

8: Malfeasance and Misconduct

A. Definitions

The definition of Research Misconduct has been debated for at least a decade and the Federal Government has just completed the final rule. It includes not only the definitions of research misconduct but also the regulations by which institutions must address allegations of misconduct as they apply to research in which PHS funds either support the institution or the research. The following is taken directly from the Federal Register:

Sec. 93.103 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.

Sec. 93.104 Requirements for findings of research misconduct.

A finding of research misconduct made under this part 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.

Sec. 93.105 Time limitations.

(a) Six-year limitation. This part applies only to research misconduct occurring within six years of the date HHS or an institution receives an allegation of research misconduct.

(b) Exceptions to the six-year limitation. Paragraph (a) of this section does not apply in the following instances:

(1) Subsequent use exception. The respondent continues or renews any incident of alleged research misconduct that occurred before the six-year limitation through the citation, republication or other use for the potential benefit of the respondent of the research record that is alleged to have been fabricated, falsified, or plagiarized.

(2) Health or safety of the public exception. If ORI or the institution, following consultation with ORI, determines that the alleged misconduct, if it occurred, would possibly have a substantial adverse effect on the health or safety of the public.

(3) "Grandfather" exception. If HHS or an institution received the allegation of research misconduct before the effective date of this part.

Sec. 93.106 Evidentiary standards.

The following evidentiary standards apply to findings made under this part.

(a) Standard of proof. An institutional or HHS finding of research misconduct must be proved by a preponderance of the evidence.

(b) Burden of proof. (1) The institution or HHS has the burden of proof for making a finding of research misconduct. The destruction, absence of, or respondent's failure to provide research records adequately documenting the questioned research is evidence of research misconduct where the institution or HHS 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.

(2) The respondent has the burden of going forward with and the burden of proving, by a preponderance of the evidence, any and all affirmative defenses raised. In determining whether HHS or the institution has carried the burden of proof imposed by this part, the finder of fact shall give due consideration to admissible, credible evidence of honest error or difference of opinion presented by the respondent.

(3) The respondent has the burden of going forward with and proving by a preponderance of the evidence any mitigating factors that are relevant to a decision to impose administrative actions following a research misconduct proceeding.

Applicability paraphrased from 93.100:

- a. Research misconduct involving PHS support is contrary to the interests of the PHS and the Federal government and to the health and safety of the public, to the integrity of research, and to the conservation of public funds.
- b. The Department of HHS and the institutions that apply for and receive PHS support for research, training, or research-related activities jointly share the responsibility for the integrity of the research process. HHS has the rights of oversight and recipient institutions have an affirmative duty to protect PHS funds from misuse by ensuring the integrity of all PHS-supported work, and primary responsibility for responding to and reporting allegations of research misconduct.

B. Process

Institutions have the responsibility of dealing with allegations of research misconduct in a two-step process. In the inquiry stage the facts are gathered to the extent necessary to determine whether a full-fledged investigation is necessary. The parallel legal step is an indictment by a Grand Jury. In research misconduct, a positive report of an inquiry results in an investigation, comparable to a trial, carried out by an appointed committee. This is a quasi-legal activity, with lawyers present, disclosure rules, requirements for detailed record keeping and a requirement for decisions of guilt or innocence regarding each allegation.

At the initiation of an investigation, the Office of Research Integrity must be notified. The ORI can be helpful in advising the institution so that the investigation will be carried out with precise adherence to the rules. The results of the investigation are reported to the institutional leadership and to the ORI. If a finding of research misconduct is made, (see above for definitions), then the institution and funding agency determine the appropriate sanctions.

The ORI has the authority to review research misconduct investigations as well as the primary data and to suggest a government investigation if warranted.

Sometimes the complainant (the whistleblower) or the respondent (the accused) is not satisfied with the results of the investigation. They can appeal

to the ORI in writing and if deemed warranted, the case can be presented to an administrative law judge for final adjudication. This is a big change in response to great criticism of the appeals carried out by the ORI directly.

C. Whistleblowing

If you perceive a situation or activity that you think constitutes research misconduct, as a scientist and professional you have a responsibility to report it. While that is part of the underlying bargain of accountability that professionals make with society, whistleblowers usually act on the basis of personal hurt or outrage. However, an allegation of research misconduct must be handled as a very serious matter. Therefore, if you are contemplating making an allegation, consider the following, derived from practical suggestions by Chris Gunsalus.

1. Consider it an inquiry rather than an accusation
2. Talk it over with friends
3. Try to figure out whether there is another side to the story
4. Write it down. Focus on the science and the exact details rather than the person
5. Try to develop support from others in the lab
6. Do not illegally examine someone's data

Other things you should consider prior to making an allegation

1. You may not have a right to know what's going on. Is that okay for you?
2. What kind of satisfaction do you want from the inquiry?
3. If it's your boss, you may have to move. Is that okay for you?
4. Is there a way to achieve your goals without going to the "authorities"?
5. Are you prepared for the long haul and for a bad outcome?

Although federal and state legislation and institutional regulation protect whistleblowers, the outcome of the process is often deleterious to their careers and their incomes.

D. Litigation, the new approach to research management

When the tort bar finds a weakness in any of our industries or enterprises, the stakes immediately go up and the costs of paying out or preventing legal liability add substantial burdens. However, this system of management has played a significant role in the protection of citizens against malfeasance, much to the enrichment of the plaintiffs' lawyers involved. In recent years, the clinical research establishment has been subject to litigation and the results have been a great tightening up of subject protections.

Historical - informed consent claims for medical treatment go back to 1914. Now the clinical research enterprise is subject to new legal claims, an increased number and types of defendants, and use of class action suit technique that can multiply the number of claims. Examples include:

- 1. The Gelsinger case:
Defective informed consent and process
Product liability
Fraud - failed to reveal that previous subjects died and that the investigators had serious conflicts of interest.**

Penn settled eventually for a substantial amount of money.

- 2. Robertson vs Oklahoma- Melanoma Vaccine
Consent failures
Trial was negligently run -investigator malpractice
Fraudulent representation of the purposes, risks and benefits**
- 3. Wright vs Hutchinson Clinic -preventing graft failure in bone marrow transplantation. Tried lymphocyte depletion, which didn't work.**

Seattle Times series called it "Uninformed Consent" They claimed that subjects were lured by greedy doctors into trials where they weren't told all the risks. They were applying current consent rules to 20 year old studies.

The legal claims were:

**Defective consent, research malpractice,
Failure to disclose COIs
Failure to report deaths to IRB appropriately
Failed to update consent forms
"breach of the right to be treated with dignity" under due process clause of the 14th amendment**

The "Hutch" fought it and won in a landmark decision.

This section derived from Mello, Studdert and Brennan: 2003 Ann Int Med; 139:40-45.

Fraud cases can result in punitive damages and really big awards. Lawyers are now suing everyone including:

- The University,**
- The teaching hospital,**
- The PI,**
- The sponsor**
- Top university officials**
- Individual IRB members**
- The hospital's patient advocate (Abiomed)**

The additional defendants make the costs of litigation much higher and favor the plaintiffs. With many individuals in the same study, the conditions are ripe for class-action suits, which provide great rewards to the attorneys.

Impacts of successful litigation:

- More suits are inevitable**
- It has tightened up research on humans - a good thing**
- It may make IRBs super-conservative, which is a bad thing**
- It may make monitoring of research mandatory**
- It may create a spate of rule-making**

E. The Importance of Trust

Research on humans is based on trust that the truth is told about the study. Subjects trust that the institution is fulfilling its responsibilities to the participants.

Subjects trust that those conducting the study have their best interests at the top of their agenda.

They also expect that conflicts of interest are disclosed to them and to others.

If we fail, the consequences could be disastrous to ourselves, to our institutions and to our standing with the public that supports our endeavors.

CASES Chapter 8

Case: Fabrication

In 1984 a faculty member was up for a tenured position in a clinical department. He was a shoo-in having already published over 100 papers in peer-reviewed journals, mostly as first author.

As it turned out, one member of the promotion committee decided to review some of the papers and found that a number of them used the same instead of different control groups. When doubts were expressed to the chair, co-authors were called and they reported that they had never seen the papers and knew nothing about them. It was discovered that there were no notebooks and no animals had been ordered to do the studies. The miscreant broke down and confessed.

1. What is the most cost-effective way to produce research results?
2. Why did this person behave like this?
3. Could this happen today?
4. Could you believe the co-authors?

Case: Data Falsification

CAST

Patricia Frankel **Professor and department chair**

George Frankel	Patricia's husband, businessman
Edward Milani	Associate Professor, in same department
Jennie Foster	Graduate student in Milani's laboratory
Jim Liu	Assistant Prof at Yale, former post-doc of Milani's
Jeremy Stoessel	Dean

Narrator: Patricia Frankel is a harried department chair, scrambling for talent and trying to keep her own laboratory afloat in the face of ferocious competition. She is having a quiet dinner out with her husband, George, a businessman.

Patricia: Today, Jennie Foster, one of Edward's (Milani, Associate Professor) graduate students, pulled me aside after a seminar. She told me that she had been unable to duplicate the critical purification of an alkaloid regulator of signal transduction that Jim Liu, the post-doc had discovered last year before he went to Yale. The published paper did not contain all the necessary technical data. Jennie figured that she was lucky to be able to go to the lab's original notebooks.

George: The importance of good laboratory documentation.

Patricia: But that's the problem. Jennie said that the notebooks were not helpful. In fact, she said there were many erasures in the dataset, the procedural details were vague and it wasn't proven that they really had pure regulator. Jennie said that when she called Jim at Yale for help, he was friendly and offered to look up his personal notes and get back to her in a week. She said that when she related the conversation to Ed Milano, he said he didn't know the details well enough to help her directly, but he was going to take the notebooks home for review. He would get back to her. That was three weeks ago and she didn't hear from either of them. She saw Ed almost every day.

George: What did you say to her?

Patricia: I told her to be patient. But there's something funny going on here. Why did Ed take the notebooks home? Why would Jim have personal notes? I wonder whether the data in the notebooks supported the conclusions in the paper, which caused quite a stir when it was published.

George: No matter. It's not your responsibility to pursue every suspicious statement or puzzling action that goes on in your department.

Patricia: Well, it's not so simple. As scientists we have responsibility for the integrity of the research record and that means uncovering misconduct. Jennie told me that she made copies of the relevant notebook pages to study and volunteered to show them to me. I wonder whether I should look at them.

George: Well, you know I like Ed. Hasn't he been a productive researcher and inspired teacher? It's hard to believe that he participated in anything dishonest. Maybe Jennie, in her naiveté has it all wrong.

Patricia: That's the dilemma. The suspicion here is of data falsification, a most serious form of research misconduct. Perhaps Jennie was completely off base but she's not naive—in fact, she's really smart. She isn't pointing a finger, yet what she's saying is quite serious.

Patricia: I wonder how to discuss this with Ed. Should I request his notebooks? Should I take this to the dean? I really could use some advice because reporting to the dean will probably initiate an official inquiry.

George: You should think about the potential consequences to you and to Jennie. This could get out of control. Maybe a colleague can help.

Questions:

1. As a colleague of Dr. Frankel's what would you suggest?
2. Did Jennie make an allegation on misconduct?
- 3. Is the proposed crime the process of research or the possibility of a false outcome?**

Narrator: Professor Frankel meets with Prof. Milani

Professor Frankel: I hear that there is some problem replicating the purification of your transduction factor.

Professor Milani: Don't worry about it. There is nothing to it. Don't get involved. Leave it entirely to me and I will clear it up. I am reviewing the notebooks and will get back to you soon.

Narrator: After a month without progress, Prof. Frankel takes the problem to Dean Jeremy Stoessel.

Prof. Frankel: Jeremy, we have this little matter that may or may not involve research misconduct. I am puzzled as to what to do because Ed is my friend and the grad student is pretty new but the lack of willingness to communicate led me to take it to you.

Dean Stoessel: Well, this is a serious matter and we can't just let it go by. These things have a tendency to have lives of their own. I am going to have to call for a formal inquiry. Both you and Ms. Foster have to submit written statements to me within 48 hours and be prepared to testify before the inquiry board.

Questions:

1. Prof Milani refused to cooperate with Prof. Frankel, precipitating the inquiry. What is his responsibility here and can this be held against him?
2. How much discretion does the integrity officer, the dean in this case, have when approached with this kind of allegation?
3. Should Prof. Frankel be required to tell Milani that she is going to the Dean?

Narrator: The meeting with Jennie.

Prof. Frankel: Dean Stoessel requested that you and I write a statement describing the problem with Dr. Milani's work. He felt that he had to convene an inquiry to

determine whether there was enough here to result in a formal research misconduct investigation.

Jennie: Why did you go to the Dean without telling me first? I really don't want to do this. It will seem as though I am a whistleblower, which was never my intention. I am really into research and this is likely to ruin my career.

Prof. Frankel: It's too late. The cat is out of the bag. Besides, being a whistleblower will protect your fellowship. You must do this.

Narrator: Jennie was asked to leave Prof Milani's lab and the only other lab that would accept her was Prof. Frankel's. She was shunned by the other graduate students, began to lose sleep and ability to concentrate. At his point she was worried that she had gotten it all wrong and was ruining not only her own career, but those of Prof Milani whom she liked and Jim Liu whom she never met. And for what!

Questions:

1. For what indeed?
1. Does Jennie have any culpability here?
3. Should she have received counseling? When and what kind?
4. Does removal from lab constitute retaliation against a whistleblower?

Narrator:

The inquiry panel impounded all of the relevant laboratory notebooks. It tried to get Jim Liu's personal notes but he denied their existence. With the help of an expert from another university, the panel decided that the combination of the paper and the laboratory notes were not sufficient to allow anyone to prepare the regulator in question. They could not determine whether the purification had indeed been accomplished. The experimental notes had been altered in a suspicious manner. They recommended a full investigation.

Dean Stoessel was concerned that the inquiry panel was too eager to suggest misconduct in what to him seemed to be sloppy science, that was facing validation in other laboratories. Couldn't Ed Milani just repurify the transduction regulator, define the conditions and make the whole problem disappear? However, the report of the inquiry board constrained him to notify the Office of Research Integrity and initiate a full-blown investigation.

Questions:

1. What are Dean Stoessel's degrees of freedom in this case?
 - a. Can he ignore the committee?
 - b. Can he defer or delay action?
2. How should the proposed investigation committee be organized?

1. expertise
2. lawyers

Narrator:

When notified of the impending investigation, Professor Milani initiated legal action for defamation of character and named Jennie Foster, Patricia Frankel and the University.

Ms. Foster, unprotected by the University, refused to testify further and under the advice of her attorney, attempted to withdraw her statement, which, she said, was made under duress.

Professor Frankel carried on her duties gamely but she knew that feelings in her department supporting Professor Milani ran high. Why, they remonstrated, was she so ready to accuse a longstanding and productive colleague? She felt her chairmanship slipping away. She used her influence to get Ms. Foster a training position at the NIH, but Jennie, discouraged, was beginning to think about other career possibilities.

Question:

1. How can society provide adequate protection for righteous whistleblowers without providing excessive protection that would allow chronic malcontents to harass their bosses?

Narrator:

The investigation committee petitioned Yale to request all notes and notebooks that Jim Liu took with him when he left. The Dean at Yale approached Jim but he claimed to have taken nothing whatsoever with him. When asked whether he could prepare a batch of transduction regulator to demonstrate the validity of the process, Jim stated that he did nothing wrong and had no interest in having his career sidetracked, even temporarily. Professor Milani refused to try to prepare a new batch of regulator for testing because, he claimed, the allegation was frivolous.

He told the investigation committee that there was no intended deception and that even if the preparation could not be duplicated, the prepared batch was good and the paper remained well accepted.

Of course, by this time the investigation had gotten out to the scientific public. Professor Milani's lab was being shunned by potential graduate students, as were other laboratories in the department, which was now considered to be "troubled."

The editors of the journal in which the paper was published were disturbed that an investigation was under way.

The ORI listed Professor Milani's case among the investigations it was monitoring.

Question:

1. What do you think about the refusal of Milani and Liu to attempt to prepare a new batch of regulator and define the procedure?

Narrator:

The investigation panel considered three questions, whether the notebooks validated the paper, whether the result was correct and whether there was a pattern of deception either prior to publication or after the allegation of misconduct was aired. After much sifting of evidence they concluded that actual evidence of misconduct was too limited to warrant a positive conclusion. They believed that the data in the notebooks were not adequate to support the results in the paper or permit replication but that the reported experiments had been carried out. They believed that the attitudes of both Jim Liu and Edward Milani were reprehensible in not helping to resolve the issue, and suggested that the journal publish a statement shedding doubt on Liu and Milani's paper.

Questions:

1. What are the risks and benefits of the journal publishing a comment on the paper?

2. At this point what is dean Stoessel's responsibility?

3. The newspapers have been reporting on the case. What are the institution's obligations toward the press and the principals?

Narrator:

At the conclusion of the investigation Professor Milani demands a University statement exonerating him and Jim Liu, a letter of apology for the accusation, and removal of Professor Frankel from her administrative duties. Jennie Foster, learning that the suit against her was not dropped, sends the NIH office of the Inspector General her copies of the notes, suggests a cover-up and requests a full investigation. The IG requests the entire file for re-examination.

Questions:

1. What lessons are there to be learned here?

2. Was science served in this case?

Case – Expropriation of trainees work

A graduate student wrote a thesis detailing a new method for teaching nutrition to schoolchildren. She claimed that one of her thesis advisors appropriated her ideas, began lecturing on her work and eventually got a grant to carry out her proposal, excluding her. All agree that he did that, using it to teach obese adults rather than school children.

She complained, got her Ph.D. but her university did not protect her. The complaint to the ORI at the Department of HHS was examined and dismissed eventually because it did not involve the quality of the scientific record and did not violate the misconduct trio of Fabrication, Falsification or Plagiarism. The faculty member had not plagiarized because he admitted his source, indicating that the thesis was published and thus was in the public domain. The thesis was only available in the institutional library and was not in a peer-reviewed journal.

Questions: 1. What rights does an entrepreneurial faculty member have over the work of a trainee?

2. If you suspected that this was going to happen to you what would or could you do?

3. What protections do trainees need?

Case: Possible Misconduct

As the university ombudsperson you find yourself meeting with Al Gianni a distinguished faculty member who appears somewhat distraught. He explains his predicament as follows:

“About three months ago I fired a post-doctoral fellow for chronic absence and lateness and for trying to get others to do her work. The remainder of the lab

had brought her failings to my attention and with regret I let her go. She promptly found a comparable position in another lab in a nearby research building.

As part of a new paper I recently started writing up a series of experiments she carried out on samples from a clinical trial. Both the statistician and I independently found that the data were tampered with. She altered the computer print outs and enhanced the information in the database so that the results became highly significant instead of indeterminate. We checked this over and over and we are sure she falsified the data. The studies had been completed before we began the process of firing her. I am glad we found it before publication and can prevent it from ever seeing the light of day.

I am worried that she could do this again in current and future positions and contaminate the scientific literature. I really don't know how to proceed and thought I'd see you right away to help me out.

- Questions:
1. What would you ask Dr. Gianni?
 2. What would you tell him about his responsibilities?
 3. Would you give him advice? If, so what advice?

Case: Unsatisfactory Study

A large drug company identified a series of small molecules that stimulated the release of growth hormone leading to the increased production of the anabolic hormone IGF₁, which normally declines profoundly with aging. It decided to conduct trials in elderly physically disabled people with low IGF₁ levels to increase the circulating IGF₁, and thus produce the beneficial effects of GH therapy, but using a single pill a day. If there were beneficial effects, they could thus be achieved inexpensively. Extensive animal trials showed enhanced GH secretion without perceived adverse effects. Phase I and phase II trials were quite successful in that there were no short-term ill effects and the drug reliably increased IGF₁ levels in a dose-dependent manner.

The phase III trial was double blinded and involved 35 centers. The participant population was that of partially disabled persons over the age of 65. Most of them were over 75. (65 is considered young these days). In addition to several blood collections, utilizing a machine that gave objective recordings of power and load, numerous measures of muscle strength were taken every two months in a six-month trial. During the conduct of the study the clinical trials coordinators saw that some of the participants experienced functional improvements but that was not seen in the muscle strength testing. One man stopped using a cane, for example and several others improved their ambulation significantly. About four months into the study, a few participants developed overt hyperglycemia while a few others experienced a decrease of glucose sensitivity.

The company stopped the study at six months and has denied numerous entreaties by the investigators to analyze and publish it. The investigators do not have access to the data. It is rumored that the company gave up research into the whole category of compounds.

Recent studies of GH administration to the elderly have shown deterioration of glucose tolerance and some instances of overt diabetes. GH is being utilized at an increasing rate in the care of older persons who can afford its costs, even though it is not approved for that purpose and insurance companies will not pay for it.

Questions:

- 1. What are the issues raised by this case?**
- 2. Is there research misconduct here?**
- 3. Would there be different issues if the drug had been FDA approved and the trial was a Phase IV trial.**
- 4. How would society best be served?**

Bibliography

(2004). Clinical Trials on Trial. The Wall Street Journal. New York. March 3, 2004

Kennedy, D. (2006). "Editorial Retraction." Science 311(5759): 335b-.

This formally retracts the editorial about human stem cell cloning previously published in Science.

Normile, D., G. Vogel, et al. (2006). "CLONING: South Korean Team's Remaining Human Stem Cell Claim Demolished." Science 311(5758): 156-157.

This news report in Science describes in some detail the investigation of Dr. Hwang's research and the conclusion that human stem cell lines did not exist but that the cloning of a dog did take place.

Agres, T. (2002). "Science on the Sly: Guilty plea in Cleveland Clinic case becomes latest example of theft from research labs." The Scientist Summer: 16-18.

This unusual case involves the stealing and transfer of scientific materials from one lab to another and then out of the country. The perpetrator was accused of economic espionage, altering and destroying trade secrets, and interstate and international transfer of stolen materials. This case underscores the increasing value of research materials and the need for security even in academic labs. The irony is that these materials could have been shared under a material transfer agreement.

Baltimore, D. (1993). "Shattuck Lecture--Misconduct in Medical Research." N Engl J Med 329(10): 732-3.

Barinaga, M. and J. Kaiser (1999). "MISCONDUCT:Fraud Finding Triggers Payback Demand." Science 285(5431): 1189a-1190.

This news report indicates that the National Cancer Institute asked the Lawrence Berkeley national labs for a return of \$800,000 in research funds when they exposed allegedly fraudulent research by a colleague. The work had put electromagnetic fields in play as influencing cellular function. The lab agreed to return unspent money but not the whole grant.

Brody, J. (2004). A Top Scientist's Research is Under Attack. *The New York Times*. New York, NY. May 6.

A major nutrition investigator's work was published then seriously challenged as being statistically invalid. The investigator was supporting the use of a vitamin preparation that he designed for cognitive maintenance and licensed to his daughter's company. He left Canada and moved to India after the news broke.

Dayton, L. (2002). "Scientific misconduct. Hall probe continues; no 'willful' fraud." *Science* 296(5568): 641.

This report of an Australian case in which allegations of willful conducting scientific fraud were lodged against a prominent clinical investigator. Although he was reprimanded and asked to do some restitution, he was not judged to have committed research misconduct pending a second investigation. A lesson for those who run laboratories.

Ding, Y. (2002). "SCIENTIFIC MISCONDUCT: Beijing U. Issues First-Ever Rules." *Science* 296(5567): 448-.

These parallel western rules regarding research.

Enserink, M. (2003). "NEUROSCIENCE: Singapore Trial Halted, British Scientist Fired." *Science* 300(5617): 233a-.

The PI, a well known neurologist was found to have misled subjects as to the research protocol and provided an inadequate consent. He also obtained the names of potential subjects and called them directly, violating their privacy rights.

Fitzgerald, M. H. (2004). "Big Basket or Mission Creep?" *Professional Ethics Report* 17(2).

Grinnell, F. (1999). "Ambiguity, trust, and the responsible conduct of research." *Sci Eng Ethics* 5(2): 205-14.

Ambiguity associated with everyday practice of science has made it difficult to reach a consensus on how to define misconduct in science. This essay outlines some of the important ambiguities of practice such as distinguishing data from noise, deciding whether results falsify a hypothesis, and converting research into research publications. The problem of ambiguity is further compounded by the prior intellectual commitments inherent in choosing problems and in dealing with the skepticism of one's colleagues. In preparing a draft code of ethics for the American Society of Biochemistry and Molecular Biology (ASBMB), an attempt was made to take into account the ambiguities of practice. Also, the draft code adopted trust as its leading principle, specifically the importance of trust as a condition necessary for there to be science. During revision of the code, the focus on trust was changed. The new orientation was on trust as a consequence of carrying out science responsibly. By addressing the obligations necessary to engender trust, the ASBMB ethics code not only sets professional standards, but also makes a clear statement of public accountability.

Gunsalus, C. K. (1998). "How to Blow the Whistle and Still Have a Career Afterwards." *Sci Eng Ethics* 4(1): 51-64.

This paper is must reading for everyone entering science and teaching. The author uses her vast experience to report the necessity of whistle blowing and the difficult road that whistleblowers may tread despite much legal protection. She carefully teaches how to be an effective whistleblower, something that every member of a research team should read.

Guterman, L. P., W. (2003). Former Graduate Student Sentenced to Prison for Faking Theft of Research. *Chronicle of Higher Education*, August 21.

Here's a good one. A graduate student who had done no work for several years (good mentoring here) just reported all his notebooks stolen. He was quickly caught and jailed for 10 months for theft. (The notebooks didn't belong to him.)

Gwynne, P. (1999). "Corporate Collaborations." *The Scientist* 13(11): 1, 6.

Hagmann, M. (1999). "SCIENTIFIC MISCONDUCT: Researcher Rebuked for 20-Year-Old Misdeed." *Science* 286(5448): 2249a-2250.

The seamy history of the availability of human growth hormone for Genentech to develop was elucidated when Peter Seeberg admitted to taking samples from his UCSF lab when he moved to Genentech and not indicating the source in a major subsequent paper. Subsequently Genentech built UCSF magnificent laboratories in payment for the stolen materials.

Hagmann, M. (2000). "SCIENTIFIC MISCONDUCT: Panel Finds Scores of Suspect Papers in German Fraud Probe." *Science* 288(5474): 2106-2107.

This news report characterizes the extent of fraudulent papers turned out by a German oncologist. The suspect papers were in numerous journals and will take years to recover from. They involved 52 papers and 357 apparent manipulations.

Healy, B. (1993). "Sounding Board: The Dingell Hearings on Scientific Misconduct." *N Engl J Med* 329(10): 725-7.

Dr. Healy, Secretary of HHS responds to congressional accusations against the ORI and NIH. It's good reading.

Hoeksema, H. L., J. Troost, et al. (2000). "Fraud in a pharmaceutical trial." *The Lancet* 356(9243): 1773.

The report illustrates how the Dutch handled a case of clinical research misconduct in which they reconstructed the data and determined that the investigator had surely fabricated the submitted data and sent mixed blood from a few persons rather than individual draws to the core lab. A useful example of quiet competent pursuit of the question.

Horton, R. (1999). "Scientific misconduct: exaggerated fear but still real and requiring a proportionate response." *The Lancet* 354(9172): 7.

This editorial discusses national committees to deal with allegations of scientific misconduct. He mentions pressures to more effectively regulate research. However, others decry the dead hand or regulators inhibiting research. These questions are still with us.

Hotz, R. L. (2003). *Medical Tests Skewed, Study Finds. Commercial ties are the outcome of research at universities, Yale investigators say.* Los Angeles Times. Los Angeles. January 22, 2003.

A very nice brief summary of the problem of institutional Conflict of Interests and the potential consequences.

Office of Research Integrity. (1999). *Scientific Misconduct Investigations: 1993-1997.* Department of Health and Human Services.

This provides a statistical analysis ORI materials relating to investigations. They have a new one that is a lot better.

Jacobson, P. D. and S. D. Pomfret (2000). "ERISA Litigation and Physician Autonomy." *JAMA* 283(7): 921-926.

The Employee Retirement Income Security Act (ERISA), enacted in 1974 to regulate pension and health benefit plans, is a complex statute that dominates the managed care environment. Physicians must understand ERISA's role in the relationship between themselves and managed care organizations (MCOs), including how it can influence clinical decision making and physician autonomy. This article describes ERISA's central provisions and how ERISA influences health care delivery in MCOs. We analyze ERISA litigation trends in 4 areas: professional liability, utilization management, state legislative initiatives, and compensation arrangements. This analysis demonstrates how courts have interpreted ERISA to limit physician autonomy and subordinate clinical decision making to MCOs' cost containment decisions.

Physicians should support efforts to amend ERISA, thus allowing greater state regulatory oversight of MCOs and permitting courts to hold MCOs accountable for their role in medical decision making.

Johnson, W. B. and N. Nelson (1999). Mentor-Protégé Relationships in Graduate Training: Some Ethical Concerns. *Ethics & Behavior*. 9: 189-210.

The authors, dealing with psychology graduate students analyze the mentor-mentee relationship and define the characteristics of an appropriate mentor. They indicate that mentoring involves a number of ethical dilemmas. In this article, they deal with competence to mentor, equal access to mentoring, exploitation in mentoring relationships, and multiple role demands related to mentoring as well as describing to the mentee the nature of the mentoring relationship. They conclude with recommendations for both mentor and mentee.

Kaiser, J. (1999). "POLICING OF SCIENCE: A Misconduct Definition That Finally Sticks?" *Science* 286(5439): 391a-.

This news report details the final version of definitions of research misconduct.

Kaiser, J. (1999). "SCIENTIFIC MISCONDUCT: Shalala Takes Watchdog Office Out of the Hunt." *Science* 286(5441): 883a-.

This news story documents the downgrading of the Office of Research Integrity by taking away its investigative powers and making it primarily an educational agency.

Kaiser, J. (2004). "PATIENT RECORDS: Privacy Rule Creates Bottleneck for U.S. Biomedical Researchers." *Science* 305(5681): 168-169.

Kennedy, D. (2002). "More Questions About Research Misconduct." *Science* 297(5578): 13-.

Kennedy, D. (2002). "Not Wicked, Perhaps, but Tacky." *Science* 297(5585): 1237-.

An introduction to research malfeasance that falls short of "misconduct" but is much more prevalent. Do we really have to do these things?

Kuznik, F. (1998). "Medical Whistle-Blowers." *Hippocrates* October: 39-47.

This is a very useful article detailing the stories of a number of whistleblowers in cases of medical care and research. It validates the point that as a group they do poorly careerwise but their consciences gave them no choice but to seek the truth.

Malakoff, D. (2000). "CLINICAL RESEARCH: Flawed Cancer Study Leads to Shake-Up at University of Oklahoma." *Science* 289(5480): 706-707.

This news report details the changes in clinical research oversight initiated at the Univ. of Oklahoma in response to findings of terrible sloppiness in carrying out studies. A major vaccine study for cancer was stopped. This was one of the first examples of institutions needing to clean up their research management.

Malakoff, D. (2002). "Student Charged with Possessing Anthrax." *Science* 297(5582): 751-2.

This little news report probably warned everyone who possesses controlled biological agents to follow the law, register the agents and keep them under tight lock and key. Institutions also have to monitor their inventories of these substances and deal very carefully with their transfer.

Malakoff, D. (2003). "SCIENTIFIC MISCONDUCT: The Multiple Repercussions of a Fudged Grant Application." *Science* 300(5616): 40-.

This news report describes the consequences of fudging preliminary work on a research grant and being caught. The allegation from an administrative assistant provoked an investigation and an admission of guilt. The grant still got funded but the investigator was no longer in charge of the program. Beware.

Mariner, W. K. (2000). "What Recourse? -- Liability for Managed-Care Decisions and the Employee Retirement Income Security Act." *N Engl J Med* 343(8): 592-596.

Marshall, E. (1995). "Suit Alleges Misuse of Peer Review." *Science* 270(5244): 1912-4.

When the money is substantial the temptation to use the information that you are supposed to keep confidential may become overwhelming. Be careful, however, you may be sued. An instructive case.

Marshall, E. (1999). "SCIENTIFIC ETHICS: Two Former Grad Students Sue Over Alleged Misuse of Ideas." *Science* 284(5414): 562-563.

This news report deals with allegations that Pis took graduate student's ideas and used them for their own grants. What the investigator did was surely bad manners and perhaps worse but it was not considered to be research misconduct. Could it have been violation of fiduciary responsibility to a mentee? This again emphasizes the unknowns in the relationship between investigators and trainees.

Marshall, E. (2000). "SCIENTIFIC MISCONDUCT: How Prevalent Is Fraud? That's a Million-Dollar Question." *Science* 290(5497): 1662-1663.

This news article reviews estimated misconduct frequency in research. The most striking finding was that one half of students were willing to fake data to get ahead. Investigators claim to know of instances of misconduct, but that has to be taken with a grain of salt.

Marshall, E. (2002). "Cancer Study Lawsuit Dismissed in Oklahoma." *Science* 295(5557): 949-50.

Medical Research Law and Policy Report. (2002). Current Climate Fostering More Misconduct, But Education, Monitoring Can Reduce Risks. Bureau of National Affairs.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1979). "The Belmont Report: ethical principles and guidelines for the protection of human subjects of research." US Government Printing Office.

Normile, D. (2004). "RESEARCH ETHICS: South Korean Cloning Team Denies Improprieties." *Science* 304(5673): 945-.

Pascal, C. (1999). "The History and Future of the Office of Research Integrity: Scientific Misconduct and Beyond." *Sci Eng Ethics* 5(2): 183-198.

The director of the ORI gives his view of the functioning of the agency in the past and the concerns to which they will be directed in the future.

Petersdorf, R. G. (1986). "The Pathogenesis of Fraud in Medical Science." *Ann Int Med* 104(February): 252-254.

Discussion of fraud in medical science has always been with us. Some of the underlying causes were discussed in this paper, which focuses on hypercompetitiveness, and inadequate supervision and oversight.

Rhoades, L. (2004). New Institutional Research Misconduct Activity 1992-2001. O. o. R. Integrity, Department of Health and Human Services.

Rhoades, L. (2004). ORI Closed Investigation into Misconduct Allegations Involving Research Supported by the Public Health Service 1994-2003. O. of. R. Integrity, Department of Health and Human Services.

Stein, R. (2005). Researcher Fabricated Data in Studies on Women. *Washington Post*. March 18, 2005

This famous case of fabrication shocked the establishment because the perpetrator was well known and slated to receive an important award. He had misused about \$11 million and had published fraudulent data. He had to pay back some money and be barred from NIH research support for life.

Steneck, N. (1999). "Confronting misconduct in science in the 1980s and 1990s: what has and has not been accomplished?" *Sci Eng Ethics* 5(2): 161-76.

He details the state of affairs before attention began to be directed at research misconduct, the formation of the ORI and the changing attitudes of investigators and institutions until the time of publication. He deals with confronting misconduct, promoting integrity and ensuring integrity. He points out that ensuring integrity has not been addressed. In the context of today's situation, perhaps we are now finally addressing the latter. I think the lawyers made us do it.

Swazey, J. P., M. S. Anderson, et al. (1993). "Ethical Problems in Academic Research: A survey of doctoral candidates and faculty raises important questions about the ethical environment of graduate education and research." *American Scientist* 81: 542-553.

This study has become a classic because it clearly demonstrated the extent of questionable behavior in both faculty and trainees in a variety of fields of science. It is worthwhile reading – and don't think that your field is any more honorable.

Taubes, G. (1993). "Misconduct: Views from the Trenches." *Science* 261: 1108-11.

This news item describes effective misconduct processes at UCSF, UCSD, Harvard and Univ. of Illinois as well as interviewing some of the responsible persons. The process at UCSF is described in some detail.

Trounson, R. O. et al (2003). *Researchers Violated Rules, UCLA Says*. Los Angeles Times. Los Angeles, CA. April 16, 2003.

This is a tricky one. The investigator arranged to work on data and blood samples obtained from an unapproved study in China without getting permission from his own institution's IRB. He was sanctioned even though he did not participate in the original study.

Woodward, J. and D. Goodstein (1996). "Conduct, Misconduct, and the Structure of Science." *American Scientist* 84(5): 479-91.

This analysis is concerned with the true structure of science as it differs from the homilies that pretend to describe this most complicated of human endeavors. The authors take apart a series of ethical principles used to characterize science and try to demonstrate that, for misconduct the only important thing is whether the scientific record was damaged by falsification or fabrication, results that it takes expertise to detect. They propose that the definition of scientific misconduct be limited to those activities. Much of their view has been adopted, finally in the new definition although plagiarism was not purged as they suggested.

Youngner, J. S. (1998). "The Scientific Misconduct Process: A Scientist's View From the Inside." *JAMA* 279(1): 62-64.

The author analyzes the activities of the Office of Research Integrity as an investigatory body and concludes that the requirement for confronting the purported perpetrator and allowing a defense was only met during the appeal process. The ORI was downgraded not long after this paper and the misconduct review now resides in the institutions and in the Inspector General's office of the Federal granting agencies. Investigations seem to be going much better at this point.

Cho, M. K., G. McGee, et al. (2006). "RESEARCH CONDUCT: Lessons of the Stem Cell Scandal." *Science* **311**(5761): 614-615.

This brief Policy Forum reflects on the reasons for the Hwang stem cell scandal. They reflect on the importance of trust in science. They indicate that scientific self-management works best in a questioning flat rather than a hierarchical laboratory environment and that widespread understanding of and buy-in regarding research ethics is required. It was not present in Korea. In my view, the Koreans were acting from a survivalist mentality in their effort to compete with America. In that mental mode, the only thing that counts is success.

<http://www.sciencemag.org/cgi/content/full/311/5761/614>