

SYLLABUS

MCB Scientific Integrity

A brief course intended to encourage recognition, understanding and discussion of issues of scientific integrity

January 15, 16, 22, 23, 2020

10 am- noon

Bio Labs 1058

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COURSE ORGANIZATION: The course will be based on (i) class discussion of selected topics, case studies and publications; and (ii) presentations by the instructor and guests. The designation "NAS" refers to the book "On Being a Scientist", 3rd edition, National Academy of Sciences Press 2009. The entire book is posted on the course web site.

First Meeting: Wednesday, January 15, 10 am- noon
The Culture of Science; Personal Integrity; Scientific Misconduct; Record Keeping
Human Subjects and Non-human Vertebrate Animals in Research
Team presentation of publications

Second Meeting: Thursday, January 16, 10 am- noon
Communicating with Peers and Public
Case studies

Third Meeting: Wednesday, January 22, 10 am- noon
Intellectual Property; Technology Transfer; Conflict of Interest
Team presentation of publications
Case studies

Fourth Meeting: Thursday, January 23, 10 am- noon
Sample Size Planning, Pre-Registration, Reproducible Data Analysis
Team presentation of publications

TEAMS: Each student is assigned arbitrarily to a team, each with a team leader, as listed on the following pages. Each team will present a designated publication and will guide the ensuing class discussion. Team leaders will arrange to meet with their team members in advance to plan their presentation, including the design of relevant questions to be posed to the class.

COURSE WEBSITE: https://internal.mcb.harvard.edu/?page_id=365

First Meeting
Wednesday, January 15, 10 am- noon
The Culture of Science; Personal Integrity;
Scientific Misconduct; Record Keeping
Human Subjects and Non-human Vertebrate Animals in Research

Guest presenter: Dr. Kathleen Pritchett-Corning (Senior Clinical Veterinarian, FAS Office of Animal Resources)

Discussion team and publications:

Team: **Barradale, Joisher, Savage**

Retraction of *Science* article by Frances Arnold; please also read the Forbes and BBC articles for some background and reactions.

Readings:

NAS, pp 1-3 (Introduction); 8-11 (The Treatment of Data); 15-18 (Research Misconduct); 19-23 (Responding to Suspected Violations of Professional Standards)

NAS pp 24-27 (Human Participants and Animal Subjects in Research)

Richard Feynman, "Surely You're Joking, Mr. Feynman" excerpts pp 341-343

Posted publications regarding the Frances Arnold *Science* retraction

Discussion Topics:

The culture and worldwide community of science

Scientific integrity as a shared value and personal integrity

Research Misconduct: Fabrication, Falsification, Plagiarism

The PHS Office of Research Integrity: <http://www.ori.hhs.gov>

Laboratory notebooks and record keeping

Harvard resources for research on non-human vertebrates

Animal rights; Experiments with people: Informed consent, confidentiality

Institutional review boards

What to do if you think there is a case of research misconduct at Harvard:

1) Talk with your advisor, department chair or other faculty member

2) Consult the MCB Ombudsperson: Jessica Manning, 190.06 Northwest Building

3) Consult the Harvard Ombudsperson: Lydia Cummings

<http://www.universityombudsman.harvard.edu/> To schedule an appointment: 495-7748

4) Read the Harvard "Grey Book", Chapter VI: *Procedures for Responding to Allegations of Misconduct in Research* <http://www.fas.harvard.edu/~research/greybook/misconduct.html>

U.S Department of Health and Human Services definition of "research misconduct":

Research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

(a) Fabrication is making up data or results and recording or reporting them.

(b) 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.

(c) Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

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

(From: § 93.103 Research misconduct. Federal Register Vol. 70, No. 94 / Tuesday, May 17, 2005.

From "Surely You're Joking, Mr. Feynman"
by Richard Feynman, W.W. Norton, 1985 excerpts, pp 341-343

... It's a kind of scientific integrity, a principle of scientific thought that corresponds to a kind of utter honesty—a kind of leaning over backwards. For example, if you're doing an experiment, you should report everything that you think might make it invalid—not only what you think is right about it: other causes that could possibly explain your results; and things you thought of that you've eliminated by some other experiment, and how they worked—to make sure the other fellow can tell they have been eliminated.

Details that could throw doubt on your interpretation must be given, if you know them. You must do the best you can—if you know anything at all wrong, or possibly wrong--to explain it. If you make a theory, for example, and advertise it, or put it out, then you must also put down all the facts that disagree with it, as well as those that agree with it. There is also a more subtle problem. When you have put a lot of ideas together to make an elaborate theory, you want to make sure, when explaining what it fits, that those things it fits are not just the things that gave you the idea for the theory; but that the finished theory makes something else come out right, in addition.

In summary, the idea is to try to give *all* of the information to help others to judge the value of your contribution; not just the information that leads to judgment in one particular direction or another.

The easiest way to explain this idea is to contrast it, for example, with advertising. Last night I heard that Wesson oil doesn't soak through food. Well, that's true. It's not dishonest; but the thing I'm talking about is not just a matter of not being dishonest, it's a matter of scientific integrity, which is another level. The fact that should be added to that advertising statement is that no oils soak through food, if operated at a certain temperature. If operated at another temperature, they *all* will—including Wesson oil. So it's the implication, which has been conveyed, not the fact, which is true, and the difference is what we have to deal with.

We've learned from experience that the truth will come out. Other experimenters will repeat your experiment and find out whether you were wrong or right. Nature's phenomena will agree or they'll disagree with your theory. And, although you may gain some temporary fame and excitement, you will not gain a good reputation as a scientist if you haven't tried to be very careful in this kind of work...

The first principle is that you must not fool yourself—and you are the easiest person to fool. So you have to be very careful about that. After you've not fooled yourself, it's easy not to fool other scientists. You just have to be honest in a conventional way after that.

Second Meeting
Thursday, January 16, 10 am- noon
Communicating with Peers and Public

Faculty: Nao Uchida

Readings:

NAS pp 8-14 (The Treatment of Data; Mistakes and Negligence)
NAS pp 29-38 (Sharing of Research Results; Authorship and the Allocation of Credit)
Posted publications on “*STAP*” and *RIKEN* report; *Nature* article by Rothman and *Neuron* challenge paper by Sweeny

Discussion teams and publications:

Team: **Berg, Jou, Tillman**
“STAP” and RIKEN report

Team: **Brookner, Kao, Wiratan**
Nature article by Rothman and Neuron challenge paper by Sweeny.

Discussion Topics:

Audiences
Pre-publication: Informal discussions, presentations, pre-prints, personal web sites
Publications: types of scientific journals, policies regarding research misconduct
What to include
Describing weaknesses in the data and alternative interpretations of results
Authorship
Acknowledgements
Literature Citations
Declaration of financial interests
Corrections and retractions
Sharing strains, reagents, etc.
Peer review
Informing the public

Discussion cases:

Case #1: "Fabrication in a Grant Proposal" NAS page 17
Case #2: "Is it Plagiarism?" NAS page 18
Case #3: "The Selection of Data" NAS page 10
Case #4: "Discovering an Error" NAS page 14
Case #5: "Appropriate Attribution or Plagiarism?"
Case #6: "A Change of Protocol" NAS page 26

Third Meeting
Wednesday, January 22, 10 am- noon
Intellectual Property; Technology Transfer; Conflict of Interest

Guest presenter: Yelena Bisharyan, PhD (Director of Business Development, Office of Technology Development) and Karen Sinclair, JD (Director of Intellectual Property, Office of Technology Development)

Readings:

NAS pp 39-42 (Intellectual Property)
Posted *Wall Street Journal* article on *Theranos*

Discussion Topics:

Confidentiality and secrecy
Patents: purpose, requirements and consequences
Ownership of ideas, the concept of "inventor"
Material Transfer Agreements
Conflict of interest
Harvard policies and practices

Discussion teams and publications:

Team: **Burgin, Foianini, Koob**
Theranos Case

Discussion cases:

Case #7: "A Commercial Opportunity?" NAS page 42

Fourth Meeting
Thursday, January 23, 10 am- noon
Sample Size Planning, Pre-Registration, Reproducible Data Analysis

Guest presenter: Prof. Bob Calin-Jageman, Dominican University, IL

Readings:

Posted publications by *Calin-Jageman, Ioannidis, Begley and Ellis, Begley, Camerer et al, Open Science Collaboration; Lane et al* article on publication bias in oxytocin research and the original trust study by *Kosfeld et al.*

Discussion teams and publications:

Team: **Conway, Liu, Rivard**
Lane et al. article on publication bias in oxytocin research; please also read and discuss the original trust study by *Kosfeld et al.*

Food and discussion!

Case #1
Responsible Conduct of Research Class
January 2020

NAS page 17: "Fabrication in a Grant Proposal"

Fabrication in a Grant Proposal

Vijay, who has just finished his first year of graduate school, is applying to the National Science Foundation for a predoctoral fellowship. His work in a lab where he did a rotation project was later carried on successfully by others, and it appears that a manuscript will be prepared for publication by the end of the summer. However, the fellowship application deadline is June 1, and Vijay decides it would be advantageous to list a publication as "submitted" rather than "in progress." Without consulting the faculty member or other colleagues involved, Vijay makes up a title and author list for a "submitted" paper and cites it in his application.

After the application has been mailed, a lab member sees it and goes to the faculty member to ask about the "submitted" manuscript. Vijay admits to fabricating the submission of the paper but explains his actions by saying that he thought the practice was not uncommon in science. The faculty members in Vijay's department demand that he withdraw his grant proposal and dismiss him from the graduate program.

1. Do you think that researchers often exaggerate the publication status of their work in written materials?
2. Do you think the department acted too harshly in dismissing Vijay from the graduate program?
3. If Vijay later applied to a graduate program at another institution, does that institution have the right to know what happened?
4. What were Vijay's adviser's responsibilities in reviewing the application before it was submitted?

5. If you were the faculty member in this case how would you respond to Vijay's assertion that he "thought the practice was not uncommon in science"?

Case #2
Responsible Conduct of Research Class
January 2020

NAS page 18: "Is it Plagiarism?"

Is It Plagiarism?

Professor Lee is writing a proposal for a research grant, and the deadline for the proposal submission is two days from now. To complete the background section of the proposal, Lee copies a few isolated sentences of a journal paper written by another author. The copied sentences consist of brief, factual, one-sentence summaries of earlier articles closely related to the proposal, descriptions of basic concepts from textbooks, and definitions of standard mathematical notations. None of these ideas is due to the other author. Lee adds a one-sentence summary of the journal paper and cites it.

1. Does the copying of a few isolated sentences in this case constitute plagiarism?
2. By citing the journal paper, has Lee given proper credit to the other author?

3. What would you think of using the Golden Rule or the Platinum Rule as a guide in deciding what Professor Lee should have done in this case?

Golden Rule: One should treat others as one would like others to treat oneself.

Platinum Rule: Do unto others, wherever reasonable, as they want to be done by.
(Karl Popper, *The Open Society and Its Enemies*, Vol. 2)

Case #3
Responsible Conduct of Research Class
January 2020

NAS page 10 "The Selection of Data"

The Selection of Data

Deborah, a third-year graduate student, and Kamala, a postdoctoral fellow, have made a series of measurements on a new experimental semiconductor material using an expensive neutron test at a national laboratory. When they return to their own laboratory and examine the data, a newly proposed mathematical explanation of the semiconductor's behavior predicts results indicated by a curve.

During the measurements at the national laboratory, Deborah and Kamala observed electrical power fluctuations that they could not control or predict were affecting their detector. They suspect the fluctuations affected some of their measurements, but they don't know which ones.

When Deborah and Kamala begin to write up their results to present at a lab meeting, which they know will be the first step in preparing a publication, Kamala suggests dropping two anomalous data points near the horizontal axis from the graph they are preparing. She says that due to their deviation from the theoretical curve, the low data points were obviously caused by the power fluctuations. Furthermore, the deviations were outside the expected error bars calculated for the remaining data points.

Deborah is concerned that dropping the two points could be seen as manipulating the data. She and Kamala could not be sure that any of their data points, if any, were affected by the power fluctuations. They also did not know if the theoretical prediction was valid. She wants to do a separate analysis that includes the points and discuss the issue in the lab meeting. But Kamala says that if they include the data points in their talk, others will think the issue important enough to discuss in a draft paper, which will make it harder to get the paper published. Instead, she and Deborah should use their professional judgment to drop the points now.

1. What factors should Kamala and Deborah take into account in deciding how to present the data from their experiment?
2. Should the new explanation predicting the results affect their deliberations?
3. Should a draft paper be prepared at this point?
4. If Deborah and Kamala can't agree on how the data should be presented, should one of them consider not being an author of the paper?

Case #4
Responsible Conduct of Research Class
January 2020

NAS page 14 "Discovering an Error"

Discovering an Error

Two young faculty members—Marie, an epidemiologist in the medical school, and Yuan, a statistician in the mathematics department—have published two well-received papers about the spread of infections in populations. As Yuan is working on the simulation he has created to model infections, he realizes that a coding error has led to incorrect results that were published in the two papers. He sees, with great relief, that correcting the error does not change the average time it takes for an infection to spread. But the correct model exhibits greater uncertainty in its results, making predictions about the spread of an infection less definite.

When he discusses the problem with Marie, she argues against sending corrections to the journals where the two earlier articles were published. "Both papers will be seen as suspect if we do that, and the changes don't affect the main conclusions in the papers anyway," she says. Their next paper will contain results based on the corrected model, and Yuan can post the corrected model on his Web page.

1. What obligations do the authors owe their professional colleagues to correct the published record?
2. How should their decisions be affected by how the model is being used by others?
3. What other options exist beyond publishing a formal correction?

Case #5
Responsible Conduct of Research Class
January 2020

Appropriate Attribution

Richard Yates, a postdoctoral student at Old Ivy University and Simon, a postdoctoral student at Dixie State University, are both investigating the enzymology of DNA damage repair. Meeting at a conference, Richard tells Simon about his discovery that a class of enzymes involved in DNA double-strand break repair requires two unusual cofactors, A and B, for activity. Shortly before the conference, Richard had submitted a manuscript for publication describing his discovery of the cofactor requirements and his isolation of a class of DNA repair enzymes thereby made possible.

Upon his return to Dixie State, Simon adds cofactors A and B to his previously inactive system, providing an assay that enables him to isolate a DNA repair enzyme of the same class as the enzymes isolated by Richard.

In the manuscript reporting his results, Simon acknowledges receiving information about the two cofactors from Richard in a footnote in the Methods section stating:

"The requirement for co-factors A and B in my experiments confirms the requirements for these cofactors in a closely related system, personal communication Richard Yates."

1. Has Simon made it clear that it was Richard who discovered the co-factor requirements? Explain. How do you decide if an attribution of credit for a discovery, idea, *etc.* is appropriate?
2. An individual familiar with both publications upon being asked for a confidential appraisal of Simon in connection with a possible faculty appointment writes that Simon is an excellent scientist. In another part of his letter of evaluation he writes that Simon was somewhat less than generous to Richard in attributing the discovery of the cofactors. Is this fair to Simon?
3. How would you have accorded credit to Richard if you were writing the manuscript instead of Simon? Explain.

Prepared by M. Meselson, 2013

Case #6
Responsible Conduct of Research Class
January 2020

NAS page 26 "A Change of Protocol"

A Change of Protocol

Hua is doing a postdoctoral fellowship in a laboratory that studies cancer treatment. In the experiment she is overseeing, a cancer-prone strain of mice is allowed to develop visible tumors and then receives experimental drugs to observe the effects on the tumors.

Hua notices that the tumors are interfering with the ability of some of the mice to eat and drink. She also notices that some of the mice are weaker and more emaciated than the others, which she suspects is a consequence of their feeding difficulties. The protocol for the experiment states that the mice will be treated only if they exhibit obvious signs of pain or discomfort.

When she mentions her concerns to another postdoctoral fellow, he suggests not raising the issue with the rest of the lab. The mice will be euthanized as soon as the experiment is over, and their nutritional status probably has little or no effect on the drug treatment. Furthermore, if it proved necessary to change the experimental protocol, the previous work would be invalidated and the Institutional Animal Care and Use Committee would need to be notified.

1. What can Hua do to get more information about the issue?
2. If she decides to raise the issue with others, what is the best way to do so?
3. Should the original protocol have been approved?

Note: Not said here is the nature of Hua's "concerns". For purposes of discussion, assume that the protocol makes no mention of what to do if malnutrition becomes a complicating factor that might affect the effectiveness of the drugs being tested and that the experiment is therefore of dubious utility.

Case #7
Responsible Conduct of Research Class
January 2020

NAS page 42: "A Commercial Opportunity?"

A Commercial Opportunity?

Shen was always interested in bioinformatics and decided to use some of his free time to write a program that others in his microbial genetics laboratory would find useful. Starting with a popular spreadsheet program on his university-provided computer, he wrote the program over the summer and posted it on his personal Web page as a bundle that combined the spreadsheet program and his own program. Over the next academic year, he improved his program several times based partly on the feedback he got from the people in his laboratory who were using it.

At national meetings, he discovered that researchers in other laboratories had begun to download and use his program package, and friends told him that they knew of researchers who were using it in industry. When the issue arose in a faculty meeting, Shen's faculty adviser told him that he should talk with the university's technology transfer office about commercializing it. "After all," his adviser said, "if you don't, a company will probably copy it and sell it and benefit from your hard work."

The director of the technology transfer office was much more concerned about another issue: the fact that Shen had been redistributing the spreadsheet in violation of its license. "You do have rights to what you created, but the company that sells this spreadsheet also has rights," he said. "We need to talk about this before we talk about commercialization."

1. What obligations does Shen have to the developer of the original spreadsheet program? To the university that provided the spreadsheet and computer?
2. What are the pros and cons of trying to commercialize a program that is based on another's product?
3. What conflicts and practical difficulties might Shen encounter if he tries to operate a business while working on his dissertation?