Everyday Practices that Compromise Integrity in Research & How to Respond to Them

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Goals:

✓ Brief history of research misconduct
✓ How to think about responsibilities in research
✓ Brief summary of important areas

Lessons

✓ Responsibility is often more complicated than we assume
✓ Best option: confront problems/dilemmas before they become problems/dilemmas

Break-out sessions

✓ Essential elements in a code of best practice for research
Case study

2006 Study (NEJM)

- Cancer early detection study
- CT scan vs. X-ray
- With CT, 80% of cases could be cured

Support for research:

- Supported in part by the National Institutes of Health (R01-CA-633931, to Dr. Henschke, and R01-CA-78905, to Dr. Yankelevitz); the Department of Energy (DE-FG02-96SF21260, to Dr. Markowitz); the Department of Defense to Dr. Tockman; Department of Health and Mental Hygiene of the City of New York; New York State Office of Science, Technology, and Academic Research; American Cancer Society; Israel Cancer Association; Starr Foundation; New York Community Trust; Rogers Family Fund; Foundation for Lung Cancer: Early Detection, Prevention, and Treatment; Foundation for Early Detection of Lung Cancer; Dorothy R. Cohen Foundation; Research Foundation of Clinic Hirslanden; Clinic Hirslanden; Swedish Hospital; Yad-Hanadiv Foundation; Jacob and Malka Goldfarb Charitable Foundation; Auen–Berger Foundation; Princess Margaret Foundation; Tenet Healthcare Foundation; Ernest E. Stempel Foundation, Academic Medical Development; Empire Blue Cross and Blue Shield; Eastman Kodak; General Electric; Weill Medical College of Cornell University; New York Presbyterian Hospital; Christiana Care Helen F. Graham Cancer Center; Holy Cross Hospital; Eisenhower Hospital; Jackson Memorial Hospital Health System; and Evanston Northwestern Healthcare.

“No potential conflict of interest relevant to this article was reported.”
Conflicting interests

March 28, 2008 NY Times*

☑ Did not report study funded by Tobacco company
  ▪ Vector Group (Liggett) ➔ $$$ ➔ Early Screening Foundation

☑ Did not report held patents on CT-scan-related technology
  ▪ Impact/profit: 48M former smokers / 40M current smokers (US)

☑ Did not report others with role in Early Screening Foundation
  ▪ Dean & Vice-Chair Board of Overseers, Weill Cornell Medical College
  ▪ Other researchers

What decisions could the funding have influenced?

☑ PI and co-PIs interpretation of result—smoking-related lung cancer can be cured

☑ Conflict of Interest Committee, which presumably approved

☑ Financial Office, which oversaw mixing of funds

☑ Dean’s agreement to accept

☑ Medical School’s policies on accepting grant funds

Does funding impact research results?

*see also Paul Goldberg, Cancer Letter Inc. (2008)
Impact of financial interests

Bekelman (2003), *JAMA*

- Meta-analysis of 37 COI studies (1,000s of trials)
- Positive correlation (3.60 OR), industry sponsorship & positive outcomes

Lexchin (2003), *BMJ*

- Meta-analysis of 30 COI studies
- Positive correlation (4.05 OR), industry sponsorship & positive outcomes

Friedman (2004)

- 398 publications, *NEJM* and *JAMA*
- Correlation (2.35-2.64 OR), industry/positive outcomes

Conclusion: Funding does affect research findings
Correcting the record…

**NEJM response (early April):**
- Two “corrections by authors”
  - COI revision: Vector provided “virtually all of the Foundation’s funding”
  - Financial conflict amended to include conflict

**Weill Cornell Medical College statement**
- WCMC takes seriously the need for transparency and integrity in research and the protection of patients who participate in research studies, and has policies and procedures in place to ensure the highest degree of integrity in the research conducted at WCMC.

**Question:**
- Did the policies ensure integrity and protect patients?
- Does this case reflect efforts to ensure “highest degree of integrity”? 
RCR, FFP (Misconduct), and QRP

Practices that deviate from RCR:

✓ Questionable research practices (QRP)
✓ Research Misconduct (FFP)
Researchers’ approach to misconduct

- Misconduct emerged as issue in late 1970s

Community reaction to the situation:

- Serious misconduct is rare
- Self-regulation keeps in check
- Misconduct is difficult to detect
- Misconduct cannot be prevented
- Apart from misconduct, standards for integrity in research are high

Reaction based on hypothesis & “experience”

- Supporting evidence was weak, absent, or contradictory
- Recent research suggests most of the early assumptions were inadequate or wrong
Definition of misconduct has narrowed

- Serious deviation from accepted practice ... to
- FFP that deviates from accepted practice

Evidence of scope of misconduct has broadened

- 1980s, major cases dominated the news and policy making
- Today, other “questionable research practices” recognized
Changing definition of Misconduct

1986-HHS:
✓ (1) serious deviation, such as fabrication, falsification, or plagiarism, from accepted practices in carrying out research or in reporting the results of research; or (2) …

1987 NSF:
✓ (1) fabrication, falsification, plagiarism, or other serious deviation from accepted practices in proposing, carrying out, or reporting results from research; (2) …

2000 OSTP
✓ Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results
✓ [must be a] significant departure from accepted practices of the relevant research community
Shift to proactive approach ~ training

- 1980s, RCR assumed, no special training needed
- 1989, first national recommendation:
  - IOM, *The Responsible Conduct of Research in the Health Science*
- 1989, first required training:
  - NIH/ADAMHA Training Grant Requirement
  - Recommended cover six key areas (1994)

Impact
- Increase in number of courses and web programs
- Development of an “RCR community”
- Increase in resources: textbooks, course outlines…
Effort peaks in 2000

  - All PHS-funded research
  - All research staff
  - 9 core areas
- NSF required RCR on IGERT awards
  - Must include: “instruction in ethics and the responsible conduct of research”
- 2007 America Competes
  - NSF must provide RCR and mentoring

**Core Areas**
1. Data acquisition, management, sharing, and ownership
2. Mentor/trainee responsibilities
3. Publication practices and responsible authorship
4. Peer review
5. Collaborative science
6. Human subjects
7. Research involving animals
8. Research misconduct
9. Conflict of interest and commitment

RCR suspended

suspended

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Current assessment of research behavior

- Misconduct ~ 0.1% <-> 1%
- QRP ~ 10% <-> 50%
- High or highest standards??

Graph showing frequency and integrity with QRP and FFP/RCR categories.
Flagrant cases are well known

- Flagrant misbehavior = misconduct = FFP
  - Fabrication, falsification, & plagiarism
- FFP have significant short-term impacts
  - Damages the image of science/research
  - Waste funds & time (€ 10s M/case)
  - Undermines validity
- Long-term impact less significant
  - Are caught & the record corrected
  - Occasional fines & penalties
- Covered by both University & Federal regulations
- Some protection for whistleblowers
What is known about prevalence?

**Scientists behaving badly**
To protect the integrity of science, we must look beyond falsification, fabrication and plagiarism, to a wider range of questionable research practices, argue Brian C. Martinson, Melissa S. Anderson and Raymond de Vries.

** Martinson, Nature (June 2005)**
- **Goal:** factors that influence research behavior
- **Method:**
  - Developed peer-based list of major offenses
  - Survey to 6,000+ researchers (3,000+ response)
  - Major question: “have you done ... in last three years?”

**Results**
- Major offenses, ca. 0.3%
- Questionable Research Practices (QRP) ca. 5-15% or higher
Studies continued

- **Gardner, Contemporary Clinical Trials (2005)**
  - Authors pharmaceutical clinical trials (64% response)
  - 1% reported target article misrepresented the research
  - 5% reported fabrication in a study they had participated in over the last 10 years
  - 17% knew personally of fabrication in a study over the last 10 years

- **Rossner, Journal of Cell Biology**
  - 11 in 1,100 papers had serious improper digital image manipulation

Research misconduct more common than generally admitted

- between 1/1,000 and 1/100
QRP may be more important

- Can have devastating consequences
  - Improper and unreported conflicts
  - Improper literature review
  - Poor design and/or review

- At a minimum, costly and wasteful
  - Geoffrey Chang retraction
    - Lab did not check work carefully
    - Editors & funders ignored reviewers
    - Who more important than what

- FFP vs. QRP
  - FFP more visible, receives most attention
  - QRP more common / more impact
Martinson study

Ten Top Behaviors

1. Falsifying or ‘cooking’ research data
2. Ignoring major aspects of human-subject requirements
3. Not properly disclosing involvement in firms whose products are based on one’s own research
4. Relationships with students, research subjects or clients that may be interpreted as questionable
5. Using another’s ideas without obtaining permission or giving due credit
6. Unauthorized use of confidential information
7. Failing to present data that contradict one’s own previous research
8. Circumventing certain minor aspects of human-subject requirements
9. Overlooking others' use of flawed data or questionable interpretation
10. Changing the design, methodology or results of a study in response to pressure from a funding source

*Martinson et al., Nature 435 (5 June 2005)
Diagnosis by researchers

Practices likely to occur & adversely impact research*

- 83% Over-interpretation of “significant” findings in small trials
- 80% Selective reporting based on p-values
- 76% Selective reporting of outcomes in the abstract
- 75% Subgroup analyses done without interaction tests
- 68% Negative or detrimental studies not published
- 68% Putting undue stress on results from subgroup analysis
- 64% Inappropriate subgroup analyses
- 64% Selective reporting of (i) subgroups (ii) outcomes (iii) time points
- 60% Selective reporting of positive results/omission of adverse events
- 60% Failure to report results or long delay in reporting
- 59% Post-hoc analysis not admitted
- 56% Giving incomplete information about analyses with non significant results
- 54% Analysis conducted by the sponsor of the trial

*Al-Marsouki, Contemp Clin Trials 26(2005)
Duplicate publication

Garner, Nature 2008

\[ \frac{14}{1,000} \times 400,000 = 5,600 \text{ suspected, 2005} \]
\[ 4,000/\text{article} \times 5,600 \text{ duplicates} = 22,400,000 \]
Duplicate publication

Garner, Nature 2008

\[ \frac{14}{1,000} \times 400,000 = 5,600 \text{ suspected, 2005} \]
\[ \times $4,000 \text{/article} \times 5,600 \text{ duplicates} = $22,400,000 \]
Other problems in publications

- **Ghost and honorary authorship**
  - Person who wrote the paper is not listed
  - Person who is listed did not contribute to the article

- **Bias in abstracts and reviews:**
  - Abstracts oversell results, ignore deficiencies
  - Reviews favor reviewer’s speciality or country

- **Review bias**
  - Established researchers get more favorable reviews
  - Institutional importance impacts reviews

- **Peer Review Congresses major impetus**
  - Article: *JAMA*, June 5, 2002
Citation errors

- Inaccurate information/claim in notes
  - Grouped as major and minor (or)
  - Citational vs. quotational
  - Pre-2000, rates ranged from >10% to <30%

- Recent findings:

<table>
<thead>
<tr>
<th>Field</th>
<th>All</th>
<th>Major</th>
</tr>
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<tbody>
<tr>
<td>Otolaryngology (2000)</td>
<td>37.5</td>
<td>11.9</td>
</tr>
<tr>
<td>Primary Care/AIDS (2003)</td>
<td></td>
<td>3% / 8%</td>
</tr>
<tr>
<td>Manuel Therapy (2004)</td>
<td></td>
<td>20 to 59% citational</td>
</tr>
</tbody>
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- Rate appears high & constant
Rule-based decisions

❖ Must follow
✓ National regulations
✓ State regulations
✓ Institutional regulations
✓ Journal policies

❖ Should follow
✓ Guidelines
✓ Commonly accepted practices
✓ Laboratory policies

Do not expect rules and regulations to answer all questions
Diverse standards for responsible behavior

Nine core areas:

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<thead>
<tr>
<th>Misconduct</th>
<th>Collaboration</th>
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<tbody>
<tr>
<td>Human subjects</td>
<td>Mentoring</td>
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<tr>
<td>Animal subjects</td>
<td>Publication</td>
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<tr>
<td>Conflict of Interest</td>
<td>Peer review</td>
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<tr>
<td>Data management</td>
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Other areas

<table>
<thead>
<tr>
<th>Lab safety</th>
<th>Biohazards</th>
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<tr>
<td>Grant management</td>
<td>Radioactive materials</td>
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<tr>
<td>Workplace rules</td>
<td>Stem cells</td>
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<td>IT rules</td>
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☑ Rules are complicated & sometimes conflict
Your role in fostering integrity?

- Know and understand your responsibilities
- Follow best practices
- Ask if you are not sure something is proper
- Do not ignore problems
- Do not do something just because “everyone does it that way”

- Report misconduct and questionable practices
Reporting is not easy

Experience of clinical trial coordinators*

✓ 18.3%, first-hand knowledge of misconduct prior year
  ▪ 21.9% in academic settings
✓ Competitiveness and funding pressures, major cause
✓ Perceptions of prevalence
✓ Coordinator response?
  ▪ 10.4% do nothing
  ▪ 37.3% object to PI but not report
  ▪ 26.7% ask PI to report report if did not
  ▪ 25.7% report to appropriate authority

Failure to take responsibility (to report) is a major problem in research today

<table>
<thead>
<tr>
<th>Misbehavior</th>
<th>Often</th>
<th>Some</th>
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<tbody>
<tr>
<td>Plagiarism</td>
<td>.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Falsifying</td>
<td>.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Enrollment violations</td>
<td>1.2</td>
<td>7.5</td>
</tr>
<tr>
<td>Procedure violations</td>
<td>1.2</td>
<td>9.1</td>
</tr>
<tr>
<td>Selective dropping data</td>
<td>.7</td>
<td>3.7</td>
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Developing responsible practices

Fundament values of UC

- The University of Cincinnati is dedicated to maintain the integrity of the research enterprise as well as openness to public scrutiny, and expects its scholars to be honest and conduct their research with the highest standards and integrity. (Conflict of Interest Policy)
- At its core, academic integrity requires honesty. This involves giving credit where it is due and acknowledging the contributions of others to one's own intellectual efforts. It also includes assuring that one's own work has been completed in accordance with the standards of one's course of discipline.

Next step, define best practices
Discussion assignment

**Assignment one.** Develop a prioritized (1, 2, 3… in order of importance) list of simple rules or best practices for the responsible conduct of research that could be posted in any research setting.

- Cover all aspects of research: planning, conducting, reporting, reviewing ....
- Be brief; for posting on a door or wall.

**Assignment two.** Do best practices differ fundamentally from field to field or could one set of best practices be developed to cover all research undertaken at the University of Cincinnati?

- “Fundamental” = change methods and content of science
- Order of authors is a “custom,” not fundamental
For more information...

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