



## Tri-I Responsible Conduct of Research Course

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# Case Studies for Small Group Discussion

**October 2018:**

- Research Misconduct**
- Data Acquisition, Management, Sharing, & Ownership**
- Enhancing Reproducibility (videos)**
- Safe Laboratory Practices**
- Animal Welfare**

### Instructions:

**Two or more of these case studies (fictional or real or video) may be discussed in your session.**

**Please read/view them in advance and come prepared to analyze and discuss with the group.**

***Keep in mind that reality is often far more complex than fiction.  
There may be several RCR-related concerns interwoven throughout the case.  
Do you see others not listed below?***

“Fictional” Case Studies – Could these happen to you?

“Real” Case Studies in Alphabetical Order:

- **Bhriгу** - Sabotage - Lab Safety, Whistleblowing
- **Chandok v. Klessig** - Data Management, Whistleblowing, Responsible Publication
- **Darsee/Breuning** - Fabrication, Falsification
- **Das** - Fabrication and Falsification, Responsible Publication
- **Maria Cristina Miron Elqutub** - Fabrication and Falsification
- **Hauser** - Data Management, Animal and Human Cognition, Whistleblowing
- **Imanishi-Kari** - Data Management, Falsification, Whistleblowing, Authorship, Collaboration
- **Gareth John** - Falsification
- **Milikan** - Data Management, Falsification
- **Poehlman** - Fabrication, Falsification, Whistleblowing, Responsible Publication
- **Potti** - Falsification, Data Management, Conflict of Interest, Use of Human Subjects, Responsible Publication
- **Sezen** - Falsification, Fabrication, Plagiarism, Mentoring
- **Summerlin** - Fabrication, Fraud, Animal Welfare
- **Wanchick** - Fabrication

Video Scenarios - Enhancing Reproducibility:

- [Lack of Transparency](#)
- [Blinding and Randomization](#)
- [Biological and Technical Replicates](#)
- [Sample Size, Outliers, Exclusion Criteria](#)



Videos from:  
NIH / NIGMS

[Clearinghouse for Training Modules to Enhance Data Reproducibility](#)

## "Fictional" Case Studies – Could these happen to you?

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### **Falsification** (*Research Misconduct*)

Helen, a professor of cell biology, found herself mentoring a young woman named Julie. Julie had sought work in Helen's lab as a technician. She had to drop out of the graduate program because of health and family issues. She felt stuck in the role of lab technician and complained a lot. Even though Helen gave Julie a lot of support and encouraged her to resume her PhD work in the near future, Julie became bitter and uncooperative.

A problem arose in connection with an autoradiography process Julie used to detect proteins. Julie presented the data she had gathered using that process at one of the weekly lab meetings in which researchers, research assistants, and students bring their lab notebooks and present their data in its raw form. After the first part of her presentation, Julie said she had repeated the experiment and had gotten the same result. She showed her slide (a PowerPoint slide of a film from an autoradiogram) from Experiment 1, in which proteins were transferred to a membrane and an X-ray film then laid on top of the membrane, and then showed another slide from Experiment 2 showing the same thing.

Helen didn't spend a lot of time looking at the raw data of her lab staff, but liked to keep track of questions she had from the presentations at lab meetings. She often followed up later, asking any questions she might have about people's data. She had noted that the two slides Julie had shown looked more than similar—they seemed identical. After the presentation, Helen asked Julie whether she might have shown the same image twice, in error. Julie said no—she had done two separate experiments, had labeled the images correctly, and had noted that the experiments yielded the exact same result. Julie's unable to repeat the experiments since the original membranes were accidentally destroyed in the lab.

Helen was still troubled. After everyone had left the lab, Helen went to Julie's notebook and looked at the films much more closely. Helen held the two films over each other, and they matched exactly. Clearly, this was a duplication of the same film since ordinarily, in this type of analysis, each membrane inevitably produces idiosyncratic artifacts.

Helen consulted with others who used this technique. All of the senior scientists and post docs she talked to agreed that the film looked like a duplicate. The following day, Helen called Julie into her office and said, "Julie, I've looked at these two films carefully, and all the imperfections in the film indicate that it is the same sample."

To her dismay, Julie again insisted that she had done two individual experiments and obtained identical results.

### **Additional Questions to Consider:**

- Is Julie's story believable?
- What is Helen's role as a mentor of Julie?
- What kind of evidence is required in order to make a fair determination?
- What issues do you think are weighing on Helen's mind as she tries to decide what to do?
- What other kinds of experts might Helen consult if she thought it possible that the identical slides came from two separate experiments?
- What would be the cost to Helen if she makes the wrong decision?
- What would be the cost to Julie if Helen makes the wrong decision?
- How important is it to science that a correct decision be made?
- How important is it to the lab personnel that a correct decision be made?
- Have you ever suspected a colleague of research misconduct? How did you deal with it, and what lessons did you learn?

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From: <http://www.ori.dhhs.gov/case-one-were-these-slides-falsified>

### **Fabrication in a Grant Proposal** (*Research Misconduct*)

Vijay, who has just finished his first year of graduate school, is applying to the National Science Foundation for a pre-doctoral fellowship. His work in a lab where he did a rotation project was later carried on successfully by

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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 action 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.

### Additional Questions to Consider:

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

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From: Committee on Science, Engineering, and Public Policy, National Academy of Sciences, National Academy of Engineering, and Institute of Medicine. (2009). *On Being a Scientist*, Third Edition. The National Academies Press: Washington, D.C.

### A Career in the Balance (*Research Misconduct – Whistleblowing*)

Peter was just months away from finishing his Ph.D. dissertation when he realized that something was seriously amiss with the work of a fellow graduate student, Jimmy. Peter was convinced that Jimmy was not actually making the measurements he claimed to be making. They shared the same lab, but Jimmy rarely seemed to be there. Sometimes Peter saw research materials thrown away unopened. The results Jimmy was turning in to their common thesis adviser seemed too clean to be real. Peter knew that he would soon need to ask his thesis adviser for a letter of recommendation for faculty and postdoctoral positions. If he raised the issue with his adviser now, he was sure that it would affect the letter of recommendation. Jimmy was a favorite of his adviser, who had often helped Jimmy before when his project ran into problems. Yet Peter also knew that if he waited to raise the issue, the question would inevitably arise as to when he first suspected problems. Both Peter and his thesis adviser were using Jimmy's results in their own research. If Jimmy's data were inaccurate, they both needed to know as soon as possible.

### Additional Questions to Consider:

- What kind of evidence should Peter have to be able to go to his adviser?
- Should Peter first try to talk with Jimmy, with his adviser, or with someone else entirely?
- What other resources can Peter turn to for information that could help him decide what to do?

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From: Committee on Science, Engineering, and Public Policy, National Academy of Sciences, National Academy of Engineering, and Institute of Medicine. (2009). *On Being a Scientist*, Third Edition. The National Academies Press: Washington, D.C.

### Advisor steals student's work. (*Plagiarism*)

A graduate student prepares a research proposal as part of her dissertation requirements. Her faculty advisor reviews the proposal but otherwise provides only minimal assistance in developing the concept. The student later learns that her advisor has paraphrased sections of her proposal and incorporated them into his/her own application to a different funding agency.

### Additional Questions to Consider:

- Is this plagiarism? If so, is it research misconduct?  
    **"A finding of research misconduct made under this part (45 CFR 96.104) requires that:**
  1. There be a significant departure from accepted practices of the relevant research community; and

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2. The misconduct be committed intentionally, knowingly, or recklessly; and
  3. The allegation be proven by a preponderance of the evidence.”
- How should the student respond?

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From: <http://ori.hhs.gov/blog/page/2/>

### **Creating a Public Archive of Sensitive Data** (*Data Management*)

Frances is a researcher studying the molecular basis of cancer. She plans to sequence the genomes of children with cancer. Frances also intends to make such sequencing data publicly available on line. Internet-based DNA sequence databases would allow other scientists to analyze the data and ideally come up with important findings more quickly. This may lead to rapid identification of targets for new pediatric cancer treatments.

If a large amount of sequence data is made available, it may be possible for individuals to eventually be re-identified, which could have negative consequences. For example, participants in childhood cancer studies could become known to future employers or insurers based on their genetic information (their history of cancer and their publicly archived data). Further, data obtained for one study might later reveal other information such as susceptibility to other diseases or previously unknown family relationships. If a subject in a genome-wide sequencing study later released a small set of genetic information to another party for a different purpose, that information might be matched to the more extensive sequence data on the internet, revealing more about the subject to that party than the subject intended. This is a risk that subjects of such research should be made aware of during the informed consent process.

However, children, unlike adults, cannot legally consent. Publishing their personal DNA sequence would be based on parental permission. Since publication of such data is irreversible, parents would have to agree to this on their children’s behalf.

Federal regulations permit pediatric research that has no direct benefit to the child only when risks are minimal. The determination that a study involves only minimal risk requires the evaluation of the magnitude of possible harms as well as the probability of such harms.

### **Additional Questions to Consider:**

- Can you describe scenarios in which the data could be re-identified?
- What are some possible harms of re-identification?
- What are ways in which publicly available DNA sequencing data are used by others?
- How might a subject learn about actual occurrence of breaches of confidentiality?
- Do you think that children should have an opportunity to refuse requests to assent to the public use of their genetic information?

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From: <http://www.ori.dhhs.gov/case-one-creating-public-archive-sensitive-data>

### **Data Acquisition, Management, Sharing and Ownership**

Dr. Bernard Sears is the Principal Investigator on a grant from the National Institutes of Health. The primary aim of the research is the chemical modification of specific natural products for use as anti-cancer agents. Part of this research involves phase I clinical trials in humans, testing these chemically modified derivatives for toxicity. During the fourth year of this five-year grant, Dr. Sears develops health problems and is diagnosed as being terminally ill. During the first several months of his illness he is able to work from his home office. He has his research technician bring all of the relevant data books from the chemical synthesis phase of the research to his home. He begins analyzing and organizing the data with the intention of preparing manuscripts for publication. When Dr. Sears becomes too ill to work, the institution contacts the NIH and requests appointment of an interim Principal Investigator. NIH approves of this request. The phase I clinical trials move ahead smoothly during the last year of the proposal and the results are promising. Unfortunately, before the grant funding period ends, Dr. Sears dies. The financial books on the grant are closed at the end of the five-year funding period. A final financial report is filed

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with the NIH several months later. During this time Dr. Sears' household, has been liquidated and his assets assumed into an estate. The NIH sends a request for a final scientific report on the project. The Director of Sponsored Programs gives this request to the interim Principal Investigator. After several weeks of investigation, no information can be gained on the location of the data books that Dr. Sears took home with him in order to write his manuscripts. Following an investigation by the University legal office and the campus police, it is concluded that the data books were destroyed when Dr. Sears' household was sold.

### **Additional Questions to Consider:**

- What are the problems or issues in this case? Who or what is affected?
- Is there any recourse to salvage this important study?
- Who should be held accountable for these events?
- Should anyone be punished?
- Has scientific misconduct been perpetrated?
- Are you aware of your institution's rules regarding data removal, retention, and storage?
- Have any federal regulations been violated?

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## Case Study: Sabotage – Lab Safety, Whistleblowing

Source: Maher, B. Published online 29 September 2010 | *Nature* 467, 516-518 (2010) Retrieved on June 2, 2011 from: <http://www.nature.com/news/2010/100929/full/467516a.html>

Heather Ames, an MD-PhD student at the University of Michigan, first noticed a problem with her research in December 2009. As part of a study on the epidermal growth factor receptor, a protein involved in some cancers, she was running a western blot assay to confirm the presence of proteins in a sample. It was a routine protocol. But when she looked at the blot, four of her six samples seemed to be out of order — the pattern of bands that she expected to see in one lane appeared in another. Five days later, it happened again. She thought it might have been her mistake, but it was weird that they had gone wrong in exactly the same way. The only explanation was that the labelled lids for her cell cultures had been swapped, and she immediately wondered whether someone was sabotaging her work. To be safe, she devised a workaround: writing directly on the bottoms of the culture dishes so that the lids could not be switched.

Next, Ames saw an additional protein in the sample lanes, showing that an extra antibody was staining the blot. Once again, it could have been a mistake, but it happened twice. She was certain that someone was tampering with her experiments, but she had no proof and no suspect. Her close friends suggested that she was being paranoid.

Some labs are known to be hyper-competitive, with Principal Investigators pitting postdocs against each other. At the time that Ames was noticing problems, it housed just one other graduate student, a few undergraduates doing projects, and the lab manager, a nine-year veteran of the lab whom Ames' supervisor called her "eyes and ears." And then there was Vipul Bhriugu, a postdoc who had come to the US from India in 2003, and completed his PhD under a cancer biologist at the University of Toledo, Ohio and joined the lab in April 2009.

In February 2010, Ames encountered what she thought was another attempt to sabotage her work. She was replacing the media on her cells and immediately noticed that something wasn't right. When she sniffed it, the smell of alcohol was overpowering. This, she thought, was the proof she needed. Her supervisor came and sniffed the medium too and agreed that it didn't smell right, but she didn't know what to think.

Some people were convinced that Ames was hitting a rough patch in her work and looking for someone else to blame. But Ames was persistent, so the matter went to the university's office of regulatory affairs, which advises on a wide variety of rules and regulations pertaining to research and clinical care. The university officials had never dealt with anything like it before. After several meetings and two more instances of alcohol in the media, they contacted the department of public safety — the university's police force. They immediately launched an investigation — into Ames herself. She endured two interrogations and a lie-detector test before investigators decided to look elsewhere.

In mid April, officers installed two cameras in the lab: one in the cold room where Ames's blots had been contaminated, and one above the refrigerator where she stored her media. Ames came in that day and worked until 5:00pm. On Monday morning, she found that her medium had been spiked again. When Ross reviewed the tapes of the intervening hours she says that her heart sank. Bhriugu entered the lab at 9:00 am on Monday and pulled out the culture media that he would use for the day. He then returned to the fridge with a spray bottle of ethanol, usually used to sterilize lab benches. With his back to the camera, he rummaged through the fridge for 46 seconds. Ross couldn't be sure what he was doing, but it didn't look good.

Bhriugu was escorted to the campus police department for questioning. When Bhriugu was told about the cameras in the lab, the postdoc confessed, saying that he was trying to slow the student down. He said that he had been sabotaging Ames's work since February. (He denied involvement in the December and January incidents.) He was fired and taken to court, where he pleaded guilty to malicious destruction of property. He was subsequently ordered to pay more than \$30,000 total in fines and restitution.

Additional Questions to Consider:

- What risk considerations in terms of lab safety are in play here?
- How big an issue is "hyper-competitiveness" in a laboratory situation? What behaviors might develop? Are there any positive outcomes? Are there mechanisms in place to deal with any unfortunate circumstances that may arise?
- What impact, if any, do the US government sanctions have on Dr. Bhriugu's ability to continue his science in India or elsewhere abroad?
- What damage, if any, is done to Dr. Ames' reputation as a result of her making accusations (even if well-founded) against a more senior colleague?

## Case Study: Data Management, Whistleblowing, Responsible Publication

Source: Samantha Weidner, JD, Presidential Management Fellow, National Cancer Institute. *Court Finds Qualified Immunity for Whistleblower*. Retrieved on June 3, 2011 from: [http://www.ori.dhhs.gov/documents/newsletters/vol19\\_no2.pdf](http://www.ori.dhhs.gov/documents/newsletters/vol19_no2.pdf)

Scientists, Dr. Meena Chandok and Dr. Daniel Klessig worked together at the Boyce Thompson Institute for Plant Research (BTI), an affiliate of Cornell University, where Klessig was a senior scientist. He directed a research team focusing on immune response mechanisms in plants and on the production of nitric oxide by plants to offset attacks by pathogens. Chandok was tasked with working to find and purify nitric oxide synthase (NOS).

In 2002, Chandok sent Klessig data indicating that she was successful in developing a recombinant protein with NOS activity. The reported results were widely publicized, and as a result of the reported data, Klessig's laboratory received a grant from NIH of more than \$1 million to fund further NOS research.

In 2004, Chandok resigned from BTI. Subsequent to her departure, the other scientists in Klessig's lab were unable to replicate the results that Chandok reported. Chandok declined to return to BTI to assist in replicating the results, and Klessig became concerned that Chandok had engaged in scientific misconduct. Klessig proceeded to notify BTI, NIH, NSF, and the Office of Research Integrity (ORI) of the potential misconduct.

Klessig also retracted articles published in *Cell* and in the *Proceedings of the National Academy of Sciences of the United States (PNAS)* regarding the reported results. Klessig emailed fellow scientists interested in NOS research to inform them that the *Cell* and *PNAS* articles were retracted in light of the inability to replicate or confirm Chandok's reported NOS results.

Chandok sued Klessig in August 2005 for defamation, claiming that Klessig made numerous false statements about the accuracy or veracity of her NOS research, thereby causing significant damage to her reputation in the scientific community.

### Additional Questions to Consider:

- Should Dr. Chandok's results have been "widely publicized" prior to attempts to duplicate her efforts? Why, or why not? Could data management and sharing policies and procedures have made a difference? If so, in what way(s)?
- What do you think about all the actions taken by Klessig to inform others about his suspicions? Did he do enough, not enough, too much? What could he have done differently?
- Was Dr. Chandok justified to initiate legal action for defamation? What could she have done differently to avoid litigation?
- Would fear of counter lawsuits affect your decision to "do the right thing?"

## Case Study: Fabrication, Falsification, Authorship, Whistleblowing, Human Subjects (Vulnerable Populations)

Source: "Case Study: Overly Ambitious Researchers - Fabricating Data" Online Ethics Center for Engineering 7/20/2006 National Academy of Engineering Accessed: Monday, May 16, 2011 [www.onlineethics.org/Education/precollege/scienceclass/sectone/cs1.aspx](http://www.onlineethics.org/Education/precollege/scienceclass/sectone/cs1.aspx)

### The Darsee case

Dr. John Darsee was regarded a brilliant student and medical researcher at the University of Notre Dame (1966-70), Indiana University (1970-74), Emory University (1974-9), and Harvard University (1979-1981). He was regarded by faculty at all four institutions as a potential "all-star" with a great research future ahead of him. At Harvard he reportedly often worked more than 90 hours a week as a Research Fellow in the Cardiac Research Laboratory headed by Dr. Eugene Braunwald. In less than two years at Harvard he was first author of seven publications in very good scientific journals. His special area of research concerned the testing of heart drugs on dogs.

All of this came to a sudden halt in May 1981, when three colleagues in the Cardiac Research Laboratory observed Darsee labeling data recordings *24 seconds, 72 hours, one week, and two weeks*. In reality, only minutes had transpired. Confronted by his mentor, Darsee admitted the fabrication; but he insisted that this was the only time he had done this, and that he had been under intense pressure to complete the study quickly. Shocked supervisors spent the next several months checking other research conducted by Darsee in their lab. Darsee's research fellowships were terminated, and an offer of a faculty position was withdrawn. However, he was allowed to continue his research projects at Harvard for the next several months (during which time his work was supervised very closely).

In October, a comparison of results from four different laboratories in a National Heart, Lung and Blood Institute (NHLBI) Models Study revealed an implausibly low degree of invariability in data provided by Darsee. In short, his data looked "too good." Since these data had been submitted in April, there was strong suspicion that Darsee had been fabricating or falsifying data for some time. Subsequent investigations seemed to indicate questionable research practices dating back as far as his undergraduate days.

A cloud of suspicion hung over all the work with which Darsee was associated. Not only was Darsee's own research discredited, but insofar as it formed an integral part of collaborative research, a cloud was thrown over published research bearing the names of authors whose work was linked with Darsee's.

The months of outside investigation also took others away from their main tasks and placed them under extreme pressure. Fifteen years later, the statistician recalled the relief his team experienced when their work was completed. There was no room for error, any mistakes would destroy the case for improbable data and severely damage careers. Even without mistakes, being able to convince lay reviewers such as a jury using statistical arguments could still be defeating. Playing the role of the prosecuting statisticians was very demanding of technical skills but also of the team's integrity and ethical standards.

### The Bruening case

In December 1983, Dr. Robert Sprague wrote an eight page letter, with 44 pages of appendices, to the National Institute of Mental Health (NIMH) documenting the fraudulent research of Dr. Stephen Breuning. Breuning fabricated data concerning the effects psychotropic medication have on mentally retarded patients. Despite Breuning's admission of fabricating data only three months after Sprague sent his letter, the case was not finally resolved until July 1989. During that five and one-half year interval, Sprague himself was a target of investigation (in fact, he was the first target of investigation), he had his own research endeavors severely curtailed, he was subjected to threats of lawsuits, and he had to testify before a US House of Representatives Committee. Most painful of all, Sprague's wife died in 1986 after a lengthy bout with diabetes. In fact, his wife's serious illness was one of the major factors prompting his *whistleblowing* to NIH. Realizing how dependent his diabetic wife was on reliable research and medication, Sprague was particularly sensitive to the dependency the mentally retarded, clearly a vulnerable population; have on the trustworthiness of not only their care givers, but also those who use them in experimental drug research.

Dr. Alan Poling, a psychologist, points out that between 1979 and 1983, Bruening was a contributor to 34% of all published research on the psychopharmacology of mentally retarded people. For those not involved in the research, initial doubts might be cast on all these publications. For those involved in the research, efforts need to be made in each case to determine to what extent, if any, the validity of the research was affected by Bruening's role in the study. Even though Bruening was the only researcher to fabricate data, his role could contaminate an entire study. In fact, however, not all of Bruening's research did involve fabrication. Yet, convincing others of this is a time-consuming, demanding task. Finally, those who cited Bruening's publications in their own work may also suffer "guilt by association." As Poling points out, this is especially unfair in those instances where Bruening collaborated with others involved no fraud at all.

Where is Bruening now? Source: <https://forbiddenpsychology.wordpress.com/2014/05/17/from-the-archives-of-scientific-fraud-stephen-breuning/>

Stephen E. Breuning was sentenced for 60 days in a halfway house and five years of probation period. The court also ordered him to pay back \$11,352, serve 250 hours of community service and abstain from psychological research for at least the period of his probation. Breuning agreed not to undertake any work as a psychologist for at least ten years. After serving his time, Breuning opened an electronics store near his home in Rochester. Today he runs his private counseling practice, or at least this is what information found on the Internet suggests.

#### Additional Questions to Consider:

The Darsee and Bruening cases raise a host of ethical questions about the nature and consequences of scientific fraud.

- The Darsee and Bruening cases raise a host of ethical questions about the nature and consequences of scientific fraud.
- What kinds of reasons are offered for fabricating data?
- Which, if any, of those reasons are good reasons--i.e., reasons that might justify fabricating data?
- Who is likely to be harmed by fabricating data? Does actual harm have to occur in order for fabrication to be ethically wrong?
- What responsibilities does a scientist have for checking on the trustworthiness of the work of other scientists?
- What should a scientist do if he or she has reason to believe that another scientist has fabricated data?
- What special considerations need to be taken into account when conducting research with vulnerable populations?

## Case Study: Fabrication, Falsification, Responsible Publication

Source: Bartlett, T. (2012 January). *UConn Investigation Finds That Health Researcher Fabricated Data*. Retrieved on January 12, 2012 from: [http://chronicle.com/blogs/percolator/uconn-investigation-finds-that-health-researcher-fabricated-data/28291?sid=at&utm\\_source=at&utm\\_medium=en](http://chronicle.com/blogs/percolator/uconn-investigation-finds-that-health-researcher-fabricated-data/28291?sid=at&utm_source=at&utm_medium=en)

A three-year investigation by the University of Connecticut has found that the director of its Cardiovascular Research Center falsified and fabricated data at least 145 times, in some cases digitally manipulating images using Photoshop.

The researcher, **Dipak K. Das**, is best known for his work on resveratrol, a compound present in grapes and other foods that some research suggests can have beneficial effects on the heart and could slow aging, though recent studies have cast doubt on the latter claim. Das has been quoted regularly in news articles, usually talking about resveratrol, and his papers have been cited often, as the blog Retraction Watch points out. But the importance of his research is unclear.

David Sinclair, a professor of pathology at Harvard University who is known for his discovery that resveratrol appears to extend the life of mice and fruit flies, said he had not heard of Das. "I've not worked with him," Sinclair wrote in an email. "Looking through it, the work is generally not published in leading molecular-biology journals."

Still, Das had published quite a bit, and the university has notified 11 journals of problems the investigation found with his research. "Whenever we get a call about resveratrol, he was our primary guy," said Chris DeFrancesco, a spokesman for the university. UConn also declined to accept nearly \$900,000 in federal grants for Das' laboratory.

The 60,000 page investigation report is not yet public, but there is a 49-page summary. Here are a few highlights:

- Das was "intimately involved in the generation of figures that were determined to have been manipulated (either by fabrication or falsification)."
- Others in his laboratory may have also been involved in wrongdoing. a spokesman, said an investigation into who else might have been involved is continuing.
- The data manipulation, investigators concluded, was "intentional" and "designed to deceive."

Plenty of questions remain unanswered. Was Das pushing a certain agenda? What will the effect be, if any, on resveratrol research, which is already the subject of some controversy?

The university did provide a copy of a response he submitted to the report. He writes in a letter dated June 5, 2010, that, in part because of a recent stroke, he cannot respond to the allegations immediately. In a subsequent letter, he writes that the university's investigation is racist, calling it a "conspiracy against Indian scientists."

### Additional Questions to Consider:

- What is the effect on science, when even "insignificant" research gets prime time press coverage?
- Would it make a difference if this research was cutting-edge or historically relevant?
- What consequences are there on an institution when one of its scientists misuses federal funds?

## Case Study- Falsification and Fabrication)

Sources: Retrieved on 6/15/18 from the Houston Chronicle article: “MD Anderson research assistant subbed in her blood for study participants” by Todd Ackerman printed on May 15, 2018 <https://www.houstonchronicle.com/news/houston-texas/houston/article/MD-Anderson-research-assistant-subbed-in-her-12917536.php> Source: <https://ori.hhs.gov/content/case-summary-elqutub-maria-cristina-miron> <https://retractionwatch.com/2018/05/14/cancer-researcher-said-she-collected-blood-from-98-people-it-was-all-her-own/>

A former member of an MD Anderson Cancer Center research team misrepresented her blood as that of nearly 100 study participants. The U.S. Office of Research Integrity (ORI) reported that Maria Cristina Miron Elqutub “intentionally and knowingly” engaged in misconduct in MD Anderson cancer genetics research by substituting her blood and falsely labeling the samples so they appeared to come from 98 human subjects. Elqutub served as a research assistant on the project. The research was supported by a grant from the National Institute of Dental and Craniofacial Research (NIDCR), National Institutes of Health (NIH)

Elqutub admitted to the misconduct. Although there was no direct impact on patients, the research was published in two academic papers. One, in the journal Cancer in 2015 was retracted. The other, in the scientific journal PLOS One in 2015, is currently under evaluation (as of June 2018) and would need to be corrected or retracted. Neither paper made a major impact: The article in Cancer was cited only eight times and the one in PLOS ONE, only twice.

The Principal Investigator of the affected \$1.3 million grant, Adel El-Naggar, and co-author on both of the papers, said he didn’t know many details of the investigation. El-Naggar said researchers at the institution realized something was wrong when they used the same blood samples for another study, and found they did not produce the same result as the one Elqutub reported.

**Where is Elqutub now?** Elqutub is currently employed as a middle school nurse.

### Additional Questions to Consider:

- What do you think motivated this research assistant, Elqutub, to use her own blood samples for this study? What did she hope to achieve by doing this?
- How did the duplicate samples go unnoticed for so long? What various levels of oversight failed? What was the responsibility of the PI?
- How does a case like this affect societal trust in human research?

## Case Study – Data Management, Animal and Human Cognition, Whistleblowing

Sources: Bartlett, T. (2011, July 19). *Marc Hauser Resigns from Harvard*. Retrieved on 4/10/12 from: <http://chronicle.com/article/Marc-Hauser-Resigns-From/128296/> Vergano, D. (2011 April 26). Harvard says Marc Hauser guilty of science misconduct. *USA Today*. Retrieved on 7/18/11 from: <http://content.usatoday.com/communities/sciencefair/post/2010/08/marc-hauser-harvard-science-misconduct-/1> Wade, N. (2010, August 10). Harvard finds scientist guilty of misconduct. *The New York Times*. Retrieved on 7/18/11 from: <http://www.nytimes.com/2010/08/21/education/21harvard.html> Retrieved on May 14, 2018 from: <https://www.chronicle.com/article/Document-Sheds-Light-on/123988>

In August 2010, Harvard University found **Marc Hauser**, a leader in the field of animal and human cognition, “solely responsible” for eight instances of scientific misconduct.

In 2006 he wrote a well-received book, “Moral Minds: How Nature Designed Our Universal Sense of Right and Wrong.” Harvard’s findings against him, if sustained, may cast a shadow over the broad field of scientific research that depended on the particular research technique often used in his experiments.

An internal document sheds light on what was going on in Mr. Hauser's lab. It tells the story of how research assistants became convinced that the professor was reporting bogus data and how he aggressively pushed back against those who questioned his findings or asked for verification.

A copy of the document was provided to The Chronicle by a former research assistant in the lab who has since left psychology. The document is the statement he gave to Harvard investigators in 2007.

The former research assistant, who provided the document on condition of anonymity, said his motivation in coming forward was to make it clear that it was solely Mr. Hauser who was responsible for the problems he observed. The former research assistant also hoped that more information might help other researchers make sense of the allegations.

It was one experiment in particular that led members of Mr. Hauser's lab to become suspicious of his research and, in the end, to report their concerns about the professor to Harvard administrators.

The experiment tested the ability of rhesus monkeys to recognize sound patterns. Researchers played a series of three tones (in a pattern like A-B-A) over a sound system. After establishing the pattern, they would vary it (for instance, A-B-B) and see whether the monkeys were aware of the change. If a monkey looked at the speaker, this was taken as an indication that a difference was noticed.

The method has been used in experiments on primates and human infants. Mr. Hauser has long worked on studies that seemed to show that primates, like rhesus monkeys or cotton-top tamarins, can recognize patterns as well as human infants do. Such pattern recognition is thought to be a component of language acquisition.

Researchers watched videotapes of the experiments and "coded" the results, meaning that they wrote down how the monkeys reacted. As was common practice, two researchers independently coded the results so that their findings could later be compared to eliminate errors or bias.

According to the document that was provided to The Chronicle, the experiment in question was coded by Mr. Hauser and a research assistant in his laboratory. A second research assistant was asked by Mr. Hauser to analyze the results. When the second research assistant analyzed the first research assistant's codes, he found that the monkeys didn't seem to notice the change in pattern. In fact, they looked at the speaker more often when the pattern was the same. In other words, the experiment was a bust.

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But Mr. Hauser's coding showed something else entirely: He found that the monkeys did notice the change in pattern—and, according to his numbers, the results were statistically significant. If his coding was right, the experiment was a big success.

The second research assistant was bothered by the discrepancy. How could two researchers watching the same videotapes arrive at such different conclusions? He suggested to Mr. Hauser that a third researcher should code the results. In an e-mail message to Mr. Hauser, the research assistant who analyzed the numbers explained his concern. "I don't feel comfortable analyzing results/publishing data with that kind of skew until we can verify that with a third coder," he wrote. A graduate student agreed with the research assistant and joined him in pressing Mr. Hauser to allow the results to be checked, the document given to *The Chronicle* indicates. But Mr. Hauser resisted, repeatedly arguing against having a third researcher code the videotapes and writing that they should simply go with the data as he had already coded it. After several back-and-forths, it became plain that the professor was annoyed. "I am getting a bit pissed here," Mr. Hauser wrote in an e-mail to one research assistant. "There were no inconsistencies! Let me repeat what happened. I coded everything. Then [a research assistant] coded all the trials highlighted in yellow. We only had one trial that didn't agree. I then mistakenly told [another research assistant] to look at column B when he should have looked at column D. We need to resolve this because I am not sure why we are going in circles."

The research assistant who analyzed the data and the graduate student decided to review the tapes themselves, without Mr. Hauser's permission, the document says. They each coded the results independently. Their findings concurred with the conclusion that the experiment had failed: The monkeys didn't appear to react to the change in patterns.

They then reviewed Mr. Hauser's coding and, according to the research assistant's statement, discovered that what he had written down bore little relation to what they had actually observed on the videotapes. He would, for instance, mark that a monkey had turned its head when the monkey didn't so much as flinch. It wasn't simply a case of differing interpretations, they believed: His data were just completely wrong. As word of the problem with the experiment spread, several other lab members revealed they had had similar run-ins with Mr. Hauser, the former research assistant says. This wasn't the first time something like this had happened. There was, several researchers in the lab believed, a pattern in which Mr. Hauser reported false data and then insisted that it be used.

They brought their evidence to the university's ombudsman and, later, to the dean's office. This set in motion an investigation that would lead to Mr. Hauser's lab being raided by the university in the fall of 2007 to collect evidence. It wasn't until this year, however, that the investigation was completed. It found problems with at least three papers. Because Mr. Hauser has received federal grant money, the report has most likely been turned over to the Office of Research Integrity at the U.S. Department of Health and Human Services.

The research that was the catalyst for the inquiry ended up being tabled, but only after additional problems were found with the data. In a statement to Harvard officials in 2007, the research assistant who instigated what became a revolt among junior members of the lab, outlined his larger concerns: "The most disconcerting part of the whole experience to me was the feeling that Marc was using his position of authority to force us to accept sloppy (at best) science." Hauser resigned from Harvard effective August 1, 2011.

#### **Additional Questions to Consider:**

- To echo de Waal: how many people knew about the misconduct or how many could have known about or suspected it? Advisors, students, postdocs, close colleagues? Is it conceivable that the scientist was solely responsible? What could have been done to prevent this from happening?
- What do you think about Premack's statement? - "Dishonesty in cognitive science is somehow more disturbing than dishonesty in biology or physical science..." Do you agree or disagree, why, or why not?
- What damage is done to a lab's credibility when one instance of misconduct is discovered? How is the lab's previous work perceived? How might these perceptions affect future funding opportunities?

## Case Study- Falsification

Source: <https://retractionwatch.com/2018/05/14/mount-sinai-multiple-sclerosis-researcher-admits-to-misconduct/>

A researcher who has received millions in funding from the U.S. National Institutes of Health and who runs a lab at the Icahn School of Medicine at Mount Sinai in New York has confessed to falsifying data in a 2014 paper.

[Gareth John](#), who studies multiple sclerosis and other neurological diseases, “has expressed remorse for his actions,” according to a [report released last week from the U.S. Department of Health and Human Services’ Office of Research Integrity](#).

John falsified data in two different figures in a 2014 paper in *Development*, “[Combinatorial actions of Tgfβ and Activin ligands promote oligodendrocyte development and CNS myelination](#),” according to the report. In one figure, a Western blot, he “removed the lower set of bands, reordered the remaining bands and used those bands to represent the actin control,” among other falsifications, and in another, he cut and pasted bands “onto a blank background and used those false bands to create a graph.” The paper was the [subject of two comments on PubPeer in August 2014](#).

According to the Office of Research Integrity (ORI), John “*notified Development that corrections to figures in the paper, but not to the text, including the conclusions in Development 2014 are required.*”

John agreed to have his research supervised for a year, to not serve on committees including peer review committees at the U.S. National Institutes of Health for the same amount of time, and to follow up with *Development* to ensure they make the corrections he requested.

The paper has been cited 13 times, [according to Clarivate Analytics’ Web of Science](#). John has received more than \$7 million in funding from the NIH, as well as funding from funding from the National Multiple Sclerosis Society.

According to [John’s] [lab’s website](#), he also receives [funding](#) from “the Guthy-Jackson Foundation, pharmaceutical and biotech industry collaborations, and private benefactors.”

ORI found that Dr. Gareth John, Professor, Department of Neurology, ISMMS, engaged in research misconduct in research supported by the National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH), grants R01 NS056074 and R01 NS062703.

**Where is John now?** Dr. John entered into a Voluntary Settlement Agreement. He is still listed on the Mount Sinai website with a description of his lab and its members.

### Additional Questions to Consider:

- The paper was cited 13 times. What effect does a misconduct finding and retraction have on the scientific community as a whole?
- What are the real or perceived conflicts of interest in this case? What pressures may John have faced due to competing interests/various funding sources.
- Are you familiar with PubPeer online journal club and its purpose? Is it beneficial for the scientific community? What are the pros/cons?

## Case Study: Data Management, Falsification, Whistleblowing, Authorship, Collaboration

Source: Retrieved on June 3, 2011 from: [http://cnmtl.columbia.edu/projects/rcr/rcr\\_misconduct/foundation/index.html#1\\_B\\_3](http://cnmtl.columbia.edu/projects/rcr/rcr_misconduct/foundation/index.html#1_B_3)

This infamous case pitted a postdoctoral researcher against a Nobel Prize winner. It became a cause célèbre in the mid-1980s, and was the subject of federal investigations and congressional hearings, which ultimately led to the establishment of regulations against research misconduct. The case took more than 10 years to resolve.

In 1986, Margot O'Toole, a postdoctoral researcher at Tufts University, could not validate the findings of some work soon to be published in *Cell* by her employer, **Thereza Imanishi-Kari** and a co-author on the paper, Nobel Prize winner, David Baltimore, of the Massachusetts Institute of Technology. O'Toole came to believe that Imanishi-Kari manipulated research data and presented her evidence to committees at Tufts and MIT. The committees ruled that misconduct had not occurred but that Imanishi-Kari had been sloppy in her research. An NIH committee at the time also cleared Imanishi-Kari.

Walter Stewart and Ned Feder, two scientists from the NIH who were involved in exposing misconduct, then became involved in the case, believing that the committees and the NIH did not do an adequate job of revealing problems with the paper. In 1988, congressional hearings were held, headed by Representative John Dingell, who chaired the Energy and Commerce Committee, which oversees the budget for the NIH. All three took up the cause because they believed that problems existed in the way that universities handled allegations of misconduct.

Dingell's committee even brought in the Secret Service, which determined that Imanishi-Kari had tampered with evidence that she had provided to the committee. The hearings were contentious in nature, and many believed that Dingell was particularly hostile to Baltimore, who continued to defend Imanishi-Kari.

In 1991, the NIH's fraud division, at that time called the Office of Scientific Integrity, found that significant portions of the data were fabricated. Thereza Imanishi-Kari was banned from receiving federal grant money for 10 years. David Baltimore resigned from his presidency of The Rockefeller University on December 31, 1991, saying that he could no longer be an effective leader because of the controversy over his role in the case. Margot O'Toole was ostracized by the science field, and at one point, for employment, she answered telephones for a moving company.

The OSI became reconstituted in HHS as the Office of Research Integrity (ORI), which upheld the OSI decision. The ORI, however, had an appeals mechanism, called the Appeals Board, which, on June 21, 1996, overturned the ORI decision. The board said that it had not been proved that Imanishi-Kari falsified the scientific record but instead that she was guilty of sloppy scientific practices.

No one emerged untarnished from the case. Soon afterward, regulations concerning the management of misconduct allegations were announced by the NIH and the NSF; they included provisions for protecting the rights of those who report misconduct and those who are accused of misconduct, and also a provision for an appeals process.

### Additional Questions to Consider:

- Although, eventually exonerated, what effect does this type of scandal have on one's career? Would this have been better or worse had it occurred earlier in her career, or later? Is it any less damaging to be guilty of "sloppy scientific practices" vs. deliberate misconduct?
- What role, if any, do you think politics plays when federal and/or state funding is involved? Would this have been as contentious if it were private or internal institutional funding? Should the source of funds make any difference?
- Is it better or worse to have well established collaborators when there is an allegation of misconduct? Does a person's celebrity or respected reputation in a particular field of study, have an effect on the process or outcome? If so, in what way?

## Case Study: Data Management, Falsification

Source: "Case Study 2: The Millikan Case - Discrimination Versus Manipulation of Data" Online Ethics Center for Engineering 7/20/2006 National Academy of Engineering Accessed: Monday, April 02, 2012 [www.onlineethics.org/Education/precollege/scienceclass/sectone/chapt4/cs2.aspx](http://www.onlineethics.org/Education/precollege/scienceclass/sectone/chapt4/cs2.aspx)

### Background

Robert A. Millikan, Nobel Prize winner in 1924, was the most famous US scientist of his time. He won largely due to his important and innovative measurement of the charge on the electron in 1910 - one of the most central physical constants that scientists of that era had been seeking to determine.

Millikan's method involved watching the behavior of oil droplets in an electrically charged field. Tiny oil droplets are ionized by passage through an atomizer; they have an extra electron or electrons riding on them. A droplet is allowed to fall between two plates, and then an electric field is created which pulls the droplet upwards. The speed of the droplet depends on the charge riding on it. Thus the basic measurement is the rise time; how long it takes a particular drop to rise a certain distance. If electrons had a spectrum of charges, one would expect a corresponding continuous spectrum of rise times. If, on the other hand, all electrons had the same charge, the charge on each ion would be multiples of a single number, a fact which would be reflected by rise times that would also be simple multiples of each other.

Millikan published tables of his measured drops and their rise times. What these tables indicated was that the charges on the droplets were, indeed, multiples of the same number - thus, the charge of the electron. He then wrote a series of papers on his experiments. He would win the Nobel Prize in Physics for this work; he was only the second American to be so honored. Millikan considered the experiment to be such a direct and irrefutable demonstration of the atomicity of electric charge that he wrote in his autobiography that he who has seen that experiment, and hundreds of observers have observed it, [has] in effect SEEN the electron.

### The Case

An examination of Millikan's own papers and notebooks reveals that he picked and chose among his drops. That is, he exercised discrimination with respect to which drops he would include in published accounts of the value of  $e$ , leaving many out. Sometimes he mentioned this fact, and sometimes he did not. Of particular concern is the fact that in his 1913 paper, presenting the most complete account of his measurements of the charge on the electron, Millikan states *It is to be remarked that this is not a selected group of drops but represents all of the drops experimented upon during 60 consecutive days*. However, Millikan's notebook shows that of 189 observations during the period in question, only 140 are presented in the paper.

Millikan's results were contested by Felix Ehrenhaft, of the University of Vienna, who claimed to have found "subelectrons." Moreover, Ehrenhaft claimed that his finding was in fact confirmed by some of Millikan's own data -- droplets that Millikan had mentioned but discounted in his published writings. The result was a decades-long controversy, the "Battle over the Electron," over whether or not there existed subelectrons, or electrons with charges of different values. This controversy makes an excellent case study because we are fortunate, thanks to Millikan's notebooks, to be able to see very specifically which drops he included and which he did not.

In retrospect, we know that Millikan was *right* and Ehrenhaft *wrong*. Electrons, to the best of our present experimental and theoretical knowledge, have a specific, discrete charge. Those scientists and other scholars who have carefully reviewed this case have failed to agree on whether Millikan was guilty of unethical behavior or "bad science" in the treatment and presentation of his data. One of the expressed opinions condemns Millikan on the simple basis of the fact that his published statement is at odds with what can be concluded from an uncritical examination of his laboratory notebooks. Others exonerate Millikan on the basis of a careful analysis and interpretation of comments on the data that appear in the notebooks. In the opinion of these Millikan defenders, the assertion that all drops were presented in the paper refers to all of the data taken under those conditions when the apparatus was working properly. Some of the scientists who have commented on this case appear to permit Millikan much discretion in the use of his "scientific intuition" to decide which data to include or exclude. This latter view seems to be guided by the principle that any scientist who consistently gets what turns out to be the correct answer is doing *good* science.

**Additional Questions to Consider:**

- Ethical questions specifically related to the Millikan case-Does the contradiction between Millikan's unqualified statement that he has published all the oil-drop data and the evidence of unpublished oil-drop measurements in his notebooks prove that he is guilty of unethical scientific behavior?
- Should the fact that Millikan was a highly successful scientist, and that he got the right answer in the controversy about the charge on the electron be a consideration in judging his scientific ethics?
- If Millikan had not claimed to have published all the data, would he still be guilty of questionable behavior?

**More general questions about the manipulation and presentation of data raised by this case:**

- What criteria should be used in deciding whether data can be legitimately discarded?
- When a scientist uses his or her "intuition" as the basis for deciding whether to ignore certain data, is the question of the ethics of this action dependent on whether the conclusion reached by the scientist is later proven to be correct?
- Is the intentional manipulation and selection of data in order to falsely prove a scientific premise less of a violation of acceptable ethical standards than the outright fabrication of data?
- Does the need for an accurate record to determine whether data have been treated and presented appropriately imply certain universal standards for the recording of observations by scientists? If so, what are these standards?

## Case Study: Falsification, Fabrication, Whistleblowing, Human Subjects, Responsible Publication

Source: Kintisch, E. (2005, March). Researcher faces prison for fraud in NIH grant applications and papers. *Science*. Vol. 307 [www.sciencemag.com](http://www.sciencemag.com) Office of Research Integrity. Retrieved on 7/18/11 from: [http://ori.hhs.gov/misconduct/cases/press\\_release\\_poehlman.shtml](http://ori.hhs.gov/misconduct/cases/press_release_poehlman.shtml)

From 1987 to 2001, Dr. Eric Poehlman held various research positions as an assistant, associate, and full professor of medicine at the UVM College of Medicine in Burlington, Vermont (1987-1993; 1996-2001), and the University of Maryland in Baltimore, Maryland (1993-1996). In these academic positions, Dr. Poehlman conducted research on human subjects related to exercise physiology and other topics that was funded primarily by grants from federal public health agencies and departments, including the NIH, the US Department of Agriculture (USDA), and the Department of Defense.

From about 1992 to 2000, Dr. Poehlman submitted seventeen (17) research grant applications to federal agencies or departments that included false and fabricated research data. In these grant applications, Dr. Poehlman requested approximately \$11.6 million in federal research funding. In most cases, Dr. Poehlman falsified and fabricated research data in the "preliminary studies" sections of grant applications in order to support the scientific basis for and his expertise in conducting the proposed research. Reviewers of these grant applications relied on the accuracy of the "preliminary studies" to determine if a grant should be recommended for award. While many of the grant applications were not awarded, NIH and USDA expended approximately \$2.9 million in research funding based on grant applications with false and fabricated research data.

Dr. Poehlman falsified and fabricated research data in grant applications and research papers related to several topics including his study of the impact of the menopause transition on women's metabolism, his study of the impact of aging in older men and women on a wide range of physical and metabolic measures, and his proposal to study the impact of hormone replacement therapy on obesity in post-menopausal women. He also presented falsified and fabricated data in grant applications and academic papers related to his study of metabolism in Alzheimer's patients and the effect of endurance training on metabolism.

Scientists say the falsified data— including work in 10 papers for which Poehlman has requested retractions or corrections—have had relatively little impact on core assumptions or research directions. But experts say the number and scope of falsifications discovered, along with the stature of the investigator, are quite remarkable. "This is probably one of the biggest misconduct cases ever," says Fredrick Grinnell, former director of the Program in Ethics in Science at the University of Texas Southwestern Medical Center in Dallas. "Very often [in misconduct cases], it's a young investigator, under pressure, who needs funding. This guy was a very successful scientist."

Poehlman, 49, first came under suspicion in 2000 when Walter DeNino, then a 24-year-old research assistant, found inconsistencies in spreadsheets used in a longitudinal study on aging. The data included energy expenditures and lipid levels for elderly patients. "[V]alues for total cholesterol, insulin, resting metabolic rate, and glucose" were falsified or fabricated, said a statement Poehlman signed. In an effort to portray worsening health in the subjects, DeNino told *Science*, "Dr. Poehlman would just switch the data points."

After DeNino filed a formal complaint, a university investigative panel looked into Poehlman's research and uncovered falsified data in three papers. These included a much-cited 1995 *Annals of Internal Medicine* study that suggested hormone replacement therapy could prevent declines in energy expenditure and increases in body fat during menopause. In that paper, Poehlman presented metabolic data on 35 women taken 6 years apart. Most of the women did not exist, according to the statement Poehlman signed. (In 2003 the paper was retracted.) Poehlman left Vermont in 2001, before the investigation ended, for the University of Montreal. A 2-year review by the Office of Research Integrity (ORI) at the Department of Health and Human Services found more falsified data in another dozen federal grant applications, ORI investigators said.

Colleagues say Poehlman's work was extensive but did not affect underlying assumptions about how the body changes during aging. Richard Atkinson, editor of the *International Journal of Obesity*, said in an e-mail that removing Poehlman's work may reduce the evidence that energy expenditure decreases across time with menopause, but "it does not

invalidate the concept.” Judy Salerno, deputy director of the National Institute on Aging in Bethesda, Maryland, says his work “wasn’t the final answer.”

Journal editors say it’s hard to guard against such misconduct. A rigorous review process can do only so much, says Harold Sox, who became *Annals’* editor in 2001: “You just have to trust the authors.”

**At his sentencing:**

Source: Interlandi, J. (2006, October 22). An unwelcome discovery, *The New York Times Magazine*. Retrieved on 7/18/11 from: <http://www.nytimes.com/2006/10/22/magazine/22sciencefraud.html?pagewanted=1>

“I need to start out by apologizing,” Poehlman said, standing at the lectern before the judge. Speaking quickly and stammering occasionally, he apologized to friends and former colleagues, some of whom were listening in the back of the courtroom. He apologized to his mother, who sat in the front row, crying. And he apologized to Walter DeNino, the former protégé who turned him in, who was also sitting in the courtroom, several rows back on the prosecution’s side.

“I have wanted to say I’m sorry for five years,” Poehlman said, without turning around to face DeNino. “I want to make it very clear I am remorseful. I accept the responsibility. There’s no way that I can turn back the clock. And I’m not that individual that I was years ago.”

Federal sentencing guidelines called for five years in prison based on the amount of grant money Poehlman had obtained using fraudulent data. But no scientist had ever spent time in prison for fabricating data. (One did spend 60 days in a halfway house.)

The sentencing judge was William Sessions, the same judge to whom Poehlman denied all allegations of misconduct at the injunction hearings four years earlier. He told Poehlman to stand and receive his sentence: one year and one day in federal prison, followed by two years of probation.

“When scientists use their skill and their intelligence and their sophistication and their position of trust to do something which puts people at risk, that is extraordinarily serious,” the judge said. “In one way, this is a final lesson that you are offering.”

**Additional Questions to Consider:**

- Colleagues seem ambivalent on the importance of Poehlman’s claims. If his work (either actual or fabricated) had appeared significant would this change the perceptions about his misdeeds? Would the depth of deception or misdirection have affected the verdict and/or sentence?
- Is it possible that just one research assistant was aware of what was happening? Who else should have known and what could they have done about it? Do you know what your options are at MSKCC if you suspect someone of research misconduct?
- Would the knowledge that one could be sent to federal prison affect one’s decision to commit research misconduct? Would it matter if these were not federal monies? Should the punishment be the same regardless of the funding source?
- Do you agree that journal editors “just have to trust the authors?” What, if anything, could journal editors do to prevent them from accepting fraudulent manuscripts?

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## Case Study - Falsification, Data Management, Conflict of Interest, Responsible Publication, Human Subjects

Sources: <http://www.ithenticate.com/plagiarism-prevention-blog/bid/78874/Biggest-Offender-of-Medical-Research-Misconduct-in-History>  
Misconduct in science - An array of errors. (2011 September 10). *The Economist*. Retrieved on April 13, 2012 from:  
<http://www.economist.com/node/21528593> Goldberg, P. (2010, July 23). By defending Potti, Duke officials become target of charges of institutional failure. *The Cancer Letter*. Vol.36. No. 28

In 2010, after five years of research, it was discovered that oncological researcher, **Dr. Anil Potti**, had manipulated the data in a number of his widely distributed papers to prove a theory worked. Potti was considered by many as being at the forefront of ovarian cancer research.

Potti, Joseph Nevins and their colleagues at Duke University in Durham, North Carolina, garnered widespread attention in 2006. They reported in the *New England Journal of Medicine* that they could predict the course of a patient's lung cancer using devices called expression arrays, which log the activity patterns of thousands of genes in a sample of tissue as a colorful picture. A few months later, they wrote in *Nature Medicine* that they had developed a similar technique which used gene expression in laboratory cultures of cancer cells, known as cell lines, to predict which chemotherapy would be most effective for an individual patient suffering from lung, breast or ovarian cancer.

From [the Huffington Post](#):

*"Potti's work in individualized treatments for cancer was regarded as "the holy grail of cancer," Dr. Rob Califf, the vice chancellor of clinical research at Duke, said on a CBS 60 Minutes segment. "Personalized cancer treatments, if they work, could be a last hope for people whose bodies don't respond to the conventional treatments." -*

It was eventually discovered that Potti had falsified information about his education; saying that he was a Rhode Scholar. This was not true and it triggered a further investigation into verification of his research, which turned out to be falsified.

To date, ten papers on individual cancer treatment and related topics have been retracted, five have been corrected and one has been partially retracted ([Retraction Watch](#), April 2012). The blog [Retraction Watch](#) reported that Duke has said about a third of Potti's 40-some-odd papers would be retracted, and another third would have "a portion retracted with other components remaining intact," so this list will continue to grow. Journals to retract his work include *Nature Medicine*, *The Lancet Oncology*, *PLoS ONE* and *Blood*. It's important to point out, that while attention has focused on Potti, he was just one of many authors on these papers.

Because of the fraudulent trials, a group is now filing suit against Duke University: *"Seeking compensatory and punitive damages in the case, alleging that Duke tried to cover up questions about the research and performed unnecessary chemotherapy on people in hopes of patenting and spinning off a cancer-screening test."*

According to *The Economist* (2011 September), Duke's lapses and errors included being slow to deal with potential financial conflicts of interest declared by Dr. Potti, Dr. Nevins and other investigators, including involvement in Expression Analysis Inc. and CancerGuide DX, two firms to which the university also had ties. Moreover, Dr. Califf and other senior administrators acknowledged that once questions arose about the work, they gave too much weight to Dr. Nevins and his judgment. That led them, for example, to withhold criticisms from the external-review committee in 2009. They also noted that the internal committees responsible for protecting patients and overseeing clinical trials lacked the expertise to review the complex, statistics-heavy methods and data produced by experiments involving gene expression.

### Additional Questions to consider:

- Are there greater implications of this misconduct that go beyond data corrections? What about the patients who had already enrolled in clinical trials for treatments?
- Do patients and their families have the right to sue the Institution?
- Do you believe the Institution's alleged financial conflicts of interest guided its decisions as to whether or not to continue the trials, even after doubts were uncovered about the project?
- How can institutions fairly lead misconduct investigations when the institution itself may be culpable?
- What about Potti's co-authors – what culpability do they have for the falsified data? What lessons about collaborations and co-authorship can be learned from this situation?

## Case Study: Fraud, Falsification, Fabrication, Plagiarism, Mentoring

Source – Excerpted from:

Schulz, W. G. (July 11, 2011). Reports Detail a Massive Case of Fraud Misconduct: Documents reveal Bengü Sezen's winding trail of deception. *C&EN*. Volume 89. Number 28. p. 4. Retrieved on 7/15/11 from: <http://pubs.acs.org/cen/news/89/i28/8928notw1.html>

**Bengü Sezen** was found guilty of 21 counts of research misconduct by the federal Office of Research Integrity (ORI). Sezen falsified, fabricated, and plagiarized research data in three papers and in her doctoral thesis. Some six papers that Sezen had coauthored with Columbia chemistry professor Dalibor Sames have been withdrawn by Sames because Sezen's results could not be replicated. The ORI findings back Columbia's own investigation.

The Sezen case began in 2000 when the young graduate student arrived in the Columbia chemistry department. "By 2002, concerns about the reproducibility of her research were raised both by members of the [redacted] and by scientists outside" Columbia, according to the documents, obtained by C&EN through a Freedom of Information Act request. The redacted portions of the documents are meant to protect the identities of people who spoke to the misconduct investigators.

By the time Sezen received a PhD degree in chemistry in 2005, under the supervision of Sames, her fraudulent activity had reached a crescendo, according to the reports. Specifically, the reports detail how Sezen logged into NMR spectrometry equipment under the name of at least one former Sames group member, then merged NMR data and used correction fluid to create fake spectra showing her desired reaction products.

The documents paint a picture of Sezen as a master of deception, a woman very much at ease with manipulating colleagues and supervisors alike to hide her fraudulent activity; a practiced liar who would defend the integrity of her research results in the face of all evidence to the contrary. Columbia has moved to revoke her PhD.

Worse, the reports document the toll on other young scientists who worked with Sezen: "Members of the [redacted] expended considerable time attempting to reproduce Respondent's results. The Committee found that the wasted time and effort, and the onus of not being able to reproduce the work, had a severe negative impact on the graduate careers of three (3) of those students, two of whom [redacted] were asked to leave the [redacted] and one of whom decided to leave after her second year."

In this matter, the reports echo sources from inside the Sames lab who spoke with C&EN under conditions of anonymity when the case first became public in 2006. These sources described Sezen as Sames' "golden child," a brilliant student favored by a mentor who believed that her intellect and laboratory acumen provoked the envy of others in his research group. They said it was hard to avoid the conclusion that Sames retaliated when other members of his group questioned the validity of Sezen's work.

After leaving Columbia, Sezen went on to receive another PhD in molecular biology at Germany's Heidelberg University. At some point during the Columbia investigation, however, Sezen vanished, though some reports place her at Turkey's Yeditepe University. Her legacy of betrayal, observers say, remains one of the worst cases of scientific fraud ever to happen in the chemistry community.

### Additional Questions to Consider:

- Should being found guilty of research misconduct have an impact on whether or not to lose one's degree or prevent one from earning another? Does it matter if the misconduct was perpetrated at the degree granting institution? Why, or why not?
- In your view, does mentor favoritism play a big role in lab personnel dynamics? If so, how can this type of climate be avoided? What mechanisms, policies or resources could be used to create balance and open communication? Had the respondent in this case been an outcast or an insignificant player all along, would this have made a difference in how people reacted?

## Case Study: Fabrication, Fraud, Animal Welfare

Sources: Where are they now? *NATURE MEDICINE* VOLUME 12 | NUMBER 5 | MAY 2006

[http://ccnmtl.columbia.edu/projects/rcr/rcr\\_misconduct/foundation/index.html#1\\_B\\_3](http://ccnmtl.columbia.edu/projects/rcr/rcr_misconduct/foundation/index.html#1_B_3)

[http://www.bme.unc.edu/~bob/scientific\\_misconduct.pdf](http://www.bme.unc.edu/~bob/scientific_misconduct.pdf) "On Being a Scientist", Committee on the Conduct of Science, National Academy of Sciences. National Academy Press, Washington, D.C., 1989, page 15, ISBN 0-309-04091-4

In 1973 **William Summerlin** came to the Sloan-Kettering Institute where he subsequently became chief of a laboratory working on transplantation immunology. For the previous six years, he had been studying the rejection of organ transplants in humans and animals. He believed that by placing donor organs in tissue culture for a period of some days or weeks before transplantation, the immune reaction that usually causes the transplant to be rejected could be avoided.

The work had become well-known to scientists and to the public. However, other scientists were having trouble replicating Summerlin's work. Another immunologist at Sloan-Kettering was assigned to repeat some of Summerlin's experiments, but he, too, could not make the experiments work. As doubts were growing, Summerlin began a series of experiments in which he grafted patches of skin from black mice onto white mice. One morning as Summerlin was carrying some of the white mice to the director of the institute to demonstrate his progress he took a felt tipped pen from his pocket and darkened some of the black skin grafts on white mice.

After the meeting, a laboratory assistant noticed that the dark color could be washed away with alcohol and within a few hours the director knew of the incident. Summerlin subsequently admitted his deception to the director and to others. Summerlin was suspended from his duties and a six-member committee conducted a review of the veracity of his scientific work and his alleged misrepresentations concerning that work. In particular, in addition to reviewing the "mouse incident," the committee examined a series of experiments in which Summerlin and several collaborators had transplanted parts of corneas into the eyes of rabbits. The committee found that Summerlin had incorrectly and repeatedly exhibited or reported on certain rabbits as each having had two human corneal transplants, one unsuccessful from a fresh cornea and the other successful from a cultured cornea. In fact, only one cornea had been transplanted to each rabbit, and all were unsuccessful.

When asked to explain this serious discrepancy, Summerlin stated that he believed that the protocol called for each rabbit to receive a fresh cornea in one eye and a cultured cornea in the other eye. Summerlin subsequently admitted that he did not know and was not in a position to know which rabbits had undergone this protocol, and that he only assumed what procedures had been carried out on the rabbits he exhibited. After reviewing the circumstances of what the investigating committee characterized as "this grossly misleading assumption," the report of the investigating committee stated: "The only possible conclusion is that Dr. Summerlin was responsible for initiating and perpetuating a profound and serious misrepresentation about the results of transplanting cultured human corneas to rabbits."

The investigating committee concluded that "some actions of Dr. Summerlin over a considerable period of time were not those of a responsible scientist." There were indications that Summerlin may have been suffering from emotional illness, and the committee's report recommended "that Dr. Summerlin be offered a medical leave of absence, to alleviate his situation, which may have been exacerbated by pressure of the many obligations which he voluntarily undertook." The report also stated that, "for whatever reason," Dr. Summerlin's behavior represented "irresponsible conduct that was incompatible with discharge of his responsibilities in the scientific community".

### Additional Questions to Consider:

- Did you know about this case, before reading about it here? How do you feel knowing that this happened at our institution? Can you imagine this happening in today's MSKCC research community? Why or why not?
- How does behavior such as this reflect on an institution as a whole? Do you think there are irreparable damages or does "time heal all wounds?"
- Does a case like this cause wonder about whether there are appropriate institutional safeguards and policies in place to prevent this type of behavior and/or to recognize when employees are showing extreme signs of duress or illness? Could this have been prevented? If so, how?

## Case Study: Fabrication, Human Subjects

Source: Source: <http://clinicaltrials.gov/ct2/show/NCT00870506> and <http://www.ori.dhhs.gov/misconduct/cases/Wanchick.shtml>

In 2009, **Jennifer Wanchick**, Research Assistant, MetroHealth System (an affiliated hospital of Case Western Reserve University), by her own admission, engaged in research misconduct by fabricating information in the electronic database purportedly collected from 150 individuals about their willingness to sign up to be an organ donor at the time they obtained a driver's license. Ms. Wanchick also admitted to fabricating the information on several survey instruments.

The study at issue was entitled "Community Based Intervention to Enhance Signing of Organ Donor Cards." The purpose of this study was to determine the effect of a 5-minute video intervention regarding organ donation and transplantation on increasing the number of organ donor cards signed in Northeastern Ohio Bureau of Motor Vehicles (OBMV) branches and on willingness to donate organs while living. The investigators hypothesized that persons in the intervention group would sign more donor cards and be more willing to donate organs while living than persons in the control group.

### Additional Questions to Consider:

- How would you feel knowing that similar survey data fabrication has happened at this institution?
- Should a respondent's cooperation with the investigation have an impact on the verdict? Does her cooperation mitigate the impact of her actions on the research or the reputation of the institution?
- Who are the "victims" of this type of scientific misconduct? Does the fact that this is not a clinical situation, where patient/subject welfare was at stake, make it any less unconscionable?
- Although not stated here - what responsibility, if any, should her supervisors have had for preventing such behavior? What types of policies, procedures or standard operating procedures could be instituted to prevent future instances of this type of misconduct?

### NIH Rigor and Reproducibility: Lack of Transparency

Video from: NIH / NIGMS [Clearinghouse for Training Modules to Enhance Data Reproducibility](#)

#### Starting Points:

- Transparency: accurately and openly providing all key information on the design, execution, and analysis of experiments<sup>1</sup>
- In order to reproduce another's findings adequately, the experimental methods, rationale, and other pertinent information must be accessible and understandable

#### Lead-in Questions:

- Do you think most people knowingly display a lack of transparency or inadequate reporting of methodological details in published papers?
- Do journals have a role in determining this? If so, what do you think their role is to assist investigators? What additional actions could be taken? [Current NIH-involved efforts<sup>2</sup>]

#### Follow-up Questions:

- Can you relate to a similar experience in your own lab?
- Do you think the corresponding author should have handled the situation differently?
- Was there anything the graduate student or PI could have done to determine this without multiple conversations with the corresponding author?
- The corresponding author was very open and transparent with the PI. Do you think this would always be the case?
- In this instance, the PIs had been in communication previously, so it provided Dr. Hansen the opportunity to look for the experimental details. Do you think it is realistic that he would have known specifics about the experiment had this not been the case?
- How would you handle the situation if the corresponding author did not want to provide data or discuss the experiments beyond generalities?
- Would it always be so easy to locate the corresponding author? Alternatively, do you think the corresponding author always would be able to locate the details, particularly if the person who had done the experiments had left their lab and/or if several years had passed since the original paper was published?
- Do you think you or your PI would have been as rigorous about determining why the results weren't reproducible if you encountered a similar situation?
- Would you have made the controls fresh each time or frozen them for reuse, assuming there would be no degradation?
- Was the experiment designed poorly or was it a simple mistake by those in the lab performing the experiments?
- This mistake may seem obvious to any experienced or well-trained scientist, but more subtle differences often can lead to variations in results. With the amount of detail frequently reported in manuscripts, how confident are you that you could determine there were differences in the preparation of the controls?
- How can you be sure that an initial experiment is designed in the most thoughtful and rigorous manner?
- Do you think a set of best practices for developing a methods section would have eliminated or greatly reduced the likelihood of this situation arising?

<sup>1</sup> Landis, et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nature*. 2012 Oct 11; 490(7419): 187–191.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3511845/>

<sup>2</sup> <http://www.nih.gov/about/reporting-preclinical-research.htm>

### NIH Rigor and Reproducibility: Blinding and Randomization

Video from: NIH / NIGMS [Clearinghouse for Training Modules to Enhance Data Reproducibility](#)

#### Starting Points:

- Blinding: keeps the investigators unaware of assigned sample designations (e.g., wild-type vs. mutant, untreated vs. treated) until after completion of the experiment and, if possible, analysis of the results<sup>1,2</sup>
- Randomization: experimental method to reduce bias and minimize the likelihood of chance altering the results of an experiment<sup>3</sup>
- Sample blinding and randomization are key elements to reduce selection and other biases, permit reliable statistical testing, and are critical particularly to the interpretation of preclinical proof-of-concept studies<sup>4</sup>

#### Lead-in Questions:

- Can you think of a particular instance in which blinding and randomization could have a dramatic impact on the results?
- Have you ever blinded and/or randomized samples in your own experiments?

#### Follow-up Questions:

- Here, the reviews state that the paper will be accepted for publication if the authors can demonstrate a particular result, which will increase the paper's significance. Have you ever felt pressure, either from your PI or reviews of a submitted paper, to obtain a specific result?
- Are you aware of the distinction between two types of experimental approaches – hypothesis-driven or discovery-driven? Is one better than the other? What are the advantages and pitfalls of each?
- Was there a general problem here with concepts of randomization and appropriate sample size?
- What specific problems in experimental design and execution can you identify?
- Do you think the PI suggested the best approach to blind and randomize the experiment? Is there an additional element that should have been included? Do you think most PIs would suggest blinding an experiment, unless they had an experience in the past that warranted it?
- In your own lab/department, how willing do you think someone would be to blind samples for you? Should this be a priority for you? How would you randomize samples?
- How realistic is the feasibility of blinding (expertise in the lab, contact with potential blinders)?
- The electrophysiological experiment discussed here was unable to be performed on the two channels simultaneously by the same individual. Do you think there was a better way to test the drug?
- The drug used in this example apparently degrades dramatically over the course of a few hours. This is a property that ideally should have been obvious to the graduate student, Miles, but do you think it's easy to overlook a detail like this?
- If you were in Miles' situation, do you think you or your PI would have discovered that the drug was degrading?
- Would you have confirmed that the drug degraded over time? If so, how? Run a positive control? Let the drug degrade for a period of time (all day) and then do the experiment?
- If the results were what they hoped/expected – in this case, if the mutant showed a greater effect because they recorded from those cells first, do you think they would have thought about drug degradation and explored this further? Would you have done so? (Confirmation bias)

<sup>1</sup> Modified from Schulz, KF and DA Grimes. Blinding in randomized trials: hiding who got what. *Lancet*. 2002 Feb 23; 359(9307): 696-700.

[http://apps.who.int/rhl/LANCET\\_696-700.pdf](http://apps.who.int/rhl/LANCET_696-700.pdf)

<sup>2</sup> Modified from Festing, MFW et al. Guidelines for the design and statistical analysis of experiments using laboratory animals. *ILAR J*. 2002; 43(4): 244-258.

<http://ilarjournal.oxfordjournals.org/content/43/4/244.full>

<sup>3</sup> Modified from Suresh, KP. An overview of randomization techniques: An unbiased assessment of outcome in clinical research. *J Hum Reprod Sci*. 2011 Jan-Apr;

4(1): 8-11. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3136079/>

<sup>4</sup> Unger, EF. All is not well in the world of translational research. *J Am Coll Cardiol*. 2007; 50(8): 738-740.

<http://content.onlinejacc.org/article.aspx?articleid=1138418>

### NIH Rigor and Reproducibility: Biological and Technical Replicates

Video from: NIH / NIGMS [Clearinghouse for Training Modules to Enhance Data Reproducibility](#)

#### Starting Points:

- Replication: requires a precise process where the exact same findings are reexamined in the same way with identical design, power, subject selection requirements, and level of significance as the original research study.<sup>1</sup>
- Biological replicates are parallel measurements of biologically distinct samples that capture random biological variation, which may itself be a subject of study or a source of noise.
- Technical replicates are repeated measurements of the same sample that represent independent measures of the random noise associated with protocols or equipment.<sup>2</sup>

#### Lead-in Questions:

- Within an individual experiment, what do you think is the best approach to determine the appropriate number of replicates?
- How did you learn about the need for replicates and the difference between certain types of replicates?

#### Follow-up Questions:

- Do you think it is common to report data from a single experiment (technical replicates) to generate an “exciting” finding? How often is this type of practice viewed as a way to expedite the research process?
- Since this is a grant application with preliminary results, is it acceptable to include results in such a manner?
- Is it appropriate for the applicant to purposely leave information about the type of replicates out and plot the data in such a way as to suggest significance over multiple experiments? Can it be considered falsification and therefore possible misconduct? If so, what are the potential consequences? What if it was simply an oversight?
- If this was your grant application, how would you have portrayed the data? Would you clearly state the “n” in the figure legend and/or describe this in the body of the grant? Would you have indicated the exclusion of data?
- Do you think papers or grant applications should delineate the use of biological vs. technical replicates in the figure legends (or elsewhere in the document)?
- The reviewer provides an analogy of “taking a thousand cells from one animal” and getting “just one point” from the resulting data. Is this always the case?<sup>3</sup>
- Do you think the review of the project will be affected?
- Do you think a typical review session discussing this issue would be as collegial?
- The reviewers appeared to be convinced easily that the figure was misleading. Do you think this transition in thought would have been so quick and painless if it were a real review session?

<sup>1</sup><http://grants.nih.gov/grants/guide/pa-files/PAR-13-383.html>

<sup>2</sup><http://www.nature.com/nmeth/journal/v11/n9/full/nmeth.3091.html>

<sup>3</sup>Aarts, E et al. A solution to dependency: using multilevel analysis to accommodate nested data. *Nature Neuroscience*. 2014 April; 17(4): 491-496.  
<http://www.nature.com/neuro/journal/v17/n4/full/nn.3648.html>

### NIH Rigor and Reproducibility: Sample Size, Outliers, and Exclusion Criteria

Video from: NIH / NIGMS [Clearinghouse for Training Modules to Enhance Data Reproducibility](#)

#### Starting Points:

- Sample: here, a sample is defined as a single value or observation from the larger set of values
- Sample size: the optimal number of samples that should be used to reach sufficient statistical power; also referred to as 'n'
- Outliers: an observation that lies an abnormal distance, typically +/- 3 standard deviations, from other values in a random sample from a group of results<sup>1</sup>
- Exclusion criteria: standards set out before a study or review to determine whether a sample should be included or excluded from the study or analysis<sup>2</sup>
- Characterization of "normal" for a specific experiment is an important component to identifying outliers and determining exclusion criteria

#### Lead-in Questions:

- Do you have a standard approach to determining the appropriate sample size and setting criteria for outliers – how you determine the numbers that go into your power analysis?
- How do you know what "normal" is if you don't know the result? Can you do this initially? Will determination of the best statistical method and approach be useful in defining normal?

#### Follow-up Questions:

##### *Lab Management*

- Can you relate to this situation – not being able to generate similar results, whether from unpublished data in your own lab or a published paper?
- Have you ever tried to replicate someone's experimental approach and discovered that information was missing in their lab notebook? Did you feel as though you needed a "Rosetta Stone" to decrypt their handwriting/abbreviations?
- Do you maintain a thorough laboratory record? If so, what methods do you follow to ensure that your lab notebook is comprehensive?
- Do you think an electronic lab notebook would have helped identify the issue(s) faster? What characteristics would the electronic lab notebook need to have?

##### *Statistical Methods and Issues*

- Have you ever had data that was "close" to significance? If so, what did you do? How did you interpret these results?
- Would Dr. Fielding (Harry) have suggested adding a few more samples and trying a different statistical test if they had initially defined their sample size and exclusion criteria, and identified the most appropriate statistical approach?
- Jamal told Robin to drop outliers above a certain value, as it is outside the physiologic range. Do you think this should have been considered further when they established their exclusion criteria? Do you think they actually developed exclusion criteria, or just considered that point as valid (potentially, without confirming) and made it their sole criteria for determining outliers?

##### *Other Issues*

- Do you think Dr. Fielding was too hard on Robin? Was there a more appropriate and effective approach that he could have taken when Robin was struggling to replicate Donna's results?
- Is it realistic to think that most PIs would admit they provided inadequate guidance?
- Do you also think most PIs would take the time to review the lab notebooks themselves to determine what may be causing the discrepancy in the results?

##### *Sex as a Biological Variable*

- One of the fundamental variables in preclinical biomedical research is sex: whether a cell, tissue, or animal is female or male.<sup>3</sup> Do you generally consider sex as a variable when designing experiments?
- Have you or someone you know only used male mice in an experiment as a way of avoiding the "sex issue?" Do you think this is appropriate? Does it depend on the type of experiment being done?
- Can an experiment be considered rigorous if sex is not considered?
- A commonly used example advocating for the consideration of sex as a biological variable in research is the zolpidem (Ambien) dosage that was amended in 2013. The drug was found to affect men and women differently, which resulted

in a decrease in the recommended dosage for women<sup>4</sup>. Would this have occurred if sex was considered in the preclinical and clinical experiments?

<sup>1</sup> National Institute of Standards and Technology, Engineering Statistics Handbook (7.1.6) <http://www.itl.nist.gov/div898/handbook/prc/section1/prc16.htm>

<sup>2</sup> Modified from the Agency for Healthcare Research and Quality Glossary of Terms <http://effectivehealthcare.ahrq.gov/index.cfm/glossary-of-terms/?pageaction=showterm&termid=105>

<sup>3</sup> NIH Office of Research on Women's Health <http://orwh.od.nih.gov/news/scientificseminars.asp>

<sup>4</sup> <http://www.fda.gov/Drugs/DrugSafety/ucm352085.htm>; <http://abcnews.go.com/Health/fda-recommends-slashing-sleeping-pill-dosage-half-women/story?id=18182165>