Complying with Federal Regulations on Research Misconduct

Randy Mason
Vice President, Research Operations
Institutional Official for Research
Beth Israel Deaconess Medical Center
Boston, MA

Agenda

- BIDMC Background
- Case Studies
- Current Events
- The Regulations
- Office of Research Integrity
- The Process
- Frequency and Cost

June 4, 2012
BIDMC Facts & Figures

- Major teaching hospital of Harvard Medical School
- $1.4B annual revenue
- 600 licensed beds
- ~5,000 births a year
- 41,864 Inpatient Discharges
- 537,014 Outpatient Visits
- 55,771 Emergency Department Visits
- 1,200 physicians on active medical staff
- #3 recipient of NIH research funding of independent hospitals

Facts and Figures

- For the 10th time – and the sixth in seven years – Beth Israel Deaconess Medical Center has been named one of the Top 100 Hospitals in the United States based in overall organizational performance, the only Boston hospital cited in the annual study released by Thomson Reuters*.

* Thomson Reuters researchers evaluated 2,886 short-term, acute care, non-federal hospitals
How the Harvard Model Differs

- Research is typically awarded to and administered by Universities and Medical Schools, not hospitals.
- In the Harvard medical system, hospitals are free-standing, financially independent entities that “own” and manage their own research portfolios, in addition to those of the medical school and university.
- Separate and distinct research admin staff, systems, policies, structures.

BIDMC Research

- $271M revenue in FY11, ~20% of medical center
- 250 key Principal Investigators
- 1600 other research faculty, fellows, technicians and students
- 240 research administrative staff
- 400,000 NASF of research space under management
- 1575 human subject protocols processed
- 375 active animal protocols underway
Misconduct Experience

- VP of Research Operations serves as Institutional Official (IO) for human, animal programs as well as Research Integrity Officer (RIO)
- In conjunction with Harvard Medical School, pursued 5-10 initial allegations of scientific misconduct in FY11

Landmark Cases

Dr. Eric T. Poehlman, University of Vermont (2000-2005)
- Barred for life from seeking or receiving funding from any federal agency in the future
- Agreed to pay $180,000 to settle a civil complaint related to numerous false grant applications
- Sentenced to a year and a day in prison
Landmark Cases

- Dr. Luk Van Parijs (2009)
  - Former Graduate Student, Department of Pathology, HMS
  - Former Research Fellow and Instructor of Pathology, BWH
  - Former Postdoctoral Fellow, Department of Biology, CalTech
  - Former Associate Professor, Department of Biology, MIT
- Engaged in scientific misconduct in research supported by:
  - National Institute of Allergy and Infectious Diseases (NIAID) grants U19 AI56900, R21 AI49897, R01 AI42100, P01 AI35297, R37 AI25022, R01 AI32531
  - National Cancer Institute, grant R01 CA51462
  - National Institute of Environmental Health Sciences (NIEHS) grant P30 ES02109
  - National Institute of General Medical Sciences (NIGMS) grant R01 GM57931

Specifically, PHS found that Respondent engaged in scientific misconduct by including false data in seven published papers, three submitted papers (with two earlier versions submitted for one of these), one submitted book chapter, and multiple presentations.
- Fired from MIT
- February 2011 US authorities filed criminal charges in US District Court in Boston
- Sentenced to 6 months house arrest, community service, financial restitution
Recent Issues

- Researchers often fail to report relevant clinical trial data
- “We are not dealing here with trial design, hidden bias or problems of data analysis—we are talking simply about the absence of the data,” the authors wrote. This behavior, in turn, biases research, wastes health care resources and may harm patients, the editorialists said.
- “Moreover, researchers or others who deliberately conceal trial results have breached their ethical duty to trial participants,” they wrote.

Recent Issues

- Investigators showed that the addition of unpublished data to published meta-analyses of drug trials often changed the results (BMJ 2012;344:d7202).
- Study researchers integrated previously unpublished data into existing meta-analyses of nine FDA-approved drugs
- The recalibrated trial data produced identical estimates of drug efficacy in three of 41 cases (7%), but 46% greater and 46% lower drug efficacy in the remaining 38 cases (19 for each).
Retractions On the Rise

A study of the PubMed database found that the number of articles retracted from scientific journals increased substantially between 2000 and 2009.

- Fraud or fabrication: 196 total
- Scientific mistake: 235 total
- Other: 311 total

Call for Reform

“The current hypercompetitive environment has created an insecure working environment for scientists, fostered poor scientific practices, including frank misconduct, and created widespread disillusionment throughout the scientific community, from trainees to senior investigators.”

Reforming Science: Structural Reforms. Ferric C. Fang, Editor in Chief, Arturo Casadevall, Editor in Chief, mBio
The Regs

- 42 CFR Part 93 Public Health Service Policies on Research Misconduct
- The proposed part 93 was published for public comment on April 16, 2004
- Final rule became effective June 16, 2005.

The Regs

- Any institution that applies for or receives Public Health Services (PHS) support for biomedical or behavioral research, research training or activities related to that research or research training are subject to ORI’s guidelines defining and enforcing research misconduct.
- Many institutional policies are agnostic to funding source.
### The Regs

Activities applicable to ORI guidelines include:

- Grant applications or proposals;
- Research training or activities related to that research or research training and training programs;
- Activities related to research or research training, such as the operation of tissue and data banks or the dissemination of research information;
- Plagiarism of research records produced in the course of PHS supported research, research training or activities related to that research or research training.”

(DHHS 2005)

### Scientific Misconduct

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

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

(b) **Falsification** is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

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

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

- Research Integrity Officers (RIOs) are institutional officials who have responsibilities related to the handling of allegations of research misconduct involving biomedical or behavioral research or research training supported by the Public Health Service (PHS).
- ORI Sample P&P has a (three page!) list of RIO responsibilities
- “Don’t be a friend, don’t be a bureaucrat”
Video – Role of the RIO

http://ori.hhs.gov/video-role-rio

Office of Research Integrity

- Mission
- Mindset
- Website
- Videos
- Sample Misconduct Policy
- Newsletter
Office of Research Integrity

Director reports to the Secretary of HHS; and will:

1. Direct Public Health Service (PHS) research integrity activities on behalf of the Secretary *with the exception of the regulatory research integrity activities of the FDA*;

2. Recommend …findings of research misconduct and administrative actions in connection with research conducted or supported by the PHS;

3. Coordinate the development of research integrity policies designed to ensure that subjects of investigations and whistleblowers are treated fairly…;

4. Oversee and direct the research misconduct and integrity activities of the office, including the oversight of research misconduct inquiries and investigations, education and training in the responsible conduct of research, activities designed to promote research integrity and prevent misconduct, and research and evaluation programs.

ORI Statement

- “Responding to an allegation of research misconduct tends to be a unique rather than a routine event at most institutions. Few institutions have any significant experience in responding to allegations, and the uniqueness of the event makes it difficult for an institution to develop expertise in conducting inquiries and investigations.”

* ORI home page
The Process

- **Preliminary Assessment**
  - Authorship dispute? HR matter? Sufficient evidence to proceed?

- **Inquiry**
  - A preliminary evaluation of the available evidence and testimony of the respondent, whistleblower, and key witnesses to determine whether there is sufficient evidence to warrant an investigation.
  - The purpose of the inquiry is not to reach a final conclusion about whether misconduct definitely occurred or who was responsible.
  - The findings of the inquiry should be set forth in an inquiry report.
Video – Responding to an Allegation

http://ori.hhs.gov/video-role-rio

The Process

• Investigation
  • Explore in detail the allegations, examine the evidence in depth, and determine specifically whether misconduct has been committed, by whom, and to what extent.
  • Will also determine whether there are additional instances of possible misconduct that would justify broadening the scope beyond the initial allegations.
The Process

• A finding of research misconduct made under Sec. 93.104 requires that
  (a) There be a *significant departure from accepted practices* of the relevant research community; and
  (b) The misconduct be committed intentionally, knowingly, or *recklessly*; and
  (c) The allegation be proven by a *preponderance of the evidence*.

• Findings of the investigation need to be set forth in an investigation report that is submitted to ORI for oversight review.

The Process

• Institutional Decision
  • Final decision made by the institution’s Deciding Official (usually Dean / CEO)
  • Notification to both the respondent and the complainant (courtesy – no facts)
  • Notification to other agencies, journals, societies, collaborators, sponsors, etc.
  • Implementation of actions
The Process

- ORI/HHS Decision, Actions
  - ORI reviews the report for timeliness, objectivity, thoroughness, and competence
  - If in agreement, ORI may negotiate with the respondent a Voluntary Exclusion Agreement (VEA) or make a finding of research misconduct and recommend imposition of administrative actions to HHS
  - Actions include but are not limited to:
    - Debarment from eligibility to receive Federal funds, prohibition from service on PHS committees, certification of data by institution, imposition of supervision by the institution, submission of correction / retraction of published articles by respondent

Public Notification


Findings of Research Misconduct

Notice Number: NOT-OD-12-104

Key Dates

Issued by
Department of Health and Human Services (2/21/11)

Purpose

SUMMARY: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Peter J. Francis, M.D., Ph.D., Oregon Health Sciences University. Based on the report of an investigation conducted by Oregon Health Sciences University (OHSU) and additional analysis conduct

Respondent claimed that after the conduct of [22] described PPE cells 21 days postinfection, the cells were killed at the 55 control patient sample, and that the pathologic injury of host tissues cells, comparisons to necrotic control, showed enhanced photodsonogram preservation and no adverse effects. Respondent admitted that this experiment had not been conducted either by the grant application has been submitted or by the time the later-R01 (19825274-1-1) application was submitted.

Dr. Francis has entered into a Voluntary Settlement Agreement (VSA) and has voluntarily agreed for a period of 2 years, beginning on March 16, 2012.
The Process

- Department of Justice / US Attorney General becoming more interested in misconduct cases
- Respondents prosecuted via the False Claims Act for false statements made against the Federal government
- Consider use of “attorney – client privilege”, outside counsel?

Responses

- Journals have become much more sophisticated in their analysis of submitted manuscripts
- Tools for analysis are much more widely used and accessible to the public.
- As such, becoming more common for journals or the wider scientific community to identify potential integrity issues.
Responses

• Journal of Cell Biology (JCB) has one full-time employee checking the figures of every paper accepted in the journal, looking for digital traces of manipulation.
• As many as 50% of papers require at least one figure to be redone because it did not conform to standards.
• In about 10–15% of cases the authors are asked to send in original data for checking.
• In about 1% (roughly 35 papers in the 10 years JCB that has been looking), efforts to manipulate are so egregious that acceptance of the paper is revoked.

Nature News Blog
The new gatekeepers: reducing research misconduct
21 Mar 2012 | 06:26 GMT | Posted by Brendan Maher

Responses

• An anonymous whistleblower created a YouTube video that details alleged duplication of images by a prominent Japanese scientist.
• 6-minute video presents a series of still shots of over 60 allegedly duplicated and manipulated images in 24 papers  http://youtu.be/FXaOqwanWnU
• Whistleblower has created separate Web sites for half a dozen cases in Japan of alleged scientific misconduct; January 2012 posted details of an allegation of image manipulation by researchers at a U.S. institution (MD Anderson)
Why is This So Difficult?!?

Research on Research Integrity

Under What Conditions Are Researchers Likely to Engage in Research Misconduct?

- Pressure For Grants/Funding: 626 (17.5%)
- Advancement/Money/Career/Tenure/Promotion: 487 (13.6%)
- Pressure For Publication: 427 (12.0%)
- Pressure For Results/To Produce: 253 (7.1%)
- Competitive/Ambition/Pressure To Succeed: 235 (6.6%)
- Pressure (Other): 216 (6.1%)
- Positive/Specific Results Needed: 198 (5.5%)

Total: 3569 (100%)

Note: 1789 scientists provided one or more responses.

Research on Research Integrity

Mentoring and Research Misconduct: An Analysis of Research Mentoring in Closed ORI Cases

- Explored the role of the mentor in the cases of trainee research misconduct on three specific behaviors that we believe mentors should perform with their trainee: (1) review source data, (2) teach specific research standards and (3) minimize stressful work situations.
- Found that almost three quarters of the mentors had not reviewed the source data and two thirds had not set standards.
- Important for mentors and institutions to devote more attention to teaching mentors about the process of education and their responsibilities in educating the next generation of scientists.

Science and Engineering Ethics
Volume 14, Number 3 (2008), 323-336. D. Wright et al

Research on Research Integrity

Truth and Consequences:
ORI officials estimate that between a third and half of nonclinical misconduct cases—those involving basic scientific research—are brought by postdoctoral fellows or graduate students like those in Goodwin’s lab. And the ones who come forward, admits ORI’s John Dahlberg, often suffer a “loss of time, loss of prestige, [and a] loss of credibility of your publications.”

Science 1 September 2006: Vol. 313 no. 5791 pp. 1222-1226
DOI: 10.1126/science.313.5791.1222
The $ Costs of Misconduct

Summary Points

- The consequences of scientific misconduct are far-ranging and the costs associated with their investigation are substantial.
- It is possible to estimate the cost (direct and indirect) of investigating a single case of scientific misconduct.
- For a specific investigation for which costs were estimated for all phases of the review process, direct cost estimates approached $525,000.


Thank You

Randy Mason
Vice President, Research Operations
Institutional Official for Research
Beth Israel Deaconess Medical Center
Boston, MA
rmason@bidmc.harvard.edu