay that can support the claims, with minimum sample sizes to complete their work within the 3-month resubmission deadline. Although a postdoc has lost some of the primary data, they agree to send just enough to satisfy the journal. Their division director is sympathetic to these efforts, and they think they understand him to say: "Because research is often handicapped by imperfect instruments and biological variability, judicious selection of methods and data is sometimes necessary to support visionary ideas and success in our tough field."

1. Which of Dr. Garcia's points are the most important problems, and which are less important?
2. How important is it to preserve original data and why? When should they be shared?
3. Are lab environment and hierarchy important for research reproducibility? How did these differ between the Smith and Garcia labs?

VI. A. With hard work and skillful revisions, each paper is accepted for publication in *High-impact*. When members of the two labs see posters from the other lab at a major conference, they discover to their surprise that their protein sequences are identical. Each group is sure that the other is wrong because they see contradictory effects on tumor cells.

1. Is it possible that both labs are correct? How might this occur, and can you provide any examples?
2. Might local lab environmental or other conditions in their institutions affect the results, such as conditions in their cell culture and animal facilities, different chow, etc.?
3. If you were Dr. Smith or Dr. Garcia, what would you do?
4. What if you were a lab member?

VI. B. Each lab races to repeat/refute the other group's findings, and they request key materials from each other. Dr. Smith provides some missing information but balks at providing their cell lines because these cell lines are widely available. Although a new postdoc in Dr. Smith's lab initially encounters trouble repeating the lab's findings, she is able to do so after guidance from an experienced postdoc. Dr. Garcia hesitates to share their transgenic mice because Dr. Smith may conduct similar follow-up studies, but she provides some additional unpublished information.

1. Have you encountered problems in trying to replicate results from another research group or even from your own?
2. Do authors currently provide sufficiently detailed methods in papers and subsequent access to tools including plasmids, cells used for the experiments, animals, and computer code?
3. How can doing an experiment "the right way" affect results, and more broadly, how can experimental, environmental, and biological variability alter findings and conclusions?

APPENDIX: Factors that Can Compromise Research Reproducibility

Conceptual weaknesses and cognitive bias

- Not distinguishing between exploratory research examining multiple hypotheses/possibilities and testing of a specific hypothesis
- Trying to "prove" and defend a hypothesis rather than trying to answer a question
- Concluding "my experiment worked" if it is the preferred answer
- Lack of concern about approaches that might lead to research misconduct
- Insufficiently rigorous peer reviewers and journal editors

Research background and cultural differences

- Insufficient or ineffective training in responsible conduct of research
- Hierarchy in which the boss/mentor's hypotheses are favored over actual findings
- Cutting corners and sloppy research
- Selective interpretation of data
- Problematic lab culture (social dynamics)

Internal and external pressures

- Perceived need to publish in high-visibility journals
- Needing large numbers of publications, even if in poor or predatory journals
- Requirements by journals for exciting novel results, not negative findings
- Demands for clean, definitive, complete stories with impressive-looking data
- Deciding not to publish unwanted or controversial findings
- Demands from reviewers and editors for specific supportive findings
- Needing to find jobs, get tenure, or keep funding to take care of one's staff

Biological variability

- Local environmental factors: type of housing, water, feed, climate control, physical activity
- Strain, sex, or age of animals or cells
- Effects of microbiome, or undetected infection
- Incomplete penetrance, wide variations of expression or phenotype

Experimental design and performance

- Failure to retain primary data
- Lack or misuse of appropriate controls
- Not considering that effects can be dose-dependent, or differ *in vitro* versus *in vivo*
- Not distinguishing between technical and biological replicates for data points
- Low power (e.g., small n) leading to false-positive results
- Piecemeal add-ons to sample size
- Small effect size
- Insufficient number of repeat experiments
- Exclusion of certain experiments or data points
- No randomization, observer blinding, or checking by independent evaluator(s)
- Faulty use of statistics (failure to correct for multiple variables, over-dependence on $P < 0.05$, selecting a statistical test because it gives a preferred answer)
- Use of only a single approach

- Inconsistent or unreliable sample handling (faulty collection, storage, thawing)
- Poorly performing assays and/or failure to keep up with the newest, best technologies
- Vague or loose outcome definition (especially clinical endpoints)

Technical issues
- Incorrect instrument settings, e.g., background, sensitivity
- Pushing beyond the limits of a technology
- Insufficient antibody validation
- Off-target effects of inhibitors or stimulators
- Complete faith in purchased kits that may have sub-optimal validity
- Non-availability of key reagents/animal models
- Contaminated cell lines or sequence errors in plasmids
- Poor communication or failure to fully assist another lab struggling to reproduce one's finding

Presentation
- Incomplete methods (sloppy or deliberate)
- Lack of availability of primary data, metadata, computer codes, and unique reagents
- Selective presentation of "representative" data
- Not following best practices in the field, e.g., imaging or FACS guidelines, antibody validation, performing RNA interference, etc.

INTERNET RESOURCES

NIH website on research reproducibility: http://www.nih.gov/science/reproducibility/

NIH policy on sharing of unique research materials: https://grants.nih.gov/grants/sharing.htm

Guidelines from journal editors: http://www.nih.gov/science/reproducibility/principles-guidelines.htm

Video reproducibility training modules: https://oir.nih.gov/sourcebook/ethical-conduct/research-ethics/committee-scientific-conduct-ethics-csce/responsible-conduct-research-training/instruction-responsible-0

Reproducibility of data collection and analysis in modern technologies: Potentials and pitfalls
Cell Biology http://videocast.nih.gov/summary.asp?Live=15277&bhcp=1
Structural Biology http://videocast.nih.gov/summary.asp?Live=15910&bhcp=1
Genome Technology http://videocast.nih.gov/summary.asp?Live=16381&bhcp=1

As scientists, we hold a position of responsibility in society based on specialized knowledge we have and seek to expand. This responsibility extends across scientific fields, but for biomedical scientists entrusted with taxpayer's dollars given in the hope that our research will eventually improve global health, there is a special duty to the broader society. This year's ethics cases address multiple aspects of this responsibility. These range from recognizing and dealing responsibly with potentially hazardous materials, to promoting sound, reproducible research and communicating it effectively to both the public and research community. Scientists feel pressure from inside --competition within and between labs -- as well as from outside --citizens expecting their investment in science to rapidly translate into better treatments and health. While competition and pressure fuel innovation, they can also lead to short-sighted decisions to cut corners in order to achieve career goals and secure ongoing funding. In labs, cutting corners can lead to problems with reproducibility. In society, especially in the current social media environment with news constantly going "viral", the pressure to act on preliminary, poorly validated or clinically unproven new results can be misleading, counterproductive and even dangerous. The anti-vaccine movement and its claims of causation in autism provides a good example of this danger.

As you go through the 2017 research ethics cases, consider what pressures you may be experiencing in your own work and how you can maintain high quality standards. Do not lose sight of the broader impact your work might have on society, even if you are not involved in clinical research. Think about what you can do to make the consequences of your research relevant and effectively communicated to the public.

Deciding What Study Results to Publish and Transparency in Research Publication

Dr. Wyck is the lead investigator for a cohort-based case-control study of the genetic and environmental factors related to Parkinson's Disease (PD) that compares 1,000 patients with 1,000 matched controls. Her team's analysis discovers that having a history of head trauma (p=0.005), high blood pressure (p= 0.01), or exposure to agricultural pesticides (p=0.04) is related to 25-60% higher risk of PD. Surprisingly, Dr. Wyck found that current cigarette smokers were at 40% lower risk of PD as compared to non-smokers (p=0.02). The analysis also indicated that non-smokers exposed to second-hand smoke had 12% lower PD risk as compared to non-smokers without exposure to second-hand smoke, but this association was not formally statistically significant (p=0.07).

Dr. Wyck is concerned that the findings for smoking exposure may have a negative impact on public health by discouraging people from quitting (i.e., as a way to avoid developing PD). While preparing the study manuscript, she is considering whether or not to report the findings related to smoking (and if so, how to address those findings in the discussion).

Questions:

1. Should Dr. Wyck report all of her findings, including those related to smoking? Why or why not? What if the result for smoking was opposite; i.e., it was related to *higher* PD risk?
2. Should she only report findings with p-values <0.05?
3. Which findings should Dr. Wyck emphasize in title, abstract, and discussion?
4. How should she discuss the apparent protective association with smoking; e.g., should she speculate on possible mechanisms, such as nicotine's role in increasing brain dopamine levels?
5. What, if anything, should the authors say about the second-hand smoke finding?
6. What aspects of the many health risks associated with smoking are relevant to the findings?

Handling Select Agents

Several years ago, Dr. Antonelli completed his postdoctoral training in the NIH laboratory of Dr. White and returned to his home country to run his own lab. Drs. Antonelli and White continued to collaborate and in 2009 Dr. Antonelli brought Dr. White a viral construct to use in their joint projects. The original virus was the Newcastle Disease Virus (NDV), a virulent chicken virus, which is extensively used in immunology to induce interferon expression in dendritic cells.

Dr. White did not have any written agreements in place to receive these materials, nor did he consider the material to be a select agent because it was only a chicken virus and is generally assumed to pose no hazard to human health (although it can still cause mild conjunctivitis and influenza-like symptoms). Also, Dr. Antonelli had confirmed in an email that no vaccinations or special handling precautions were needed for this virus, leading Dr. White to assume it was the less virulent *LaSota* strain of NDV, which would not require registration.

Dr. White and the other members of his lab, including postdocs and graduate students, continued to work with the virus for several years and published two papers. However, the methods section of both papers - copied largely from an early article by White and Antonelli - indicated that the construct was based on the highly virulent *Herts* strain of the NDV, indicating that it was in fact a select agent (and should therefore have been registered). Unfortunately, Dr. White did not realize this, as he usually only focuses on editing the abstract, introduction, results and discussion sections of the manuscript drafts from his fellows.

No one ever pointed out to Dr. White that they likely were dealing with the virulent strain of NDV, and it went unnoticed until the "Clean Sweep" initiative at the NIH in 2014, led by the NIH's Division of Occupational Health and Safety. At that time, it turned out that Dr. White had no proof that the virus was harmless, meaning that that he and his fellows could have been exposed to, or inadvertently released, a potential biohazard.

Questions:

1. What are the risks associated with research on select agents? How does one know if something **is** a select agent or a dual-use agent? Can animal pathogens be select agents?
2. What are Material Transfer Agreements (MTA), why are they important? Was it appropriate for Dr. Antonelli to bring a viral clone to the United States and share it with Dr. White without getting the proper documentation? What other ethical and legal problems do you see in this case?
3. Whose responsibility was it to check the manuscript methods section and make sure that the virus construct used was safe for use in the lab (or alert the group if it was not)?
4. How would you react if it turned out that you have been using a poorly characterized (and potentially harmful) bacterium or virus? How would you deal with the paper(s) that used this construct and provided questionable (erroneous?) info?

Resources:

https://www.selectagents.gov/SelectAgentsandToxinsList.html
http://osp.od.nih.gov/office-biotechnology-activities/biosecurity
https://osp.od.nih.gov/biotechnology/biosafety-guidance-and-resources/

Research Competition and Reproducibility

Dr. Park is a tenure-track investigator searching for a novel method to de-differentiate cells from adult tissues to produce stem cell lines that might be used in organ regeneration. At his third-year tenure-track review, the committee expresses a concern that he has no recent high-impact publications.

Part 1

Dr. Park presents his postdoctoral fellows, Drs. Sanchez and Aero, a list of the ten most-promising chemicals and growth factors he has identified for further testing. As motivation, he reminds them that whoever successfully publishes such a breakthrough approach will have a great career. After the initial screening indicates that a derivative of trichostatin A is the most promising compound, Dr. Park assigns both fellows to work on this chemical separately, using the same commercially available cell line. At first, the fellows get along collegially and have some productive discussions about how to design their experiments, but they have a falling out when Dr. Sanchez suggests that they collaborate on both projects and share first-author status.

After four months of independent, intense (and secretive) experimentation by the two postdocs, Dr. Aero presents at a lab meeting beautiful preliminary results demonstrating that incubating isolated adult cells with the compound produces de-differentiation and rapid cell proliferation, and that removal of the drug results in fully functional re-differentiation. Dr. Sanchez, however, can show only a weak, seemingly toxic response to the drug, and she wonders to herself whether Dr. Aero may have sabotaged her experiments. She notices that both her experimental and control cells have abnormally high death rates and suspects that someone is tampering with her experiments. One morning she discovers that her incubator was set at 40^{o}C, and that the set points had also been altered so as not to trigger the alarm when the temperature exceeded 37.5^{o}C (36-37^{o}C is the optimal temperature for growing these cells).

Questions:

1. Should the head of a lab put two trainees on the same project? What are the advantages and disadvantages?
2. What can or should Dr. Sanchez do if she suspects that her work has been tampered with? Should she talk to Dr. Park about this?
3. What should Dr. Park do if Dr. Sanchez claims that her work has been sabotaged?
4. Is tampering with an experiment unethical? Does it fit the definition of research misconduct?
5. If the group is successful in discovering an agent that can induce de-differentiation, this discovery could be patentable and could have significant economic value. Should they pursue a patent prior to making any decisions regarding publication?

Part 2

After Dr. Park warns the fellows not to sabotage each other's experiments, Dr. Sanchez is also able to demonstrate that the drug produces de-differentiation, but the effect size is only 50% of Dr. Aero's experiments. He asks them to both repeat their experiments and they both obtain results which are similar to those they obtained earlier. Dr. Park decides that the group has successfully replicated the experiments, and they submit a paper to a high impact journal reporting Dr. Aero's impressive findings. The paper lists Dr. Aero as the first author, followed by Dr. Sanchez, two graduate students, and Dr. Park. The paper does not include data from Dr. Sanchez's experiments and only reports data from Dr. Aero's two experiments. It says that the group has replicated his findings, with data available upon request.

Questions:

1. Does Dr. Sanchez' experiment constitute a successful replication of Dr. Aero's work?
2. Should they have reported the results of both experiments?
3. Should they have attempted to determine why Dr. Sanchez' experiments consistently had a much smaller effect size than Dr. Aero's? What factors could lead to different outcomes in such experiments?
4. Is failure to report Dr. Sanchez's results data falsification?

Part 3

The paper is accepted for publication and is highlighted with an accompanying editorial. The institute prepares a press release and several reporters interview Dr. Park. Based on the promising findings, Dr. Park's lab chief prepares a compelling departmental application on the urgent need for a next-generation sequencer and bioinformatics support. The request is funded unusually rapidly because of the potential high impact of the work, even though other labs with long-term consistent productivity had competing requests for the funds.

Questions:

1. What responsibilities do lab chiefs and supervisors have in this type of situation?
2. How do we prepare trainees and other researchers for professional survival and career success in the current competitive research environment while instilling and preserving high ethical standards?
3. How can competition for limited resources be made fairer?

Part 4

Another lab headed by Dr. Williams tries to repeat Park's work using commercially available cell lines but is not able to obtain the larger effects reported in the paper and cannot determine why; their effect size is closer to that of Dr. Sanchez. They contact Dr. Park and ask for their protocols, samples, and primary data of Drs. Sanchez and Aero. They conduct a genetic analysis of Dr. Aero's and Dr. Sanchez's cell lines and detect some variations. They suspect that Dr. Aero's cell line may have mutations that made it more sensitive to the trichostatin A derivative, and plan to investigate this hypothesis in future work.

Questions:

1. How did the failure to report Dr. Sanchez's experiments impact the reproducibility of this research and the overall understanding of the effects of the trichostatin A derivative on de-differentiation?
2. What other biological factors could contribute to the source of the differences?

Societal Aspects of the Responsible Conduct of Research

Part I

You are a post-doctoral fellow working with a prominent senior investigator on a project examining risk factors for dementia. You, as first author, and the lab are drafting the report of an investigation of the association between flu vaccination and dementia. In reviewing the manuscript, you notice that the data summarized in one of the tables are not consistent with the raw data in the chart reviews. In particular, the time between last exposure to the vaccine and date of dementia diagnosis for several patients is substantially shorter than what your own records indicate. This shorter latency implies a stronger link between vaccination and disease than would be observed otherwise. You request a meeting with the PI where you indicate that the data in the table do not match those in the chart reviews. You are told somewhat dismissively that some statistical adjustments had to be applied to "smooth" the data, that these methods are standard and have been validated, and that you shouldn't worry about these apparent discrepancies.

Questions:

1. What are your responsibilities as a coauthor for understanding analyses performed on data? Should you investigate this further? If so, what steps would you take?
2. Are there risks to you as a young researcher in this situation? Should you be worried that continuing to voice your concerns might impact your relationship with the PI?
3. Should you be concerned that the data were perhaps manipulated to generate more interesting findings?

Part II

Despite your concerns, the main findings of the study are published in a respected medical journal. Several prominent dementia researchers immediately refute the primary findings and conclusions, and request access to the primary data. After a while, a formal NIH misconduct investigation is launched and finds sufficient evidence of data falsification to warrant retraction of the paper. Despite the scientific criticism and discrediting of the study, however, both traditional and social media had already translated the findings into the message that an increase in dementia in the elderly is linked to taking the flu vaccine. Consequently, there is now a decrease in flu vaccine compliance not just in the elderly, but in all age groups.

Questions:

1. In what ways do news or social networks communicate scientific results differently from the scientific literature? To what extent are authors of research papers and other scientists responsible for the eventual public dissemination of messages derived from the primary studies and publications?
2. Do you think the scientific literature is self-correcting and, if so, to what extent does this also apply to the much larger lay literature?

2022 Ethics Case Study - Use of Human Biospecimens and Informed Consent

Key Take Home Points

1. Before sharing human biospecimens or private data, it is essential to check with the IRB-approved informed consent document to determine whether and exactly what sharing is permitted. If participants have opted not to allow their biospecimens or private data to be shared with other researchers outside of the original study team, their wishes must be respected.
2. **Secondary research** on human private data or biospecimens is research that **is not part of the original IRB-approved protocol**, such as investigation of a new question or hypothesis, or a new analysis of the data.
3. **Secondary research involving the use of identifiable**, private human data or identifiable human biospecimens **must be approved by the IRB**.
4. Human data or biospecimens are considered **identifiable** if they include personal identifiers (such as name or medical record number), or they are coded and a member of the research team has access to the key needed to decipher the code.
5. Secondary research on **non-identifiable private**, human data or biospecimens does not require IRB approval, provided that it is consistent with the IRB-approved protocol and consent form.
6. It is always a good idea to consult with the IRB if you have any questions about sharing human biospecimens or data or conducting research on private human data or biospecimens.

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Part I: Inclusion of Underrepresented Populations in Clinical Trials, Statistics, Demographics

Dr. Maxwell is a cell biologist and a Senior Investigator at the NIH who has been collaborating with Dr. Liu, an oncologist and Clinical Investigator at the NIH. Maxwell and Liu have published numerous articles in high-impact journals on using RNA-interference (RNAi) to treat liver cancer. The RNAi treatment works by blocking expression of a genetic variant that plays a key role in liver cancer cell proliferation. After successfully treating liver cancer in laboratory mice and completing a Phase I trial which showed the treatment was well tolerated, they began a Phase II trial. However, few subjects receiving the treatment had stable tumor volume for 12 months, the study's efficacy measure. Interestingly, the treatment was more effective in African American/Black males than in other racial, ethnic, or gender groups, although the proportion of African American/Black males with stable tumor volume compared to other groups was not statistically significant ($p = 0.07$). The trial recruited a diverse population of subjects but was insufficiently powered to establish efficacy in isolated demographic groups.

1. Is $p = 0.07$ considered to be a statistically significant difference between demographic groups? How should the investigators address this finding?

2. How should the investigators have designed their Phase II trial if the goal had been to distinguish between treatment effects in different demographic groups? Would this change in strategy have created any issues for completing their study?

3. What are some strategies for including underrepresented populations in research?

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Part II: Scientific Disagreements

Following the disappointing Phase II trial, the investigators try to understand, at a cellular level, why the treatment works in some participants but not others. They decide to try to model their RNAi treatment in mouse organoids (self-organized tissue constructs derived from stem cells) to elucidate molecular, genetic, and epigenetic mechanisms and interactions. Maxwell invites Dr. Mehta, a Visiting Fellow, to join the team and puts Mehta in charge of the animal organoid experiments. Mehta and Maxwell discover a genetic variant that interferes with the RNAi treatment in mouse liver tumor organoids. They also discover that it is possible to use a different RNAi treatment to block expression of the variant.

At a lab meeting, Maxwell announces plans to test this two-pronged RNAi approach to liver cancer in their mouse model. Mehta asks whether additional analysis of the organoid data needs to be done before proceeding further, but Maxwell rejects this idea Later that day, Maxwell asks Mehta for an impromptu meeting in which Maxwell says "Dr. Mehta, I have a great deal of respect for your judgment and expertise but if you disagree with me about a scientific issue, we should discuss it in private and not in front of the group."

4. How should disagreements about scientific issues be handled? What are the advantages and disadvantages of discussing them with the whole research team?

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Part III: Research with Human Biospecimens, Sharing Biospecimens, Consent

After a year, the team has completed the animal experiments, which show that the new, two-pronged RNAi treatment is 95% effective at halting tumor growth in their mouse model. Maxwell and Mehta discuss these findings in Maxwell's office. Maxwell believes the experiments should be replicated as soon as possible in human organoids, but Mehta thinks they need to do some additional work with animals before proceeding further. Maxwell dismisses this concern and says that the lab already has some cancer stem cells in storage from the Phase II collaboration with Liu that they can use to develop human, liver tumor organoids. Later, Maxwell emails Liu about this project, who is excited about the idea.

At a lab meeting the following day, Maxwell informs the group about the plans for the human tumor organoid experiments and puts Mehta in charge of the project. Maxwell also says they will send aliquots from the human organoids to Dr. Kennedy, who runs an NIH Genomics Core Facility and will test for the variant that blocks the original RNAi treatment. Kennedy will also perform gene expression assays on the aliquots. Mehta, who recently attended an NIH workshop for trainees on the responsible conduct of research, asks if they will need Institutional Review Board (IRB) approval before they proceed. Maxwell quickly and forcefully responds that the project will not be considered human subjects research because the cells are marked with a code and only Liu has access to the key needed to decipher the code, but Liu is not part of the research team. Mehta feels that Maxwell was irritated by the question and does not pursue the matter further.

5. Do the researchers need to ask the IRB for permission to send human biospecimens to Dr. Kennedy or any other collaborators?

6. Does it matter what the consent form says about future use and sharing of human biospecimens?

7. Should Mehta have said something to Maxwell about the human subjects issue before the lab meeting? What difference might that have made?

8. Does secondary research with human biospecimens require IRB approval if the biospecimens are coded and none of the members of the research team working with biospecimens have the key to the code?

9. If someone has questions about whether a study requires IRB approval, who should they contact for advice?

10. Generally, who is responsible for ensuring the regulatory issues, including human and animal subjects issues, are properly addressed?

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Part IV: Human Subjects Research and IRB Review

After six months, the researchers have enough data to show that the two-pronged RNAi approach is highly effective at stopping liver tumor growth in human organoids. During a lab meeting, Maxwell discusses their exciting results and the possibility of initiating another clinical trial in collaboration with Liu. Maxwell asks Mehta to assemble individual, participant-level data from their research for Liu. Maxwell believes the data are compelling enough for Liu to revisit the clinical data from the Phase II study so that Liu can determine whether participants without the variant of interest responded better to the original RNAi treatment than those with it. Mehta is still concerned about the IRB issue, since they are now planning to share individual, participant-level coded data with Liu. Mehta is hesitant to discuss these regulatory/ethical issues with Maxwell, given the tensions in their relationship.

11. What should Mehta do at this point?

12. Is IRB approval needed to share the coded participant-level data with Liu? Is it needed for Liu to perform this new analysis of the clinical data from the Phase II study?

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Part V: Manuscript Clearance/Submission, IRB, and Non-Compliance

Mehta deliberates about what to do but doesn't want to further jeopardize the relationship with Maxwell and ultimately decides to say nothing. Liu receives the individualized data and begins the analysis using the prior Phase II data. Liu finds that participants in their Phase II study without the variant of interest were five times more likely to respond well to the original RNAi therapy than participants with the variant. Maxwell drafts a paper to submit to the *Journal of Breakthrough Medical Results*. After the paper makes it through the NIH manuscript clearance process—Maxwell checked the "no" boxes when asked whether the manuscript was based on a clinical study protocol or exemption—the authors submit it to the journal. After 6 weeks, journal accepts the paper with minor revisions. One of the reviewers asks whether they had IRB approval for this study. Liu reads the comment and is floored because Liu realizes that IRB approval was needed but was not obtained. Maxwell realizes they had incorrectly completed the manuscript clearance form. Liu feels angry and embarrassed, wondering if excitement about moving forward with this project led to neglect of IRB issues. Liu meets with Maxwell to discuss their problems.

13. How should they proceed from here? Should they contact the IRB?

14. Should the researchers withdraw the paper?

15. Should the reviewer for NIH publication clearance have checked to see if the authors checked the wrong box?

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Part VI: Research Non-Compliance, Corrective Actions, and Publication

Liu contacts the NIH IRB about what happened. The Executive IRB Chair, Dr. Anderson, tells Liu to stop all research on this project and submit a Reportable Event Form (a form for reporting non-compliance, protocol deviations, and other problems with research). Anderson reviews the Reportable Event Form and the protocol and consent forms from the Phase II study and notices that the consent form includes the following language:

"Check yes or no for each statement:

I agree to allow my biological specimens and data to be stored and used for other research studies [Yes__No__]

I agree to allow my biological specimens and data to be shared with other researchers [Yes__No__]

Anderson asks Liu if they kept records of what the subjects consented to and honored their requests. Liu contacts the study coordinator who reports the following breakdown:

I agree to allow my biological specimens and data to be stored and used for other research studies [Yes: 75, No: 15, No Answer: 10]

I agree to allow my biological specimens and data to be shared with other researchers [Yes: 75, No: 15, No Answer: 10]

Anderson realizes that the non-compliance is potentially more serious than it seemed to be initially because 15% of the subjects did not want their biospecimens or data used in other studies and 15% did not want their biospecimens to be shared with other researchers. Anderson discusses this issue with Liu and learns that biospecimens and data from all of the participants were included in the research and biospecimens from all of the participants were shared with Kennedy. The IRB reviews the reportable event at its next meeting and decides that this is serious non-compliance. The IRB is required to report this non-compliance and corrective actions to the HHS Office of Human Research Protections, which oversees NIH-funded research.

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The IRB is trying to decide what type of corrective actions need to occur.

16. Which of the following corrective actions should be taken (if any)?

    a. Contact the participants whose consent was violated and tell them what happened and what is being done about it and apologize;
    b. Require additional training for Liu and Maxwell and their research groups on human subject protections;
    c. Require more training throughout the NIH on IRB approval for secondary uses of biospecimens and data;
    d. Prohibit Liu and/or Maxwell from doing research with human subjects for a period of time, such as a year or more;
    e. Require the paper to be withdrawn;
    f. Require that all of the human data be destroyed.
    g. Require that the human data where consent was violated be destroyed.

17. Generally, what could have or should have been done to prevent these problems?

18. Who is/was responsible for ensuring that they had appropriate IRB approvals for their research? Maxwell, Liu, other members of the lab present at group meetings, the NIH publication clearance reviewer, the reviewers and editors at the journal?

[End of case study]

Please take the survey by either clicking on the link below or scanning the QR code on your hand-held device:

https://www.surveymonkey.com/r/6MRQTVW

Epidemiological and Clinical Data Management

Case 1 - Dr. Wood is the principal investigator for a large, multi-center cohort study of cancer in adults. Over the last year, two postdoctoral fellows, each working with their respective tenure-track mentor, had embarked on studies examining risk factors for finger cancer. Because he had noted a strong north-south gradient in the U.S. Atlas of Cancer Mortality, PD 1 studied the relationship with climate and temperature, while PD 2 examined the associations with occupation, pollution, and genes.

Eager to confirm his hypothesis and impress his mentors, PD 1 started his analyses, identifying his main residential history questions, creating new variables related to annual seasonal temperatures from a NOAA database, and working up other covariates for potential confounding. Meanwhile, based in part on her previous experience implementing field studies, PD 2 was painstakingly reviewing the questionnaires, cataloging the myriad exposures that had been quantified, and drafting a careful and complex analytical plan.

The initial analyses of PD 1 showed substantial variation in the geographic distribution of finger cancer in the cohort, and there was a striking risk-annual ambient temperature gradient such that the persons in warmest regions were at greatly and significantly reduced risk. (A lower temperature threshold effect was also suggested by the data, however.) PD 1 was very excited by these ground-breaking results, which he explained on the basis of hemodynamics, and shared them with his mentor, TT 1. TT 1 agreed that PD 1 should complete the analyses and get internal clearance in time for an upcoming AACR late-breaking session abstract deadline, even though consideration of the entire database was lacking. The abstract was accepted for oral presentation and PD 1 was invited to participate in a press conference at the meeting. PD 1, TT 1, and Dr. Wood were ecstatic, and planned for rapid submission to a high profile journal.

At the same time, PD 2 had begun to produce some very interesting results, including age and sex differences, and had DNA samples from a nested case-control set sent to the genotyping facility. Dr. Wood was not impressed with her progress, however, especially in light of PD 1's AACR acceptance, and she asked PD 2 to present her initial findings at the next Branch meeting.

After going over the data and slides with TT 2, PD 2 presented her results to the group. She had found independent, positive associations for the 45-65 age range (in men only) and showed a RR (Relative Risk) of 10 for the use of argon-infused, sub-zero gloves (included in the Apparel module of the study questionnaire only after two visits to the TEQ (Technical Evaluation of Questionnaires Committee) and at the insistence of a previous fellow). A gasp went around the room, and eyes turned to PD 1 and TT 1. They revealed that they had looked at the glove variable but did not keep it in the final models owing to "some" attenuation of the main finding. Also, they had learned of specific factories in Montana, North Dakota, Wisconsin, Michigan, and New York that could have been explored in the data but were not. Dr. Wood was not looking forward to her next meeting with the Division Director.

Questions

What should the investigators and Branch do with this new information?

What steps could have been taken earlier to avoid the present situation?

What are the implications for the abstract accepted by AACR? How do pressures of meeting submissions and publishing in competitive fields affect decisions regarding which data to include?

What are the steps in evaluating and managing the data before they are analyzed? Where can the most critical errors occur? Who has oversight of data linkages and database integrity?

What responsibility does the PI have for monitoring data-related tasks and knowing which piece of primary data was used in each analysis, which was not, and why?

What are some of the pitfalls regarding a priori and post-hoc hypotheses? Data exploration? Testing for confounders?

What constitutes original data in epidemiology? Is it the primary record, the questionnaire, the lab assays? Is it the electronic entry? Edited data on the servers?

Case 2 - You do an analysis of a risk factor, say body mass index, and multiple outcomes—i.e. diabetes incidence, risk of disability, risk of heart disease, and death. All the data are consistent with the exception of one endpoint.

How should you handle this?

Case 3 - You are involved in a clinical protocol comparing a clinical intervention with usual care. Overall, there is no difference between your intervention and control. However, on careful analysis, you see that there is a clear dichotomy in response—with a large group having a modest response but a small group with a very substantial response.

How do you analyze the data?

Case 4 - You are conducting a multicenter trial and note that all centers but two have results consistent with a positive outcome for the trial. You determine that the intervention was not applied as rigorously at these centers as in others.

Can you exclude these centers from the analysis?

Guiding Principles for Data Management

The proper management, interpretation, and representation of scientific data are central to all scientific inquiry. A wide range of scientific approaches are incorporated into the research carried out at the NIH, but two guiding principles underlie all data management and presentation. First, data should faithfully reflect the experimental results, qualitatively and quantitatively, without misrepresentation. Images (microscopy, blots, gels, etc.) should be representative of all the results obtained. Second, sufficient documentation of the experimental methods and the data should be kept in the laboratory for at least five years, such that any trained individual would be able to independently examine and interpret the data. The cases selected for 2005 (available as a pdf file with Figure 1 as a separate image) cover these topics thoroughly. There are five cases related to the management and representation of different types of data in laboratory settings, and an additional four cases related to epidemiological and clinical data management, and we encourage each group to discuss those cases that most pertain to the types of experiments they carry out.

We strongly encourage facilitators to provide the following two documents as supplements to the 2005 case discussions.

Document 1 -- The NIH Catalyst article entitled "What's in a Picture? The Temptation of Image Manipulation" which provides guidelines for proper handling of digital image data with powerful examples of what can go wrong (the images from the article can also be found in the pdf file). **We strongly recommend that this brief article be required reading before the case discussions.**

Document 2 -- Three retractions published in Cell in 2004 (pdf file). How could these retractions have been avoided?

Original figures from:

What's in a picture? The temptation of image manipulation

Mike Rossner and Kenneth M. Yamada

***The NIH Catalyst 12*: 8-11 (May-June 2004)**

http://www.nih.gov/catalyst/2004/04.05.01/page4.html

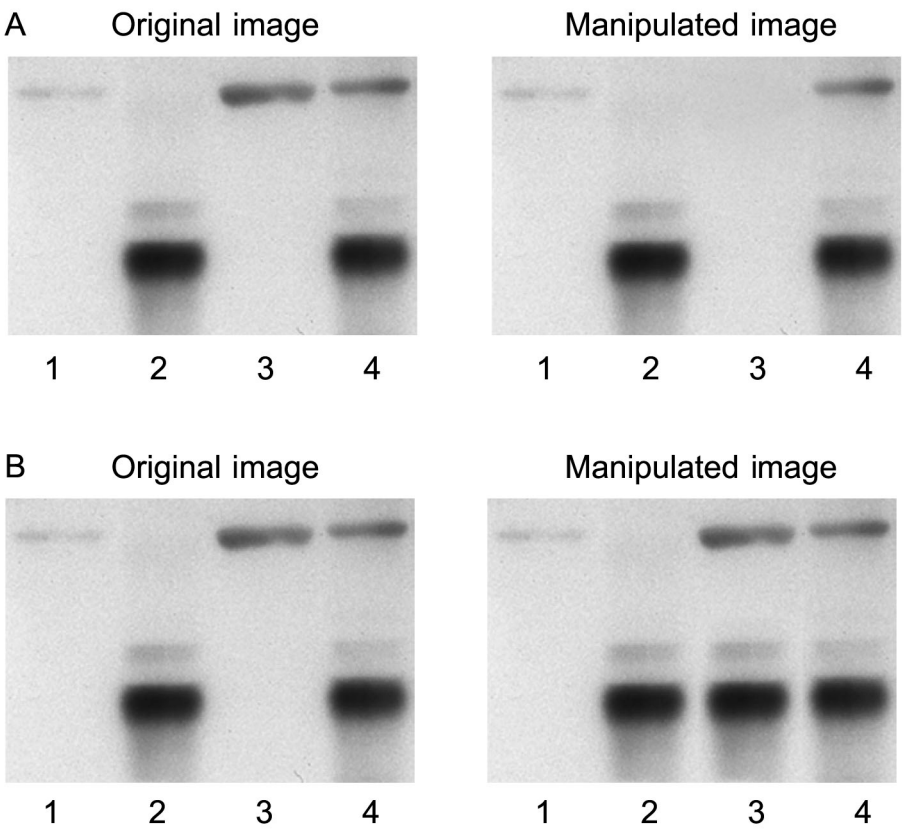
- Also reprinted with permission in *J. Cell Biol. 166:* 11-15 (2004) to make it available to non-NIH researchers.

- The original JPEG files are available from the following public download URLs at Rockefeller University:

  Stuffit format for Mac: http://gingerx.rockefeller.edu/~rossner/Image_Feature_Figures.sit

  Zip format for PC: http://gingerx.rockefeller.edu/~rossner/Image_Feature_Figures.zip

Figure 1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Original image
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Figure 2

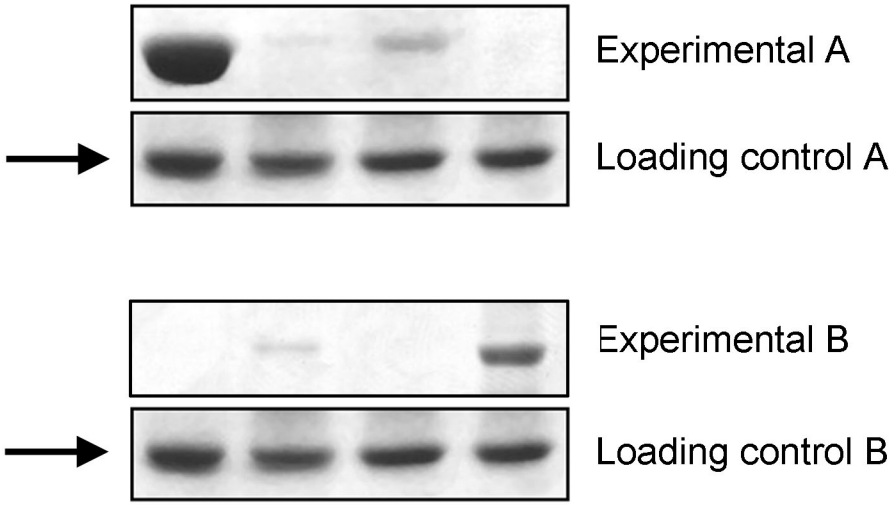

Experimental A
Loading control A
Experimental B
Loading control B

Figure 3

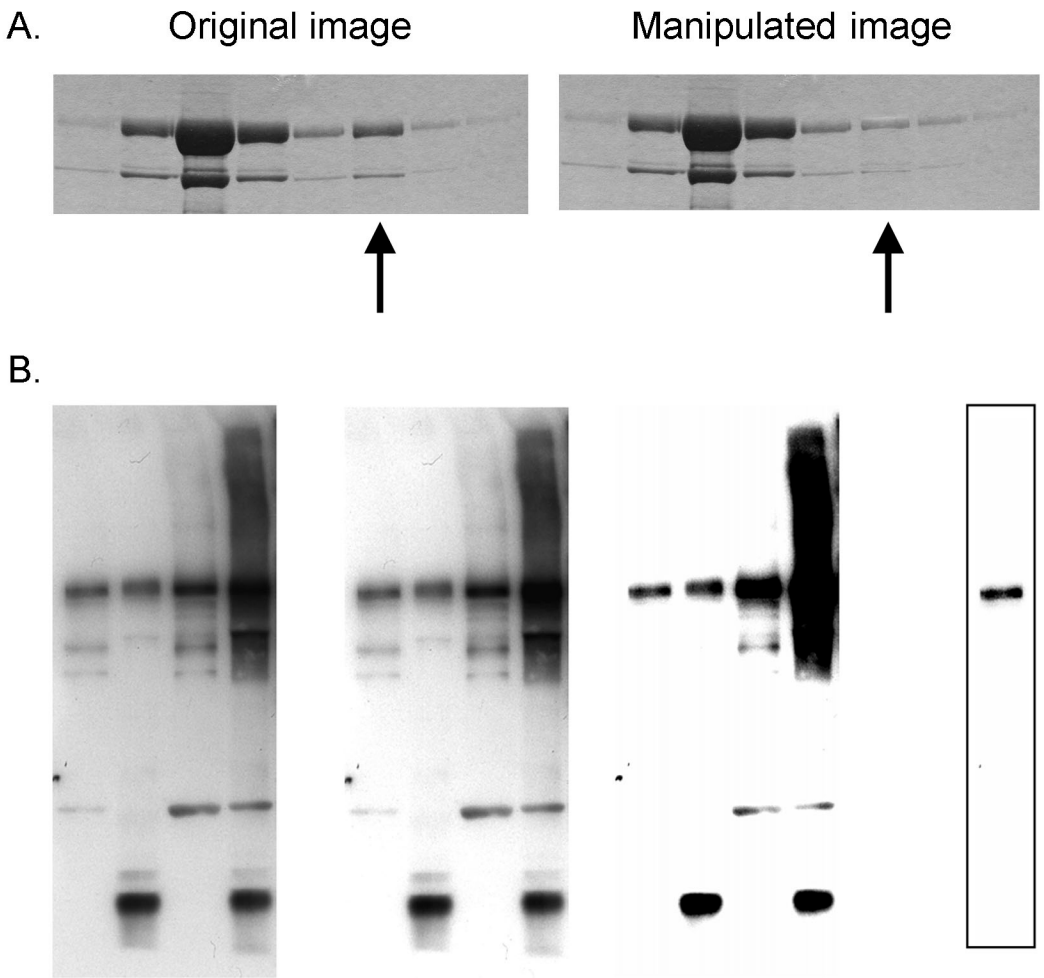


Figure 4

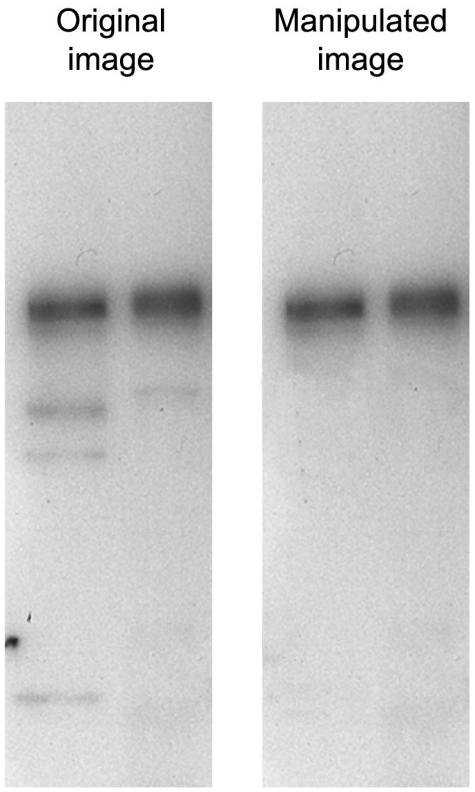
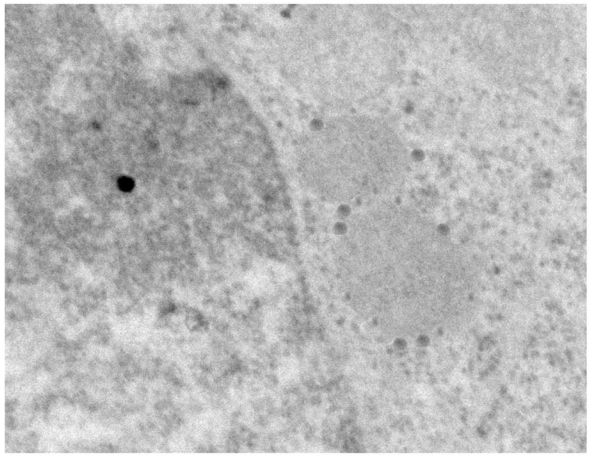


Figure 5

Original image



Manipulated image

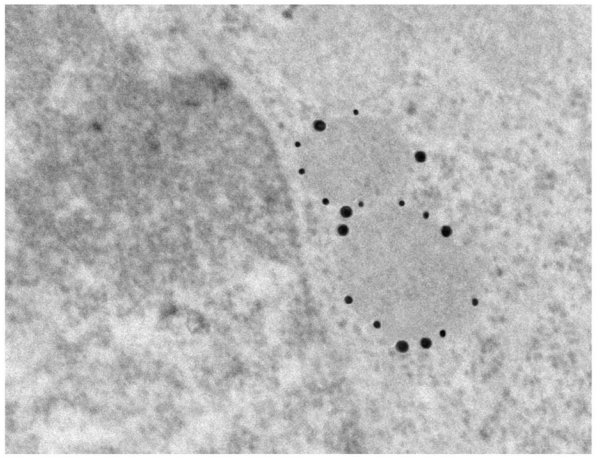
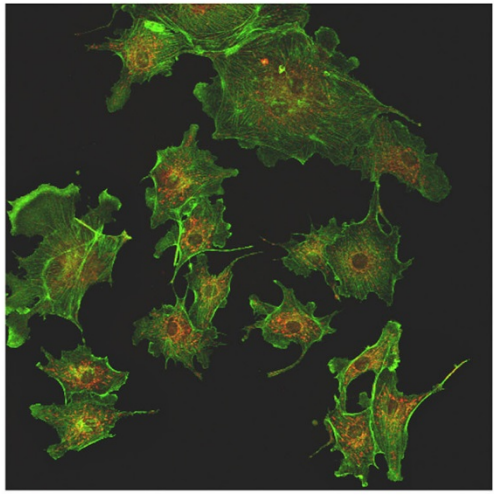
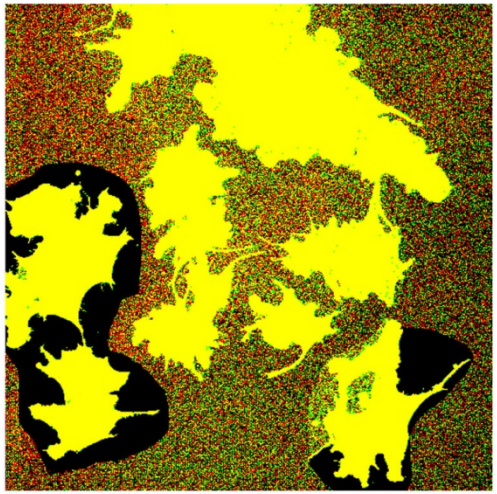


Figure 6

Manipulated image



Manipulation revealed by contrast adjustment



Recent *Cell* Retractions

Chan, S.-K. and Struhl, G. (2002) Cell *111*, 265-280

This paper presents a series of experiments that challenge the conventional view that Armadillo transduces Wingless by combining with Pangolin to form a transcriptional activator. The challenge rests principally on experiments performed by my coauthor, S.-K. Chan, the results of which are shown in the Figures 2D, 4, and 5. These experiments test the function of altered forms of Armadillo that are targeted inside or outside of the nucleus or that contain heterologous transcriptional activator or repressor domains. Recently, in seeking to extend these findings, I personally obtained the opposite result for the key negative control for the experiments in Figure 5 (Figure 5B). When confronted with this discrepancy, S.-K. Chan informed me that most of the results shown in Figures 2D, 4, and 5, including the negative control shown in Figure 5B, were either not performed or gave different results than presented in the paper. I therefore withdraw this paper and the conclusions it reports. I deeply regret and apologize for any adverse consequences that may have resulted from its publication. S.-K. Chan concurs with this retraction.

Chandok, M.R., Ytterberg, A.J., van Wijk, K.J., and Klessig, D.F. (2003). Cell *113*, 469–482.

The above paper describes the purification and characterization of a pathogen-inducible NOS-like activity from tobacco plants and its identification as a variant form of the P subunit of the glycine decarboxylase complex. The demonstration that recombinant *Arabidopsis* variant P protein has NO-synthesizing activity was a critical piece of evidence leading to the above conclusion. Further experiments by other members of the Klessig laboratory reveal difficulties in reproducing the data with recombinant variant P and in addition suggest that the data on recombinant variant P presented in Tables 1 and 2 and in Figures 5B and 5C of this paper are unreliable. Since we cannot substantiate the major conclusion presented in this paper, we wish to retract the entire paper and its conclusions in order to avoid wasted efforts by other investigators whose studies might be influenced by the results and conclusions reported. The first author, M.R. Chandok, has not approved this retraction. We deeply regret that this serious incident occurred and sincerely apologize to our colleagues.

Yamaguchi, R. and Newport, J. (2003) Cell *113*, 115-125

This paper (Cell 113, 115-125, April 4, 2003) reports results of experiments that together strongly support the conclusion that, in metazoan cells, formation of a complex consisting of the GTP binding protein Ran, the exportin Crm1, and the DNA helicase MCM plays a critical role in limiting DNA replication to a single round each cell cycle. This conclusion is largely based on two experimental results: (1) Experiments which show that a Ran mutant, RanQ69L, that binds GTP but cannot hydrolyze it inhibits incorporation of the MCM helicase into pre-replication complexes (pre-RC's) in Xenopus egg extracts. (2) Equally important is the observation that addition of a Ran mutant that cannot bind GTP, Ran T24N, induces both re-binding of MCM

helicase to DNA following a single round of DNA replication and induces a second round of replication. Together these results suggested that sequestration of MCM into a Crm1-Ran complex within nuclei during S phase of the cell cycle functioned to limit replication to a single round. In the course of pursuing this model further, a postdoctoral fellow in my laboratory, Dr. Peter Trabold, was able to reproduce results reported using the RanQ69L mutant. However, he was unable to reproducibly observe either the substantial reloading of MCM onto DNA or the robust re-replication reported to occur following addition of RanT24N. Occasionally, modest excess replication was observed following addition of RanT24N. However, further investigation demonstrated that this replication was most likely due to the transient permeablization of nuclei caused by addition of RanT24N. Therefore, although experiments using RanQ69L support a model involving the Crm1-MCM complex to limit re-replication, the inability of RanT24N to induce re-replication leaves the model unproven. In light of these new results, I am withdrawing the paper and the conclusions included in it.

The first author of this article, Ryuji Yamaguchi, is not a coauthor on this retraction because he stands firmly by the data presented in the article.

Case Scenarios for 2005 Ethics Training

Case 1. Dr. Wode's project has been to characterize the complex of proteins that interact with "protein Z". The material that elutes from an affinity column is fairly pure, and Dr. Wode only detects ~ 7 other bands on his silver stained-protein gel. He carried out mass spectrometric analysis and was able to identify five of the bands. Two of the proteins (X and Y) make sense with respect to the current model in the field. However, the three highest molecular weight proteins correspond to membrane proteins (A, B and C) that do not make sense to Dr. Wode. Dr. Wode has carried out co-immunoprecipitation experiments that showed that the X and Y proteins do in fact interact with critical protein Z in a cell cycle-dependent manner. As a control, Dr. Wode also assayed for the membrane proteins and found that A and B also co-immunoprecipitate with protein Z. The field is very competitive, and Dr. Wode is now writing up these results for publication.

Should Dr. Wode show the entire silver-stained gel, which might lead to questions about proteins A, B and C from the reviewers? Or should Dr. Wode cut off the top of the gel and not mention proteins A, B and C? One of the bands that Dr. Wode is not able to identify is present in material from both the affinity column and a control column. Should Dr. Wode eliminate this extra band using Photoshop?

Unfortunately the protein size marker lane was badly distorted on the gel where the samples electrophoresed nicely, and the marker lane ran nicely on a gel where the samples ran poorly. Can Dr. Wode splice the good sections of the two separate gels together?

By another stroke of bad luck, the autoradiograph showing the controls for the co-immunoprecipitation was ruined when water leaked on Dr. Wode's notebooks during a heavy rainstorm. Can Dr. Wode mention these controls as data not shown? If so, what should Dr. Wode do if reviewers ask for these data? What should Dr. Wode do to avoid this disaster in the future? How should critical data be protected?

Dr. Wode happens to be in a lab where the PI takes a "hands off" approach to manuscript preparation and preparation of figures. What responsibility does the PI have for monitoring these tasks and knowing which piece of primary data was used in each figure?

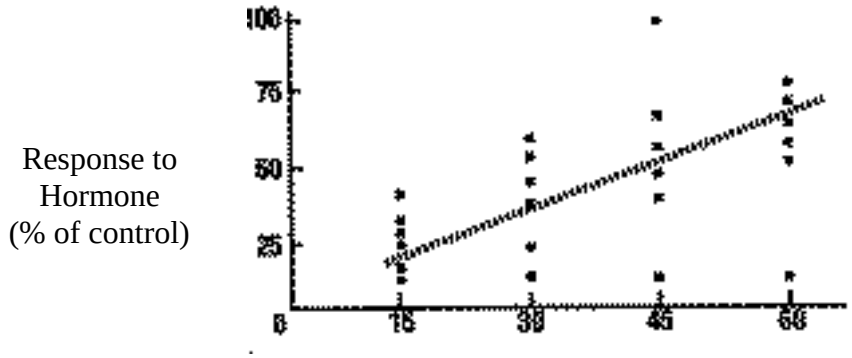
Case 2. Dr. Margaret Clint, a second year postdoctoral fellow in a neuroendocrinology laboratory, has just completed a series of experiments characterizing the receptor for a new class of hormones. During the course of this work, Dr. Clint carried out binding assays for a receptor mutant three times. In two experiments, the data were very consistent and supported the working hypothesis that Dr. Clint and her mentor were evaluating. However, in a third independent experiment, several of the samples showed the opposite effects.

Dr. Clint is supposed to present her data at the weekly meeting of her laboratory group and is now considering how to do so. In this analysis of the binding of hormone to the mutant receptor, should she average all three experiments? Should she average the two sets of data that are the

most consistent? Alternatively, could she present the data of one of the experiments and state that the findings are representative of three independent determinations? What if the experiment had been repeated six times and two of the experiments showed opposite effects?

In a parallel study, Dr. Clint investigated the hormonal response of several clonal cell lines transfected with receptor variants. In analyzing the data, Dr. Clint 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 to the hormone. The data from one cell line, with each symbol representing the response of one culture plate, are provided in Figure 1.

Figure 1



Dr. Clint was also perplexed as to how to present the hormone response data shown in Figure 1. She consulted Dr. Joseph Atwood, a senior research fellow in the laboratory. Dr. Atwood responded, "Why don't you clean up the data? Seriously, you may never get the paper published unless you do." He then suggested that the four culture points failing to show a response (along the X-axis at approximately 10% response) be dropped because the cells were probably dead. He also pointed out that she might eliminate the top data point at the 45 minute interval as an outlier. She said, "Perhaps I should repeat a few of the experiments or try to improve the culture conditions?" "No," said Dr. Atwood, "If you're convinced of your results, why go through the time and expense of more repetitions?" Somewhat dismayed, Dr. Clint thanked him and turned back to her work.

What do you think about Dr. Atwood's comments on publication practices and his suggestions for "cleaning up" the data? How should Dr. Clint go about determining which points to include and which to exclude in Figure 1? What other course(s) of action would you recommend to her?

Dr. Atwood'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?

One day, Dr. Clint's mentor asked her to prepare an abstract for an upcoming meeting, as

well as a preliminary report of her findings for publication. Unfortunately, the abstract was due in one week.

Is Dr. Clint ready to write an abstract? How should she present the data discussed above? What should Dr. Clint discuss with her mentor?

Case 3. Dr. Fong, a postdoctoral fellow in your laboratory, has been characterizing the offspring of smart-gene knockout mice. The construct was made by inserting a neo gene into the third exon. This knock out strain has just been generated and therefore is still in a mixed genetic background. Furthermore the protein blots of brain tissue show an unexpected smaller band that is faint but may specifically be reacting with the anti-smart gene anti-peptide antibodies (possibly a truncated derivative of the smart protein?). Dr. Fong presents her results in a group meeting and concludes that 70% of the offspring are slower in two of the behavioral assays the lab routinely carries out. Dr. Bhat examines another set of offspring in the same assays but concludes that only two or three out of the ten offspring are abnormal. You have heard that another laboratory has recently generated a similar mutant mouse and are worried about the competition. How should you proceed in light of these results? How should these behavioral data be documented? How much effort should be put into characterizing the immunoreactive protein band?

Case 4. Dr. Cott has been studying the subcellular localization of the "Key" protein. The favored model in the lab is that the "Key" protein moves between endosomes and the plasma membrane. In examining the Key protein labeled with GFP in living cells, Dr. Cott sees predominantly peri-nuclear staining consistent with endosomes, but no clear plasma membrane staining. However, by changing the filters used for visualization and exposing for very long periods, Dr. Cott can also observe some signal at the plasma membrane even though the rest of the cell is then badly over-exposed. How should Dr. Cott present these data? Can he show the plasma membrane localization by itself as a separate figure?

Dr. Cott also has been imaging the subcellular localization of the "Lock" protein, and has cells that are transiently transfected with a construct expressing GFP-labeled Lock. Before treatment with his favorite inhibitor, the Lock protein is in the Golgi in 55% of the cells (though most of the other cells show low signal or a diffuse distribution of Lock-GFP). After treatment with the inhibitor, the Lock protein is in the endoplasmic reticulum in 65% of the cells (again many cells show low signal or a diffuse distribution, and a few also show Golgi localization). Dr. Cott thinks that the redistribution of the Lock protein to the endoplasmic reticulum makes sense with respect to what is known about his favorite inhibitor. How can Dr. Cott present his data? Can he present a field of cells that show Golgi localization for his "without inhibitor" figure and a field of cells that show localization in the endoplasmic reticulum for his "with inhibitor" figure? What is the definition of a "representative example"?

Case 5. Dr. Williams is a Prinicipal Investigator who has a large laboratory at one of NIH's institutes. The laboratory includes about 15 junior researchers, post-doctoral fellows, and

graduate students. Twelve members of his group have been working on a project related to the relationship between hormones and obesity. They have isolated a key hormone in mice that is necessary to maintain normal weight. They publish a paper on this new finding, with Dr. Williams as the senior author. Two months after the paper has been published, Dr. Williams receives an inquiry from a researcher at a large university who has had difficulty replicating some of the group's work. The researcher requests to see the orginal data used to support a figure presented in the paper. Dr. Williams asks members of his team for the original data related to the figure and they report that the experiments that generated that data were conducted by Dr. VF, a post-doctoral fellow who recently left the laboratory to return to his native country. When Dr. VF left the institute, he was told to leave the original data at the institute and to take copies. A search of the laboratory for the original data has been less than satisfactory. The group discovers that there are several problems with the data, including the lack of a bound notebook and the availability of some “post-it” sticky notes written in Dr. VF's native language. They also have trouble retrieving data that were stored on his computer, which has been infected by a virus.

How should Dr. Williams deal with this issue?

2020 Ethics Case #1 – Data Access, Analysis and Reporting within a Research Group

As you go through this case, keep in mind that some key details are intentionally missing to encourage everyone to think through how the scenario might play out differently depending on some of the further case details you might want to know about.

When Dr. John Thomas (an M.D./Ph.D.) joined Dr. Rick Peterson's lab as a clinical fellow, Dr. Peterson told him about an exciting new compound they were studying that showed promise for treating schizophrenia. The lab was currently completing a Phase 1 clinical trial under the leadership of Dr. Sally Simpson, a staff clinician in Dr. Peterson's lab, who served as Lead Investigator (LI) and Medically Accountable Investigator (MAI) on the study with Dr. Peterson as Principal Investigator (PI). Dr. Simpson had just gone on early maternity leave unexpectedly due to complications, and the project needed someone to take over. Dr. Peterson suggested that Dr. Thomas take over the project and start planning the Phase 2 trial because Dr. Simpson wasn't expected to return for at least six months and Dr. Peterson was eager to keep the project moving. While Dr. Thomas found the science and experimental findings very interesting, he felt uneasy about taking over the project of another investigator who would be returning to the work. Dr. Peterson told him not to worry about it because as a staff clinician, Dr. Simpson would always have projects to work on and it didn't matter if she stayed with any one study through completion because she wasn't 'ambitious in that way'.

1. How can disruptions in workflow due to unexpected absences be dealt with?
2. Are there other ways Dr. Peterson could have approached this?
3. What if the Phase 1 trial had been funded by a bench-to-bedside grant (or other outside funding mechanism) obtained by Dr. Simpson? What if Dr. Simpson had served as PI on the study within Dr. Peterson's lab?
4. How could Dr. Simpson have handled the situation differently?

While Dr. Thomas still felt unclear about Dr. Simpson's future role on the protocol, he was excited about the opportunity to work with this compound and agreed to Dr. Peterson's plan. He learned all he could about the compound and the Phase 1 trial and took over the day-to-day supervision of data gathering and safety monitoring, reporting back to Dr. Peterson regularly. At Dr. Peterson's suggestion, Dr. Thomas occasionally emailed Dr. Simpson about potential side effects/adverse events in the participants since she had the most experience with the compound. He then began writing up the Phase 2 protocol, which was generally very straight-forward, but after his extensive review of the preclinical data, Dr. Thomas added a novel assessment of cognitive function to the standard clinical measures of psychosis. Again at Dr. Peterson's suggestion, he sent the protocol to Dr. Simpson, who was still on leave recovering from her complicated pregnancy and caring for her premature son, for input. Dr. Simpson reviewed the protocol, raised several helpful points, and suggested that a novel assessment of mood also be included.

5. Is it appropriate for Dr. Peterson to repeatedly suggest Dr. Thomas involve Dr. Simpson in ongoing work while she is on leave? What issues should be considered in a situation like this?
6. What other actions might Dr. Thomas take in this situation?

Dr. Simpson returned to the lab after about 6 months and opted for a flexible work schedule to accommodate childcare responsibilities she shared with her husband. She worked 10-hour days in the office on Mondays and Tuesdays (days her husband was responsible for childcare issues) and 20 hours flexibly the rest of the week, some of which could be unscheduled telework, in order to be available for any emergencies that might arise with her young son. Dr. Simpson told Dr. Peterson she wished to resume her work with the compound she had already spent so much time and effort developing but Dr. Peterson told her that Dr. Thomas needed to stay on that project because he was going to be applying for faculty positions and needed to demonstrate his ability to see a big project through the many phases required for developing a new treatment. Dr. Peterson also told her he thought

the project needed someone who would be reliably in the office every day in order for it to continue running smoothly. He did, however, encourage her to continue to help Dr. Thomas with the protocol and told her she would be included on any publications from the project. Dr. Peterson assigned Dr. Simpson to another protocol that he felt was more suited to her irregular schedule. Dr. Simpson saw little difference in the needs of the two protocols except that her new protocol was decidedly less likely to result in high-impact results.

7. Does Dr. Simpson have a 'right' to return to the project she was working on prior to her leave?
8. Would it matter if Dr. Simpson had taken the lead on the early development of the compound?
9. What issues arise when 'ownership/leadership' of a project has changed hands?

Dr. Thomas struggled to get FDA approval for his phase II protocol. Dr. Simpson, who had extensive experience getting FDA approval for protocols, helped him navigate several rounds of queries and get the approvals from both the FDA and IRB so he could start enrolling participants. Dr. Thomas finally began enrolling participants, but recruitment was slow, and it was difficult to maintain adherence through the one-year follow-up visit, which is far longer than typical Phase 2 studies. Dr. Peterson wanted the longer follow-up because it would allow for a more clinically relevant assessment of the drug and because long follow-up phases are possible at NIH where it's part of the mission to do long-term studies that are not feasible in other settings.

In the third year of his clinical fellowship, Dr. Thomas had a motorcycle accident, badly breaking several bones and requiring an extensive leave of absence. Dr. Peterson tapped Dr. Simpson to fill in while Dr. Thomas was recuperating, which she was easily able to do since she already knew the protocol well and had covered for Dr. Thomas for 10 days when his mother unexpectedly passed away. Recruitment picked up with Dr. Simpson in charge because she had relationships with community psychiatrists who felt comfortable referring their patients knowing she was running the study. When Dr. Thomas was ready to return to work about 6 months later, Dr. Simpson again asked to stay on the project and let Dr. Thomas manage another project for the remainder of his clinical fellowship. Dr. Peterson again said that it was important for Dr. Thomas's job prospects to remain in charge of the project he had started with, while Dr. Simpson already had a stable job and didn't need this project for her CV or advancement.

10. What do you think of Dr Peterson's decision-making process regarding management of this project?
11. What assumptions is Dr. Peterson making about Dr. Simpson's career, including her future plans? Is this appropriate? Might it reflect bias?

With the papers from his Ph.D. research and one publication from the Phase 1 data, which Dr. Peterson had allowed him to write up as first author, Dr. Thomas applied for jobs and was offered a soft money position as an Assistant Professor at a large research university. He negotiated some start-up funds but needed to apply for grant money as soon as he started. He asked Dr. Peterson to unblind the trial's treatment-arm data for participants who had completed the protocol to date (about half of the planned cohort) so he could analyze the study and use it as preliminary data for grant applications, without discussing this with Dr. Simpson.

12. Is this an appropriate reason to unblind an ongoing protocol? Why might Dr. Peterson refuse to unblind?
13. Would the situation be any different if this protocol was a preclinical study investigating the impact of the compound in a preclinical model?

Dr. Peterson agreed to unblind the completed participants, and Dr. Thomas analyzed the unblinded data quickly and began writing grants. He discovered that the compound appeared to have marginal efficacy for the primary outcome of psychotic symptoms, no effect on the cognitive functions he had hypothesized would benefit, but a strong effect on some aspects of mood that was already significant at the one-month follow-up in this initial

cohort sample. The mood measures had been added at Dr. Simpson's suggestion. He formulated his next hypotheses around these mood findings and started writing up a manuscript as well, since the findings were very interesting, even if preliminary, and having a paper would help his chances of securing grant funding.

Dr. Simpson found out about Dr. Thomas's analysis and results when he sent around a manuscript with himself as first author, Dr. Peterson as senior author, and Dr. Simpson as second author. Dr. Simpson complained to Dr. Peterson that the mood assessment was her contribution to the protocol and that she had planned to present the data at a conference and serve as first author. She also thought it was premature to publish the data as a paper, since the study was ongoing and had not yet met its planned enrollment numbers. Dr. Peterson mentioned that Dr. Thomas was submitting a grant to follow up on the mood findings. Dr. Simpson was not happy, as she had planned to follow up on this hypothesis if the data looked promising.

14. Who should control use of the data in this situation?
15. Is it appropriate to publish an interim analysis of an ongoing study? To include it in a grant application or present it at a conference?

After two more years, the protocol completed its final one-year follow-up visit. With the assistance of the current clinical fellow, Dr. Simpson analyzed the data and found that the compound significantly improved psychotic symptoms, mood, and cognition after a year of treatment. She drafted the findings for the three outcomes, with herself as first author, Dr. Peterson as senior author, the current clinical fellow as second author, and Dr. Thomas in the middle of the author list. Dr. Thomas, now three years into his new position and struggling to secure grant funding, was upset that Dr. Simpson had included all the data in one manuscript and thought the cognitive findings warranted their own paper which he wanted to write. He complained to Dr. Peterson.

16. How should decisions about publishing and authorship be handled after a post-doc has left the lab?
17. Is it reasonable to publish results separately in order to provide first-authorship opportunities for more study team members? What considerations should go into deciding what data get published together vs. separately?

2020 Ethics Case #2 – Moving On

Dr. Pat Suarez has been a highly productive postdoc with Dr. Jones at the NIH for three years. Though excited to begin a second postdoc at the University of GreatState (UofG) in a week's time, Pat is torn. He just received data back for samples he had submitted to the NIH Sequencing Core. The data are from patients with the disease that the Jones lab studies, and the results are expected to provide insights into why some patients are unresponsive to treatment.

Pat offered to undertake the bioinformatics analysis of the data even though he was formally leaving the lab, but Dr. Jones was resistant. He gave as his reason that Pat should immerse himself in the work of his new lab, but he also had in mind that the analysis would be a good first project for the new computationally-trained postdoc scheduled to join the lab in a few days. Dr. Jones reminds Pat of all he has accomplished in three years and assures Pat that he would be co-first author on the primary publication from the project.

Though Pat highly respects Dr. Jones, he decides that Jones couldn't possibly be unhappy if he was able to rapidly analyze the sequencing data after leaving the lab (working evenings and weekends). On his way into lab on his last day, Pat stops to purchase a high capacity flash drive at his favorite computer supply store and copies the data files. He finally finishes late in the evening, grabs the three lab notebooks he's filled over the years and heads for the door.

1. Who owns the data generated by an NIH lab or research group?
2. Does Pat have the authority to take copies of the sequencing data with him? What about the lab notebooks?
3. How could this situation have been better managed by Dr. Jones?

A few days later Pat starts work in his new lab. His new PI had purchased a laptop for him, which Pat configures for use on UofG's network. He is eager to get a start on analyzing the data from the Jones lab before getting too busy with new work. When Pat gets home, he immediately loads the data from the flash drive to his new laptop and gets to work.

4. Apart from the right or wrong of taking a copy of the data, how have Pat's actions put the security of the data at risk?
5. It is not uncommon for trainees (as well as other NIH scientists) to finish up projects after leaving the NIH. For someone in Pat's situation (i.e., leaving NIH for another training position), what is the appropriate arrangement consistent with NIH data use policy?
6. What additional or different considerations would there be if Pat were leaving NIH to accept a position as independent investigator at a university? Or what if Pat were starting a job in industry?

Over the next few weeks and on his own time, Pat analyzes the sequencing data he brought from the Jones lab. He is pleased because he had been taught to use some sophisticated, home-grown bioinformatics tools in his new lab at UofG and they have proved very useful for analyzing the Jones lab data. He has found some exciting results, and when he emails his analysis to Dr. Jones he feels sure that Dr. Jones will be impressed.

But Dr. Jones is NOT happy. He tells Pat that a new computationally trained postdoc in his lab had been doing some nice analysis of the same data set with the understanding that it was HER project. And he is very concerned about Pat using software tools developed at his UofG lab. Pat is dismayed.

7. Should Dr. Jones be upset? What are his interests and obligations in this situation?

THEME 1: SCIENTIFIC MISCONDUCT

CASE 1

Adapted from: **Research Ethics: Cases and Materials**, **by Robin Levin Penslar**

Scientific Misconduct : by **Karen Muskavitch, Boston College**

Chapter 4 *What Is It and How Is It Investigated?*

This hypothetical case is loosely based on several scientific misconduct cases that have occurred in the last few years. It does not involve a whistle-blower and therefore does not involve such issues as whistleblower victimization, officials failing to heed warnings and take action, or the need to ensure accusers' confidentiality during an investigation while providing due process to the accused. While these are important issues which can be explored if time allows, the intended focus here is on three equally important topics:

1. Proper laboratory practices, particularly in the management of data and its manipulation as manuscripts are prepared.

2. The definition and identification of scientific misconduct.

3. The way in which investigations of alleged scientific misconduct are and should be carried out.

Part A (One Day in August)

David Dunbar, one of the postdocs in Professor Steve Grey's lab at Big Tech, has just finished presenting the results of his latest set of experiments to the lab group at the weekly lab meeting. Grey's lab is a large group, with 22 technicians, research associates, graduate students, and postdocs all working on the identification and mechanism of action of genes associated with cancer. Dunbar presented the results of a series of experiments investigating the expression of the *tnc* cancer gene in normal cells and a variety of cancer cell lines. (The *tnc* gene is associated with toenail cuticle cancer, a rare cancer usually seen only in certain at-risk families.) It was a nice presentation. For instance, his table of RNA levels was beautiful, as well it should be. It was the last figure in a manuscript he and Grey just submitted to the Prestigious Cancer Journal, Dunbar's fourth paper on which he was first author since joining the lab two and a half years ago.

Shortly after the meeting, Erik Larson, a graduate student, comes into Professor Grey's office, shutting the door behind him. "David couldn't possibly have done all the analyses he reported in group meeting," asserts Larson angrily. "Unless he's got a lab at home. In fact, I'll bet some of the cell lines he showed numbers for in that last table haven't even grown up enough yet for RNA isolation." "Have we ever had reason to doubt David's work?" asks Grey. "No," Grey continues, not waiting for Larson's response. "We have always been able to follow up on his results, to the benefit of many in the lab. Yes, I know he gets a lot done during his time in lab,

but he's just more experienced and better organized than most others. Now, how is that work of yours going on the search for tnc-related genes in yeast?". After a short discussion of his recent experimental results, Larson leaves Grey's office. Grey sits at his desk, reflecting on their conversation. "I guess Dunbar's success just makes others uncomfortable," concludes Grey, wishing that personnel management had been part of his training.

Questions for Discussion

1. Was Larson right to bring his concerns to Grey? Could Larson have presented his concerns in a better, more persuasive way? Should Larson do anything further now that he has spoken to Grey?

2. Was Grey's response to Larson appropriate? Is there some way in which you think it could be improved?

Part B (One Month Later)

Jeff Adams, a new postdoc who has just arrived in Grey's lab, pulls Larson aside. Adams is supposed to pick up the work on human tnc, since Dunbar will be leaving soon. "Hey, what's with these papers you guys have published?" Adams asks, waving a paper of which Dunbar, Larson, and Grey were authors. "What do you mean?" Larson responds. "Well, look at this autorad in figure 1. All the lanes are the same!" fumes Adams. "Sure," replies Larson, "that's the point of the paper. We see the same, odd rearrangement to give a new 7.2 kb band in all the cell lines from toenail cuticle tumors." "No, that's not what I mean," says Adams, shaking his head. "Look at the background dots on the film. The same dots are in each lane. These aren't the results from different tumor lines; these are copies of the same photograph!" "Oh, my heavens!" exclaims Larson. "I never noticed that before. I was a new student in the lab when this work was done and all I did was help on the cell growth and DNA isolations. I have no idea how Dunbar made this figure. We'd better talk to Steve right away."

After talking with Adams and Larson and seeing the published figure in a whole new way, Grey calls in Dunbar and angrily accuses him of fabricating data. Dunbar appears genuinely shocked. "I didn't make up any data!" he asserts. "I did all those analyses and got those results; I can show you the autorads. I was just trying to make the nicest-looking figure for publication." "But these aren't the results for the cell lines indicated in the figure. It's all copies of one of them. You can't do that," replies Grey. "Why not? It's the same thing as cutting up the autorad to make figure 4. I didn't try to deceive anyone," says Dunbar. "And besides, no one said anything. Not people in the lab, not you, not the reviewers. I thought that was how it was done."

Questions for Discussion

1. At the end of the case are drawings of the two figures from the published paper (figures 1 and 4), as well as the two original autoradiograms from which they were derived (figures 2 and 3). Did Dunbar fabricate data in his production of figure 4? In the production of figure 1? Explain your criteria for determining fabrlcation.

2. Does it matter that the primary data show that the results are the same as shown in figure 1? Does it matter that the avowed intent was to produce a prettier picture, not to deceive?

3. Should Larson have been a coauthor on the paper if all he contributed were some routine

laboratory manipulations?

4. What are the responsibilities of coauthors for the authenticity of the contents of a paper? What are the responsibilities of reviewers in this area?

5. How could Grey change the practices in his laboratory to minimize the possible recurrence of a problem of this sort?

Part C

Although somewhat relieved that the autorads Dunbar produced verified that his creative graphic artistry did not alter the basic results or conclusions of the published paper, Grey is still shaken and worried. He decides to check all of the work Dunbar did while in the lab. Grey asks three senior postdocs in the lab, Xavier, Yates, and Zimm, to begin a review of Dunbar's notebooks and published work. Grey then heads for the department chair's office to inform him of what has been discovered and what is being done.

Questions for Discussion

1. Should Grey have contacted the departmental chair at this point?

2. Are there any other interested parties who should be informed?

Part D

Dunbar returns to the lab after lunch to discover Xavier, Yates, and Zimm looking through his notebooks. Dunbar is furious, asserting that notebooks are, like diaries, private. "I thought I made it clear to the lab last year, when that new student was pawing through my notebooks, that no one was to touch them without my permission," says Dunbar.

Yates can't believe what he's hearing. "It was Steve who asked us to check over your work," Yates says, "and I think you know why. Besides, where do you get these ideas about notebooks? When I was a grad student my Ph.D. advisor routinely checked each student's notebook every evening, and anyone in the lab was free to look up any information needed for their work."

"Actually, it's a good thing you're back. We have a couple questions," interjects Zimm. "Where are the data for the first paper you published from this lab? We can only find this box of autorads."

"I threw those notebooks out a few months ago. I figured the work was all published long ago, and I needed more space on my bookshelves," replies Dunbar.

"\Vell, then, what about the instrument printouts for the analyses you presented in the second paper? We can only find tables recording mean values. There doesn't seem to be any record of the actual, individual determinations," says Xavier, jumping into the discussion.

"I never keep instrument printouts," replies Dunbar, getting angrier by the second. "Who does? I don't need all that useless paper cluttering up my desk. I just analyze the data and ditch that

stuff. I've got better things to do than play filing clerk."

Questions for Discussion

1. To whom do laboratory notebooks belong? The individual? The principal investigator (PI)? The department? The laboratory? The university? The funding agency? The NIH?

2. Who should have access to laboratory notebooks and other experimental data? Are there only certain circumstances under which some people should have access?

3. What types of data should be retained, in what form, and for how long? Whose responsibility is it to see that data are appropriately retained?

4. Where should the data be retained? For instance, do the notebooks go with a finishing student or should they stay in the lab?

Part E

Larson, rather shaken by the revelations of the day, wonders about the effect that this business will have on his career. He was so pleased to have his name on a paper published in his first year in the lab; now he's not so sure it will be to his advantage at all. In the cell culture facility, Larson, remembering Dunbar's lab meeting last month, decides to take a look at the culture logs and compare them with the lines listed in Dunbar's RNA level table in the submitted manuscript. Unfortunately, his unease was justified. Two of the lines listed in the table were not even in the lab at the time of the meeting. They arrived since then from the stock center and are being grown, but Dunbar couldn't have obtained data from them when he said he did. Larson makes a copy of the log and goes to look for Grey.

When Grey and Larson confront Dunbar with the cell culture log the next day, Dunbar admits that the numbers reported in the table were not derived from RNA analyses but were his best estimates of what the results would be. "Look," says Dunbar, "I knew what the results would be. You know how long it takes to go through the review process for the Prestigious Cancer Journal. It's been more than a month, and we haven't heard a thing. If I had waited for the cells to come in and grow up and for the review, it would have been a year, and I could have gotten scooped! Don't worry, I didn't do anything wrong. When the paper was accepted pending a few requested revisions, I planned to just put the real data in the table and everything would be fine."

"Sure," says Larson. "How can I believe that you really would put in the real data?

"Easily," replies Dunbar, "because that's just what I've done before."

"What! When else have you submitted 'estimated data' for review?" asks an astonished Grey.

"Lots of times. Like in that first paper with the figure you're so upset about. What's the big deal? I've never tried to deceive anyone. I've never had to change the conclusions of a paper."

Grey searches for and finally finds a disk with the file of the two-year-old manuscript (in the form in which it was submitted), calls it up on his computer, and compares it with the reprint he keeps in his top desk drawer. Sure enough, the numbers listed in the table show the same basic trend

in the two versions, but are not the same.

Questions for Discussion

1. Does Dunbar's method of preparing his manuscripts for publication constitute fabrication or falsification? Is it, rather, a questionable research practice? Or is it simply a novel way to speed the progress of science?

2. Is it important to consider that the conclusions drawn in the submitted and final versions are the same?

3. Is it important to consider that, as Dunbar asserts, he did not intend to deceive anyone?

4. Is it important to consider that, in the end, only the real data were actually published?

5. What are the consequences to science of this approach to publishing?

6. Suppose that, in his fury, Larson threatens to call the editor of the Prestigious Cancer Journal and tell all. Should he do this? Is it warranted and proper, is it premature, or is it unwarranted and inappropriate?

Part F

While all this was going on in the Grey lab, the departmental chairman, Jack Washington, was also busy. After Grey informed him of the problematic figure, Washington consulted with the dean for research at Big Tech to see what was expected of him. He was told that he was to see that an initial inquiry was undertaken to determine whether an investigation was in order. It was up to Washington to appoint those who would conduct the inquiry. Above all, the dean cautioned, keep this quiet. "Well, if all we have to do is gather information while keeping a lid on this, the people Grey has got looking into it will make a perfect inquiry committee," he decides. "No one else need be involved." So Washington calls Grey to request that Grey send him a written report when Xavier, Yates, and Zimm finish.

Within three weeks, the three postdocs give Grey a written summary of their findings which mentions the figure produced by creative graphic artistry and the "estimated data" submitted for review, as well as the missing laboratory notebooks and primary data. Grey reads it over, edits it a bit, and sends it to Washington. Washington then forwards it to the dean for research as the report of the inquiry committee he was told to appoint.

Questions for Discussion

1. Are other members of the same lab the best people to review Dunbar's work? If not, who would be a better choice and why?

2. Should the head of the laboratory, who is also a coauthor, be involved in the initial inquiry in the manner described here? What arguments for and against his involvement can you make?

3. Has Washington fulfilled his obligations to the institution and the accused?

Part G

After reviewing the inquiry report, the dean for research and other administrators at Big Tech decide that a full misconduct investigation of Dunbar is required. They further conclude that no investigation need be carried out for Grey or the other coauthors, as the suspect conduct seems to be Dunbar's alone. They so inform Dunbar, Grey, Washington, and the National Institutes of Health (NIH) which funded this research.

Grey contemplates what he should do. Concluding that the best way is full disclosure and a clean break with Dunbar, he dismisses Dunbar from the laboratory and terminates his salary, which had been drawn from an NIH grant awarded to Grey. Then, after consulting with the other coauthors but not with Dunbar, Grey writes to the journals retracting all the published papers on which Dunbar was an author and withdrawing the manuscript still in review.

Questions for Discussion

1. Do you also conclude that an investigation of Dunbar is warranted? If so, what would be the components of scientific misconduct of which you would accuse Dunbar?

2. Do you conclude as well that only Dunbar should be subject to a misconduct investigation?

3. Are Grey's actions proper and warranted? Which, if any, are inappropriate and why?

Part H

All of this couldn't have happened at a worse time for Dunbar. After a series of successful interviews, he was looking forward to starting his own lab at another university. With the research he had done in Grey's lab and previous publications from his Ph.D. research, Dunbar figured he had a pretty good shot at a good job. Now getting a good job looked impossible because, in addition to everything that had already happened, Grey sent letters to each of the universities to which Dunbar applied telling them of the accusations against Dunbar and the planned investigation and retracting what had been very strong letters of recommendation. In response, the one university that had already offered Dunbar a position withdrew its offer.

Questions for Discussion

1. At the time the concerns about Dunbar's work were raised, Grey had already sent letters of recommendation in support of Dunbar's job applications. Was he under any obligation to inform the institutions to which Dunbar had applied of changes in his evaluation of Dunbar since writing his letters?

2. Suppose Grey has not yet written his recommendation letters when these matters come to light. Is he under any obligation to inform potential employers of the pending investigations?

Part I

The dean for research appointed a five-member committee to conduct the investigation. All five members were from the Biological Sciences Division of Big Tech. They reviewed the evidence and interviewed people at Big Tech and other universities.

When Dunbar was interviewed, he did not deny any of the actions of which he was accused, but he did deny that he was guilty of scientific misconduct. He asserted that it was never his intent to deceive and that all of the data presented in his papers were derived from actual primary data. He denied ever fabricating anything.

"I thought that was how you prepared a paper for publication," Dunbar said. "No one told me any differently. In fact, the first manuscript I ever prepared was when I came to Grey's laboratory. When I was a graduate student at Enormous State University, my advisor wrote all the papers that came out of the lab. Yes, some of my original data are gone. I didn't know that I was expected to keep them even after they were published, or that people thought instrument printouts were important. So I'm a poor document clerk; that's no crime!"

Questions for Discussion

1. Was the composition of the investigating committee appropriate?

2. Should naivete be an adequate defense in a situation like this?

3. How can the scientific community ensure that others in the future will not also be able to say, "But I didn't know."

Part J

The Big Tech investigating committee concluded that Dunbar was guilty of scientific misconduct, having found the multicopied lanes on the autoradiogram and the submission of 'estimated data" for review to be examples of fabrication. In addition, they concluded that Dunbar had engaged in many questionable research practices, such as prematurely destroying data, failing to record or keep primary data, and denying other scientists access to his data.

The findings of the investigating committee then went to Big Tech's administration for action. As required, a report was sent to NIH, but no further action was taken to punish Dunbar because he was no longer associated with Big Tech and was no longer engaged in scientific research. When last contacted, Dunbar had enrolled in an MBA program and was trying to put his life together again.

Questions for Discussion

1. Is this an appropriate conclusion for this tale?

2. What, if anything, could and should Big Tech or NIH do to punish Dunbar?

FIGURE 1

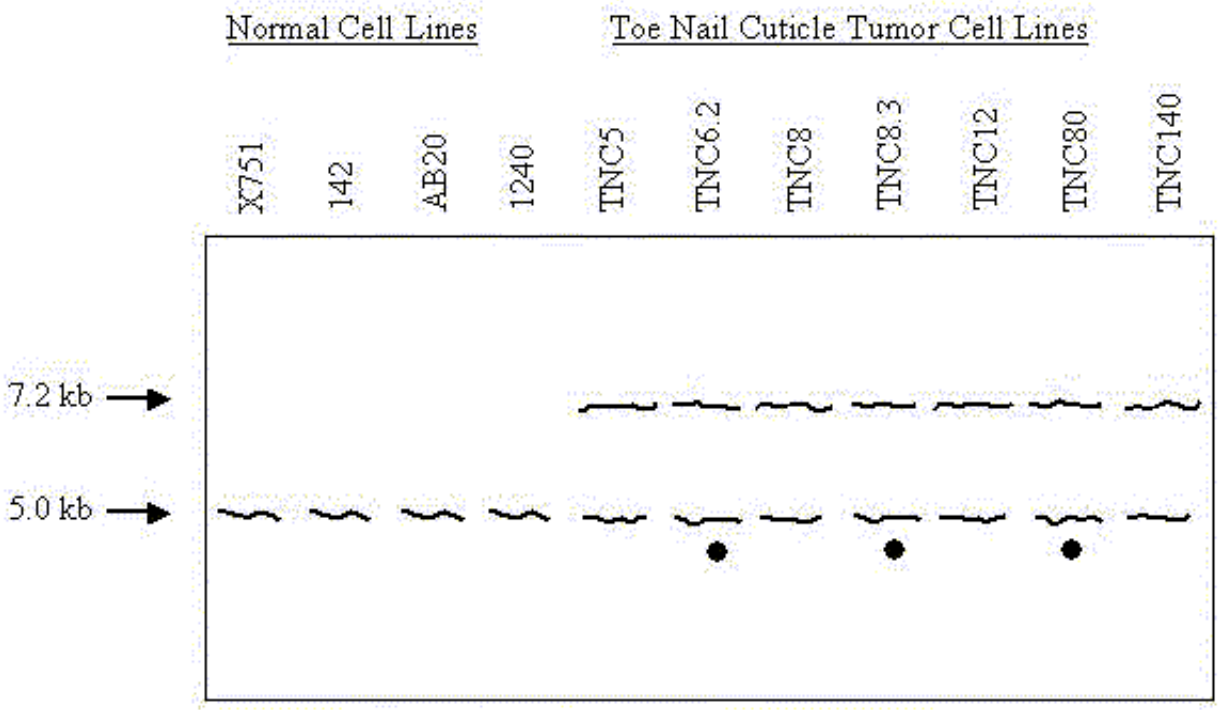


Figure 1.

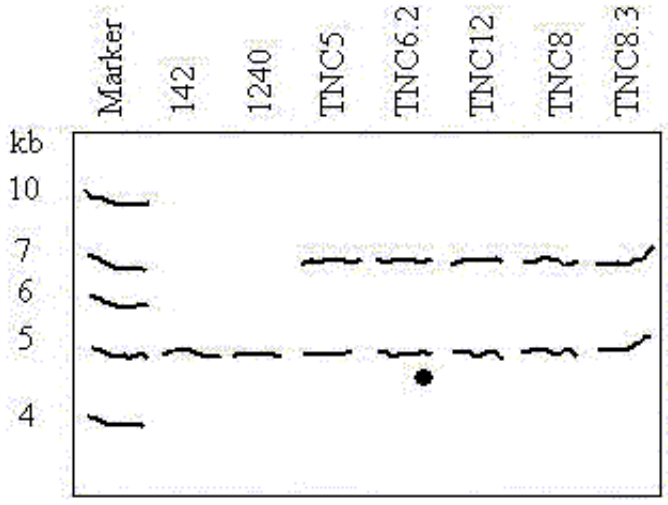


Figure 2.

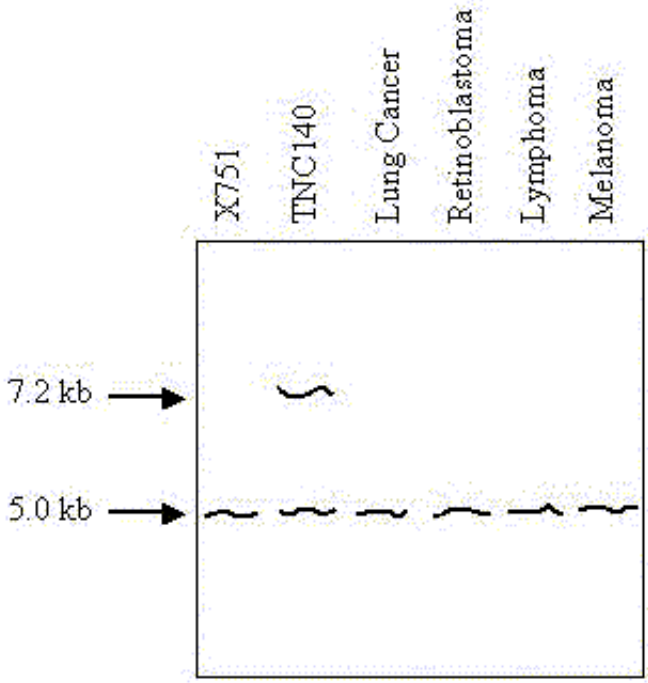


Figure 4.

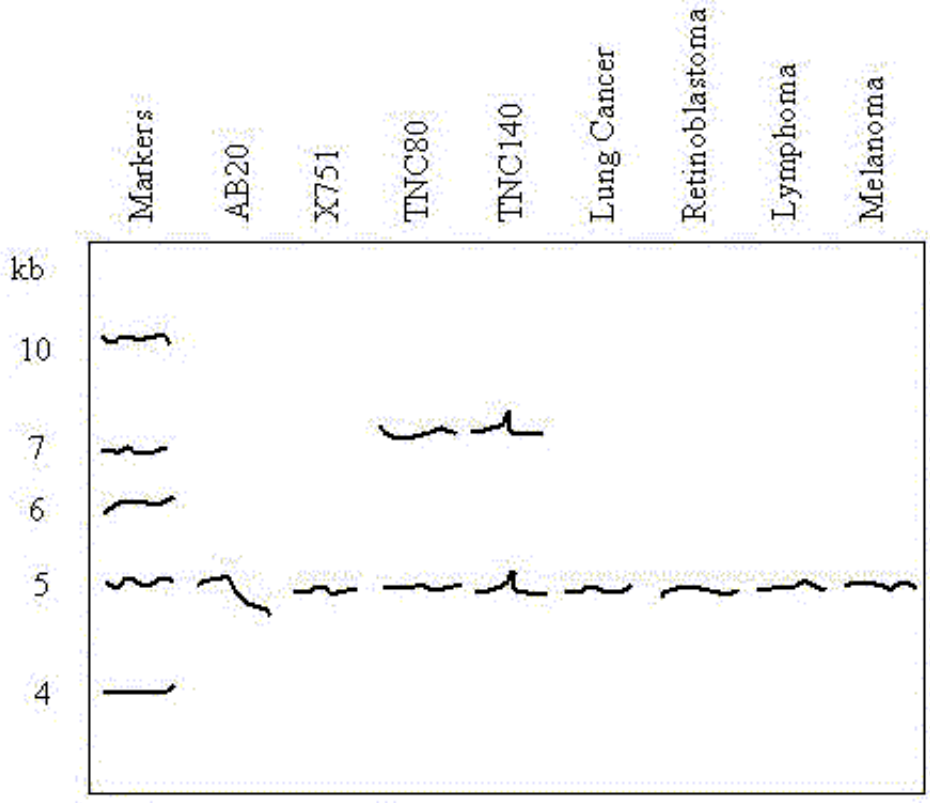


Figure 3.

THEME 1: SCIENTIFIC MISCONDUCT

CASE 2

From: ***Teaching the Responsible Conduct of Research Through a Case Study Approach: A Handbook for Instructors:*** With permission from the Association of American Medical Colleges

Dealing with Suspicions of Misconduct

CASE FI

Eric Woodworth is an oncology nurse working in a clinical research center (CRC) at a large academic medical center. Dr. Philip Thomas is an oncologist and clinician researcher who conducted a trial in the CRC of a drug being evaluated for its safety and efficacy in alleviating the nausea and discomfort associated with cancer chemotherapy. Eric assisted on Dr. Thomas's project in several ways. He attended to the patients' routine clinical needs and administered their cancer chemotherapy by I.V. He also gave the patients participating in Dr. Thomas' protocol oral doses of what may have been either the experimental drug or a placebo. The vials were numerically coded, so Eric did not know which he was providing. Finally, he interviewed patients concerning their symptoms, following a standardized questionnaire prepared by Dr. Thomas.

At times, Eric tried to guess, based on their responses, which patients were getting the placebo, and which were getting the real drug. In fact, he did not observe much difference in any of his patients and was convinced that the experimental drug was ineffective. He conveyed his opinion to Dr. Thomas, who merely shrugged and said, "We'll see."

After Eric's role in this protocol concluded, he was quickly engaged in other responsibilities. Meanwhile, Dr. Thomas compiled and analyzed the data that Eric collected and wrote up the results. Months passed, and the research ultimately was published in a well-known oncology journal. Eric was curious to read the results of this project, particularly since he was to be acknowledged for his contributions to the effort. Upon locating a copy of the journal, Eric read with astonishment Dr. Thomas's conclusion that the experimental compound was highly effective in alleviating the physical distress precipitated by chemotherapy. Eric read the article closely and decided that Dr. Thomas's recounting of the survey results was inaccurate, describing alleviations of discomfort that Eric never observed or recorded.

Questions for Discussion

1. If you were Eric, what would you do at this point to address these concerns?

2. Does Eric have a responsibility to take action toward correcting what he believes is an erroneous report?

Eric wondered what he should do in response. He hesitated to tell his supervisor, the head CRC nurse, because they did not have a very good relationship. Although Eric thought of himself as assertive and conscientious -- never hesitating to point out ideas for improving the operations within the CRC -- he understood that his boss viewed him more as a thorn in her side. He reported his concerns to her, nonetheless, figuring that, at worst, she would discount his report as another in a long list of complaints. As he predicted, his supervisor advised Eric that it would be in his best interest to focus on his current responsibilities and to stop looking for problems. That earlier project was so subjective, she added, that differing opinions on the results were not surprising in any case. Eric indeed recognized a certain subjective quality to the study, having wondered at times if he was recording patient reports consistently.

Questions for Discussion

3. Did Eric's supervisor respond appropriately to Eric's concern? How might you have responded were you in her position?

4. Having received such a response, what might Eric do next?

One day, when crossing the medical center complex, Eric ran into Dr. Thomas and expressed his surprise at the paper's findings. Dr. Thomas stated that once the survey results were decoded, a significant difference between patients receiving the placebo and the experimental drug became evident. Eric then stated that he would be fascinated to learn which patients were getting the drug and which weren't; he asked if he could take a look at the completed surveys now that they were unblinded. Acting hurried, Dr. Thomas stated that they had been sent to storage and that it would be too much trouble to retrieve them. He then dashed off. This behavior seemed suspicious to Eric and made him inclined to believe that some deliberate misrepresentation had taken place.

Questions for Discussion

5. Eric suspects that Dr. Thomas misrepresented the findings of the survey, but he cannot empirically support his suspicions without access to the surveys. Does he have a right to those materials since he is acknowledged in the paper?

6. Given Eric's lack of access to the surveys, how should he follow up on his suspicions?

7. Does Eric have an appropriate basis for lodging an allegation of scientific

misconduct? Is there a distinction to be made between an "allegation" and an "expression of concern"?

Eric tried on several more occasions to get the survey data from Dr. Thomas, without success. Knowing his supervisor was unsympathetic to his concerns, and upon the advice of a trusted

colleague, he decided to approach the administrator of the medical center's institutional review board (IRB). The IRB reviews the ethical and legal ramifications of proposed clinical research and its administrator would certainly be interested in his suspicions, he reasoned.

Questions for Discussion

8. Does the IRB or its administrator have authority to deal with instances of scientific misconduct?

9. Whom would you approach at your institution if you suspected research misconduct?

Upon meeting with the IRB administrator, Eric explained his belief that Dr. Thomas had misrepresented the findings of his research. In response, the IRB administrator informed Eric that complaints of that nature should be taken to Dr. Holly Baird, the associate vice president for research and the institutional Research Integrity Officer. The IRB administrator counseled Eric that he should not take his concerns any further, though, unless he were fairly certain of them. His allegations seemed to be based on sketchy recollections of data collected long ago, she said, adding that, in her opinion, he did not have sufficient basis for a complaint.

Questions for Discussion

10. How should one decide whether a suspicion of wrongdoing is sufficiently significant to warrant lodging a formal complaint?

11. What are some considerations Eric might take into account in weighing whether to lodge a formal complaint?

12. In your opinion, does Eric have sufficient cause to register a complaint with the Research Integrity Officer?

After the conversation, Eric pondered different ways to handle this situation. One approach would be to lodge an anonymous complaint with Dr. Baird and simply let events run their course. Alternatively, he could present his concerns in person, but rather than focus on the inaccuracy of Dr. Thomas's work, he would simply assert a right to access the surveys. Both approaches seemed loaded with pitfalls.

Questions for Discussion

13. Should institutions encourage or discourage the practice of lodging anonymous complaints when individuals suspect misconduct? What problems might anonymous complaints pose for the institution? What issues of fairness might anonymous complaints pose for the accused? What advantages and disadvantages are posed by this approach for Eric?

14. If you were Dr. Baird, the institution's Research Integrity Officer, how would you handle an anonymous complaint?

15. Why might Eric's second idea, to focus on his desire to access the surveys, prove risky?

16. Would it be better for Eric or for someone else to examine the surveys? Why?

In the end, Eric approached Dr. Baird with the observation that Dr. Thomas's findings seemed inconsistent with Eric's knowledge of the surveys. He framed his concern as much as possible as an observation of fact, without suggesting that any deliberate misrepresentation had taken place. Eric was also quick to note that he repeatedly tried to access the original surveys without success.

Dr. Baird listened to Eric's report and told him that because he had questioned the integrity of Dr. Thomas' research, the institution would be compelled to explore the legitimacy of Eric's statements. This initial phase is termed an "inquiry" she said and would involve an initial review to determine whether a formal investigation would need to take place. Although the complaint might be resolved after reviewing the original survey instruments, it is possible, she explained, that an investigation might ensue, at which point Eric might need to become involved. Eric suddenly felt very queasy. Reflecting upon the prospect of having a face-to-face confrontation with Dr. Thomas, Eric wished that he had never raised the issue at all. The drug in question wasn't even that important, he thought. It's not as though patients would be harmed by it, he considered, wondering why should he take the risk of becoming further involved.

Questions for Discussion

17. Even if an investigation takes place, is it necessary for Eric to become involved in the process? Under what circumstances might his involvement be essential to permitting those conducting the investigation to arrive at a determination of what happened? Under what circumstances might his involvement not be required?

18. If Eric does become involved in the process, is it necessary for him to confront Dr. Thomas directly, as he envisions?

19. Should the clinical importance of the research weigh in the decision to pursue the allegation?

20. Eric might have wrongly accused Dr. Thomas. What should the consequences of that error be, if any?

21. If misconduct is found, what steps should the institution take?

22. If misconduct is ruled out, what steps should the institution take?

23. If Dr. Thomas is exonerated, but Eric feels certain that he misrepresented the data, what recourse does he have?

Scientific misconduct continues to be a serious and ongoing problem in the biomedical research community

Since 1994, there has been an average of two misconduct cases that have been examined by Inquiry, and in some cases, Investigation Committees in the NIH Intramural Research Program EACH year.

Recently a finding of misconduct in the extramural community resulted in a 366-day Federal prison term for a scientist because his actions led to loss of government funds, obstruction of justice, and abuse of a position of trust. The sentenced scientist had the following explanation for his actions:

"First, I believed that because the research questions I had framed were legitimate and worthy of study, it was okay to misrepresent "minor" pieces of data to increase the odds that the grant would be awarded to UVM and the work I proposed could be done. Second, the structure at UVM created pressures which I should have, but was not able to, stand up to. Being an academic in a medical school setting, I saw my job and my laboratory as expendable if I were not able to produce. Many aspects of my laboratory, including salaries of the technicians and lab workers, depended on my ability to obtain grants for the university. I convinced myself that the responsibility I felt for these individuals, the stress associated with that responsibility, and my passion and personal ambition justified "cutting corners". Third, I cannot deny that I was also motivated by my own desire to advance as a respected scientist because I wanted to be recognized as an important contributor in a field I was committed to."

Underlying this case was the issue of data management and the detection by one of the scientist's staff of inappropriate data management. He admitted to destruction of electronic evidence of his falsifications and fabrications, among other things. Scientific misconduct is detrimental to all parties involved. Everyone in a lab has a responsibility to be informed and vigilant about appropriate data management to prevent instances of scientific misconduct.

Several of the following cases are based on actual misconduct cases.

Case 1 - Data Management of Computer-generated Files

Case 2 – Handling of Images and Graphs

Case 3 – Appropriate Use of Statistics

Case 4 – Appropriate Sources of Data and Decision to Publish

Case 5 – Handling of Clinical Data

Comments and Guidelines derived from the Cases

Case 1 - Data Management of Computer-generated Files

Dr. Fred has been at the NIH for three years and is anxious because he has not published a paper and wants to begin looking for a job. He was finally able to purify all of the mutant genes needed for his analysis and recently presented a draft of a manuscript to Dr. Wilma, his mentor. Dr. Wilma found the data interesting but wanted to see the original scans for Table 1, which supposedly were carried out in February 2006. Dr. Fred could not produce a copy of the original scans because after he received a warning that his folder was full, he inadvertently deleted the data on the lab computer associated with the spectrophotometer. As a result, he had only an Excel table with the numbers he had written down from the plots produced by the lab computer. Dr. Wilma was able to obtain a backup copy of all the February scans that had been backed up on the institute's server, but none of these files contained data corresponding to the numbers in the Excel file. Since he could not produce the missing data, Dr. Fred carefully repeated the experiments and showed Dr. Wilma that all numbers were consistent with the original Table 1. Two pages from Dr. Fred's lab notebook covering February 2006 are attached.

Does this case represent scientific misconduct?

- Are there any problems regarding data management, and if so, what are they?
- Who is at fault?
- How could this case have been prevented?
- Can you show all of the primary data for each experiment that you performed a year ago?
- Could someone reproduce the details of your experiments from your lab notebook?
- What are the elements of a good lab notebook?

ligation

insert	3
vector	1
5X	2
ligase	1
	3
	10

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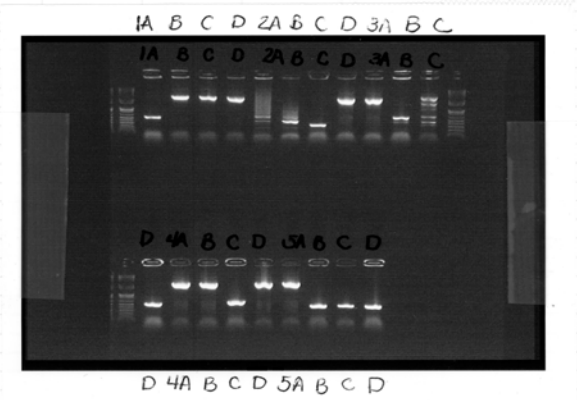


purified :

1B
1C
2D
3A
4A
4B
5A

1B	5.4	10.6	57.2		
1C	5.6	11.2	62.7		
2D	5.9	50.3	296.8		
3A	6.1	1.1	6.7		
4A	6.2	9.0	55.8		
4B	5.5	9.0	49.5		
5A	5.7	101.1	576.3		

2-17

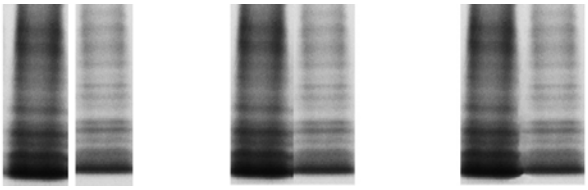
1B	5.4	110.1	594.5		
1C	5.6	10.7	59.9		
2D	5.9	53.4	315.1		
3A	6.1	0.9	5.5		
4A	6.2	8.9	55.2		
4B	5.5	9.2	50.6		
5A	5.7	102.8	586.0		

1B	6.4	9.5	60.8		
1C	6.2	10.9	67.6		
2D	5.9	54.0	318.6		
3A	6.1	0.8	4.9		
4A	6.3	9.1	57.3		
4B	6.2	8.9	55.2		
5A	5.8	105.6	612.5		

Case 2 – Handling of Images and Graphs

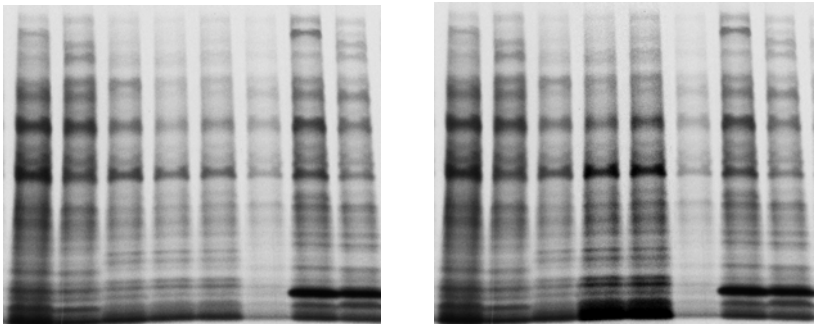
Dr. Green is preparing her manuscript for submission to a high-impact journal and is trying to decide the most effective way to present her gel and image data. Colleagues tell her that the data need to be "impressive" and "clean." She comes to you for advice about which of the following versions would be the most effective presentation of her data.

A. Spliced lanes from different parts of the same gel.



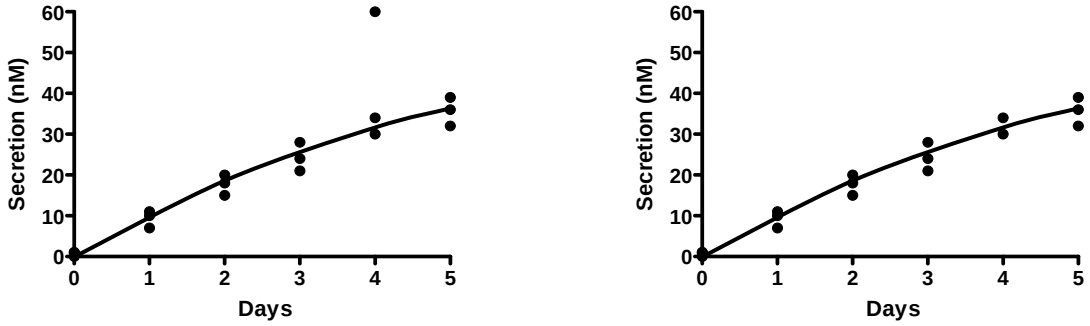
Originals Joined Blurred

B. Lanes enhanced for emphasis.



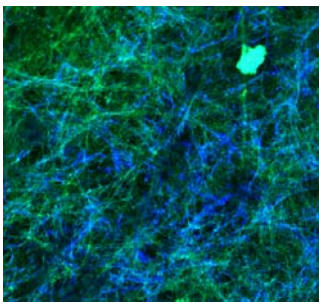
Original Two lanes enhanced

C. Deletion of outlying point.

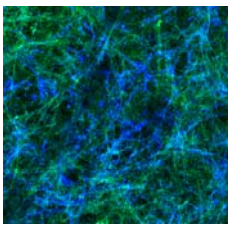


Original data and graph Anomalous point deleted

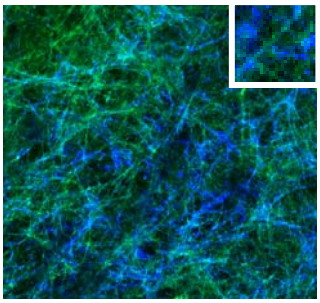
D. Cropping and cosmetic fixes.



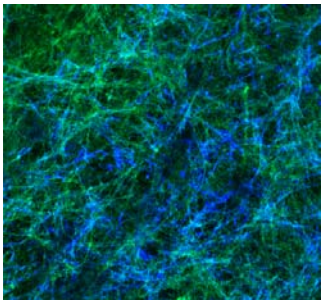
Original with “junk”



Cropped



Hidden by inset



Fixed using Photoshop

- What is your advice?
- Which changes are acceptable, borderline, or inappropriate?
- How do you choose the findings that you actually publish?

Dr. Green raises the issue that she has had two experiments that “worked,” i.e. both showed that stress increases synthesis of the protein stimulin considerably more than it increases borin. However, an earlier experiment had shown the opposite.

- What should you advise her?
- How do you decide which of multiple varying results or experiments to trust?

Case 3 – Appropriate Use of Statistics

After years of research, Dr. Venable, a gerontologist, had developed a hypothesis that dementia is strongly correlated with fish consumption. He designed a prospective, longitudinal clinical study to test this hypothesis. The study was to follow the health histories of two groups of patients over the age of 40, one of which ate fish at least three times a week, and the other essentially never ate fish. The groups were balanced for gender, race/ethnicity, and socioeconomic status, and chosen to exclude such confounding factors as smoking, substance abuse, and the use of dietary supplements. He submitted a proposal to the NIA for funding which included only one scientific aim: to evaluate the relationship between fish consumption and dementia. The only specified primary outcome measures involved assessments of cognitive function. The study section was enthusiastic about the proposal, but insisted, especially given the expense of the project, that he track the incidence not only of dementia but also of several other common disorders manifest in the geriatric population. Although Dr. Venable had no reason to believe that any of these other conditions were affected by fish consumption, he did modify his study and the revised application was funded upon resubmission.

- Was it appropriate for Dr. Venable to alter his study design in response to the study section's recommendations?
- Given that he agreed to their suggestions, what changes, if any, should Dr. Venable make to the study's scientific aims, specified outcome measures, and statistical analysis plan?

Dr. Venable's study reached its first analytic time point after five years. Using a standard statistical package, his staff calculated the following P values for positive or negative association of fish consumption with the 15 conditions evaluated:

Disease Entity	**P Value**
Dementia	0.013
Leukemia	0.78
Lymphoma	0.86
Colon Cancer	0.87
Breast Cancer	0.46
Lung Cancer	0.23
Suicide	0.0087
Hypertension	0.93
Obesity	0.67
Osteoporosis	0.18
Arthritis	0.16
Glaucoma	0.61
Nephritis	0.50
Cardiovascular Disease	0.23
Diabetes	0.51

Around this time, Dr. Venable accepted an invitation to be a keynote speaker at an international gerontology conference and met with his lab a week prior to the meeting to discuss the presentation of their long-awaited results. Dr. Gray, an assistant professor who had collected many of the case medical records, said, "The timing of this meeting is great. We'll be able to report strong evidence for a positive correlation of fish consumption with both dementia and suicide."

"Wait a minute," said Dr. Oldham, a first-year postdoctoral fellow who had performed the statistical analyses. "The P values I gave you have not been corrected for the multiple hypotheses tested, without which they cannot be validly interpreted. For example, the Bonferroni correction requires that a P value of 0.05 be divided by 15, i.e. 0.0033, for any of these results to be considered statistically significant. I'm afraid you can't report any of the clinical findings from this study as being statistically significant."

- Is Dr. Oldham correct in insisting that the P values be corrected for multiple comparisons?

"Look," said Dr. Venable, "I don't know about suicide, but my original hypothesis concerned only dementia. I set out to prove a correlation between fish consumption and dementia, and I proved it. I want to report at least that at the meeting. Including the other clinical outcomes was based on the recommendation of the study section's comments and there was no a priori hypothesis regarding their relationship to fish consumption. We can discuss the statistical analyses of the other data when we prepare the results for publication, but for now, please go back and re-analyze the data focusing on the findings for dementia so that I can show an impressive slide at the conference."

- Is Dr. Venable making a reasonable request?
- Should Dr. Oldham re-analyze the data without correcting for multiple comparisons, on the grounds that Dr. Venable's original specific aim involved only dementia?
- Should she try other less stringent correction algorithms for multiple comparisons until she finds one that yields a significant P value for the dementia correlation?

Dr. Oldham provides Dr. Venable with slides showing a significant relationship between fish consumption and dementia, which he proudly presents at the conference.

- Does Dr. Venable have an obligation to mention the other clinical outcomes included in his study, and whether and how he corrected for multiple comparisons?
- Does he have similar or different obligations for disclosure in the peer-reviewed publication?
- To what extent does this case raise issues of honest disagreement over statistical methods, rather than issues of scientific misconduct?

Case 4 – Appropriate Sources of Data and Decision to Publish

Joe Smith is a graduate student working on an M.P.H. degree with Dr. Sampler, a famous epidemiologist with an appointment at the NIH and an adjunct professorship at Jensen University. His research includes epidemiological studies of human exposure to air-borne asbestos in dust clouds that result from building demolitions. At one well-publicized destruction of a large stadium, thousands of people witnessed the event. Because of the light prevailing winds that day, the resulting dust cloud slowly drifted south over a neighborhood of nearly 4,000 residents while to the north a similar neighborhood, being upwind, remained dust-free. Mr. Smith proposed to Dr. Sampler that he analyze the exposure data derived from this one event as his master's thesis research, and Dr. Sampler agreed.

After several months, Mr. Smith came to Dr. Sampler with the preliminary results of his research: in the six months following the demolition, there was a 2-fold higher incidence of school absences among children aged 5 to 8 on the downwind (exposed) side of the old stadium compared to those on the upwind (unexposed) side. Dr. Sampler asked Mr. Smith if there was any way to confirm that the school absences were related to upper-respiratory illnesses. Mr. Smith contacted Stella Seller, a friend who works in the purchasing department of CTS, the largest retail drugstore chain in that area. Mr. Smith asked Ms. Seller if she could review the chain's records of sales of children's nasal decongestants in the months immediately prior to and following the demolition, to see if the sales at upwind and downwind stores were different. Ms. Seller provided him with a print-out that showed month-to-month changes in sales volumes for the three top-selling decongestants, for six upwind and five downwind stores. For corporate confidentiality reasons, Ms. Seller provided only aggregate sales data expressed as percent change in sales from the same period a year earlier. Nevertheless, the sales data showed a statistically significant increase in decongestant sales at the downwind stores in the three months following the demolition.

Mr. Smith proposes to Dr. Sampler that he begin writing up his thesis, so that he can graduate in June and enter medical school in the fall. He also presents Dr. Sampler with a rough draft of a manuscript he is thinking of submitting to a journal. Dr. Sampler agrees that Mr. Smith can write the thesis, but says that a publication would be premature before the study can be confirmed by analyses of similar data from other demolitions that Dr. Sampler and colleagues at Jensen University are working on. Their study will not be completed for another 2-3 years however. When Mr. Smith tells Ms. Seller about the analysis and his plans to publish the work, she tells him that she should be a co-author on the paper and that a lawyer at CTS will need to review the paper prior to publication.

- Should Mr. Smith complete his thesis even if the paper cannot be written at this time?
- Is Dr. Sampler justified in requiring that Mr. Smith wait two or three years for confirmatory data from other demolitions before publication? Does the length of time (2-3 years) he might have to wait influence the decision?

- Was it appropriate for Ms. Seller to provide data to Mr. Smith? Should Ms. Seller be a co-author on the paper?
- What rights does CTS have with respect to publication of the paper?

Case 5 – Handling of Clinical Data

Dr. Bob is a promising junior faculty member at Z University. His major clinical research project, funded by an NIH grant, is a prospective, longitudinal study of changes over time in plasma levels of protein X and their association with cardiovascular disease. Previous cross-sectional studies by others have suggested that protein X levels increase with age and are associated with increased risk of cardiovascular disease. Dr. Bob's is the first longitudinal study to address this issue. A successful study would be publishable in a high-impact journal and give a substantial boost to his achieving tenure.

Dr. Miriam, a resident at the Z University Medical School, approaches Dr. Bob for advice about a research career and he offers to let her help analyze data from the first 3 time points of his protein X study. She eagerly accepts this offer as an opportunity to gain research experience and perhaps co-authorship on a high-impact paper.

- When is it appropriate for Dr. Miriam to discuss her authorship status with Dr. Bob? Should she raise the issue now, before agreeing to analyze the data, or wait until after the results are known?

Dr. Bob gives Dr. Miriam an Excel spreadsheet which he describes as containing all the relevant data from study subjects. Dr. Miriam performs a statistical analysis, but her results are not consistent with the hypothesis Dr. Bob wrote in his grant application. Protein X levels appear unchanged over time, and there is no association with cardiovascular risk. When Dr. Miriam presents her analysis to Dr. Bob, he is noncommittal. He says he will take the Excel spreadsheet home with him over the weekend to check her work. The next week, Dr. Bob returns the spreadsheet to Dr. Miriam, explaining that he has corrected a few mistaken data entries. He asks her to re-do the analysis.

- Is it appropriate for Dr. Bob to take the clinical data home with him?
- Would it make a difference whether or not the Excel spreadsheet contained personally identifiable information about the research subjects?

When Dr. Miriam reanalyzed the data, the hypothesis was confirmed. However, she was puzzled that correction of "a few mistaken data entries" would so substantially change the outcome of the analysis. She compared the "corrected" spreadsheet with the study's case report forms and found that the majority of data entries had been changed, always in the direction consistent with the hypothesis.

- Is it appropriate for Dr. Miriam to check the new spreadsheet against the case report forms?
- Should she have accepted Dr. Bob's corrections and confined herself to the re-analysis? Under what circumstances would one check a transcribed or secondary data set against the primary or source data?

When Dr. Miriam presented the data discrepancies to Dr. Bob and asked to see the original patient files, he brushed this off as unnecessary. He blamed the apparent discrepancies on his own ineptitude with Excel and on his use of imputed data (i.e., data entries derived from a statistical model, rather than actual measurements). Concerned about the situation, Dr. Miriam began reviewing patient records on her own without telling anyone. To her dismay, she found that many data entries in the spreadsheet had been changed from their true values, that some data entries did not correspond to actual measurements, and that some patients recorded as participating in the study did not actually exist.

- Is Dr. Bob's explanation of the data discrepancies justifiable? When is it appropriate to mix measurement-derived data with imputed data in the same data set?
- Is it appropriate in this context for Dr. Miriam to access patient records? Should she first have shared her concerns with someone in authority and gotten permission?
- Does this situation represent scientific misconduct? If so, what type of misconduct is it?

Dr. Miriam continued to work with Dr. Bob while she searched for a new mentor, but did not tell him of her findings. She did share her concerns with one of Dr. Bob's former fellows and with a collaborating faculty member in his department. Dr. Bob learned of Dr. Miriam's questioning of his scientific integrity and stopped working with her. In response, Dr. Miriam lodged a formal complaint of scientific misconduct against Dr. Bob with the university.

- Should Dr. Miriam have shared her concerns with others without first talking with Dr. Bob or lodging a formal complaint?
- What other steps could she have taken before lodging a complaint? When would have been the best time to lodge a formal complaint of scientific misconduct?

Dr. Bob was eventually convicted of scientific misconduct and resigned from his faculty position. NIH demanded repayment of the grant money that funded his study. Several patients who participated in the study felt exploited because they were exposed to risk without any balancing scientific gain.

- What factors might have motivated Dr. Bob to commit scientific misconduct?
- What obligation does Dr. Bob have toward the NIH? What ethical or legal obligations does he have toward the patients in his study?

Comments and Guidelines derived from the Cases

- The honest and accurate presentation of scientific findings is the most important thing a scientist can do. The illustrations must provide an accurate representation of the data obtained. The consequences of misrepresenting data far outweigh the short-term gains.

- Many recent cases of scientific misconduct in both the intramural and extramural programs involve inappropriate data manipulation using programs such as Photoshop, or inappropriate statistical analysis. As a result, journals now analyze images to detect inappropriate manipulations or send manuscripts out for separate statistical review.

- Changes in brightness, contrast, etc. should be applied simultaneously to all panels in a figure, including positive and negative controls. Attention must be paid to avoid saturating the brightest details and to avoid changing the relative brightness of different areas. Be aware that any change to an image has implications.

- Parts of images or graphical data should not be arbitrarily modified.

- Combining of gel lanes should be indicated by a break or line in the image.

- For safety, two copies/versions of data should be kept (original + figure version, two hard copies, hard copy + scan, computer file + backup, etc.).

- For digital images, the original data file must always be kept, with its original name (as recorded in a notebook); subsequent modified versions, and versions finalized for publication must be maintained as separate files.

- The scientific integrity and credibility of clinical trial data depend on a sound trial design with clearly identified primary and secondary endpoints and a description of statistical methods to be employed. This is a requirement for clinical studies under the jurisdiction of the FDA.

Theme 19 – Civility, Harassment and Inappropriate Conduct (2019)

Introduction to Case #1 - Gender Harassment, Sexual Harassment, and Inappropriate Conduct (including Inappropriate Relationships)

This 2019 Research Ethics case is focused on the timely and important problem of sexual and other harassment as well as inappropriate conduct in our research workplace. This issue is addressed in detail by the recently released NIH Policy Manual Chapter 1311 (https://policymanual.nih.gov/1311) which opens with:

> *"The contributions of each and every member of the National Institutes of Health's community are vital to successfully improving people's health and reducing the burden of disease. An environment where people feel welcome, respected, and valued is necessary for all individuals to contribute to their fullest potential. In alignment with this, the NIH is committed to creating and maintaining a work environment that is free of harassment and other inappropriate conduct. Harassment, bullying, intimidation, threats, or other disruptive behaviors are unacceptable and will be handled with administrative and/or legal action, as appropriate. Actions that run counter to our mission and goals will be met with consequences, no matter who the offender."*

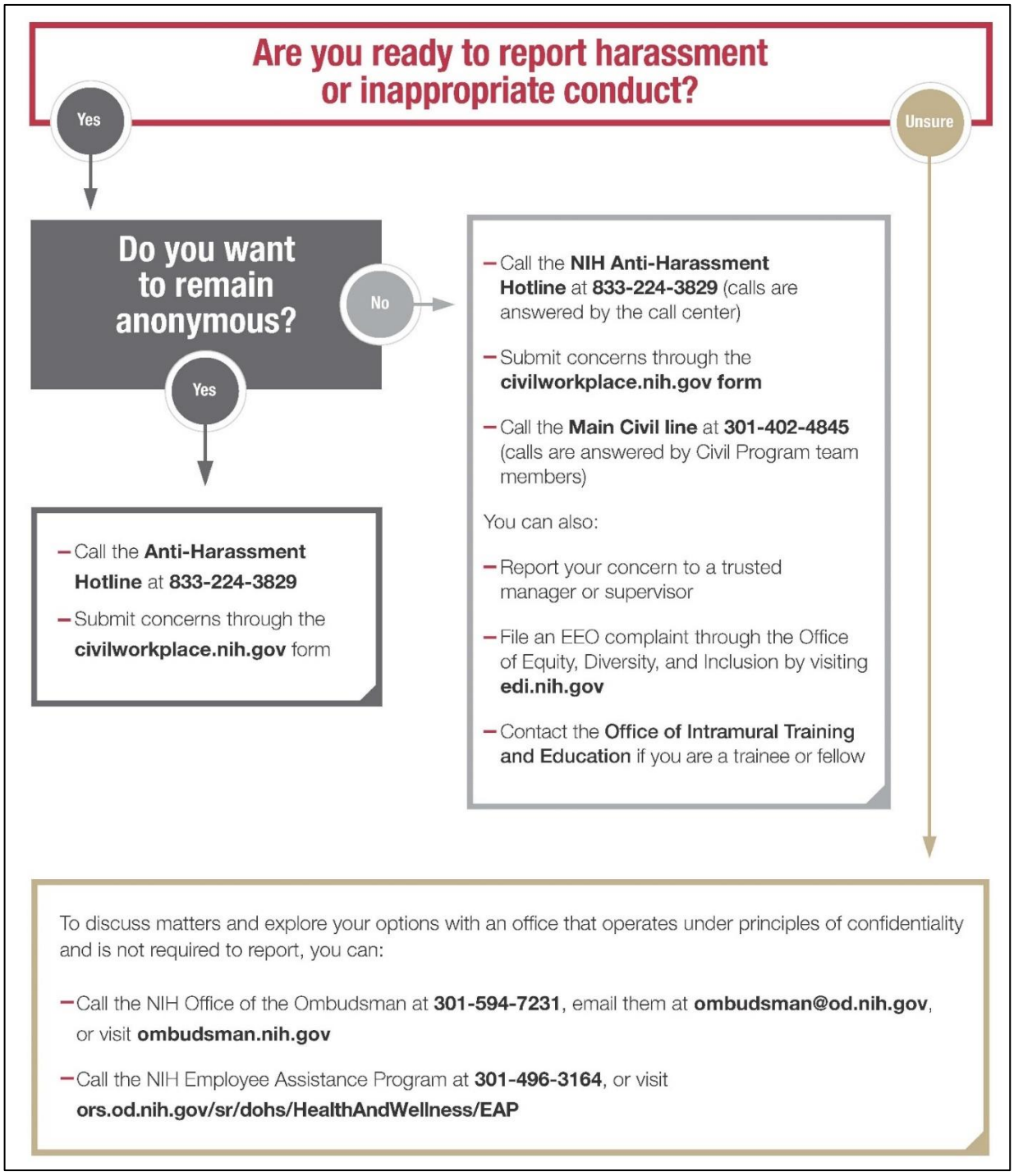
In 2018, NIH leadership initiated a comprehensive campaign aimed at increasing awareness and elimination of harassment, including sexual harassment, in the research community. This included, 1) formulation of the comprehensive Policy Manual Chapter cited above as well as a Policy Statement dealing with personal relationships in the workplace; 2) expansion of the Civil Program within the Office of Workforce Resource Development in the Office of the Director to deal with allegations of harassment (https://civilworkplace.nih.gov); and, 3) implementation of an NIH-wide survey related to staff experiences of harassment in the workplace intended to objectively identify the magnitude of the problems (an interim report on the findings from the survey may be found at https://diversity.nih.gov/building-evidence/harassment-survey/interim-executive-report-on-the-nih-workplace-climate-and-harassment-survey). Central themes of the new campaign are to substantially **increase education of the NIH community** with respect to both the wide range of inappropriate, problematic behaviors and, equally importantly, staff and manager/supervisor/leadership **responsibilities** and **avenues for reporting**, evaluating, remediating and eliminating such behaviors (including sexual harassment). Regarding the latter, reporting instances of harassment and inappropriate behavior can be made directly to the Civil Program either online at https://civilworkplace.nih.gov, or by calling either the Civil main line (301-402-4845) or the NIH Anti-Harassment Hotline (833-224-3829). Reports of concerns can also be made through other NIH offices including the NIH Office of the Ombudsman, the Employee Assistance Program, the Office of Equity, Diversity, and Inclusion, and (for trainees) the Office of Intramural Training & Education. These options are depicted in the diagram on the next page.

Important links to guidelines and resources dealing with how to report harassment, procedures and offices for remediation, and individual responsibilities can be found at the following sites.

- The NIH Director: Changing the culture of science to end sexual harassment
- NIH Manual Chapter 1311: Preventing and Addressing Harassment and Inappropriate Conduct
    - Toolkit for Employees
    - Toolkit for Supervisors
    - Toolkit for Trainees and Fellows
    - Toolkit for Contractors
    - Additional Q&As for all staff can be found by visiting: https://hr.nih.gov/working-nih/civil/nih-anti-harassment-policy-and-guidance.

- To learn more about ways to report a concern, please visit: https://hr.nih.gov/working-nih/civil/how-can-i-report-harassment-or-inappropriate-conduct.

- NIH Policy Statement: Personal Relationships in the Workplace
  - Toolkit for NIH staff, including trainees/fellows and contractors
  - Toolkit for Managers and Supervisors



Case #1: Gender Harassment, Sexual Harassment, and Inappropriate Conduct (including Inappropriate Relationships)

Dr. Kathleen Ilaazo-Firoria is a newly hired tenure-track (TT) investigator at NIH, and she is excited about starting her research program in an environment that has excellent first-class collaborators in her field, outstanding animal facilities, and a genomics bioinformatics core, which she will need for her projects. She had some concerns about joining the Institute since the senior leadership, including the SD and lab chiefs, as well as the search committee, have very few women and no members of underrepresented minorities (URM). However, the leadership of her Institute as well as NIH as a whole has recently instituted a new anti-harassment policy and program, indicating their commitment to a culture change, which she found encouraging.

Shortly after arriving, Dr. Ilaazo-Firoria is invited to join the Trans-NIH Mentoring Committee. At her first meeting, she was struck by the lack of diversity among the members, and that while the PI's and chiefs (all male) are introduced as Dr. Smith, etc., she is introduced as 'Kathleen, a new TT scientist in Institute X", a pattern she has noticed in her building. While this bothers her a bit, she wonders if it is just because her longer surname is difficult to remember and pronounce, but she worries that she might appear pretentious if she brings it up and decides to say nothing. At one point, the chair asks her to present a 'different perspective' on mentoring, and she is not sure if this related to her being a TT scientist or a woman (or both), or possibly to her recent experience in academia. The meeting is scheduled for 4-5:30pm, and at 5:15pm members are engaged in an animated discussion of a contentious point. There are still two agenda items that have not been addressed. She becomes increasingly anxious since she is a single mother and her children must be picked up from day care by 6:00pm, so at 5:40 she interrupts the discussion to excuse herself and she departs hastily. Unfortunately, there is heavy traffic and she gets to the center a few minutes late, which costs her $50.

Questions:

1. **Why do you think that Dr. Ilaazo-Firoria is called Kathleen frequently?**

2. **A senior member of the IC who also serves on the Mentoring Committee noticed that she was not fully engaged in the discussion and that she left the meeting early. He later mentions to her that being asked to join this group can help her network with important people at NIH and that he thinks she should not have departed early. How should she respond?**

3. **Dr. Ilaazo-Firoria is told by a colleague that another TT hire, Dr. Stan Brown, has said that even though she is on the 'mommy track', she doesn't need to worry about tenure since the institute is all about diversity and resolving gender inequity. Should she respond? Should the colleague respond? How?**

4. **Do these comments constitute gender harassment? Why or why not? How do they affect Dr. Ilaazo-Firoria, and other women and URM's in the labs? How do they affect the workplace in general?**

Dr. Ilaazo-Firoria's research starts off slowly because of a problem in the mouse facility that killed most of her animals. In addition, her younger child developed a serious medical problem that required many absences from the lab for about 6 months. However, after a rough first 18 months, her lab has become productive with some potentially exciting results. At her first BSC site visit, the reviewers comment that

her research is promising and potentially quite impactful, and she also receives outstanding marks for her mentorship. But concerns are raised about her not having sufficient high impact publications when she comes up for tenure.

Questions:

5. **Are there options available to help Dr. Ilaazo-Firoria with these issues? If so, what are they?**

6. **Do you think that Dr. Ilaazo-Firoria might be reluctant to use these options? Why?**

The lab chief, Dr. Fernett, has always been eager to mentor the TT's in his lab, and he meets with Dr. Ilaazo-Firoria and Dr. Brown frequently, sometimes inviting one or the other to meet at the end of the day to discuss their research progress and careers over espressos that he makes in his office. In addition, Dr. Fernett and Dr. Ilaazo-Firoria have just established a new collaboration with new post-docs from each lab so they are now meeting regularly. Dr. Ilaazo-Firoria notices that at times the discussions are personal. Dr. Fernett sometimes mentions problems in his marriage and asks her for advice. Dr. Illaazo-Firoria survived a stressful divorce herself and is more than happy to help her mentor/colleague. During the next year, Dr. Fernett's marriage dissolves and the friendship between Dr. Fernett and Dr. Illaazo-Firoria evolves into a romantic relationship. They decide to remain discrete since both are cognizant of the need to maintain a professional relationship in the workplace.

Questions:

7. **Are Dr. Fernett's frequent meetings with his TT investigator(s) appropriate? What are the circumstances that would influence your opinion?**

8. **Is the decision to remain discrete appropriate? What are the obligations for revealing this relationship to the Institute? Why is that necessary or not? At what point in the relationship should this relationship be revealed?**

9. **What are the consequences for the other members of the two labs? How could the relationship affect the post-docs working within the collaboration?**

After 5 more years, it is time for Dr. Ilaazo-Firoria to come up for tenure. Dr. Brown, who started 1½ years after her, is coming up at the same time, in part because Dr. Ilaazo-Firoria was granted extra TT time because of her child's health issues and the mouse colony disaster. Dr. Brown is somewhat resentful of this because his mother was quite ill during his tenure track and he feels that he had to work extra hard to help with his mom and keep the lab going. Dr. Brown, who is aware of the romantic relationship between Drs. Ilaazo -Firoria and Fernett, decides to file a formal complaint alleging that Dr. Ilaazo-Firoria received preferential treatment as a result of their relationship.

Questions:

10. **Do you think that Dr. Ilaazo-Firoria should have been granted additional TT time? Why or why not? Were there options available to Dr. Brown to grant him more time because of his personal family situation? If so, why did he not take them?**

11. **Do you think that Dr. Brown has a legitimate complaint? If so, whom should he contact?**

At this point, both candidates have similar packages in terms of numbers of publications, although their fields are very different. Dr. Ilaazo-Firoria knows that Dr. Fernett thinks very highly of Dr. Brown's research. To make matters worse, within the past year, the relationship between Dr. Fernett and Dr. Ilaazo-Firoria has soured. Dr. Ilaazo-Firoria decided that the relationship was not working, and despite Dr. Fernett's repeated attempts to reconcile, they have not. Dr. Fernett is quite bitter about the break-up and privately tells Dr. Ilaazo-Firoria that she 'needs to think carefully' about how he can influence the tenure decision. He is a major player in the field, and reminds her that he is good friends with many of the scientists she will want to have write letters for her tenure package. Dr. Ilaazo-Firoria is rattled by his comments and tells Dr. Jones, a tenured PI within the lab, what Dr. Fernett said.

Questions:

12. **Does Dr. Fernett's behavior constitute sexual harassment? Why or why not? Does Dr. Jones have a responsibility to report the incident?**

13. **What options are available to Dr. Ilaazo-Firoria? Should she pursue these options?**

14. **How does the break-up affect the other members of these labs? What should they do?**

Introduction to Case #2 – Freedom of Expression and Civility in the Laboratory

This introduction is not meant to constrain or even guide group discussion. It is meant to provide assistance in discussing the ethical issues raised by the case. Legal issues concerning work behavior and freedom expression are difficult. Discussion leaders are encouraged to explore these issues from an ethical perspective but are cautioned not to offer legal opinions or advice.

Appropriate Behavior in the NIH Work Environment

The purpose of employment at the NIH is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Individuals at the NIH have the right to express their opinions, but they should not interfere with the goals of employment at the NIH. Although individuals working at the NIH have considerable latitude in how they express themselves, civility and respect for others is required to ensure a productive work environment. The NIH defines inappropriate behavior as any conduct which could reasonably being perceived as be disruptive or that could adversely affect operations, productivity and/or the work environment. These include conduct that disparages or demonstrates hostility or aversion towards and/or actions that can be construed as disruptive, disrespectful, discriminatory or hostile to or offensive to others. Physically acting out such as throwing objects, slamming doors, yelling and using expletives is also inappropriate. The same rules that apply during the week apply during the weekend and during evenings at the NIH[1].

Addressing Issues of Civility at the NIH

Supervisors often have perspectives and insights that that are valuable, but employees are not limited by their supervisor's advice, nor must they report their concerns to their supervisor before reaching out for help to other office for advice and assistance.

To ensure a civil work place, multiple avenues are available for reporting concerns about inappropriate behavior. Which path individuals choose depends on the individual and the concerns they have. At any time, employees can contact the Office of the Ombudsman by phone, 301-594-7231, or by email at **ombudsman@od.nih.gov**. The ombudsmen's office coordinates and provides a full range of dispute resolution programs and services for all employee of the NIH[2]. The office of the Ombudsman can assist managers and employees in facilitating resolution of disputes. These services are provided in confidence.

The NIH's Civil program[3] exists to foster civility throughout the NIH community. Complaints of work place uncivil behavior, such as harassment, sexual harassment, inappropriate conduct, intimidation, bullying, or other unproductive, disruptive, and/or violent behaviors are appropriately made to the Civil Program. Although the discussion presented here focuses on the NIH Civil program, employees may find other paths more suitable. It should be noted that filing a complaint with the NIH Civil Programs is not equivalent to filing an EEO complaint. The office of Equity, Diversity and inclusion must be contacted within 45 days of a discriminatory incident in order to preserve the right to file an EEO complaint.

Once the Civil Program is contacted[4], staff will discuss all available options with the reporting party with the goal of addressing the issue at the lowest level possible. This may include providing guidance on how best to move forward and/or recommending additional resources and training. If the behavior is egregious or the situation is complex, the Civil Team may determine that an administrative inquiry is necessary. The purpose of an administrative inquiry is to ensure allegations are examined objectively and expeditiously and any inappropriate behavior is curtailed quickly through appropriate corrective action.

Special Concerns for PI's and Supervisors

PI's and supervisors play an important role in fostering a work environment that is free from harassment. They are required to report any allegations of harassment. While one incident of discriminatory behavior may not be enough to constitute an actionable hostile work environment claim, a supervisor's failure to act may lead to further incidents and liability on the part of the agency. Therefore, harassing conduct, even if not severe or pervasive should be deal with immediately to prevent further incidents. In these cases, PI's and supervisors are encouraged to contact the Civil Program for a consultation by calling the **Anti-Harassment Hotline**, the **Main Civil Line** or visiting the **civilworkplace.nih.gov**.

Political Speech and the Hatch Act

Political speech in the federal government falls under a separate category and is constrained by the Hatch Act[5]. Although employees may express their opinions in a respectful manner while at work, wearing a shirt or campaign button supporting a political candidate who is running for office is deemed as activity directed at the success of that candidate and is considered a violation of the Hatch Act and therefore prohibited at all times on NIH property[5,6]. Although federal employees can support whatever candidate they choose when on their own time, there is a 24/7 prohibition on federal employees raising campaign funds for political candidates. This ban extends to posting fund raising information on personal social media pages[7]. Before re-posting information from a political site, employees should make certain that any message they post in support of a candidate or party does not contain an embedded fund-raising appeal for that candidate or party. (Employees should be aware that posting threats or defamatory remarks on social media, even if apolitical, could subject them to legal or even disciplinary work actions.)

Today's social environment is affected by the 24h news cycle, acrimonious commentary, divisive politics and a winner take all mentality. Although these are good for ratings, they are not helpful when trying to achieve a productive workplace. In the case presented here Jessica's shirt was the catalyst for the ensuing argument, but both John and Jessica behaved inappropriately. The employees of the NIH are in large part responsible for the work environment at the NIH. At work, civility, thoughtful discussion tempered by respect for other's opinion, is the desired goal.

[1] **https://policymanual.nih.gov/1311: This site defines inappropriate conduct in the NIH workplace**

[2] **Ombudsman.nih.gov: This site describes the conflict resolution services offered by the ombudsman.**

[3] **Civilworkplace.nih.gov: This site describes Civil Program's Mission.**

[4] **hr.nih.gov/working-nih/civil/civil-program-process: This webpage describes the Civil Program Process.**

[5] **osc.gov/pages/hatchact-affectsme.aspx: This web page describes the restrictions place on political speech and action for further restricted and less restricted employees. Specifically, states wearing political T-shirts or buttons while employees are on duty is forbidden.**

[6] **https://ethics.od.nih.gov/topics/political-act.htm:** This website further describes limits on employee speech and actions by NIH employees.

[7] **https://osc.gov/Resources/Social%20Media%20Quick%20Guide%20FINAL%20updated%207.3.pdf** A brief summary of Hatch Act permitted and forbidden social media actions. Specifically states that reposting information soliciting funds for political campaigns on individual social media sites by federal employees is banned by the Hatch Act.

NIH Resources for conflict resolution

https://ombudsman.nih.gov/: The NIH ombudsman provides policy clarifications, assistance with exploring options for solving problems, help with interpersonal problems and expertise in group processes such as scientific collaboration. The Office of the Ombudsman can also facilitate discussions between different parties.

https://hr.nih.gov/working-nih/civil: The Civil Program exists to help foster civil behavior at the NIH. Referrals to the civil program are appropriate for uncivil behavior, harassment, sexual harassment, inappropriate conduct, intimidation, bullying or other unproductive disruptive and/or violent behavior. Referral to the Civil Program is not equivalent to filing an EEO complaint, nor does it meet the EDI requirement of notification within 45 days of a perceived act of discrimination.

https://www.edi.nih.gov/: The Office of Equity, Diversity and Inclusion exists to ensure a workplace free of discrimination and to foster diversity and inclusion in the workplace. EEO complaints are filed through this office.

https://ethics.od.nih.gov/ : This site provides information on the standards of ethical conduct for federal employees.

Contact information for issues raised in this case:

https://osc.gov/Pages/HatchAct-AffectsMe.aspx : Office of Special Council's Hatch Act web page. Explicitly states who is covered by the Hatch Act and what politically related activities are prohibited and permitted for government employees.

https://ethics.od.nih.gov/topics/political-act.htm: This website further describes limits on employee speech and actions by NIH employees, and it includes information about social media policy.

https://ombudsman.nih.gov/ : The NIH ombudsman provides policy clarifications, assistance with exploring options for solving problems, help with workplace interpersonal problems and expertise in group processes such as scientific collaboration.

https://hr.nih.gov/working-nih/civil : The Civil Program helps with resolution of workplace problems involving uncivil behavior, such as harassment, sexual harassment, inappropriate conduct, intimidation, bullying or other unproductive, disruptive and/or violent behavior.

https://www.edi.nih.gov/ : The Office of Equity, Diversity and Inclusion web site. This website provides help with issues of workplace discrimination, inclusion and diversity. It is also the site for filing EEO complaints.

Case #2: Freedom of Expression and Civility in the Laboratory

John and Jessica share the same workspace at the NIH, but that is about all they share. They have diametrically opposing social, religious and political views. They co-exist in the lab with a thin veneer of civility, but there is always some underlying tension between the two. Both are competent and valuable researchers in the lab. Both work exceptionally hard, and both are high strung. One summer weekend day, Jessica comes into the lab wearing a T-shirt advocating for a particular social view while John and 3 other lab members are present. John approaches Jessica and bluntly tells her that he finds the T-shirt offensive. Jessica responds bluntly to John and things soon escalate into a yelling match. Although the interaction does not become physical, the entire episode makes everyone in the lab uncomfortable. The following Monday, one of the fellows in the lab who was present during the weekend exchange goes to the lab PI to tell her about the incident and how uncomfortable the exchange made the lab feel.

Question:

1. **How does the NIH define inappropriate work place behavior?**

At the end of the day, the PI asks John and Jessica into her office, tells them their behavior is unacceptable. As a result, the PI reminds both John and Jessica of expectations regarding professional work attire.

Question:

2. **In the workplace there is always a balance between employee actions and accomplishing workplace goals. How might this balance be affected by employment in the NIH compared to a laboratory in the private sector? In this case do you think that the lab PI's actions were reasonable? What factors do you think are important in resolving this issue? If Jessica's comments were related to partisan politics, how might the Hatch Act affect this discussion? What resources are available to employees and PI's for conflict resolution?**

Going home after this meeting, Jessica feels he has been treated unfairly. She posts a picture of her shirt and a video on a social media site stating that her shirt neither contained graphic images or espoused violence or hate, but merely her honest beliefs on the subject. People with the same point of view as Jessica see her post and re-post it on their social media pages. Jessica's post goes viral overnight. The next afternoon, a reporter from a cable news network contacts the lab PI and the institute director, and requests interviews with them.

Question:

3. **What, if any issues, do you think Jessica should have considered before posting her grievances on social media? In the workplace, how do you think NIH staff should deal with their beliefs regarding political and social issues? Who is responsible for assuring that civility moderates our discussion of such issues in our research environment?**

Introduction to Case #3 - Mentoring

Surveys of the mentoring experiences of NIH postdoctoral fellows have pointed to three key factors that define the quality of the fellowship experience. These include the achievement of training goals, the achievement of career goals, and the overall quality of the mentoring. Predictors of these three elements include factors such as scientific direction given by the mentor, level of independence in research projects, feedback from the mentor regarding whether the research is going well or is stalled, appropriate recognition for work in publications and presentations, introductions to scientists outside their laboratory/branch by their mentor (including notification of job announcements), and discussion of training and career goals with the mentor. These same predictors can be applied to all trainees in the NIH IRP. Mentorship agreements, available from the NIH Office of the Ombudsman, the Office of Intramural Training & Education, and several Institute/Center training offices, can be used to establish the goals and research plan for a given mentor-trainee relationship. Key among the knowledge and skills that all trainees should develop is the ethical framework within which research and collaborations should be carried out. Trainees and their mentors are encouraged to build strong relationships based on mutual trust and respect, including, especially, awareness of the inherent supervisor-supervisee "power" inequity. Trainees must also recognize the need for team effort and collaborative interactions. This includes certain responsibilities such as attendance at lab/branch meetings, working regular hours, and maintaining a professional attitude at all times. Mentors are responsible for overall trainee research and career guidance, including timely review of research data and manuscripts.

This 2019 case address issues related to the ethical framework for research and how trainees and their mentors should interact. In discussing the cases, consider whether the rules for handling a specific issue would be different if the person were in a different position; i.e., should graduate students be treated differently than postdoctoral fellows? Do tenure-track investigators need mentoring? If so, from whom should they receive it?

Case #3: Biases in Mentoring of Fellows and Sexual Harassment

Dr. North, a PI in the NIH intramural program, regularly receives letters advertising early career academic positions inside and outside NIH. He usually posts these on the laboratory bulletin board or distributes them to faculty or postdoctoral fellows via the lab email list, but occasionally gives a letter selectively to one postdoctoral trainee without posting it more widely.

Drs. Brian Smith and Kathy Jones are currently senior postdoctoral trainees in Dr. North's lab. During lunch, Dr. Smith learns that Dr. Jones has applied for a position at a prestigious medical center and is considered a good candidate. Dr. Smith had not seen this position posted. Furthermore, Dr. Jones reveals that North had provided the job announcement only to her.

Upset, Dr. Smith confronts Dr. North who asserts a policy of dealing with such letters selectively, and states that "based on Kathy's skill set and work history, the position suits her better". Dr. North also points out that the position in question was widely advertised in scientific journals and thus available to everyone who reads those journals on a regular basis.

Questions:

1. **If you were a postdoctoral fellow in this laboratory, what would be your expectations about being given information regarding job opportunities? Why?**

2. **As a mentor, what would be your policy about position announcements? Why?**

Dr. Jones is aware that the lab members feel she is singled out and favored by Dr. North. In the past, she was invited by Dr. North to attend a number of important meetings with him, and he included her on some publications where her contributions were viewed as "minimal" by Dr. Smith and some other staff in the lab. This apparent favoritism has fostered gossip and resentment among her peers and diminished the perception of her own contributions the lab's research.

Question:

3. **In what ways does favoritism (or the perception of it) negatively impact the lab environment? Does it matter that Dr. Jones is a woman?**

Dr. Jones sings in a community choral group where Dr. North is also a member. Both Dr. Smith and Dr. North belong to the same wine-tasting club where Dr. Smith exhibits boorish and condescending behavior towards other members.

Question:

4. **How can interactions between the mentor and fellows outside of the lab influence relationships? Could they lead to differences in treatment within the lab? How should Dr. Jones deal with what appears to be favoritism?**

Over beers one night, Dr. Smith comments to other fellows, both male and female, that perhaps he too could get special treatment if he wore a short skirt to lab meetings and volunteered to stay late and help with Dr. North's cell cultures. This is not the first time Dr. Smith had made disparaging remarks about Dr. Jones as well as other women formerly in the lab. These insinuations about her have fostered a growing unease among female lab members.

Questions:

5. **Could this kind of gossip be considered sexual harassment? Could the lab now be viewed as a toxic work environment for women? How should this situation be defused?**

6. **In the end, both post-docs in the lab apply for the position. Dr. North provides a glowing letter of recommendation for Dr. Jones but feels unable to write an equally strong letter for Dr. Smith.**

7. **Could Dr. Smith's behavior have biased Dr. North's recommendation for him? What are Dr. North's responsibilities? What if Dr. Smith is a talented scientist?**

It is unlawful to harass a person because of that person's sex. Harassment can include "sexual harassment" or ***unwelcome sexual advances****,* ***requests for sexual favors****, and other* ***verbal or physical harassment of a sexual nature****.… Harassment does not have to be of a sexual nature, however, and can include* ***offensive remarks about a person's sex****. For example, it is illegal to harass a woman by making offensive comments about women in general…. Although the law doesn't prohibit simple teasing, offhand comments, or isolated incidents that are not very serious, harassment is illegal when it is so frequent or severe that it creates a hostile or offensive work environment or when it results in an adverse employment decision* (such as the victim being fired or demoted).

–Equal Employment Opportunity Commission

NATIONAL INSTITUTES OF HEALTH
INTRAMURAL RESEARCH PROGRAM
POLICIES & PROCEDURES FOR
RESEARCH MISCONDUCT PROCEEDINGS

Revised: November 19, 2018

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ATTACHMENTS

NIH INTRAMURAL RESEARCH PROGRAM POLICIES & PROCEDURES FOR RESEARCH MISCONDUCT PROCEEDINGS

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I. INTRODUCTION

The research community and the community at large rightly expect adherence to exemplary standards of intellectual honesty in the formulation, conduct, and reporting of scientific research. Allegations of research misconduct are taken seriously by the National Institutes of Health (NIH) Intramural Research Program (IRP). The process of reviewing allegations must be balanced by equal concern for protecting the integrity of the research as well as the careers and reputations of researchers.

These NIH IRP Policies & Procedures for Research Misconduct Proceedings (hereinafter referred to as the "Policy") are intended to enable allegations of research misconduct to be processed fairly, confidentially, and promptly. Fairness allows all of those who become involved in research misconduct proceedings to have the opportunity to participate appropriately in addressing the relevant issues and seeks to protect innocent participants from adverse consequences. Confidentiality helps protect innocent people who are incorrectly or unjustly accused and those who bring the allegations. A prompt response to an allegation helps to minimize any harm to the public that could result if research misconduct is found and allows those who are incorrectly accused to clear their names without going through a long process. Allegations of research misconduct that prove to be untrue, even if made in good faith, can damage careers and have a chilling effect on research. Fair, confidential, and prompt treatment of research misconduct allegations is important and also fosters an institutional climate supportive of honest, good-faith reporting of possible research misconduct.

II. APPLICABILITY AND SCOPE

Consistent with the NIH's responsibilities under the Public Health Service (PHS) Policies on Research Misconduct, 42 C.F.R. Part 93 (*i.e.*, the PHS Regulations, available at https://ori.hhs.gov/statutes-regulations), this Policy applies to alleged or actual research misconduct involving biomedical or behavioral research, research training, or activities that are related to research or research training, such as the operation of tissue and data banks and the dissemination of research information:

1. carried out in NIH facilities by any person;

2. funded by the NIH Intramural Research Program (IRP) in any location; or

3. undertaken by NIH staff as part of official NIH duties or NIH training activities, regardless of location.

This Policy does not apply to authorship or collaboration disputes. It applies only to research misconduct that occurred within six years prior to the date the NIH or the U.S. Department of Health and Human Services (HHS) receives the allegation, subject to the exceptions discussed in the PHS Regulations.

III. DEFINITIONS

Unless otherwise indicated below, terms used in this Policy have the same meaning as defined in the PHS Regulations. For convenience, several of the definitions from the PHS Regulations have been reproduced without change below.

A. AIRIO – NIH Agency Intramural Research Integrity Officer – the NIH official responsible for: (1) assessing allegations of research misconduct to determine if they fall within the definition of research misconduct, are covered by the PHS Regulations, and warrant an Inquiry on the basis that the allegation is sufficiently credible and specific so that potential evidence of research misconduct may be identified; (2) overseeing Inquiries and Investigations in the intramural program; and (3) other responsibilities as described in this Policy.

B. ARILO – NIH Agency Research Integrity Liaison Officer – the NIH official responsible for overseeing the NIH's research integrity programs, both intramural and extramural.

C. Allegation – A disclosure of possible research misconduct through any means of communication (*e.g.*, by written or oral statement) to an NIH or HHS official. In accordance with this Policy, allegations should be communicated to the AIRIO.

Good Faith Allegation – An allegation made by an individual having a belief in the truth of the allegation that a reasonable person in the individual's position could have, based on the information known to the individual at the time.

Bad Faith Allegation – An allegation made by an individual with knowing or reckless disregard for information that would negate the allegation.

D. Assessment – The review of an allegation of research misconduct to determine whether an Inquiry is warranted based on the following factors: whether the allegation is sufficiently credible and specific so that potential evidence of research misconduct may be identified; whether the allegation is within the jurisdictional criteria of the PHS Regulations; and whether the allegation falls within the definition of research misconduct in the PHS Regulations. The AIRIO is responsible for assessing allegations of research misconduct subject to this Policy.

E. Complainant – A person who in good faith makes an allegation of research misconduct.

F. CSCE – NIH Committee on Scientific Conduct and Ethics.

G. DO – Deciding Official – The Deputy Director for Intramural Research (DDIR) is the Deciding Official for Inquiries. The NIH ARILO is the Deciding Official who makes a final determination on recommended findings of research misconduct by an Investigation Committee. The Deciding Official will not be the same individual as the AIRIO and should have no direct prior involvement in the allegation assessment, Inquiry, or Investigation.

H. Evidence – Any document (hard copy or electronic, including e-mail), tangible item, or testimony offered or obtained during a research misconduct proceeding that tends to prove or disprove the existence of an alleged fact.

I. Inquiry – The process of gathering information and initial fact-finding to determine whether an allegation or apparent instance of research misconduct warrants an Investigation. An Inquiry must meet the criteria and follow the procedures of the PHS Regulations.

J. Intentionally – Purposefully acts to propose, perform, review research, or report research results that included falsified, fabricated or plagiarized materials.

K. Investigation – The formal development of a factual record and the examination of that record leading to a decision not to make a finding of research misconduct or to a recommendation for a finding of research misconduct, which may include a recommendation for other appropriate actions, including administrative actions. An Investigation must meet the criteria and follow the procedures of the PHS Regulations.

L. Knowingly – Uses falsified, fabricated, or plagiarized material to propose, perform, review research, or report research results knowing that the material has been falsified, fabricated or plagiarized.

M. NIH research misconduct proceeding or **NIH proceeding** – Any actions taken by or through the NIH intramural research program related to a research misconduct proceeding subject to this Policy including, but not limited to, allegation assessments, Inquiries, Investigations, and administrative actions taken by NIH following completion of an Investigation.

N. NIH staff – NIH employees, as well as trainees, fellows, contractors, special government employees (SGEs), volunteers, former employees, and other persons engaged to perform a service in support of NIH.

O. Notice – A written communication served in person, or sent by mail or its equivalent to the last known street address, facsimile number, or e-mail address of the addressee.

P. ORI – The Office of Research Integrity – The office to which the HHS Secretary has delegated responsibility for addressing research integrity and misconduct issues related to PHS-supported activities.

Q. PHS Regulations – The Public Health Service (PHS) Policies on Research Misconduct, 42 C.F.R. Part 93.

R. Preponderance of the evidence – Proof by information that, compared with that opposing it, leads to the conclusion that the fact at issue is more probably true than not.

S. Recklessly – Uses falsified, fabricated or plagiarized material to propose, perform, review research, or report research results without exercising the proper care or caution, and disregarding or showing indifference to the risk that the materials were falsified, fabricated or plagiarized.

T. Research – A systematic experiment, study, evaluation, demonstration or survey designed to develop or contribute to general knowledge (basic research) or specific knowledge (applied research) relating broadly to public health by establishing, discovering, developing, elucidating or confirming information about, or the underlying mechanism relating to, biological causes, functions or effects, diseases, treatments, or related matters to be studied.

Q. Research misconduct – Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. Specifically:

(1) **Fabrication** is making up data or results and recording or reporting them;

(2) **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;

(3) **Plagiarism** is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit;

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

A finding of research misconduct made under the PHS Regulations and this Policy requires that: (a) there be a significant departure from accepted practices of the relevant research community; and (b) the misconduct be committed intentionally,

knowingly, or recklessly; and (c) the allegation be proven by a preponderance of the evidence.

R. Research misconduct proceeding – Any actions related to alleged research misconduct taken under the PHS Regulations including, but not limited to, allegation assessments, inquiries, investigations, ORI oversight reviews, hearings, and administrative appeals.

S. Research record – The record of data or results, both physical and electronic, that embody the facts resulting from scientific inquiry, including but not limited to, e-mails, research proposals, laboratory records, progress reports, abstracts, theses, oral presentations, internal reports, journal articles, and any additional documents and materials obtained during the research misconduct proceeding.

T. Respondent – The person against whom an allegation of research misconduct is directed or who is the subject of a research misconduct proceeding. There can be more than one Respondent in an Inquiry or Investigation.

U. Retaliation – An adverse action, such as a demotion or firing, taken against a Complainant, witness, or committee member by NIH or one of its institutional members (as defined in the PHS Regulations) in response to:

(1) a good faith allegation of research misconduct; or

(2) good faith cooperation with a research misconduct proceeding.

IV. ROLES AND RESPONSIBILITIES

A. Deciding Official (DO)

For Inquiries

The Deputy Director for Intramural Research (DDIR) is the DO for Inquiries. The DO will receive the Inquiry Report and, after consulting as needed with the AIRIO, the Inquiry Committee, and/or other NIH officials, decide whether an Investigation is warranted under the criteria in the PHS Regulations. Any finding that an Investigation is warranted must be made in writing by the DO and must be provided to ORI, together with a copy of the Inquiry Report meeting the requirements of the PHS Regulations, within 30 days of the finding. If it is found that an Investigation is not warranted, the DO and the AIRIO will ensure that detailed documentation of the Inquiry is retained for at least 7 years after termination of the Inquiry, so that ORI may assess the reasons why the NIH decided not to conduct an Investigation. Where the DO is involved in the proceeding, the NIH Director or his/her designee will assume the DO's responsibilities as described above.

For Investigations

The ARILO is the DO for Investigations and findings of research misconduct (see below). The DO will receive the Investigation Report and, after consulting as needed with the AIRIO, the Investigation Committee, and/or other NIH officials, decide whether and to what extent the NIH accepts the recommended findings of the Investigation. If research misconduct is found, the DO will decide, or will refer to other appropriate NIH officials to decide, what, if any, NIH administrative actions are appropriate. The DO shall ensure that the final Investigation Report, the findings of the DO, and a description of any pending or completed administrative actions are provided to ORI as required by the PHS Regulations.

B. NIH Agency Research Integrity Liaison Officer (ARILO)

The ARILO:

1. oversees and coordinates the NIH's activities and policies related to research integrity in both intramural and extramural research supported by the NIH;

2. represents the NIH on matters of research integrity policy; and

2. serves as the Deciding Official for Investigations and findings of research misconduct.

C. NIH Agency Intramural Research Integrity Officer (AIRIO)

The AIRIO:

1. oversees and coordinates the NIH's activities and policies related to research integrity in the NIH Intramural Research Program;

2. assesses allegations of research misconduct to determine if they fall within the definition of research misconduct, are covered by this Policy and the PHS Regulations, and warrant an Inquiry on the basis that the allegations are sufficiently credible and specific so that potential evidence of research misconduct may be identified;

3. oversees Inquiries and Investigations;

4. is authorized to act promptly and take all reasonable and practical steps to obtain custody of all research records and evidence needed to conduct a research misconduct proceeding, inventory the records and evidence, and sequester them in a secure manner, throughout the NIH Intramural Research Program;

5. provides Inquiry Reports to the DDIR and Investigation Reports to the ARILO (Deciding Officials for Inquiry and Investigation respectively); and

6. is responsible for ensuring that the NIH complies with all ORI notice and reporting requirements contained in the PHS Regulations including, but not limited to, providing to ORI in a timely manner the following: (a) for an Inquiry, the written finding by the Deciding Official that an Investigation is warranted and a copy of the Inquiry Report; and (b) for an Investigation, a copy of the Investigation Report, a statement of whether NIH accepts the Investigation's recommended findings, a statement of whether NIH found research misconduct and, if so, who committed it, and a description of any pending or completed administrative actions against the Respondent.

The AIRIO has lead responsibility for ensuring that the NIH:

- takes all reasonable and practical steps to foster a research environment that promotes the responsible conduct of research, research training, and activities related to that research or research training, discourages research misconduct, and deals promptly with allegations or evidence of possible research misconduct.

- has written policies and procedures for responding to allegations of research misconduct and reporting information about that response to ORI (*i.e.*, this Policy), as required by the PHS Regulations.

- complies with this Policy and the requirements of the PHS Regulations.

- informs NIH staff who are subject to the PHS Regulations about this Policy and the NIH's commitment to compliance with this Policy.

- takes appropriate interim action during a research misconduct proceeding to protect public health, federal funds and equipment, and the integrity of the NIH- and PHS-supported research process.

In a given NIH research misconduct proceeding, the AIRIO may delegate, as necessary, one or more of the above-referenced responsibilities to authorized NIH staff.

D. Complainant

The Complainant is responsible for making allegations in good faith, maintaining confidentiality, and cooperating with the research misconduct proceeding, including any Inquiry or Investigation.

During the Inquiry stage, the Complainant, if known, usually is interviewed and, when feasible, an audio recording of the interview is made. Upon the request of an Inquiry Committee, the AIRIO has the discretion to approve preparation of a transcript of the recording. When a transcript is prepared, the Complainant is provided an opportunity to correct errors in transcription. The transcript (or, if no transcript is prepared, the audio recording) is entered into the record of the proceeding. The NIH may choose to provide the Complainant the portions of the draft Inquiry Report that address the Complainant's role and statements in the Inquiry and give the Complainant an opportunity to submit comments.

During an Investigation, the Complainant is interviewed, if known. An audio recording of the interview is made and, when feasible, professionally transcribed. When a transcript is prepared, the Complainant is provided an opportunity to correct errors in transcription. The transcript (or, if no transcript is prepared, the audio recording) is entered into the record of the proceeding. The NIH may choose to provide the Complainant the portions of the draft Investigation Report that address the Complainant's role and statements in the Investigation and give the Complainant an opportunity to submit comments.

The Complainant may:

- consult with his/her own legal counsel or a non-lawyer personal adviser (who may not be a principal or witness in the NIH proceeding) and, subject to the AIRIO's prior approval, bring the counsel or personal adviser to interviews or meetings during the NIH proceeding. When a counsel or personal adviser is present at an Inquiry or Investigation Committee interview or meeting, his/her activities will be limited to

advising the Complainant, as opposed to representing the Complainant before the Committee. The adviser or counsel should not direct questions to the Committee.

- request that an interpreter for him/her be present during an interview or meeting in the course of the NIH research misconduct proceeding.

E. Respondent

The Respondent is responsible for maintaining confidentiality and cooperating with the research misconduct proceeding, including any Inquiry or Investigation. The Respondent may:

- expect a good faith effort by the AIRIO to notify the Respondent of the allegation(s) in writing at the time of, or before beginning, an Inquiry and receive a copy of, or reference to, this Policy and the PHS Regulations.

- have an opportunity, at both the Inquiry and Investigation stages, to object to a proposed committee member based upon a personal, professional, or financial conflict of interest. The Respondent must inform the AIRIO of any objections within seven (7) calendar days. The AIRIO will then determine whether a personal, professional, or financial conflict of interest exists that cannot be resolved and, as a result, necessitates replacement of the challenged committee member.

- be interviewed during the Inquiry stage if requested by the Inquiry Committee. When feasible, an audio recording of the interview is made. Upon the request of an Inquiry Committee, the AIRIO has the discretion to approve preparation of a transcript of the recording. When a transcript is prepared, the Respondent is provided an opportunity to correct errors in transcription. The transcript (or, if no transcript is prepared, the audio recording) is entered into the record of the proceeding.

- consult with his/her own legal counsel or a non-lawyer personal adviser (who may not be a principal or witness in the NIH proceeding) and bring the counsel or personal adviser to interviews or meetings during the NIH proceeding. When a counsel or personal adviser is present before an Inquiry or Investigation Committee during an interview or meeting, his/her activities will be limited to advising the Respondent, as opposed to representing the Respondent before the Committee. The adviser or counsel should not direct questions to the Committee.

- consult with others who may assist Respondent in his/her defense, consistent with the responsibility to maintain confidentiality within the bounds established under the PHS Regulations (see section V(C) below). Individuals who are consulted will be asked to sign a Confidentiality Statement provided by the AIRIO (see Attachment 1).

- request that an interpreter for him/her be present during an interview or meeting in the course of the NIH research misconduct proceeding.

- have an opportunity to comment on the draft Inquiry Report and have his/her comments attached to the Report.

- be notified of the outcome of the Inquiry, and receive a copy of the final Inquiry Report.

- if there is to be an Investigation, be notified in writing of the allegations to be investigated within a reasonable time after the determination that an Investigation is warranted, but before the Investigation begins (which is to occur within 30 days after NIH decides to begin an Investigation), and be notified in writing of any new allegations, not addressed in the Inquiry or in the initial notice of Investigation, within a reasonable time after the determination to pursue those allegations.

- be interviewed during the Investigation stage. An audio recording of the interview is made and, when feasible, professionally transcribed. When a transcript is prepared, the Respondent is provided an opportunity to correct errors in transcription. The transcript (or, if no transcript is prepared, the audio recording) is entered into the case record.

- request that any witness who has been reasonably identified by the Respondent as having information on relevant aspects of the Investigation be interviewed during the Investigation. An audio recording of the interview is made and, when feasible, professionally transcribed. When a transcript is prepared, the witness is provided an opportunity to correct errors in transcription. The transcript (or, if no transcript is prepared, the audio recording) is entered into the record of the proceeding.

- receive a copy of the draft Investigation Report and, concurrently, a copy of, or supervised access to the evidence on which the report is based, and be notified that any comments must be submitted within 30 days of the date on which the copy was received and that the comments will be considered by the NIH and addressed in the final report.

- where no finding of research misconduct is made, request the AIRIO and other NIH officials to undertake, as appropriate, all reasonable and practical efforts to protect or restore the Respondent's reputation.

At any time during the NIH research misconduct proceeding, the Respondent has the opportunity to admit that research misconduct occurred and that he/she committed the research misconduct. With the advice of the AIRIO and/or other NIH officials, the Deciding Official may terminate the NIH's review of an allegation that has been admitted, if the NIH's acceptance of the admission and any proposed settlement is

approved by ORI. The ORI typically will prepare a Voluntary Settlement Agreement (VSA) for review by the Respondent (see Attachment 5 for a sample VSA). Once the VSA is approved and signed by the Respondent and HHS, the NIH proceeding is terminated.

F. Institute/Center Director

The NIH Institute and Center (IC) Directors assist the AIRIO and others, as needed, in the NIH research misconduct proceeding. At the close of the NIH proceeding, they assist with the implementation of administrative actions, if any, as directed by the Deciding Official or other appropriate NIH official.

G. Institute/Center Scientific Director and Deputy Scientific Director

NIH IC Scientific Directors (SDs), Deputy SDs, and other NIH officials as needed, are informed of the NIH research misconduct proceeding and may notify other NIH staff on an as needed basis to manage effectively agency resources and protect agency programs, consistent with the provisions described in section V(C), below. If requested by the AIRIO during an NIH proceeding, the Executive Officer, Chief Information Officer, and/or Administrative Officer, or their agents of a Respondent's IC may assist in the securing of evidence, and in other matters as needed. Typically, the Deputy SD of the Respondent's IC serves as Co-Executive Secretary during the NIH proceeding. The Deputy SD also serves as the AIRIO's point of contact with regard to financial expenditures related to the NIH proceeding, which are the responsibility of the Respondent's IC. For an IC that does not have a SD or Deputy SD, or in a case where a SD or Deputy SD has unresolved personal, professional, or financial conflicts of interest, the IC Director will designate another individual to carry out these responsibilities.

V. GENERAL POLICIES AND PRINCIPLES

A. Responsibility to Report Misconduct

All NIH staff are expected to report observed, apparent, or suspected research misconduct. Reporting procedures are described in section VI(A) below.

B. Cooperation with NIH Research Misconduct Proceedings

All NIH staff will cooperate with the AIRIO and other NIH officials in NIH research misconduct proceedings, including the review of allegations and the conduct of Inquiries and Investigations. NIH staff, including Respondents, have an obligation to provide evidence relevant to research misconduct allegations to the AIRIO or other NIH officials.

C. Confidentiality

In accordance with the PHS Regulations, disclosure of the identity of Respondents and Complainants in research misconduct proceedings is limited, to the extent possible, to those who need to know, consistent with a thorough, competent, objective and fair research misconduct proceeding, and with implementation of its findings, as allowed by law. However, the NIH must disclose the identity of Respondents and Complainants to ORI pursuant to an ORI review of research misconduct proceedings under the PHS Regulations. 42 CFR 93.108.

Confidentiality must be maintained for any records or evidence from which research subjects might be identified, except as may otherwise be prescribed by applicable law. Disclosure is limited to those who have a need to know to carry out a research misconduct proceeding, or to implement its findings. The disclosure of the identity of Inquiry or Investigation committee members and Inquiry or Investigation witnesses should be limited, to the extent possible, to those who need to know.

Records related to NIH research misconduct proceedings are part of a Privacy Act system of records, "NIH Records Related to Research Misconduct Proceedings, HHS/NIH," 09-25-0223 (77 Fed. Reg. 52043 (Aug. 28, 2012)). The AIRIO may use written confidentiality statements or other mechanisms to help maintain confidentiality of NIH research misconduct proceedings. (See Confidentiality Statement, Attachment 1).

D. Interim Administrative Actions; Notification of Special Circumstances

Throughout an NIH research misconduct proceeding (*i.e.*, the assessment, Inquiry, and Investigation stages), the AIRIO will review the situation to determine if there is any threat of harm to public health, federal funds and equipment, or the integrity of the NIH- or PHS-supported research process. In the event of such a threat, the AIRIO will, in consultation with other NIH officials and ORI, take appropriate interim action to protect against any such threat. Interim action might include additional monitoring of the research process and the handling of federal funds and equipment, reassignment of personnel or of the responsibility for the handling of federal funds and equipment, additional review of research data and results, or delaying publication.

The AIRIO shall, at any time during a research misconduct proceeding, notify ORI and appropriate NIH officials immediately if the AIRIO has reason to believe that any of the following conditions exist:

- Health or safety of the public is at risk, including an immediate need to protect human or animal subjects;

- HHS resources or interests are threatened;

- Research activities should be suspended;

- There is a reasonable indication of possible violations of civil or criminal law;

- Federal action is required to protect the interests of those involved in the research misconduct proceeding;

- The research misconduct proceeding may be made public prematurely and HHS action may be necessary to safeguard evidence and protect the rights of those involved; or

- The research community or public should be informed.

If the AIRIO has reason to believe that there has been a violation of applicable safety regulations, financial irregularities related to federal funds, discrimination, or sexual harassment, not covered by the criteria set forth above, the AIRIO shall inform appropriate NIH officials.

E. Correction of the Research Record; Communication with Publishers

Subject to the Confidentiality provisions in section V(C) above, if an NIH research misconduct proceeding involves published research, the corresponding author has a responsibility to contact the publisher and have the research record corrected as soon as feasible, which may be prior to completion of the NIH proceeding as described below. Where the Respondent is the corresponding author on the publication, this responsibility typically can be handled by the Respondent's supervisor for the research in question (*e.g.*, lab chief or principal investigator). The AIRIO should be consulted for guidance.

If an NIH proceeding is not yet complete or if no finding of research misconduct has been made, communication with a publisher can reference errors in the research without attributing individual responsibility. Unless and until NIH has made a finding at the conclusion of an NIH research misconduct proceeding, a proposed correction or retraction notice should not characterize the errors as research misconduct. Information regarding the existence of a pending NIH research misconduct proceeding, or details of such proceeding, should not be shared with the publisher unless necessary for NIH to obtain information from the publisher to assist review of allegations in an NIH proceeding. The AIRIO shall coordinate any request for assistance or information collection from third parties, including publishers, during an NIH proceeding.

A corresponding author (or supervisor) should work with the AIRIO to avoid the need for multiple corrections of a publication, if feasible. For example, if errors are identified in a single table, the corresponding author should review the remaining figures in the publication to confirm accuracy before contacting the publisher about the errors.

If NIH makes a finding at the conclusion of an NIH research misconduct proceeding and has informed ORI of the finding, NIH may make a disclosure to research collaborators of the Respondent, professional journals, other publications, news media, professional societies, other individuals and entities, and the public. The disclosure may include information concerning the research misconduct finding and the need to correct or retract research results or reports that have been affected by research misconduct, unless NIH determines that release of the specific information in the context of a particular case would constitute a clearly unwarranted invasion of personal privacy. Such disclosure constitutes a "routine use" as described in the applicable Privacy Act system of records notice, "NIH Records Related to Research Misconduct Proceedings, HHS/NIH," 09-25-0223 (77 Fed. Reg. 52043 (Aug. 28, 2012)).

VI. ASSESSMENT OF ALLEGATIONS OF RESEARCH MISCONDUCT

A. Bringing an Allegation of Research Misconduct

Allegations of research misconduct may be communicated through any means (*e.g.*, by written or oral statement) to an NIH or HHS official. Individuals who are uncertain whether they have evidence of, or have observed, research misconduct may discuss their concerns with, or seek advice from, individuals they trust, including the NIH Ombudsman, before bringing a formal complaint. The NIH encourages allegations to be communicated directly to the Agency Intramural Research Integrity Officer (AIRIO), Office of Intramural Research, Office of the Director, NIH (AIRIO@nih.gov, 301-827-7745).

Where possible, the allegation should be provided, or subsequently documented, in sufficient detail to enable the NIH to assess it appropriately. This may include details such as relevant parties, witnesses, dates, locations, publications, and the subject matter of the research in question.

A person (or persons) who makes an allegation of research misconduct may do so anonymously, or otherwise request that his/her name be withheld; however, in some cases, an Inquiry or Investigation may not be able to proceed without identifying and/or obtaining further information from the person who made the allegation (*i.e.*, the Complainant). An anonymous complaint may include a situation in which the AIRIO is notified about an anonymous comment or blog posted online regarding alleged research misconduct that has occurred in published research available on the internet.

If a person is unsure whether a suspected incident falls within the definition of research misconduct, he/she may contact or meet with the AIRIO to discuss the suspected research misconduct informally and confidentially, which may be presented as a hypothetical situation and/or anonymously. If the circumstances described by the individual do not meet the definition of research misconduct, the AIRIO may refer the individual or

allegation to other offices or officials with responsibility for resolving the problem. If the AIRIO concludes that the allegation meets the definition of research misconduct, he/she will proceed with an assessment.

B. Assessment of Allegations

Upon receiving an allegation of research misconduct, the AIRIO will immediately assess the allegation to determine whether the allegation is:

(1) sufficiently credible and specific so that potential evidence of research misconduct may be identified;

(2) within the jurisdictional criteria of the PHS Regulations and this Policy;

(3) within the definition of research misconduct in the PHS Regulations and this Policy.

If these criteria are met, an Inquiry is warranted (see section VII below). If no Inquiry is initiated, the matter shall be closed and the AIRIO's records related to the allegation will be retained for seven (7) years (or longer, if other record retention requirements apply to the records).

The assessment period should be brief. In conducting the assessment, the AIRIO need not interview the Complainant, Respondent, or other witnesses, or gather data beyond any that may have been submitted with the allegation, except as necessary to determine whether the allegation is sufficiently credible and specific so that potential evidence of research misconduct may be identified. The AIRIO's assessment may include, as needed, confidential consultation with NIH staff who have scientific expertise relevant to the subject matter of an allegation.

If no Inquiry is initiated, the AIRIO may notify the Complainant, if known, and anyone else of whom the AIRIO is aware who has knowledge of the allegation, as appropriate, to resolve any questions that may exist concerning the status of the AIRIO's assessment.

VII. CONDUCTING THE INQUIRY

A. Purpose and Initiation of the Inquiry

If the AIRIO determines that an Inquiry is warranted, he or she will immediately initiate the Inquiry process. The purpose of the Inquiry is to conduct an initial review of the available evidence to determine whether to conduct an Investigation. It is not for the purpose of reaching a final conclusion as to whether research misconduct has, or has not, occurred.

An Inquiry does not require a full review of all the evidence related to the allegation, although the process usually involves interviewing of key witnesses, including the Complainant(s) and Respondent(s).

B. Notice to Respondent

At the time of, or before beginning, an Inquiry, the AIRIO will make a good faith effort to notify the Respondent in writing, if the Respondent is known. The AIRIO will attempt to provide to the Respondent a notification memo, signed by the AIRIO, which explains the nature of the allegation(s) of research misconduct, as well as a copy of this Policy and/or related materials explaining NIH and PHS policies and procedures regarding research misconduct.

The allegation(s) described in the notification memo should be as specific as feasible given the facts available at the time. Unless further amended during the Inquiry, the allegation(s) as described in the notification memo should provide the basis on which the Inquiry Committee's review is focused. ORI has provided the following example as a recommended format for framing an allegation: *Respondent falsified (Figure X) in (paper X) by (describe what is false and how the figure was falsified)*.

The AIRIO will lead the notification process. The AIRIO will make a good faith effort to arrange that this process be performed, where feasible, in a private place in an undisruptive manner in order to minimize disturbance to the laboratory and embarrassment to the Respondent. When feasible, the Respondent's supervisor (as long as he/she is not the Complainant), or another IC official, will be present.

In addition to providing the notification memo and policy information, when feasible, the AIRIO will seek to explain verbally the Inquiry process to the Respondent and to inform the Respondent that he/she may acquire his/her own legal counsel. If there is more than one Respondent, the AIRIO will seek to notify each Respondent separately when feasible. If the Inquiry subsequently identifies additional Respondents, they will be notified in writing. If additional allegations are added during the Inquiry, or if the original allegations described in the notification memo are amended, the Respondent(s) should be notified in writing.

C. Sequestration of Research Records

On or before the date on which the Respondent is notified, or the Inquiry begins, whichever is earlier, the AIRIO will take all reasonable and practical steps to obtain custody of all the research records and evidence needed to conduct the research misconduct proceeding, inventory the records and evidence (*i.e.*, prepare a record of the proceeding), and sequester them in a secure manner. Starting at the time of sequestration, the AIRIO or designee will seek to maintain a chain of custody for all sequestered materials, as well as any additional research records or evidence gathered during the

Inquiry, in order to preserve the integrity of the original research records and evidence received by the AIRIO. The AIRIO may establish and update as needed one or more Standard Operating Procedures that describe aspects of the intended sequestration process in greater detail.

When the research records or evidence encompass scientific instruments shared by a number of users, custody may be limited to copies of the data or evidence on such instruments, so long as those copies are substantially equivalent to the evidentiary value of the instruments. When appropriate, the Respondent may be provided copies or supervised access to the materials to facilitate continuation of research. The AIRIO may consult with ORI for advice and assistance in this regard.

D. Appointment of the Inquiry Committee

The AIRIO, in consultation with other NIH officials as appropriate, will appoint an Inquiry Committee, usually consisting of three voting members, as soon after the initiation of the Inquiry as is practical. The Inquiry Committee should include individuals who are federal employees and who have the appropriate scientific expertise to evaluate the evidence and issues related to the allegation(s), interview the principals and key witnesses, as appropriate, and conduct the Inquiry. The Inquiry Committee may include members of the CSCE. Individuals who have unresolved personal, professional, or financial conflicts of interest with those involved with the Inquiry, including the Respondent(s) and Complainant(s), may not serve on the Inquiry Committee.

If necessary to secure additional scientific expertise or to avoid conflicts of interest, the AIRIO may appoint employees of other federal agencies. Except under extraordinary circumstances, the Inquiry Committee should not include as a member an individual who was consulted or was otherwise involved in the assessment of allegation(s). When appointment of an individual with previous involvement in the NIH research misconduct proceeding is determined to be useful, the AIRIO will document the basis for the NIH's conclusion that the appointment satisfies the PHS Regulations' requirement to ensure a fair investigation, and include such documentation in the record of the Inquiry.

At the time of appointment, a proposed Inquiry Committee member will be asked to sign a Federal Employee Participant Statement. (See Attachment 2).

Typically, the Deputy SD of the Respondent's IC serves as Co-Executive Secretary for the Committee. The other Co-Executive Secretary will be designated by the AIRIO. One or more attorneys from the HHS Office of the General Counsel may be present at committee meetings and/or interviews.

The AIRIO will notify the Respondent of the names of the proposed Inquiry Committee members and provide an opportunity for the Respondent to object to a proposed member based upon a personal, professional, or financial conflict of interest. The Respondent

must inform the AIRIO of any objections within seven (7) calendar days. The AIRIO will then determine whether a personal, professional, or financial conflict of interest exists that cannot be resolved and, as a result, necessitates replacement of the challenged committee member.

E. First Meeting and Charge to the Committee

1. Charge to the Committee

The AIRIO may prepare a written charge for the Inquiry Committee that:

- describes the allegations (which should be consistent with allegations provided to the Respondent in the notification memo per section VII(B) above).
- describes any related issues identified during the allegation assessment.
- identifies the Respondent(s).
- defines research misconduct.
- states that an Inquiry is the process of gathering information and initial fact-finding, which usually includes interviews with the Respondent, Complainant, and key witnesses, if desired, to determine whether an allegation or apparent instance of research misconduct warrants an Investigation.
- states that an Investigation is warranted if the Committee determines that the criteria of the PHS Regulations and this Policy, described below in section VII(F), have been met.
- informs the Committee that it must prepare, or direct the preparation of, a written Inquiry Report that meets the requirements of this Policy and the PHS Regulations.
- describes the timeline for completion of the Inquiry.
- describes NIH's expectation that confidentiality will be maintained consistent with this Policy and to the extent required by law. Outside of the Committee meetings and interviews, Inquiry Committee members are directed not to discuss the NIH proceedings with the Respondent, Complainant, witnesses, or anyone not otherwise authorized to discuss the Inquiry.

2. First Meeting

At the Inquiry Committee's first meeting, the AIRIO may review the charge with the Committee; discuss the allegations, any related issues, and the process for conducting the Inquiry; assist the Committee with organizing plans for the Inquiry; and answer any questions raised by the Committee. The Inquiry Committee should be provided a copy of this Policy and the PHS Regulations. One member of the Committee will serve as Chair. The AIRIO will be present or available throughout the Inquiry to advise the Committee as needed.

F. Inquiry Process

The Inquiry Committee usually interviews the Respondent, the Complainant, if known, and key witnesses as needed, as well as examine relevant research records and materials. An audio recording of each interview is made and, when feasible, professionally transcribed. When a transcript is prepared, the interviewee is provided an opportunity to correct errors in transcription. Changes to a transcript will only be made to correct errors in transcription, but an interviewee may add comments or additional information that will be included with his/her transcript as an addendum. The transcript (or, if no transcript is prepared, the audio recording) is entered into the record of the proceeding.

The Inquiry Committee will evaluate the evidence, including testimony obtained during the Inquiry. After consultation with the AIRIO and, if necessary, the Office of the General Counsel, the Committee will decide whether or not to recommend that an Investigation is warranted.

Under the PHS Regulations and this Policy, an Investigation is warranted if the following criteria are met:

1. There is a reasonable basis for concluding that the allegation falls within the definition of research misconduct and is within the jurisdictional criteria of the PHS Regulations and this Policy (see section II above); and

2. The allegation may have substance, based on the preliminary information-gathering and preliminary fact-finding conducted by the Committee during the Inquiry.

The Committee's decision need not be unanimous. The scope of the Inquiry is not required to, and does not normally include, deciding whether research misconduct definitely occurred, determining definitively who committed the research misconduct, or conducting exhaustive interviews and analyses. If a legally sufficient admission of research misconduct is made by the Respondent, a finding of research misconduct may be determined at the Inquiry stage if all relevant issues are resolved. In that case, the NIH will promptly consult with ORI regarding the sufficiency of the admission statement and

to determine the next steps that should be taken, as described in section XI below and Attachment 5.

Inquiry Committee members are expected to be present for all Committee meetings and interviews. When necessary (*e.g.*, to ensure attendance or to avoid prolonged delay or unreasonable expense), the AIRIO may make arrangements to use video conference, audio conference, or similar technology for an Inquiry Committee meeting or interview. In the event a Committee member is absent from one or more meetings or interviews, the AIRIO may in his or her discretion determine whether the Inquiry process should be modified, *e.g.*, by having the member continue to serve on the Committee in a non-voting capacity only, or by removing the member from further participation on the Committee.

G. Timeline for Completion

The Inquiry, including preparation of the final Inquiry Report and the decision of the DO on whether an Investigation is warranted, is to be completed within sixty (60) calendar days of its initiation (defined as the date of the first meeting of the Inquiry Committee), unless the AIRIO determines that circumstances clearly warrant a longer period. If the AIRIO approves an extension, the Inquiry record must include documentation of the reasons for exceeding the 60-day period. In addition, the AIRIO should notify the Respondent of the extension.

VIII. THE INQUIRY REPORT

A. Elements of the Inquiry Report

The Inquiry Committee and the AIRIO are responsible for preparing a written draft report for the Inquiry. The Inquiry Report must include the following information:

1. The name and position of the Respondent;
2. A description of the allegations of research misconduct (which should be consistent with the allegations provided to Respondent in the original notification memo or, if applicable, an updated version thereof);
3. The PHS support (*e.g.*, if applicable, a statement that the research was funded and carried out within the NIH IRP);
4. The basis for recommending, or not recommending, that the allegations warrant an Investigation, including a summary of the relevant evidence (or lack of evidence) on which the Committee's recommendation is based;
5. If an extension of time was granted for completion of the Inquiry, documentation of the reasons for exceeding the 60-day period;
6. In the final version of the report, any comments submitted by the Respondent or the Complainant on the draft report, per section VIII(B) below.

In addition, the Inquiry Report should include the following information:

7. The names, titles, and affiliations of the Inquiry Committee members;
8. The dates of Committee meetings and interviews;
9. The Inquiry Committee's reply to any comments submitted by the Respondent or the Complainant on the draft report, per section VIII(B) below, including a description of any changes made to the draft Report as a result of the comments;
10. As an attachment, a list of the documentary evidence examined and interviews conducted.

The Inquiry Report may include Committee recommendations as to whether any actions should be taken if an Investigation is not recommended. When the Inquiry Committee's decision is not unanimous, the Report also may include a separate statement summarizing the minority viewpoint.

An outline for an Inquiry Report is provided in Attachment 3.

A draft report will be provided to the HHS Office of the General Counsel for legal review. Modifications may be made as appropriate and in consultation with the AIRIO and the Inquiry Committee.

B. Notice to Respondent and Complainant; Opportunity to Comment

The AIRIO shall notify the Respondent of the Inquiry Committee's recommendation as to whether or not an Investigation is warranted, and will include a copy of the draft Inquiry Report and a copy of, or reference to, this Policy and the PHS Regulations. The NIH may choose to provide the Complainant, if known, that portion of the draft Report that addresses the Complainant's role and statements in the Inquiry. The Respondent and Complainant will provide their comments, if any, to the Inquiry Committee within fourteen (14) calendar days of receipt. Any comments that are submitted by the Respondent or Complainant will be attached to the final Inquiry Report. Based on the comments, the Inquiry Committee may revise the draft report and/or add a written reply to the comments, as appropriate, and prepare the report in final form. The Committee will deliver the final report to the AIRIO.

C. NIH Decision and Notification

1. Decision by Deciding Official (DO)

The AIRIO will transmit the final Inquiry Report and any comments to the DO, who will determine whether an Investigation is warranted and document that decision in writing. The Inquiry is completed when the DO makes this determination.

2. Notification to ORI

Within thirty (30) calendar days of the DO's decision that an Investigation is warranted, the AIRIO will provide ORI with the DO's written decision and a copy of the Inquiry Report. The AIRIO will also notify those NIH officials who need to know of the DO's decision as part of their official duties. Upon ORI's request, the AIRIO must also provide to ORI the following information: (1) the NIH policies and procedures under which the Inquiry was conducted; (2) the research records and evidence reviewed, transcripts or recordings of any interviews, and copies of all relevant documents; and (3) the charges to be considered in the Investigation.

3. Documentation of Decision Not to Investigate

If the DO decides that an Investigation is not warranted, the AIRIO does not need to notify ORI. However, the AIRIO must secure and maintain for seven (7) years (or longer, if other record retention requirements apply) after the termination of the Inquiry sufficiently detailed documentation of the Inquiry to permit a later assessment by ORI of the reasons why an Investigation was not conducted. These documents must be provided to ORI or other authorized HHS personnel upon request.

If no Investigation is initiated, the AIRIO will notify the Respondent. The AIRIO may also notify the Complainant, if known, and anyone else of whom the AIRIO is aware who has knowledge of the NIH research misconduct proceeding, as appropriate, to resolve any questions that may exist concerning the status of the NIH proceeding. At the request of the Respondent, the AIRIO will undertake, as appropriate, all reasonable and practical efforts to restore the Respondent's reputation, as further described in section XIII(B) below.

4. Return of Sequestered Materials

If the DO decides that an Investigation is not warranted, the AIRIO will arrange for all sequestered materials to be returned to the Respondent or other parties, as appropriate, as soon as practicable following closure of the case.

IX. CONDUCTING THE INVESTIGATION

A. Purpose and Initiation of the Investigation

The Investigation must begin within thirty (30) calendar days after the determination by the DO that an Investigation is warranted. The purpose of the Investigation is to develop a factual record by exploring the allegation(s) in detail and examining the evidence in depth, leading to recommended findings on whether research misconduct has been

committed, by whom, and to what extent. The Investigation will also determine whether there are additional instances of possible research misconduct that would justify broadening the scope beyond the initial allegations. This is particularly important where the alleged research misconduct involves clinical trials or potential harm to human subjects or the general public or if it affects research that forms the basis for public policy, clinical practice, or public health practice. In accordance with the PHS Regulations, the findings of the Investigation must be set forth in an Investigation Report.

B. Notice to ORI and Respondent; Sequestration of Research Records

On or before the date on which the Investigation begins, the AIRIO must (1) notify the ORI Director of the decision to begin the Investigation and provide ORI a copy of the Inquiry Report; and (2) notify the Respondent in writing of the allegations to be investigated and provide the Respondent a copy of the Inquiry Report and a copy of (if not previously provided), or reference to, this Policy and the PHS Regulations. The AIRIO must also give the Respondent written notice of any new allegations of research misconduct within a reasonable amount of time of deciding to pursue allegations not addressed during the Inquiry or in the initial notice of the Investigation. If there is more than one Respondent, each should be notified separately.

The AIRIO will, prior to notifying the Respondent of the allegations, take all reasonable and practical steps to obtain custody of and sequester in a secure manner all research records and evidence needed to conduct the research misconduct proceeding that were not previously sequestered during the Inquiry. The need for additional sequestration of records for the Investigation may occur for any number of reasons, including the NIH's decision to investigate additional allegations not considered during the Inquiry stage or the identification of records during the Inquiry process that had not been previously secured. The procedures to be followed for sequestration during the Investigation are the same procedures that apply during the Inquiry. The AIRIO may establish and update as needed one or more Standard Operating Procedures that describe aspects of the intended sequestration process in greater detail.

C. Appointment of the Investigation Committee

The AIRIO, in consultation with other NIH officials as appropriate, will appoint an Investigation Committee, usually consisting of five voting members, as soon after the initiation of the Investigation as is practical. The Investigation Committee should include individuals who are federal employees and who have the appropriate scientific expertise to evaluate the evidence and issues related to the allegation(s), interview the principals and key witnesses as appropriate, and conduct the Investigation. The Investigation Committee may include members of the CSCE. Individuals who have unresolved personal, professional, or financial conflicts of interest with those involved with the Investigation or Inquiry, including the Respondent(s) and Complainant(s), may not serve on the Investigation Committee.

When feasible, one member of the Investigation Committee should be a person of similar professional designation as the Respondent. In addition, if necessary to secure additional scientific expertise or to avoid conflicts of interest, the AIRIO may appoint employees of other federal agencies.

Except under extraordinary circumstances, the Investigation Committee should not include as a member an individual who served on the Inquiry Committee or who was consulted or was otherwise involved in the assessment of allegation(s). When appointment of an individual with previous involvement in the NIH research misconduct proceeding is determined to be useful, the AIRIO will document the basis for the NIH's conclusion that the appointment satisfies the PHS Regulations' requirement to ensure a fair investigation, and include such documentation in the record of the Investigation.

At the time of appointment, a proposed Investigation Committee member will be asked to sign a Federal Employee Participant Statement. (See Attachment 2).

Typically, the Deputy SD of the Respondent's IC serves as Co-Executive Secretary for the Committee. The other Co-Executive Secretary will be designated by the AIRIO. One or more attorneys from the HHS Office of the General Counsel may be present at committee meetings and/or interviews.

The AIRIO will notify the Respondent of the names of the proposed Investigation Committee members and provide an opportunity for the Respondent to object to a proposed member based upon a personal, professional, or financial conflict of interest. The Respondent must inform the AIRIO of any objections within seven (7) calendar days. The AIRIO will then determine whether a personal, professional, or financial conflict of interest exists that cannot be resolved and, as a result, necessitates replacement of the challenged committee member.

D. First Meeting and Charge to the Committee

1. Charge to the Committee

The AIRIO may prepare a written charge to the Committee that:

- describes the allegations and related issues identified during the Inquiry.
- identifies the Respondent(s).
- defines research misconduct.
- states that an Investigation is the formal development of a factual record and the examination of that record leading to a decision not to make a finding of

research misconduct or to a recommendation for a finding of research misconduct, which may include a recommendation for other appropriate actions, including administrative actions.

- describes the Investigation process (see section IX(E) below).

- informs the Committee that it must evaluate the evidence and testimony to determine whether, based on a preponderance of the evidence, research misconduct occurred and, if so, the type and extent and who was responsible.

- informs the Committee that in order to determine that the Respondent committed research misconduct, it must find that a preponderance of the evidence establishes that: (1) research misconduct, as defined in this Policy, occurred; (2) the research misconduct is a significant departure from accepted practices of the relevant research community; and (3) the Respondent committed the research misconduct intentionally, knowingly, or recklessly. The Committee's decision need not be unanimous.

- informs the Committee that it must prepare, or direct the preparation of, a written Investigation Report that meets the requirements of this Policy and the PHS Regulations.

- describes the timeline for completion of the Investigation.

- describes NIH's expectation that confidentiality will be maintained consistent with this Policy and to the extent required by law. Outside of Committee meetings and interviews, Investigation Committee members are directed not to discuss the NIH proceedings with the Respondent, Complainant, witnesses, or anyone not otherwise authorized to discuss the Investigation.

2. First Meeting

At the Investigation Committee's first meeting, the AIRIO may review the charge; discuss the allegations, the Inquiry Report, any related issues, and the process for conducting the Investigation; assist the Committee with organizing plans for the Investigation; and answer any questions raised by the Committee. The Investigation Committee should be provided a copy of this Policy and the PHS Regulations. One member of the Committee will serve as Chair. The AIRIO will be present or available throughout the Investigation to advise the Committee as needed.

E. Investigation Process

The Investigation Committee and the AIRIO must:

- use diligent efforts to ensure that the Investigation is thorough and sufficiently documented and includes examination of all research records and evidence relevant to reaching a decision on the merits of the allegations;

- take reasonable steps to ensure an impartial and unbiased Investigation to the maximum extent practical;

- interview each Respondent, each Complainant, if known, and any other available person who has been reasonably identified as having information regarding any relevant aspects of the Investigation, including witnesses identified by the Respondent. An audio recording of each interview is made and, when feasible, professionally transcribed. When a transcript is prepared, the interviewee is provided an opportunity to correct errors in transcription. Changes to a transcript will only be made to correct errors in transcription, but an interviewee may add comments or additional information that will be included with his/her transcript as an addendum. The transcript (or, if no transcript is prepared, the audio recording) is entered into the record of the proceeding.; and

- pursue diligently all significant issues and leads discovered that are determined relevant to the Investigation, including any evidence of additional instances of possible research misconduct, and continue the Investigation to completion.

A finding of research misconduct made under the PHS Regulations and this Policy requires that: (a) there be a significant departure from accepted practices of the relevant research community; and (b) the misconduct be committed intentionally, knowingly, or recklessly; and (c) the allegation be proven by a preponderance of the evidence.

The NIH has the burden of proof for making a finding of research misconduct, based on a preponderance of the evidence. The destruction, absence of, or Respondent's failure to provide research records adequately documenting the questioned research is evidence of research misconduct where the NIH establishes by a preponderance of the evidence that the Respondent intentionally, knowingly, or recklessly had research records and destroyed them; had the opportunity to maintain the records but did not do so; or maintained the records and failed to produce them in a timely manner; and that the Respondent's conduct constitutes a significant departure from accepted practices of the relevant research community.

The Respondent has the burden of proving by a preponderance of the evidence any affirmative defenses raised, including honest error or a difference of opinion. The Respondent also has the burden of proving by a preponderance of the evidence any

mitigating factors that are relevant to a decision to impose administrative actions following an NIH research misconduct proceeding or following additional ORI proceedings.

Investigation Committee members are expected to be present for all Committee meetings and interviews. When necessary (*e.g.*, to ensure attendance or to avoid prolonged delay or unreasonable expense), the AIRIO may make arrangements to use video conference, audio conference, or similar technology for an Investigation Committee meeting or interview. In the event a Committee member is absent from one or more meetings or interviews, the AIRIO may in his or her discretion determine whether the Investigation process should be modified, *e.g.*, by having the member continue to serve on the Committee in a non-voting capacity only, or by removing the member from further participation on the Committee.

F. Timeline for Completion

The Investigation is to be completed within 120 days of its initiation (defined as the date of the first meeting of the Investigation Committee), including conducting the Investigation, preparing the report of recommended findings, providing the draft Report for comment, review and final decision by the DO, and sending the final Report to ORI. However, if the AIRIO determines that the Investigation cannot be completed within this 120-day period, he/she will submit to ORI a written request for an extension, setting forth the reasons for the delay. The AIRIO will ensure that periodic progress reports are filed with ORI, if ORI grants the request for an extension and directs the filing of such reports. In addition, the AIRIO will notify the Respondent of the extension.

X. THE INVESTIGATION REPORT

A. Elements of the Investigation Report

The Investigation Committee and the AIRIO are responsible for preparing a written draft report for the Investigation that:

1. describes the nature of the allegation(s) of research misconduct, including identification of the Respondent;
2. describes the specific allegations of research misconduct considered in the Investigation;
3. describes and documents the PHS support;
4. should include the names, titles, and affiliations of the Investigation Committee members;
5. should include the dates of Committee meetings and interviews;
6. includes the NIH policies and procedures under which the Investigation was conducted (*i.e.*, this Policy), unless those policies and procedures were provided to ORI previously;

7. if an extension of time was granted for completion of the Investigation, should document the reasons for exceeding the 120-day period;
8. identifies and summarizes the research records and evidence reviewed and identifies any evidence taken into custody but not reviewed;
9. includes a statement of recommended findings; *i.e.*, for each separate allegation of research misconduct identified during the Investigation, includes a recommended finding as to whether research misconduct did or did not occur, and if so:
   (a) identifies whether the research misconduct was falsification, fabrication, or plagiarism, and if it was intentional, knowing, or in reckless disregard;
   (b) summarizes the facts and the analysis which support the conclusion and considers the merits of any reasonable explanation by the Respondent, including any effort by Respondent to establish by a preponderance of the evidence that he or she did not engage in research misconduct because of honest error or a difference of opinion;
   (c) identifies the person(s) responsible for the research misconduct;
   (d) identifies the specific PHS support;
   (e) identifies whether any publications need correction or retraction; and
   (f) lists any current support or known applications or proposals for support that the Respondent has pending with non-PHS federal agencies.
10. may describe any recommended administrative actions that the Investigation Committee believes the NIH should take;
11. when the Committee's decision is not unanimous, may include a separate statement summarizing the minority viewpoint;
12. may document evidence that suggests an allegation may have been made in bad faith; and
13. in the final version of the Investigation Report, includes any comments submitted by the Respondent or the Complainant on the draft report, per section X(B) below, along with the Committee's written reply, which should address any changes made to the draft Report as a result of the comments.

An outline for an Investigation Report is provided in Attachment 4.

A draft report will be provided to the HHS Office of the General Counsel for legal review. Modifications may be made as appropriate, in consultation with the AIRIO and the Investigation Committee.

B. Comments on the Draft Report and Access to Evidence

1. Respondent

The AIRIO must give the Respondent a copy of the draft Investigation Report for comment and, concurrently, a copy of, or supervised access to, the evidence on which the report is based. The Respondent will be allowed thirty (30) days from the date he/she receives the draft report to submit comments to the AIRIO. The

Respondent's comments, if any, will be considered and included in the final report.

2. Complainant

The NIH may choose to provide the Complainant, if known, the portions of the draft Investigation Report that address the Complainant's role and statements in the Investigation. Any comments from the Complainant must be submitted within thirty (30) days of the date on which he/she receives the draft report, and the comments will be considered and included in the final report.

3. Confidentiality

In distributing the draft report, or portions thereof, to the Respondent and Complainant, the AIRIO should remind the recipient of his/her obligation to maintain the confidentiality of the research misconduct proceeding (see section V(C) above).

C. Decision by Deciding Official

The AIRIO will assist the Investigation Committee in finalizing the draft Investigation Report, including ensuring that the Respondent's and Complainant's comments, if any, are considered and included, and transmit the final Investigation Report to the DO, who will determine in writing: (1) whether the NIH accepts the Investigation Report, its recommended findings, and any recommended NIH actions; and (2) the appropriate NIH actions to be taken, if any, in response to accepted findings of research misconduct. If this determination varies from the recommended findings of the Investigation Committee, the DO will, as part of his/her written determination, explain the basis for rendering a decision different from the recommended findings of the Investigation Committee. Alternatively, the DO may return the report to the Investigation Committee with a request for further fact-finding, analysis or clarification of the Report.

If, in the Investigation Report, the Investigation Committee documents evidence that suggests an allegation may have been made in bad faith, the DO will review the evidence and may recommend further action (section XIII(D)).

D. Notification of NIH Findings and Actions; Requests for Comment

When a final decision has been reached, the AIRIO will notify both the Respondent and the Complainant, if known, in writing. The AIRIO will also notify those NIH officials who need to know of the decision as part of their official duties.

Unless an extension has been granted, the AIRIO must, within the 120-day period for completing the Investigation, submit the following to ORI: (1) a copy of the final

Investigation Report with all attachments; (2) a statement of whether the NIH accepts the findings of the Investigation Report; (3) a statement of whether the NIH found research misconduct and, if so, who committed the research misconduct; and (4) a description of any pending or completed administrative actions against the Respondent.

After NIH makes a finding of research misconduct and has informed ORI of the finding, NIH will determine whether notice to other parties is necessary. To the extent consistent with the "routine uses" described in the applicable Privacy Act system of records notice, "NIH Records Related to Research Misconduct Proceedings, HHS/NIH," 09-25-0223 (77 Fed. Reg. 52043 (Aug. 28, 2012)), such parties may include the following depending on the circumstances:

- Other Federal, State, local, or Tribal governmental agencies and offices;
- Law enforcement;
- Institutional Review Boards, research-sponsoring institutions, individual research subjects;
- Responsible officials of NIH- or PHS-supported institutions or organizations;
- Research collaborators of the Respondent, professional journals, other publications, news media, professional societies, other individuals and entities, and the public.

The AIRIO is responsible for ensuring compliance with all notification requirements of other funding or sponsoring agencies, if applicable.

If NIH IRP receives a request for comment regarding an NIH research misconduct proceeding, *e.g.*, a press inquiry following NIH's disclosure of a finding, a response should be coordinated through the AIRIO's office. The following statement has been approved for use in response to a request for comment:

NIH takes allegations of research misconduct seriously. NIH does not discuss whether or not a research misconduct proceeding is taking place, and does not comment on ongoing or completed NIH proceedings. The HHS Office of Research Integrity (ORI) oversees and directs Public Health Service (PHS) research integrity activities on behalf of HHS. After NIH makes a finding of research misconduct, it informs ORI of the finding. Once it has reported to ORI, NIH may, if necessary, make disclosures under certain conditions to professional journals, research collaborators, and others concerning the NIH finding and the need to correct or retract research results or reports that have been affected by research misconduct. All ORI findings of research misconduct are posted on the HHS Office of Research Integrity website: https://ori.hhs.gov/.

E. Maintaining Records for Review by ORI

The AIRIO must maintain and provide to ORI upon request "records of research misconduct proceedings" as that term is defined in the PHS Regulations (42 CFR 93.317). Unless custody has been transferred to HHS or ORI has advised in writing that the records no longer need to be retained, records of research misconduct proceedings must be maintained in a secure manner for seven (7) years (or longer, if other record retention requirements apply to the records) after completion of the proceeding or the completion of any PHS proceeding involving the research misconduct allegation, whichever is later. The AIRIO also is responsible for providing any information, documentation, research records, evidence or clarification requested by ORI to carry out its review of an allegation of research misconduct or of NIH's handling of such an allegation.

XI. ADMISSIONS AND SETTLEMENTS; REPORTING OBLIGATIONS

The NIH is expected to carry Inquiries and Investigations through to completion and to pursue diligently all significant issues. At any time during the NIH research misconduct proceeding, the Respondent has the opportunity to admit that research misconduct occurred and that he/she committed the research misconduct. With the advice of the AIRIO and/or other NIH officials, the Deciding Official may terminate the NIH's review of an allegation that has been admitted, if the NIH's acceptance of the admission and any proposed settlement (typically known as a Voluntary Settlement Agreement) is approved by ORI. A sample Respondent Admission Statement and Voluntary Settlement Agreement are included in Attachment 5.

The NIH must notify ORI in advance if it plans to close a case at the Inquiry or Investigation stage on the basis that the Respondent has admitted guilt, a settlement with the Respondent has been reached, or for any other reason, except: (1) the closing of a case at the Inquiry stage on the basis that an Investigation is not warranted; or (2) a finding of no research misconduct at the Investigation stage, which is to be reported in any event under the PHS Regulations, as described in section X(D) above.

ORI will consult with the NIH on its basis for closing the case and may conduct an oversight review of the handling of the NIH proceeding and take appropriate actions including: (1) approving or conditionally approving closure of the case; (2) directing the NIH to complete its process; (3) referring the matter for further investigation by HHS; or (4) taking a compliance action.

XII. NIH ADMINISTRATIVE ACTIONS

If, in the Investigation Report, the Investigation Committee includes a recommended finding of research misconduct, the Investigation Committee may describe any recommended administrative actions that the Investigation Committee believes the NIH should take, including appropriate actions against the Respondent.

If the DO determines that research misconduct is substantiated by the Investigation findings, he/she will decide after consultation with the AIRIO or, as necessary, will refer to other appropriate NIH officials (*e.g.*, Director of Human Resources) to decide what, if any, NIH administrative actions should be taken. The administrative actions must be consistent with applicable personnel rules and regulations and may include, for example:

- retraction or correction of all pending or published abstracts and papers emanating from the research where research misconduct was found (though earlier corrective action may be appropriate for publications, per section V(E) above);

- removal of the responsible person from the particular project, letter of reprimand, special monitoring of future work, probation, suspension, salary reduction, or initiation of steps leading to possible rank reduction or termination of employment; or

- other action appropriate to the research misconduct.

XIII. OTHER CONSIDERATIONS

A. Termination or Resignation Prior to Completing Inquiry or Investigation

The termination of a Respondent's employment at NIH, by resignation or otherwise, before or after an allegation of possible research misconduct has been reported, will not necessarily preclude or terminate a research misconduct proceeding or otherwise limit any of the NIH's responsibilities under the PHS Regulations.

If a Respondent, without admitting to the research misconduct, elects to resign his or her position after the NIH receives an allegation of research misconduct, the assessment of the allegation, as well as the Inquiry and Investigation, may proceed as appropriate based on the outcome of the preceding steps. If the Respondent refuses to participate in the process after resignation, the AIRIO and any Inquiry Committee or Investigation Committee will use their best efforts to reach a conclusion concerning the allegations, noting in the report the Respondent's failure to cooperate and its effect on the evidence available for analysis.

B. Restoration of the Respondent's Reputation

Following a final finding of no research misconduct, including ORI concurrence where required by the PHS Regulations, the AIRIO must, at the request of the Respondent and as appropriate, undertake all reasonable and practical efforts to restore the Respondent's reputation. Depending on the particular circumstances and the views of the Respondent, the AIRIO should consider notifying those individuals that are known to the AIRIO to be aware of or involved in the NIH research misconduct proceeding or the final outcome, publicizing the final outcome in any forum in which the allegation of research

misconduct was previously publicized, and requesting that all reference to the research misconduct allegation be expunged from the Respondent's personnel file, if appropriate.

An IC for which the Respondent works should seek to mitigate the impact that the NIH proceeding may have had on the Respondent's position, reputation, and responsibilities. In the case of Fellows, NIH has the discretion to permit the Fellow to move his/her fellowship to another NIH laboratory, if available. To the extent permitted by law and NIH policy, the NIH also may consider whether to extend an existing fellowship award or grant a new award in recognition of the time that the Fellow may have lost in his/her original laboratory.

Any NIH actions intended to restore the Respondent's reputation should first be approved by the DO.

C. Protection of the Complainant, Witnesses, and Committee Members

During the research misconduct proceeding and upon its completion, regardless of whether the NIH or ORI determines that research misconduct occurred, the AIRIO must undertake all reasonable and practical efforts to protect the position and reputation of, or to counter potential or actual retaliation against, any Complainant who made allegations of research misconduct in good faith and of any witnesses and committee members who cooperate in good faith with the research misconduct proceeding. The DO will determine, after consulting with the AIRIO, and with the Complainant, witnesses, or committee members, respectively, what steps, if any, are needed to restore their respective positions or reputations or to counter potential or actual retaliation against them. The DO may consult with, or refer matters to, other appropriate NIH officials, *e.g.*, the Director of Human Resources for matters that may involve employee standards of conduct and related personnel regulations. The AIRIO may assist the DO by implementing measures that the DO has approved.

D. Allegations Not Made in Good Faith

If relevant, the DO will determine whether the Complainant's allegations of research misconduct were made in good faith, or whether a witness or committee member acted in good faith. If the DO determines, based on the Inquiry Report or Investigation Report, that there was an absence of good faith, he/she will determine or, as necessary, will refer to other appropriate NIH officials (*e.g.*, Director of Human Resources) to determine, whether any administrative action should be taken against the person who failed to act in good faith.

E. ORI Review and HHS Administrative Actions

Comprehensive descriptions of ORI's authority to review and respond to an allegation of research misconduct or a research misconduct proceeding and HHS' authority to take

administrative action in response to a research misconduct proceeding are beyond the scope of this Policy. These descriptions and related matters are contained in the PHS Regulations. Additional information is also available on the ORI web site <https://ori.hhs.gov/>.

Attachment 1

CONFIDENTIALITY STATEMENT

Note: To be provided to complainants, respondents, witnesses or others, as needed, related to an NIH research misconduct proceeding

From: Deputy Director for Intramural Research, National Institutes of Health (NIH)

The NIH Intramural Research Program is conducting an NIH research misconduct proceeding to examine allegations of research misconduct about which you may have, or may acquire, some knowledge. The NIH maintains confidentiality of research misconduct proceedings as required under federal law, 42 C.F.R. Part 93. An unlawful breach of confidentiality may disrupt the NIH's ability to carry out this proceeding fairly, may cause undue damage to the scientific reputations of the individuals involved, or may constitute a breach of the Privacy Act, 5 U.S.C. sec. 552a.

It is your obligation to maintain the confidentiality of this research misconduct proceeding to the extent required by law. You agree not to disclose the identity of respondents, complainants or witnesses, except to those who need to know in order for this research misconduct proceeding to be carried out in a thorough, competent, objective and fair manner, or unless otherwise allowed by law. In addition, you agree not to disclose any records or evidence from which research subjects might be identified except to those who need to know in order to carry out this research misconduct proceeding or as otherwise prescribed by applicable law.

Unless you are a Respondent in this NIH proceeding or have received prior permission from the NIH Agency Intramural Research Integrity Officer (AIRIO), you should not make copies of any information provided to you and should return all materials that you received to the AIRIO at the conclusion of your involvement in this proceeding. For more information, you may refer to the NIH Intramural Research Program Policies & Procedures for Research Misconduct Proceedings.

Note to Respondents: To the extent consistent with the obligations described above and applicable law, a Respondent may consult with his/her own legal counsel or a non-lawyer personal adviser (who may not be a principal or witness in the proceeding), or with others who may assist Respondent in his or her defense.

Please sign below to indicate that you have received and read this statement and understand your obligation to maintain confidentiality.

Name (please print): _____

_____ _____

(signature) (date)

Attachment 2

NIH INTRAMURAL RESEARCH MISCONDUCT PROCEEDING
FEDERAL EMPLOYEE PARTICIPANT STATEMENT

I, _____ *(name)*, am an employee of the Federal Government and offer to assist the National Institutes of Health (NIH) Intramural Research Program by sharing my scientific expertise and participating in an NIH research misconduct proceeding. In making this offer, I understand and agree with the following statements:

1. To the best of my knowledge, I do not have unresolved personal, professional, or financial conflicts of interest with those involved with the NIH research misconduct proceeding, and I have appropriate scientific expertise to participate in it.
2. This assignment is within the scope of my federal employment position description, and my supervisor is aware of, and has approved, my participation in the NIH research misconduct proceeding during official business hours.
3. For purposes of this assignment, I will be under the direct supervision of the NIH Agency Intramural Research Integrity Officer (AIRIO), or designee.
4. For purposes of this assignment, I agree to be bound by the provisions of the NIH Intramural Research Program Policies & Procedures for Research Misconduct Proceedings and the Public Health Service (PHS) Policies on Research Misconduct, 42 C.F.R. Part 93 (PHS Regulations).
5. I will maintain the confidentiality of the research misconduct proceeding to the extent required by law. I will not disclose the identity of respondents, complainants, or witnesses except to those who need to know in order for the research misconduct proceeding to be carried out in a thorough, competent, objective and fair manner, or unless otherwise allowed by law. In addition, I will not disclose any records or evidence from which research subjects might be identified except to those who need to know in order to carry out the research misconduct proceeding or as otherwise prescribed by law.
6. While on the premises of NIH, and while performing services for this assignment off the premises of NIH, I will conform to all applicable administrative instructions and requirements of the Department of Health and Human Services and NIH.

I understand that my assignment becomes effective upon the date of my signature below and ends upon the completion of my services with regard to the NIH research misconduct proceeding, or as otherwise instructed by the AIRIO or designee. I also understand that my assignment may be terminated at any time by the NIH, and that a request by me to terminate my assignment may be considered by the AIRIO in his or her discretion.

_____

Signature of Federal Employee Participant Date

Attachment 3

Outline for an Inquiry Report

The PHS Regulations and this NIH Policy require an Inquiry Report to be prepared during the course of an NIH research misconduct proceeding (see section VIII of this Policy). The following outline is based, in part, on guidance received from ORI. This outline may be used to prepare an Inquiry Report, though special factors in a given NIH proceeding may necessitate a different approach. Section VIII(A) of this Policy describes mandatory, recommended, and discretionary elements of the Inquiry Report.

1. Background

   Provide sufficient background information to ensure a full understanding of the issues that concern NIH and the Public Health Service under the definition of research misconduct, including:

   a. The name and position of the Respondent;
   b. Role of the Complainant and his or her name and position (unless the allegation was made anonymously or upon request that identity be withheld);
   c. The facts leading to the Inquiry, including a description of the research at issue, relevant dates, identification of relevant persons involved, and any associated public health issues.

2. Allegations

   Describe the allegations of research misconduct against the Respondent, including any additional allegations that arose during the Inquiry. The allegations listed in this section should be consistent with those identified in the original notification memo to the Respondent or, if applicable, an updated version thereof. These allegations will form the structure or context in which the subsequent analysis and findings are presented in the report.

3. PHS Support

   For each allegation, identify the PHS support (*e.g.*, if applicable, a statement that the research was funded and carried out within the NIH IRP).

4. Inquiry Committee Members and Activities

   Summarize the Inquiry process, including the following information:

   a. The names, titles, and affiliations of the Inquiry Committee members;
   b. The dates of Committee meetings and interviews and identification of persons interviewed;

c. Reference to the policies and procedures used by the Committee for the Inquiry, *i.e.*, this Policy (The NIH IRP Policies and Procedures for Research Misconduct Proceedings);
d. If an extension of time was granted for completion of the Inquiry, documentation of the reasons for exceeding the 60-day period;
e. Any other factors that may have influenced the proceedings.

5. Evidence Examined

Summarize the evidence secured and reviewed. Describe the sequestration process, including how and when records were sequestered and the measures taken to ensure security of the records. Include as an attachment a list of the documentary evidence examined and interviews conducted.

6. Analysis

As a reminder, under the PHS Regulations and this Policy, an Investigation is warranted if the following criteria are met:

a. There is a reasonable basis for concluding that the allegation falls within the definition of research misconduct and is within the jurisdictional criteria of the PHS Regulations and this Policy (see section II of this Policy); and

b. The allegation may have substance, based on the preliminary information-gathering and preliminary fact-finding conducted by the Committee during the Inquiry.

For each allegation, the analysis should describe the basis for recommending, or not recommending, that the allegation warrants an Investigation, including a summary of the relevant evidence (or lack of evidence) on which the Committee's recommendation is based.

The analysis for each allegation should take into account all of the relevant statements, claims (*e.g.*, a claim of a significant positive result in an experiment), rebuttals, documents, and other evidence, including circumstantial evidence, related to the issue. The source of each statement, claim, or other evidence should be cited (*e.g.*, laboratory notebook with page and date, medical chart documents and dates, relevant manuscripts, transcripts of interviews, etc.).

Summarize or quote relevant statements, including rebuttals, made by the Complainant, Respondent, and other pertinent witnesses and reference/cite the appropriate sources. The analysis should describe the relative weight given to the various witnesses and pieces of evidence, noting inconsistencies, credibility, and persuasiveness.

Include discussion of each argument that the Respondent raised in his or her defense against the research misconduct allegation and cite the source of each argument. Any inconsistencies among the Respondent's various arguments should be noted.

If the allegations involve images, indicate whether the Committee reviewed them visually or by forensic image analysis in order to reach its decisions.

If applicable, any use of additional expert analysis should be discussed. The forensic, statistical, or special analysis of the physical evidence, such as similarity of features or background in contested figures, should be noted and included with attachments.

7. Conclusion

Based on the analysis in section 6 above, concisely state whether, for each allegation, the Inquiry Committee recommends or does not recommend that the allegation warrants an Investigation.

The Inquiry Committee may choose to include recommendations as to whether any actions should be taken if an Investigation is not recommended (*e.g.*, correction or retraction of a publication for errors, even if such errors were determined by the Committee not to result from research misconduct).

When the Inquiry Committee's decision is not unanimous, the Report also may include a separate statement summarizing the minority viewpoint.

8. Reply to Comments (for final version of Report)

If the Respondent or Complainant submits comments on the draft Inquiry Report, it is recommended that the Inquiry Committee include a written reply to such comments in the final version of the Inquiry Report. The reply should include a description of any changes made to the draft Report as a result of the comments.

9. Report Attachments

At a minimum, the Inquiry Report should include a list of the documentary evidence examined and interviews conducted. If feasible, the attachments also should include copies of significant documentary evidence that is referenced in the report (*e.g.*, relevant notebook pages or other research records, relevant committee or expert analyses of data, transcripts or summary of each interview, manuscripts, publications or other documents).

The final version of the Inquiry Report must include any comments submitted by the Respondent or the Complainant on the draft report.

If documentary evidence is attached, it is useful to identify the allegedly false statements, misrepresentations in figures or parts of figures, areas of plagiarism, etc. on a copy of the page or section of the questioned document (*e.g.*, a page from a research notebook). For alleged plagiarism, a side-by-side comparison with the original data or text that is alleged to have been plagiarized is helpful.

Where multiple attachments are included with the Report, add a "List of Attachments" as the first attachment.

Attachment 4

Outline for an Investigation Report

The PHS Regulations and this NIH Policy require an Investigation Report to be prepared during the course of an NIH research misconduct proceeding (see section X of this Policy). The following outline is based, in part, on guidance received from ORI. This outline may be used to prepare an Investigation Report, though special factors in a given NIH proceeding may necessitate a different approach. The Investigation Report must incorporate, at a minimum, the required elements described in section X(A) of this Policy.

1. Background

   Provide sufficient background information to ensure a full understanding of the issues that concern NIH and the Public Health Service under the definition of research misconduct, including:

   a. The name and position of the Respondent;
   b. Role of the Complainant and his or her name and position (unless the allegation was made anonymously or upon request that identity be withheld);
   c. The facts leading to the NIH research misconduct proceeding, including a description of the research at issue, relevant dates, identification of relevant persons involved, and any associated public health issues;
   d. A list of any current support or known applications or proposals for support that the Respondent has pending with non-PHS federal agencies.

2. Allegations

   Describe the allegations of research misconduct against the Respondent, including any additional allegations that arose during the Investigation. The allegations listed in this section should be consistent with those identified in the Investigation notification memo to the Respondent or, if applicable, an updated version thereof. These allegations will form the structure or context in which the subsequent analysis and findings are presented.

3. PHS Support

   For each allegation, identify the PHS support (*e.g.*, if applicable, a statement that the research was funded and carried out within the NIH IRP).

4. Inquiry Summary

   Summarize the Inquiry process, including reference to the Inquiry Report. Discuss any factors of particular relevance to the Investigation Committee's subsequent review.

5. Investigation Committee Members and Activities

Summarize the Investigation process, including the following information:

a. The names, titles, and affiliations of the Investigation Committee members;
b. The dates of Committee meetings and interviews and identification of persons interviewed;
c. Reference to the policies and procedures used by the Committee for the Investigation, *i.e.*, this Policy (The NIH IRP Policies and Procedures for Research Misconduct Proceedings);
d. If an extension of time was granted for completion of the Investigation, documentation of the reasons for exceeding the 120-day period;
e. Any other factors that may have influenced the proceedings.

6. Evidence Examined

Summarize the research records and evidence secured and reviewed, including any new evidence sequestered after the Inquiry. Describe the sequestration process, including how and when records were sequestered and the measures taken to ensure security of the records. Include as an attachment a list that identifies the interviews conducted and the research records and evidence reviewed, as well as any evidence taken into custody but not reviewed.

7. Analysis

As a reminder, a finding of research misconduct made under the PHS Regulations and this Policy requires that: (a) there be a significant departure from accepted practices of the relevant research community; and (b) the misconduct be committed intentionally, knowingly, or recklessly; and (c) the allegation be proven by a preponderance of the evidence.

Points to be Addressed

For each allegation, the analysis should summarize the relevant facts and identify and analyze the relevant evidence supporting the Investigation Committee's statement of recommended findings as set forth in section 8 (below). If not already included as background in section 1, describe the particular matter (*e.g.*, experiment or component of a clinical protocol) in which the alleged misconduct occurred and why and how the issue came to be under investigation.

The analysis should indicate the extent and seriousness of the alleged fabrication, falsification, or plagiarism, including its effect on research findings, publications, research subjects, and the laboratory or project in which the research misconduct occurred. The Report should include the significance of each incident of alleged

misconduct to the overall research results that were reported. For example, in a case involving allegedly falsified or fabricated images, the Investigation Committee should describe the significance of each image alteration to the overall results that are reported in the figure.

Similarly, the analysis should describe the basis for a determination that the alleged misconduct was (or was not) a significant departure from accepted practices in the relevant research community. Specifically, the Report should identify the relevant research community, articulate its accepted practices, and state how the alleged misconduct was (or was not) a significant departure from these accepted practices at the time the alleged misconduct occurred. For purposes of identifying accepted practices, the Committee may choose to reference publications, standards of the institution or relevant professional societies, applicable regulations, or expert opinion.

The analysis also should describe any evidence that shows that the Respondent acted with intent, that is, any evidence that the Respondent knowingly, intentionally, or recklessly engaged in the alleged falsification, fabrication, or plagiarism. Similarly, if applicable, describe the evidence supporting the possibility that honest error or differences of scientific opinion occurred with respect to the allegation in question.

Methodology and Content

The analysis for each allegation should take into account all of the relevant statements, claims (*e.g.*, a claim of a significant positive result in an experiment), rebuttals, documents, and other evidence, including circumstantial evidence, related to the issue. The source of each statement, claim, or other evidence should be cited (*e.g.*, laboratory notebook with page and date, medical chart documents and dates, relevant manuscripts, transcripts of interviews, etc.).

Summarize or quote relevant statements, including rebuttals, made by the Complainant, Respondent, and other pertinent witnesses and reference/cite the appropriate sources. The analysis should describe the relative weight given to the various witnesses and pieces of evidence, noting inconsistencies, credibility, and persuasiveness.

Include discussion as to consideration of the merits of any reasonable explanation by the Respondent, including any effort by Respondent to establish by a preponderance of the evidence that he or she did not engage in research misconduct because of honest error or a difference of opinion. Cite the source of each argument. Any inconsistencies among the Respondent's various arguments should be noted.

If the allegations involve images, indicate whether the Committee reviewed them visually or by forensic image analysis in order to reach its decisions.

If applicable, any use of additional expert analysis should be discussed. The forensic, statistical, or special analysis of the physical evidence, such as similarity of features or background in contested figures, should be noted and included with attachments.

8. Statement of Recommended Findings

Based on the analysis in section 7 above, for each allegation, include a concise statement of recommended findings. Specifically, for each separate allegation of research misconduct identified during the Investigation:

a. include a recommended finding as to whether research misconduct did or did not occur, and if so:
b. identify whether the research misconduct was falsification, fabrication, or plagiarism;
c. identify whether it was intentional, knowing, or in reckless disregard;
d. identify the person(s) responsible for the research misconduct; and
e. identify whether any publications need correction or retraction.

Where no finding is recommended for a particular allegation, the Investigation Committee may, if applicable, document evidence that suggests the allegation may have been made in bad faith.

9. Reply to Comments (for final version of Report)

If the Respondent or Complainant submits comments on the draft Investigation Report, the Investigation Committee is obligated to consider such comments prior to finalizing the Report. It is recommended that the Committee incorporate a written reply to such comments in the final version of the Investigation Report. The reply should include a description of any changes made to the draft Report as a result of the comments.

10. Recommendations for Administrative Action (Optional)

Based on its recommended findings, the Investigation Committee may recommend administrative actions that it believes should be taken. If the Committee has recommended correction or retraction of a publication, the Committee may include suggested text for a notice of correction or notice of retraction to be published. The Report also should identify any other sources of scientific information (such as data bases) that should be retracted or corrected so that NIH can take steps to ensure that appropriate officials who can effect these corrections or retractions are notified.

11. Minority Opinion (Optional)

When the Investigation Committee's decision is not unanimous, the Report may include a separate statement summarizing the minority viewpoint.

12. Report Attachments

At a minimum, the Investigation Report should include a list of the documentary evidence examined and interviews conducted. If feasible, the attachments also should include copies of significant documentary evidence that is referenced in the report (*e.g.*, relevant notebook pages or other research records, relevant committee or expert analyses of data, transcripts or summary of each interview, manuscripts, publications or other documents). These attachments should be cited in the Report and pages numbered, if possible, when the attachment consists of more than one page.

The final version of the Investigation Report must include any comments submitted by the Respondent or the Complainant on the draft report.

If documentary evidence is attached, it is useful to identify the allegedly false statements, misrepresentations in figures or parts of figures, areas of plagiarism, etc. on a copy of the page or section of the questioned document (*e.g.*, a page from a research notebook). For alleged plagiarism, a side-by-side comparison with the original data or text that is alleged to have been plagiarized is helpful.

Where multiple attachments are included with the Report, add a "List of Attachments" as the first attachment.

Attachment 5

Sample Respondent Admission Statement

CONFIDENTIAL
DRAFT

DATE: <Date>

TO: <NIH Agency Intramural Research Integrity Officer (AIRIO)>

FROM: <Respondent>
<Position, IC>

SUBJECT: Admission of Research Misconduct NIH-XX-YY

Dear Dr. Colbert,

I was a <*position*> with Dr. <*Supervisor*> in <*Branch or division*> of the <*IC*>I from <*start date*>to <*end date*>. During that time, I was an author on several publications.

On <Date>, I received a Notification of Inquiry regarding allegations of research misconduct for falsifying and fabrication data, <*which was expanded from the original allegations presented on date*>, to now include figures in <*n*> of my publications.

It is with regret and much sorrow that I admit to knowingly and intentionally falsifying and fabricating the results you identified.

1. I admit to falsifying Figure X by <*duplication, alterations, etc.*> <e.g., *The gel images in fibroblasts and melanocytes are identical in*>
   < *citation: Title, Authors, Journal, reference, year*>

2. I admit to falsifying Figure Y by <*duplication, alterations, etc.*> <e.g. *Bands have been erased from the final image in*>
   < *citation: Title, Authors, Journal, reference, year*>

3. I admit to falsifying the image in Figure Z by manipulating the image shown there. Specifically, bands have been manipulated by <*How manipulated*>… in
   < *citation: Title, Authors, Journal, reference, year*>

I was solely responsible for my actions and sincerely apologize to my mentor and my co-workers in Dr. <*Supervisor's*> laboratory for the embarrassment this has caused. I recognize that it is imperative to correct the research record as required. Please notify the HHS Office of Research Integrity that I will work with them to do what is necessary and appropriate for my case.

Signature and Date

Sample Voluntary Settlement Agreement (based on text provided by ORI)

This Voluntary Settlement Agreement (Agreement) is entered into by and between the United States Department of Health and Human Services (HHS), through the U.S. Public Health Service (PHS), the Office of Intramural Research (OIR) at the National Institutes of Health (NIH), and <*Respondent*>.

The purpose of this Agreement is to settle the Office of Research Integrity's (ORI's) research misconduct findings against Respondent, who was a <*Position* (*e.g.*, postdoctoral fellow, staff scientist, research fellow)> in the <*Branch*>, <*IC*>, NIH.

Based on Respondent's admission, an assessment conducted by NIH and analysis conducted by ORI in its oversight review, this settlement resolves ORI's research misconduct finding that Respondent engaged in research misconduct supported by <*IC*>, NIH.

ORI finds that Respondent engaged in research misconduct by reporting falsified and/or fabricated data in the following (*n*) publications <*and submitted manuscripts, grant applications, abstracts, etc.*>:

- Paper 1
- Paper 2, etc.

ORI finds that Respondent knowingly falsified and/or fabricated data and related images by alteration and/or reuse and /or relabeling of experimental data. Specifically:

- In Paper 1, Respondent falsified and or fabricated results in Figure X by…
- In Paper 2, Respondent falsified and or fabricated results in Figure Y by…

The terms of this agreement are as follows… (to be completed by ORI)

Collaborative Science

Research collaborations facilitate progress and should be encouraged; however, the ground rules for collaborations, including authorship issues, should be discussed openly among all participants from the beginning. The NIH encourages research collaborations, both within the intramural programs and with investigators at extramural sites, because they can enhance scientific progress. However, such collaborations may require the establishment of formal mechanisms, such as a material transfer agreement (MTA) or a human subjects protection review.

The NIH Center for Cooperative Resolution, directed by the NIH Ombudsman, has developed a template for use in establishing collaborations that may prove useful as you embark on a collaboration. The following cases illustrate some of the key issues that arise and therefore need to be addressed in any agreement before the collaboration starts.

CASE 1 - BASIC-CLINICAL COLLABORATION

adapted from Scientific Integrity by Francis L. Macrina

A clinical scientist and a basic molecular biologist are collaborating on a series of projects that involve patients and normal control subjects. Each investigator is funded from their IC's intramural program for work distinct from the collaborative project, and each has separate funds for the collaborative project. The clinical scientist views the patient records and diagnoses as her intellectual property and shares these data only when she is ready to prepare a manuscript. The molecular biologist has prepared and preserved cell lines, probes, and reagents that have been kept in facilities readily available to both collaborators. The molecular biologist believes that there are important results that merit publication. He prepares a manuscript up to the point of inclusion of clinical data. The clinical scientist refuses to provide the clinical data. In the dispute that follows, the clinical scientist asserts ownership of the cell lines, probes, and reagents that were developed from patient samples. The dispute is brought to you to mediate. Discuss the data ownership issues of this collaboration. Who owns the clinical data? Who owns the cell lines, probes, and reagents? Who has access to, and use of, the clinical data and the materials prepared from patient samples?

CASE 2 - WHEN DOES A COLLABORATOR DESERVE AUTHORSHIP?

adapted from Scientific Integrity by Francis L. Macrina

You have had a radical idea regarding how to get eukaryotic cells to take up DNA fragments much more efficiently than was previously possible. You tell your colleague Maria about your idea and how you plan on testing the hypothesis. Maria is not in your field of expertise, but you spend some time explaining to her the details of your study and the expected outcomes. Maria offers a number of unsolicited suggestions on how to improve the study. Because of her lack of experience, many of her ideas are not practical or are very elementary and part of your study anyway. However, Maria suggests some valuable control experiments involving DNA competition assays, which help you make a compelling case for the novelty and efficiency of your method: Maria talks to you frequently about the project and comes to several of your lab presentations. She comments critically on your work and makes other suggestions, including the idea that you try different cell types to further build your case. She offers to try your method on several cell lines that are routinely maintained in her laboratory. You are reluctant to do this, but you suggest that she give you the cell lines so you can do the experiments. She complies, and the experimental results you obtain with her cells further support your hypothesis. You decide to submit a provisional patent application and then submit your exciting results as a short communication to a prestigious journal. Maria argues strongly that her name should be included as a co-inventor on the application and a coauthor on the manuscript. How do you respond? What is the rationale underlying your response?

CASE 3 - EQUIPMENT SHARING AND AUTHORSHIP

adapted from Scientific Integrity by Francis L. Macrina

Dr. Otto Max recently was hired as a tenure-track investigator in the Laboratory of Biological Chemistry at NIH. As part of his recruitment package, the IRP has purchased a specialized, expensive instrument used to analyze macromolecules. The analytical power of this instrument and Max's expertise have PI's in several laboratories excited about the application of this technology to their research. PI's who approach Dr. Max to explore the use of the instrument in their research learn that he is happy to collaborate with them. But he spells out conditions for such collaborative research that have some PI's upset. For example, no one but Dr. Max or his technician may operate the instrument. The original printouts of all data must remain with Dr. Max. In addition, any paper submitted for publication that contains data obtained using the instrument must have Dr. Max's name on the author byline and his technician's name in the acknowledgments. Some PI's complain to Max's laboratory chief that these conditions are not collegial and are prohibitive. They argue that if IRP funds were used to purchase the instrument, its use should benefit all IRP PI's. As the laboratory chief, how would you handle this dispute?

CASE 4 - ASSAYS AND AUTHORSHIP

developed by the NIH Committee on Scientific Conduct and Ethics

Dr. Wong has developed a reputation in the local research community for performing well an effective, although somewhat tedious, method of gene expression analysis in her lab. Because the data obtained from this assay are very useful, many labs have an interest in obtaining such results but are reluctant to develop the technique. Dr. Suzuki , a fellow in a nearby lab in another Institute, approached her about performing the assay on a number of samples that he was preparing. Dr. Suzuki indicated that he considered the work to be a collaboration and Dr. Wong agreed to collaborate. A month later, Dr. Suzuki sent Dr. Wong the samples; she ran the assay within a week, providing Dr. Suzuki with the data in figure form as well as her interpretation of the data and some ideas about additional genes to analyze and experiments to perform. Approximately 9 months later, Dr. Wong was scanning the table of contents of a prestigious journal and was surprised to see an article authored by Dr. Suzuki on the topic on which she had thought that they were collaborating. On reading the article, she was surprised and a bit shocked to see the data she had provided to Dr. Suzuki as a figure in the paper and her name in the acknowledgements for performing the assay. Dr. Wong wrote by email to the Head of Dr. Suzuki's laboratory, Dr. Bigge, expressing her surprise and disappointment at seeing her data in a paper about which she was never informed. Both Dr. Bigge and Dr. Suzuki apologized by email and admitted that they were wrong in not sending Dr. Wong the manuscript and inviting her to decide whether she should be a coauthor based on her contributions. Dr. Suzuki indicated that he had decided not to include her as a

coauthor based on some training he had recently received on criteria for authorship.

Points to consider:

1. What is the proper procedure on deciding authorship, especially when a collaboration had been established?
2. Was Dr. Wong justified in being upset?
3. What role should Dr. Bigge have played regarding authorship?
4. Was it appropriate for Dr. Suzuki and Dr. Bigge to have used email to express their apologies?
5. What corrective actions might Drs Suzuki and Bigge take?

CASE 5: COLLABORATION AND CREDIT

adapted from Online Ethics Center for Engineering and Science, CASE Western Reserve University

Robert Kent, M.D., is an established and highly regarded investigator and clinician in breast cancer research and treatment. He holds a faculty position at a large medical institution, where he serves as the Director of the Schrag Center for Breast Cancer research and oversees the allocation of considerable federal monies granted to the Center. In this position, he acts as the facilitator of scientific discussions among clinicians and basic scientists doing work in breast cancer at his center. The members of the group hold appointments in various departments. While many of these investigators receive funding from the Schrag Center, all of them have their own resources as well (NIH, NSF, ACS, etc.). The investigators and members of theirs labs meet weekly to discuss the progress of each lab.

During a recent meeting, Taka, a graduate student, represented the lab of Dr. Sylvia Costa, Ph.D. Although Taka's work is not funded through a Schrag Center grant, Dr. Costa wanted to get feedback on Taka's new data. Taka presented some extremely interesting preliminary data (one set of replicates) regarding two drugs (Casodin and Fluox), both currently in clinical use. Taka's research shows that, when used together, these drugs dramatically inhibit the growth and progression of aggressive breast cancer tumors in mice. Dr. Kent and the rest of the group were very interested in Taka's findings since they held some promise for novel, efficacious therapies with drugs already in use in the clinics.

A few weeks later, Dr. Costa received a phone call from a long-time friend and colleague.

Dr. Costa: Anil, it's great to hear from you. How have you been? I read your last article; it looks like you are really on to something.

Anil: Well, I thought I was moving fast until I saw Dr. Kent give a talk with data from his lab at the International Breast Cancer Meeting last week. I remembered you two were at the same university and wanted to get your opinion of his findings.

Dr. Costa: Well, sure, I guess. To be honest, I haven't heard anything from his lab in quite a while. We both participate in our university's Breast Cancer Research Discussion Group, but those discussions are very informal. In fact, his lab skipped their turn to present data, and that was almost six months ago. What new data did he present?

Anil: He showed numerical data about a novel combination therapy he has been working on, something with Casodin and Fluox.

Dr. Costa: Oh, were these data from mice experiments?

Anil: Yeah. I thought you would be familiar with it. He claimed the results were preliminary, but the three sets of experimental replicates looked impressive.

Dr. Costa: And you're sure this was his work? He presented it as his work with replicate experiments?

Anil: Yup. Well, actually, he said his group. He's such a smart guy.

Dr. Costa: Listen, Anil, I've got to go. I'll talk to you later.

Dr. Costa immediately went to Dr. Kent's office to discuss the incident. Dr. Kent was shocked by Dr. Costa's reaction.

Dr. Kent: Listen, Sylvia, we're really on to something here, and I thought the scientific community needed to benefit from our findings. You weren't planning to attend the meeting, and this is ground-breaking stuff. As the leader of the discussion group and the senior faculty member, I felt the meeting was a great opportunity to present those data.

Dr. Costa: Excuse me, Dr Kent, but when did they become our data? Taka's work isn't even funded by the Schrag Center! This is absolutely outrageous behavior.

Dr. Kent: Well, then I wonder if you are interested in the drug company offers I have been getting to develop a combined delivery system. I really think we can work together on this, Sylvia. I hope you can put aside your reservations. This is just the way science works.

Discussion Questions

1. What should Dr. Costa do?

2. Was Dr. Kent justified in sharing Taka's data at the meeting? What if they were not preliminary data? Should Dr. Kent have any authority over the dissemination of any data discussed at the weekly group meetings?

3. What if Taka's work were funded by the Schrag Center?

CASE 6 - THE STATUTE OF LIMITATIONS

adapted from Online Ethics Center for Engineering and Science, CASE Western Reserve University

Part 1

Shanta is a professor of Biology at ESU (Enormous State University). Her recent work on the genetic structure of plant populations has been exciting and fruitful; she can hardly find the time to follow up on all her ideas. ESU has an informal "brown bag" seminar series in which graduate students and professors present and critique data and ideas. Shanta has always been an enthusiastic participant in the brown bag series, and one year ago she presented a particularly stimulating and untested idea that had spun off from her main avenue of research. Steve, a new graduate student in the department, approached Shanta after her talk and expressed enthusiasm about her idea. Steve felt that he knew just the empirical system in with which to test Shanta's idea, and he offered to collaborate with her on the project and share authorship on any resulting papers. Shanta politely declined. Steve was not her grad student, and she wanted to save the idea for one of her own students to test. A year after the brown bag, Steve approached Shanta again. None of Shanta's students had pursued the idea, and Shanta had not had time to pursue it herself. Steve renewed his previous offer. Shanta again rejected this course of action. It was her idea, and she would pursue it in due time.

Discussion Questions

1. Should Shanta have accepted Steve's offer after it became clear that none of her own current students were interested in following up the idea? When is it acceptable to reject an offer of collaboration?

2. What if Steve's proposed experiment would require seeking additional funding and would take three

years to complete? What if Steve's experiment could be done with materials and equipment on hand and would require only a few weeks? Does the type of collaboration proposed make a difference in when it is acceptable to reject a collaboration? i.e., do the duration and extent of the proposed collaboration matter? Why do you think so?

Part 2

A few days later, Steve approached Shanta a third time. This time Steve announced that he was going to go ahead and test Shanta's idea, with or without her approval. Steve promised that he would give Shanta full credit for her role in the genesis of the idea. Shanta stated that she felt that Steve's actions would be inappropriate since it would deprive her of the right to be the first to publish her new idea. Shanta approached Steve's major professor, Orlando, with her concerns about Steve's behavior. Orlando stated that he knew what Steve was doing, and furthermore he sanctioned it. Orlando and Steve felt that it was legitimate for Steve to pursue the idea, provided he properly credited Shanta as its creator. Shanta responded that her ability to develop and test the idea had been compromised and that Orlando should prevent Steve from pursuing the project. Orlando argued that after a year, the statute of limitations had run out. He asserted that the idea was public property from the moment Shanta gave her brown bag talk. Orlando then offered an indictment of Shanta's behavior.

"Look, Shanta," said Orlando. "Don't you remember how you used to tell us about that awful Professor Igneous you knew in grad school? You used to tell us how he would always claim to be working on all kinds of neat ideas, but in reality he was just trying to claim as much intellectual turf as possible. Igneous was taking advantage of the fact that most of us will avoid initiating a research project if we know someone else is already working on it; there's no sense in duplicating all that effort. You used to tell us how despicable you thought his behavior was, but now you are doing the same thing. You need to let someone pursue the idea who has time to do it now."

Shanta was outraged. "What I am doing is nothing like what Igneous used to do," she replied. "He never got around to doing anything with those projects. I, on the other hand, fully intend to follow up on the idea. What makes you think you get to decide at what point I have had enough time to pursue my own research?"

Discussion Questions

1. Are there ethical implications of "sitting" on an idea that someone else is eager to pursue? Would it change matters if Shanta's idea had potentially important applications in human medicine or the conservation of endangered species?

2. Orlando argued that the idea was fair game after Shanta's brown bag seminar. Would it matter if Shanta had published the idea in a short theoretical note? What if she had delivered the idea in a formal seminar at a national meeting as "work in progress"? Does the setting in which Shanta presented the idea (an informal, in-house presentation) matter? Why or why not?

3. Was Steve justified in pursuing the experiment on the basis that Shanta had had enough time to do the work herself? Should a statute of limitations apply to the ownership of research ideas?

4. Is Shanta's behavior like Dr. Igneous' behavior? Why or why not? Suppose her brown bag presentation had been an interesting idea she had thought of on the drive to work that morning, and the idea was pretty rough and undeveloped. Suppose instead that she had carefully developed mathematical and graphical models to support her idea and had presented those in the brown bag talk. Is the amount of work Shanta may have done relevant to assessing whether Shanta is like Dr. Igneous? Why or why not?

5. Suppose Shanta is delaying the pursuit of this idea until her current grant runs out because she does not have time to work on it until then. Suppose Shanta is teaching this term and intends to pursue it after she has finished. Do Shanta's reasons for delaying the work matter in assessing whether she is behaving like Dr. Igneous in this situation? Why or why not?

6. Should Orlando have tried to mediate the situation between Shanta and his student? Should Orlando prevent Steve from doing the study once it became clear that Shanta did not want Steve involved in the project?

7. Does Orlando and Shanta's argument suggest a tension between the concept of ownership of ideas and the value of collaborative relationships? How do you feel this situation should be resolved? Should Steve pursue the idea? Why or why not?

Collaborative Science and Authorship

Introduction

Collaborations are an important component of biomedical research at the NIH and worldwide. They serve to bring together investigators with diverse expertise for the purpose of addressing specific, important research goals and studies. Successful multidisciplinary teams are characterized by a strong sense of direction and purpose, clearly defined roles and responsibilities, joint commitments of time and effort, effective lines of communications, and a framework for evaluation of progress.

A critical dimension of successful collaborative science related to clear roles and responsibilities concerns planning for future publication(s) with the fair and appropriate allocation of credit through authorship. Written authorship agreements that reflect the substantive contributions of all the research staff and laboratories involved in the project, including students, technicians, fellows, and investigators (including in core facilities and with extramural partners), are especially important in the context of multi-team research. Where appropriate, co-first authorship designation provides a mechanism for ongoing career advancement of young research faculty, while co-senior and corresponding author designations allocate credit for project conceptualization, coordination and successful execution by the senior researchers. Flexibility amongst the study teams and co-authors may be required to maintain fairness under certain circumstances, such as extensive additional experiments being incorporated, departures of staff and completion of experiments by new fellows, or journal requests for additional data. Mechanisms for resolving authorship disputes include local mediation (e.g., by respective lab or branch chiefs), involvement of program or scientific director(s), or engagement of the NIH Office of the Ombudsman.

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Case # 1 – Intellectual Input, Core Facilities and Authorship

(adapted from Scientific Integrity by Francis L. Macrina; developed by the NIH Committee on Scientific Conduct and Ethics)

PART 1

You have a radical idea regarding how to perform genomic editing much more efficiently than was previously possible. You tell your colleague Anastasia about it and how you plan to test the hypothesis. Anastasia does not work in your field, but you spend some time explaining to her the details of your study and she offers a number of unsolicited suggestions on how to make a compelling case for the novelty of your method. After this initial conversation, Anastasia talks to you frequently about the project and comes to several of your lab presentations. She comments critically on your work and makes other suggestions, including the idea that you try different cell types to further build your case. These experiments strongly support your initial hypothesis and show that the technique can be generalized. You decide to submit your exciting results to a prestigious journal and ask Anastasia to comment on it before sending it to the journal. Anastasia returns it with some insightful comments and argues strongly she should be a coauthor on the manuscript.

Discussion Questions

1. Should you agree to include Anastasia as a co-author and what is the rationale underlying your response?

2. What is the relative importance of thinking of and planning experiments compared to being able to effectively execute them? How should these two aspects of research be reflected in authorship and authorship positions?

3. Was there a time when it would have been helpful to discuss Anastasia's role in the project?

PART 2

Based on your prior high profile publications, you are hired into a tenure-track position at the prestigious National Institutes of Health. Part of the attraction of the position is a laboratory doing state-of-the-art sequencing. You approach the head of the sequencing group, Dr. Max, to explore using the genomic sequencer for your own research. Although Dr Max is happy to collaborate with you, he spells out conditions that include that only Dr. Max's technician may operate the instrument, and that all the original data must remain with Dr. Max. In addition, any paper submitted for publication that contains data obtained using the instrument must be reviewed by Dr. Max prior to submission, and he must be included as a co-author, with his two technicians acknowledged for their expertise.

Discussion Questions

1. Are the conditions requested by Dr. Max reasonable? What if his equipment was purchased for the whole Institute and his lab was considered a core facility? What do you think of the request that Dr. Max keep all original data? What about the requirement that he be an author on the resulting publications?

2. What do you think is an appropriate way to handle the contribution of the technicians who actually operated the sequencer? What about a technician in your lab who performed several of the experiments?

PART 3

Dr. Wong has developed a novel approach for analysis of genomic sequence data that is available on open source websites but is cumbersome to implement. After meeting Dr. Wong at a lab seminar, you mention that you plan to implement the method but you haven't been able to hire someone with the right computational experience. After the discussion, you share your data with him and about a week later you receive a series of summary figures, as well as an interpretation of the data and some ideas about additional genes to analyze and experiments to perform.

Approximately 9 months later, you receive an angry email forwarded from your lab chief where Dr. Wong expresses outrage that you have published a paper using not just the analytic method but also validating some of the genes that he had proposed. Dr. Wong expressed the opinion that based on his analysis and reporting the data back to you, as well as the fact that interpretation of the results at the level of predicting specific genes and pathways, required experience and insight and that was sufficient to have warranted co-authorship.

Discussion Questions

1. Was Dr. Wong justified in being upset? Are there corrective actions that you should take?

2. What actions could you have taken to clarify collaborative and authorship roles, and when might you have taken those steps? What were your expectations when you shared your data with him originally?

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Case # 2 – Authorship Disputes in Multi-Team Collaborations

Dr. Wallace, a neurotoxicologist, and Dr. Anderson, a pathologist, have been collaborating on a research project investigating the effects of an organophosphate pesticide (OP1) on central nervous system neurons in rodents. Dr. Wallace's lab includes a visiting scientist, Dr. Wang, while Dr. Anderson's lab includes a senior postdoctoral fellow, Dr. Adams. Their experiments randomly assign the rodents to be fed a normal control diet or diets containing three different OP1 concentrations. The primary outcome measures are neurological function, neurotoxicity, and OP1 uptake by neurons. Dr. Wang had discussed the idea for the project with Dr. Wallace prior to his arrival and initiation of the collaboration, at the time suggesting they test a different pesticide of the same chemical class (OP2). In the discussions leading up to the collaboration, Dr. Adams recommended testing OP1 instead of OP2, because there were very few experiments using OP1 in the literature. As the experiments were to begin, Drs. Wallace and Anderson agreed over the phone that Drs. Wang and Adams would be co-first authors on the resulting manuscript (in that order), indicated by an asterisk and footnote stating that "Drs. Wang and Adams contributed equally to this research." Similarly, Wallace and Anderson would be listed as co-senior authors, with Wallace listed last. Dr. Adams would prepare a first draft of the paper and be listed as the corresponding author. Drs. Wallace and Anderson did not have a formal collaboration agreement, however.

The two teams completed their research and submitted the manuscript to a top-tier toxicology journal. The reviewers recommended acceptance of the paper with major revisions to incorporate data from additional tissue pathology analyses that Dr. Anderson's lab would have to complete. She agrees to this, but requests that Dr. Adams be listed as the first author, followed by Dr. Wang. The paper would still indicate they contributed equally to the research so they could still claim first author status on their CVs. Anderson also proposes that she be listed last as the sole senior author because her role and level of effort has expanded based on the journal review. Dr. Wang is very upset about this proposed change because it may impact his chances for tenure, since his university requires being first author on at least two publications in top-tier English language journals as a condition for receiving tenure. Dr. Wallace is also opposed to not being listed as co-senior author, since he needs senior author papers in top-tier journals for the lab's next site visit. He sends an email to Dr. Anderson protesting her proposed change in authorship order and designations. He reminds her that this change would be going against their prior agreement. Dr. Anderson replies that the prior agreement no longer applied because of the additional pathology required by the journal.

Discussion Questions

1. Was Dr. Wallace's reaction to the proposed change in authorship and designation appropriate? How should author order and designation be determined in this case?

2. What are the pros and cons of using co-first and co-senior author designations?

3. Would the disagreement have occurred if the authorship details had been in writing from the outset?

4. Should the authors consider publishing another paper based on the new pathology data, with different first and last authors, as a way to accommodate both teams? What potential impact might this have on the review outcome with the current journal?

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Case # 3 – Clinical Collaborations

A physician scientist and a molecular biologist are collaborating on a series of studies that involve cancer clinical trial subjects and biospecimens from those participants. The goal is to correlate genetic profiles with patient outcomes in response to the same protocol therapy. The clinician enrolls the subjects and his team obtains the samples which are processed in the molecular biologist's lab; i.e., germline and tumor DNA is prepared and preserved, and cancer cell lines are grown from the primary tumor. Both DNA and cell lines are kept in a facility readily accessible to both collaborators. The molecular biologist believes that there are important correlational genomic findings, apart from the clinical data, that merit separate publication. He prepares a manuscript that will need to have the clinical data added, but the clinician refuses to provide them, saying the report is premature. In the dispute that follows, the physician scientist asserts ownership of the DNA and cell lines from patient samples. The dispute is brought to you as the department head to mediate.

Discussion Questions

1. What are the data ownership issues for this collaboration? Who owns the clinical data? Who owns the DNA and cancer cells lines?

2. Who should have access to, and use of, the clinical data and the materials prepared from patient samples?

3. What could a publication agreement made at the beginning of the collaboration have included?

By L. Kunkel and R. Fischbach, Harvard Medical School, 1993

AUTHORSHIP AND THE ROLE OF THE ABSENT RESEARCHER

As a graduate student, Camilla Pedroza worked closely with her advisor/mentor and lab chief, Dr. Kisaki, for four years on a project developing a diagnostic test for lupus. As part of the study, she performed diagnostics for physicians, particularly Dr. Browne, who sent tissue samples from his patients to her to be tested. Shortly before her project was completed, her husband was relocated to an excellent position in their homeland, Spain. She hastily put together the material she had collected over the years which was enough to pass as her thesis. During her final meeting with Dr. Kisaki, he promised to complete her project and get it published.

Jonathan Sand has been a post-doc in the Kisaki lab for a year and a half and has little to show for his time in the lab. Dr. Kisaki feels that Camilla's project is ideal for Jonathan because it is so close to complection and would allow him to build upon it for future projects. Within three months, thanks to Camilla's excellent write-ups of her methods, Jonathan has been able to replicate several of Camilla's experiments and does some important controls.

Noting the progress, Dr. Kisaki asks Jonathan to write the first draft of the paper as he now has access to all the data. Dr. Kisaki suggests including a few of Jonathan's figures which replicated Camilla's work. Dr. Kisaki is relieved and gratified that at last, with Jonathan's efforts, the project has been successfully concluded.

Hearing that the work is close to publication, Dr. Browne calls Dr. Kisaki to remind him of their original agreement which established that he should be included as an author on this paper in return for furnishing the tissue samples.

Meanwhile, Jonathan passes in the first draft of the manuscript with his name as first author. In considering the position of authors, Jonathan believes that he should be listed first because these are his data being presented, he prepared the figures, and he wrote the paper. Camilla will be included as an author.

Dr. Kisaki sends the draft off to Camilla, who recognizes that the data are no different than those included in her thesis. She sends an immediate response to Dr. Kisaki requesting that she be first author. And she also objects to Dr. Browne being included as an author because (1) he was one of many physicians who sent in tissue samples; (2) she was performing a service for him; and (3) he contributed no intellectual effort to the project. She also questions the inclusion of the department head, Dr. Carson, as an author despite that being the custom of the department. Dr. Kisaki realizes that he has a lot of decisions to make. One solution he considers is dividing the manuscript into two submissions so that both Camilla and Jonathan can each be first author on one paper.

Discussion questions:

1. Does the person who writes the paper naturally assume first authorship? Does Camilla have a legitimate claim for first authorship? What does first authorship imply?

2. As Camilla's advisor/mentor, should Dr. Kisaki have discussed with her: (1) plans for the publication of the results of her dissertation research; (2) her role and responsibilities in the preparation of the manuscript(s); (3) commitments and arrangements for attribution for investigators who supplied tissue

samples/reagents for her studies?

3. As a departing student, what role should Camilla have played in initiating discussions relevant to the dissemination of her work product? Are the results of Camilla's thesis project her intellectual property?

4. Students and postdocs come and go in a lab. How do you decide, in a transient setting, who contributed the most to a project and has a subsequent claim to be an author? Is Jonathan guilty of intellectual plagiarism? How does the departed grad student, or postdoc, retain an ongoing role in absentia in subsequent research efforts?

5. Whose responsibility is it to determine authorship? What about the role of the mentor in deciding who should be first author, especially in settings where someone left the lab without completing the project? When should these decisions be made? What are the pressures faced by postdocs who write the first draft in determining placement and inclusion of authors? How much weight do Camilla and/or Jonathan have in these decisions?

6. Criteria for authorship have been hotly debated. The study could not have been conducted without the contribution of Dr. Browne and the others who sent in the tissue samples. So what claim does Dr. Browne have to be an author? What criteria do you set for people like Dr. Browne and others who contribute samples?

7. Many journals now request that authors state explicitly that they contributed to the publication. Dr. Browne, who has never read the manuscript, nonetheless believes strongly that he contributed to the project and would in good conscience sign any compliance form. How do you resolve this with the intent of the journal?

8. The NIH Guidelines do not recognize the concept of "honorary authorship", yet there can be compelling interests to continue this practice. Discuss the implications of honorary authorship.

9. What about accountability? Given that there are five authors listed on the paper, who is ultimately responsible for validity of the data and information contained in the publication? What is someone challenges the validity down the road?

10. "Salami publication" or publication of the "least publishable unit" is growing in frequency. Why is there concern about "republished" or duplicate publications?

TO BE OR NOT TO BE INCLUDED

Upon entering the graduate program, Alyssa decided to do start working in the laboratory of Dr. Harry Swift. She started on a project that consisted of administering and evaluating the effects of an anti-malarial agent using an animal model. Although six other graduate students were working in the laboratory (not doing rotations), none of them was involved with the project, other than occasionally assisting Alyssa with the animals. She presented her data at weekly laboratory meetings attended by all members of Swift's lab, including Swift.

Alyssa and Swift did not get along very well. Swift believed that although Alyssa was a hard worker, she required too much supervision and was not an independent thinker. Alyssa, on the other hand, believed that Swift expected too much from his students and failed to provide adequate direction. Therefore, after completing the project, which took approximately nine months, Alyssa decided to leave the lab and begin working in another laboratory in the same department. Alyssa's lab book remained in Swift's lab, and Swift told her that the work did not merit publication.

Approximately one year later, Alyssa learned that her data had been published. The paper did not list her as an author, but it did list the names of other graduate students who had worked in Swift's lab during Alyssa's tenure. Alyssa decided to bring this situation to the attention of the departmental chairman, who referred her to the Director of Student Affairs. The director formed a committee of senior faculty members from outside Alyssa's department to investigate the situation.

When the committee questioned Swift about the exclusion of Alyssa as an author, he responded that Alyssa did the work but had not contributed intellectually to the project. Rather, she had functioned primarily as a technician. Swift commented that he had had several discussions with Alyssa about her inability to add to the project, other than data collection, and she had made no effort to increase her input. The committee questioned Alyssa and reviewed her lab book. The other graduate students who had worked in Swift's laboratory were never questioned.

The committee decided that Alyssa was responsible for the data presented by Swift. They also concluded that she did not have a major input into the experimental design, nor did she carry out the statistical analysis of the data required for publication. The committee concluded that the decision to include Alyssa as an author was at Swift's discretion.

Discussion questions

1. Should Swift have notified Alyssa about the decision to publish the work?

2. Should Alyssa have been given an opportunity to analyze the data for publication?

3. Should Alyssa have approached Swift about the matter before approaching the department chair?

4. Should the committee have questioned more individuals associated with Swift, (e.g., the other graduate students working in the lab who were listed as authors on the paper)?

5. Should the university have rules about acknowledging students' contributions to laboratories?

6. What criteria should determine authorship?

7. What are the responsibilities of mentors, students, and institutions to the successful conduct of graduate/postgraduate education?

8. Did Swift fail in his responsibility to Alyssa as a graduate student adviser by allowing her to function solely as a technician?
9. Did Alyssa fail in her responsibility as a graduate student to contribute intellectually to the project rather than limiting her contribution to data collection?

10. Is it necessary for graduate programs to spell out the responsibilities of advisers and graduate students, or are they implicit?

STUDENT PUBLISHES

Stevens is a second year graduate student performing materials science research and hopes someday to have a faculty position. The material Stevens is working on is diamond. The cost of preparation and analysis of the samples is very high, and there are not many samples. Due to these high materials costs, few experiments can be conducted, and hence it is difficult for faculty and/or students to generate more than one or two publications from a given series of experiments. Students from Stevens's department generally have four or five publications by the time they finish the Ph.D.

Stevens's adviser is Professor and Department Chair Charlie Cordage. Cordage was recently elected to the position of chairman by the seven other faculty members in the department. Due to the obligations and time commitments dictated by the chairmanship position, Stevens is Cordage's only graduate student. Having a vague understanding of the importance of publications to get post-doc and faculty positions, Stevens based his decision to work with Cordage on the professor's outstanding publication record.

Stevens is making progress with his research and getting good data. He has analyzed his data well, and his relationship with Cordage is going very well. After one of their brief research meetings, Cordage believes that Stevens has enough data to publish a paper in an obscure journal. Cordage encourages Stevens to write a paper and tells him they can submit it for publication. After several revisions, Stevens and Cordage submit the paper, and it is accepted. Stevens is happy to start adding publications to his resume.

Because Cordage had been busy with administrative tasks, he hadn't taken the time to correct Stevens's paper beyond writing style and grammatical errors. Finishing up work a little early one afternoon, he decides to reread Stevens's paper. Reviewing the data carefully, he concludes that the paper probably could have been published in a more highly regarded journal. After a couple of months of clever revisions and making himself first author, Cordage submits the research paper to the more prestigious journal.

Upon its acceptance, Cordage sends Stevens a short email with the title and citation and congratulates him on adding another publication to his resume. Stevens had no idea of Cordage's action until he received Cordage's email. Stevens is delighted but confused. He asks himself, "How can I publish the same paper twice?" Stevens does not want to make waves, and he is not sure to whom he should turn. He lets the matter pass and says nothing.

Months later, Stevens is doing the literature review for his dissertation. He notices that a large fraction of the papers previously published by Cordage on the same topic seem similar. He realizes that aside from details such as title changes, Cordage is publishing each paper twice, once in conference proceedings and once in a journal. Normal practice has never been explained to Stevens, and he isn't really sure what to do.

Discussion Questions

1. Is it ethical for authors to receive credit for two publications from the same data? If so, under what conditions is it ethical?

2. Should the authors be required to inform the second publication that data has been presented or published elsewhere?

3. Would it matter that the first publication was in conference proceedings? Assume for argument sake that the paper was reviewed but not with the same scrutiny as a peer-reviewed journal.

4. In an ongoing research project, it is common for data to overlap. How much new or additional data should be required for the paper to be a new publication?

5. In his role as student and new investigator, has Stevens behaved appropriately with regard to the responsible conduct of science? To whom should he have turned with his concerns about Cordage?

6. When is information/data/research considered published?

7. Consider interdisciplinary research. Should the scientists from each discipline be allowed to publish the research in their disciplines' journals? If so, can all the scientists from each discipline be on each paper?

8. Is it acceptable to publish or present work or research without informing one's coauthors in advance?

9. Has Dr. Cordage fulfilled his responsibilities as a mentor? If not, where has he gone astray?

Source: Association of American Medical Colleges (1994). "Teaching the Responsible Conduct of Research Through a Case Study Approach." Washington, D.C., AAMC.

Authorship Case Study: CRITERIA FOR AUTHORSHIP AND ATTRIBUTION

Bob Powell, a postdoctoral fellow in biochemistry, has just completed a manuscript detailing the results from the first project in which he had taken a leading role. The focus of his project has been to discern the ways in which humans metabolize sulfites, a class of chemicals commonly used to preserve wines and dried fruits. Although he had developed the rough outlines of the project on his own, he owes much to individuals both inside and outside his lab. The assistance he received from others includes the following:

- A colleague at another university, a toxicologist specializing in food additives, shared with Bob his previous work on the in vivo activity of sulfites, information that allowed Bob to choose the ideal animal model for the experiment -- the Abyssinian field mouse.
- A friend of his, who happened to be a wildlife specialist, provided Bob with much advice on rearing and maintaining a colony of Abyssinian field mice such that he would have stable pool of animal subjects.
- A highly experienced technician in the lab gave Bob advice on modifying an assay he had been using, which finally allowed him to measure successfully sulfite metabolites in mouse urine. This technician also assisted in writing up the methods section of the paper.
- The number of assays that Bob had to conduct was quite sizable and more than he could manage on his own, given the other demands of the project. Thus, an undergraduate college student collected most of the urine samples and conducted the assays yielding the data.
- Finally, a senior researcher in a neighboring lab who took an interest in Bob's career offered to review the initial drafts of Bob's paper. By the end of the writing process, this researcher had helped Bob outline the paper, suggested a few additional experiments that strengthened the paper's conclusions, and made a number of editing changes in the penultimate draft that enhanced the paper's clarity.

Discussion questions:

1. What kind of attribution should be given to each of these individuals who contributed in one way or another to Bob's project? For example, who should be recognized as an author and who should receive an acknowledgement in the paper? Who does not merit formal recognition?

2. What criteria should be applied when determining whether:

    to list someone as an author?

    to note someone's contributions in the acknowledgement?

3. What are the responsibilities of authors in representing the contributions of others?

4. At what point in the process of conducting and reporting on one's research should decisions concerning authorship and acknowledgements be made?

5.Are decisions concerning attribution entirely Bob's responsibility? Should he consult with others? Why or why not?

CASE # 1: CO-AUTHORSHIP—WHEN CHANGING LABS, HAVE YOU DONE ENOUGH TO BE INCLUDED?

(Based on Shamoo A. and Resnik D., Responsible Conduct of Research, 2003)

Sarah is a graduate student that worked in the lab of Dr. Jones for a year studying a novel transmembrane protein found only in tumor cells. Sarah isolated some of the protein and then used a contract laboratory to develop a sensitive rabbit antibody that recognizes an extracellular portion of the protein. Her dissertation project was going to involve using this antibody (along with other methods) to study the protein and its potential role in tumor progression and metastasis.

Despite this progress, she unfortunately did not get along well with Dr. Jones and decided to leave the lab and move to Dr. Smith's lab to begin a new project.

A few months later, Sarah finds out that her former advisor is preparing a paper based on subsequent research conducted by a new graduate student, but using the antibody Sarah developed. Sarah feels that she should be a coauthor and brings this up with Dr. Jones. The former advisor explains that the data being published were obtained solely by the new graduate student, and that raising an antibody is merely a technical activity that does not justify co-authorship. Sarah argues that the isolation of the protein and the decision about what peptide to select as antigen constituted original scientific thinking. Dr. Jones disagrees, saying that the literature contains numerous examples of this type of work.

Discussion Questions

1. Should Sarah be a coauthor on the paper?

2. Dr. Jones suggests that she will write a methodological paper limited to describing the preparation and characterization of the antibody. She offers Sarah coauthorship. However, she can't get to work writing that paper until her new student's paper has been submitted. Should Sarah accept this offer?

3. Sarah brings her complaint to the chair of the department. She argues that the new student's research could not have been done without her antibody and its characterization. How should the department chair respond to this situation?

4. What could Sarah and her advisor have done prior to her departure to prevent this disagreement from occurring?

5. Would your answers be any different if Sarah had remained in the original lab, but had abandoned the project and taken up a new dissertation topic?

6. Would your answers be any different if Sarah were a technician in the Jones lab instead of a graduate student?

7. Would your answers be any different if Sarah had used core-laboratories to carry out the protein's isolation and sequencing?

CASE # 2: CRITERIA FOR AUTHORSHIP AND ATTRIBUTION

Dr. Johnson is a postdoctoral fellow at the NIH working in the laboratory of Dr. Brown exploring the relationship between insulin-like growth factor (IGF)-1 signaling and cancer. He demonstrated that IGF-1-receptor deficient mice develop 50% fewer liver tumors than normal controls, and that daily IGF-1 injections substantially increase liver tumor formation. Dr. Johnson is ready to submit a manuscript for publication. The following individuals were involved in this project:

- Dr. Johnson came up with the original idea and hypothesis (that a defect in IGF-1 signaling inhibits liver tumorigenesis), designed and supervised the experiments, analyzed and interpreted the data, and drafted the manuscript.
- The Principal Investigator, Dr. Brown, who supervised Johnson's work, obtained funding, and read and edited the manuscript.
- A tenured researcher at State University provided Dr. Johnson with the mice used in the experiments. In a note that accompanied the Material Transfer Agreement, he said that he was providing the mice with the understanding that he would be an author on the paper resulting from the experiments.
- A Staff Scientist pathologist performed the pathological analysis for the study, provided digital images for publication, read the manuscript, and drafted the pathology methods section.
- A Staff Scientist Biostatistician performed the statistical analysis for the study and provided Dr. Johnson with advice concerning sample sizes and the need for multi-variable regression models. He read the manuscript and drafted a section on the statistical analysis.
- A technician performed 50% of the experiments, and made useful suggestions for modifying experimental protocols. She read the paper and made substantial comments.
- A graduate student performed 50% of the experiments, read the paper and made no changes.
- A technician took care of the laboratory animals.
- A highly respected and well-known Oncology Principal Investigator read the paper, revised it critically for intellectual content, made some useful suggestions concerning the interpretation of the data, but disagrees with one of the findings in the paper.
- An English major at State University and friend of Dr. Johnson's helped him draft and edit the manuscript. (English is not Dr. Johnson's native language.)
- A graphics specialist helped prepare some color figures for the manuscript.

Discussion Questions

1. Who should be an author on this paper?

2. Who should receive only an acknowledgment?

3. Who should not even receive an acknowledgment?

4. Who should be first author? Second? Last?

5. Should co-first authorship be considered? Co-last author? Corresponding author?

6. When should authorship decisions be made?

7. Would it have been appropriate to use written agreements for determining authorship issues in this case? If so, with whom and when?

CASE # 3: MULTIPLE PUBLICATIONS

Miller is a second year graduate student performing materials science research on diamond. Sample preparation and analysis cost is very high, there are few samples, and not many experiments can be conducted. Because of these constraints, it is difficult for faculty and students to generate more than one or two publications from a given series of experiments, and students from the department generally have only four or five publications by the time they finish their Ph.D.

Miller selected as his adviser Professor and Department Chair, Dr. Davis, based on the professor's outstanding research career and Miller's realization of the importance of publications for his advancement. Miller is his only graduate student, he and Davis have a congenial relationship, and his research is progressing well. After one of their brief research meetings, Davis encourages Miller to assemble his current data for publication in an obscure journal. After several revisions, they submit the paper, and it is accepted soon thereafter. Miller is happy to start adding publications to his resume.

Being busy with departmental tasks, Davis hadn't thought in depth about the implications of Miller's data. Finishing up work a little early one evening, he re-reads the paper and concludes that it should have been published in a more highly regarded journal. After a couple of months of clever revisions, Davis submits the research paper to the more prestigious journal, where it is accepted after revisions. Upon its acceptance, Davis sends Miller a short email with the title, a copyright form, and the tentative citation, and congratulates him on adding another publication to his resume. Although Miller had not known Davis submitted the separate paper, he was both delighted and confused, asking himself, "How can I publish the same work twice?" Miller does not want to make waves, and is not sure to whom he should turn. He lets the matter pass and says nothing.

Discussion Questions

1. Is it ethical for authors to receive credit for two publications from the same data?
    * What if the papers are essentially the same ideas and data, but written somewhat differently?
    * What if the idea is the same, but different examples of the same experiments are presented?
    * What if it is the same dataset, but a new analysis and interpretation has been applied to it?

2. Would it matter if the first publication was in conference proceedings? Assume for argument sake that the paper was reviewed, but not with the same scrutiny as a peer-reviewed journal. Can data in a patent that is publicly available later be published?

3. Should the authors be required to inform the second publication that data were presented or published elsewhere?

4. In an ongoing research project, it is common for data to overlap. How much new or additional data should be required for the paper to be a new publication?

5. In his role as student and new investigator, has Miller behaved appropriately with regard to the responsible conduct of science? To whom should he have turned with his concerns about Davis?

6. When is information/data/research considered published? Presentations? Posted as an online lecture or database?

7. Consider interdisciplinary research. Can scientists from each discipline publish specific or methods aspects of the research in their specialty journals? If so, should all authors from the original paper be on each new paper?

8. Is it acceptable to publish or present work or research without informing one's coauthors in advance?

9. Has Dr. Davis fulfilled his responsibilities as a mentor? If not, where has he gone astray?

CASE # 4: FIRST AUTHORSHIP, PUBLICITY, AND MULTIPLE INSTITUTIONS

Dr. Williams recently joined the Population Branch as a post-doctoral fellow very interested in vitamin research. At their first formal meeting upon arrival, his primary mentor and early tenure-track investigator, Dr. Smith, suggests several timely hypotheses with data currently available for analysis and publication. They agree on three analyses to be completed in the next 12-18 months, with the first looking at vitamin D status and breast cancer risk. Williams is very excited, and he quickly submits the study mini-proposal to the parent cohort study data-base for documentation and approval, finalizes the analytical plan, and begins working on the multivariate risk models.

Upon her return 2 months later from three weeks of travel, Smith schedules a meeting to review Williams' results. She senses that he has some very exciting findings, and in fact he reports a very significant, 75% breast cancer risk reduction during the 10-year follow-up period in women who had higher vitamin D levels. This result was generally consistent with their hypothesis, but the magnitude of the preventive association was more than twice what they had anticipated, thereby elevating the potential impact of their findings and affording them likely publication in the *New England Journal of Medicine*.

Williams is very excited about this and is ready to begin drafting the manuscript. Smith is also excited, but at the same time frustrated that an analysis they believed would go to a modest journal will instead be high-profile, and could have helped her with tenure if she were first author. She relates this development to the PI of the parent study, Dr. Jones. They both quickly realize that one of them is going to miss out on much of the attention and credit by not being senior author, and decide to ask Williams if he would accept a second author position so that Smith can write the paper and be first author, thereby boosting her chances for tenure. Williams is surprised by the request and feels pressured to agree, so he asks them to give him a few days to think about it. At the same time, one of the five collaborating study centers, Seattle, informs Smith that a junior faculty member there is interested in the same hypothesis, and would like to get started and lead the analysis based on their earlier discussions with the PI, Dr. Jones.

Discussion Questions

1. Is the request by Drs. Smith and Jones for an authorship change reasonable? When should authorship roles/positions be discussed?

2. In such a situation, how does one balance the career advancement of post-doctoral fellows and tenure-track investigators?

3. How might consideration of co-first or co-senior authorship help out in this situation? What does it mean to be a senior author? Corresponding author?

4. If Williams wants to remain first author, who can he turn to for advice or advocacy? Should the branch chief or IC training office get involved or intervene on his behalf?

5. What should be done about the request from Seattle? How can such "late-breaking" overlapping requests or surprises be avoided?