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# What Constitutes Responsible Conduct of Research?

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The Responsible Conduct of Basic and Clinical Research  
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# From ethics to integrity

- **Post World War II, questions about research ethics.**
  - ✓ **Issues:**
    - **Ethical** & humane treatment of animals
    - **Ethics** of human experimentation
  - ✓ **Characteristic publications:**
    - “An **ethical** code for researchers” (Pigman, 1950)
    - “**Ethics** of scientists” (Cranberg, 1968)
- **1980s, shift to emphasis on integrity**
  - ✓ **Integrity** in science (Branscomb, 1985)
  - ✓ The **integrity** of the scientific literature (Stewart, 1987)
  - ✓ Ensuring **integrity** in biomedical publication (Woolf, 1987)
- **Late 1980s, establishment of government “integrity” offices**
  - ✓ Office of Scientific **Integrity**, HHS
  - ✓ Office of Scientific **Integrity** Review, HHS
  - ✓ National Science Foundation, Inspector General

**1992 ~ Office of  
Research Integrity**

# From fraud to misconduct

## ☛ 1970s emphasize criminal side of bad behavior

- ✓ “**Cheating** in science” (St. James-Roberts, 1976)
- ✓ “**Fraud** in science” (Weinstein, 1979)
- ✓ “**Fraud** and the structure of science” (Broad, 1981)
- ✓ “**Fraud** in Biomedical Research” (US Congress, 1981)

## ☛ 1980s, begin “soften” terminology

- ✓ “NIH grapples with **misconduct**” (Broad, 1982)
- ✓ “**Scientific misconduct**: Institutional procedures and due process considerations” (Olswang, 1983)

## ☛ Outcome = “Research **Misconduct** Policies”

- ✓ Cover worst offenses ~ fabrication, falsification, plagiarism
- ✓ Emphasize intent; exclude sloppiness & disagreement
- ✓ Left door open to “other” offenses

# Emergence of RCR

- Conflict of interest
- Responsible authorship
- Policies for handling misconduct
- Data management
- Human and animal subjects

## ☛ 1989

- ✓ Institute of Medicine, *The Responsible Conduct of Research in the Health Science*

## ☛ 1989

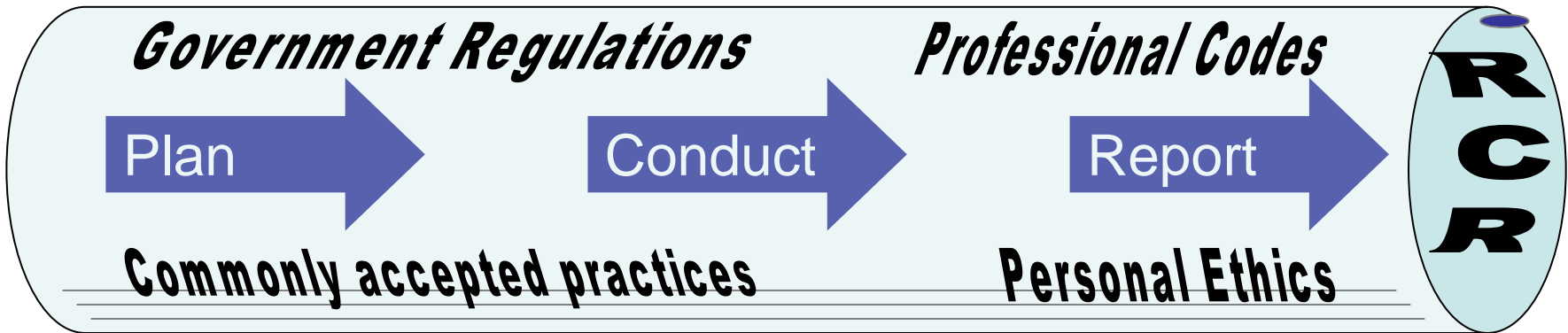
- ✓ National Institutes of Health, Training Grant Requirement
- ✓ Recommended cover six key areas (1994):

## ☛ Impact

- ✓ Increase in number of courses and web programs
- ✓ Development of an “RCR community”
- ✓ Increase in resources: textbooks, course outlines...

# RCR

## Responsible Conduct of Research



Practices that deviate from RCR:

- ✓ Questionable research practices (QRP)
- ✓ Research Misconduct (FFP)

# RCR, RI, and RE

- Responsible Conduct of Research (RCR)

...conducting research in a way that fulfills the professional responsibilities of scientists and contributes to the perpetuation of science as a social endeavor held in high repute. ORI summarizes under nine broad areas of responsibility.

- Research Integrity

...the use of honest and verifiable methods in proposing, performing and evaluating research and in reporting research results, with particular attention to adherence to rules, regulations, guidelines and commonly accepted professional codes or norms.

Should !

- Research ethics

...the critical study of the moral problems associated with biomedical and behavioral research and its application to health care decision-making.

Should ?

# How should researchers behave?

1.1 The scientist is bound by the principles of ethics of humankind, as well as by the principles of good manners in science.

**POLISH ACADEMY OF SCIENCES  
COMMITTEE FOR ETHICS IN SCIENCE**

**GOOD MANNERS IN SCIENCE  
A SET OF PRINCIPLES AND GUIDELINES**

**Warsaw 2001**

1.3 The scientist cannot justify behaviour in conflict with principles of good manners in science by reference to either obedience or loyalty.

1.13 Scientist have a particular duty to promulgate within the scientific community...the principles of reliable scientific work and the condemnation of scientific dishonesty and breaches of good practice.

# Standards for responsible science?

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European Science Foundation Policy Briefing

## Good scientific practice in research and scholarship

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### *Foreword*

**A**t a time when the need to build trust between science and society is becoming ever more important, it is vital that the conduct of science itself is based on the highest ethical considerations and that misconduct within science itself can be identified and dealt with in an open and transparent manner.

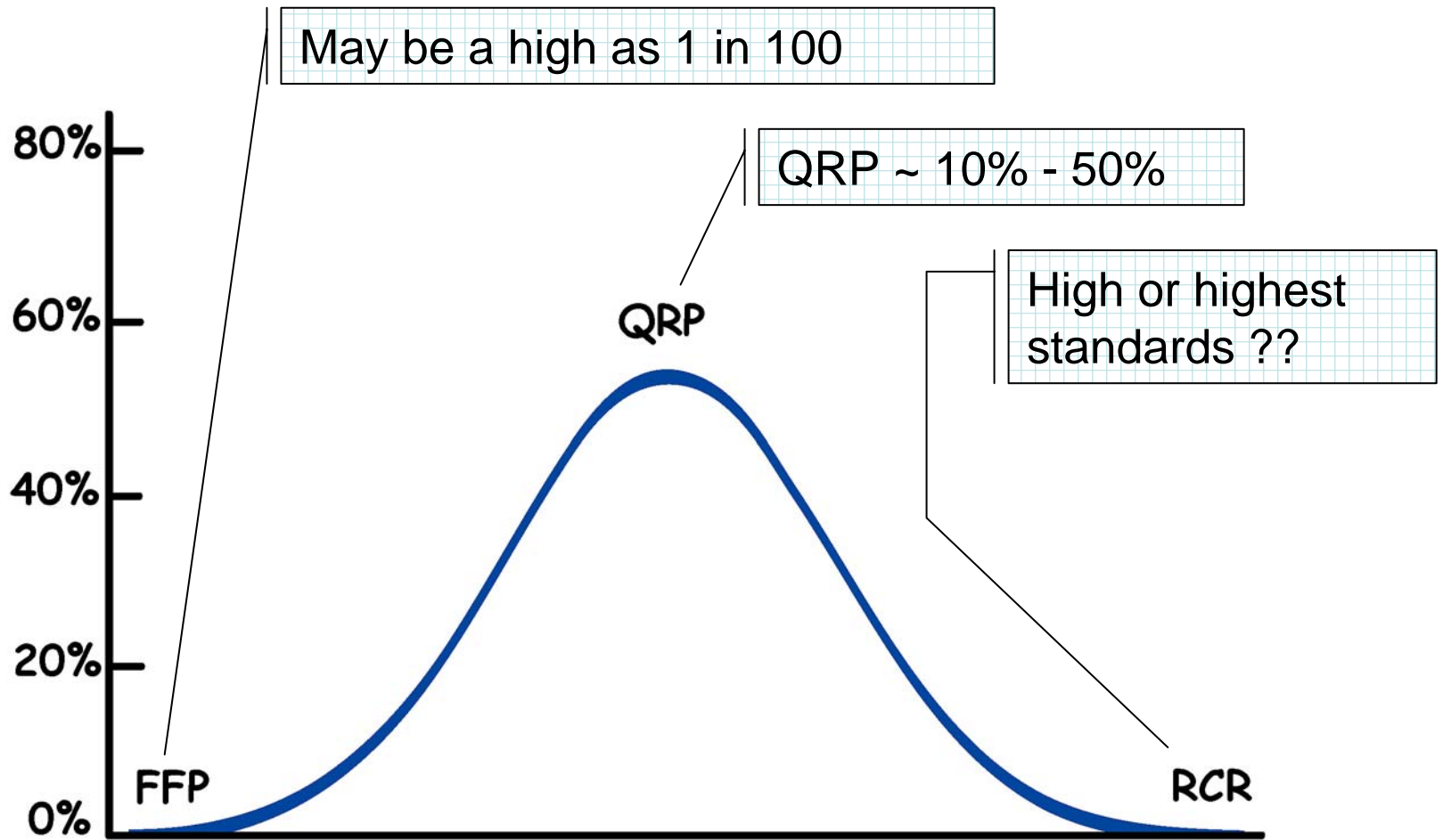
# Need for high standards widely accepted



## Guidelines on good research practice

The Wellcome Trust expects the highest standards of integrity to be adhered to by the researchers whom it funds. To facilitate this it has drawn up these 'Guidelines on Good Research Practice'.

# Ideals ≠ Actual Research Behavior



# Research misconduct (FFP)

## ☛ Three key questions:

1. How much - how many commit & how often?
2. Cause(s) of misconduct?
3. Way(s) to prevent?

## ☛ Steneck summary in 2000

- ✓ Rate: 1/100,000  $\leftrightarrow$  1/100
- ✓ Cause(s): slight evidence for personal/individual
- ✓ Prevention: suggestions but no firm evidence

## ☛ Recent research favors higher rate ~ 1/100



# Rates of FFP ~ recent studies

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## • JM Ranstam, *Control Clin Trials* (2000)

- ✓ Survey, 442 biostatisticians, 37% response
- ✓ 51% knew about fraud in medical research
  - 26% involved FF
  - 31% directly involved in projects with misconduct
- ✓ Estimates of rate, .69% → .80% (.25% standard)

## • Geggie, *J Med Ethics* (2001)

- ✓ Survey, 305 new medical consultants, 64% response
  - 55.7% observed misconduct (FF lower)
  - 5.7% committed misconduct in the past
  - 18% would commit in future
  - 17% had research ethics training

# ORI Research on RI Program

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## • Gardner, Contemporary Clinical Trials (2005)

- ✓ Sample ~ authors (549) who reported results of 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

## • Other studies in press based on self-reporting

## • Unpublished conference presentations

- ✓ Falsification & improper manipulations of digital images in journal publications

# Cost of research misconduct?

## Basic numbers

- ✓ 1-10m researchers in US
- ✓ Rate ca. .01-1%

## Estimates of FFP

## Impact

- ✓ Direct funding
- ✓ Investigations
- ✓ Publication costs
- ✓ Scientific time

## Cost of FFP?

- ✓ \$1,000s to \$1,000,000s/ case
- ✓ Recent major case (Poehlman) ca. \$2-5 M

Rate/Number	1M	5M	10M
1:10,000 (.01%)	100	500	1,000
1:1,000 (.1%)	1,000	5,000	10,000
(1%)1:100	10,000	50,000	100,000

## Total cost?

# FFP, Causes and Prevention

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## ☛ Causes

- ✓ Ranston (2000) - career & power, not financial (76%)
- ✓ Riis (2001) - inadequate guidelines
- ✓ Davis (2003) - culture & national background
- ✓ Parrish (2004) - academic standing

## ☛ Prevention

- ✓ Anderson (2000) - improved guidelines
- ✓ Riis (2001) - improved guidelines
- ✓ Geggie (2001) - education

## ☛ Incomplete understanding of cause & prevention

# Questionable Research Practices

## Definition

- ✓ Less than responsible conduct
- ✓ Falls short of good research practice
- ✓ At odds with “commonly accepted practices”

## Examples

- ✓ **Misrepresentation** of credential
- ✓ **Conflicts of interest** that impact results/actions
- ✓ Undeserving/improper **authorship**
- ✓ Sloppy and bias **publication practices**



# Misrepresentation

- ✦ False information about research on resumes
- ✦ Pre-2000 studies
  - ✓ Six studies
  - ✓ 15%-30% misrepresentation
- ✦ 2000-2004
  - ✓ Radiology (2000)-----11.0%
  - ✓ Orthopedics (2000)-----18.0%
  - ✓ Orthopedic Surgery (2003)-----10.6%
  - ✓ Emergency Medicine (2004)-----21.3%
- ✦ Are these numbers accurate?
  - ✓ Boyd (1996), numbers may be too high
  - ✓ Herbert & Smith, *Internal Medicine* (2003) agree; multiple checks reduced rate to 1%
- ✦ What is the correct rate & how can integrity be improved?

# Conflict of Interest

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## • Growing number of “journalistic” case studies

- ✓ Levine (2003) - Positive correlations, olestra research
- ✓ Krimsky (2003), *Science in the Private Interest*
- ✓ Angell (2004), *The Truth about the Drug Companies*

## • Studies of extent and characteristics of conflicts

- ✓ Boyd (2000) - faculty increased financial relationships
- ✓ Campbell (2001) - impact of market forces on research
- ✓ Campbell (2003) - presence among IRB members
- ✓ Buchkowsky (2004) - growing importance in clinical trials

## • Institutional studies

- ✓ Cho (2000) - shortcoming of institutional policies
- ✓ Krimsky (2001) - shortcoming of journal policies

# Impact of Conflict of Interest

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## ☛ 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

# Authorship & publication

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- Area that continues to produce most research
- Research covers practices relating to:
  - ✓ Abstracts
  - ✓ Authorship
  - ✓ Citations
  - ✓ Duplicate and salami publication
  - ✓ Editorial practices
  - ✓ Peer review
  - ✓ Retraction
- Peer Review Congresses major impetus
  - ✓ <http://www.ama-assn.org/public/peer/peerhome.htm#Issues>
  - ✓ 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:

Field	All	Major
Otolaryngology (2000)	37.5	11.9
Primary Care/AIDS (2003)		3% / 8%
Manuel Therapy (2004)	20 to 59% citational	

## ☛ Rate appears high & constant

# Cost of QRP?

## Number of biomedical publications

NLM Services	2001	2002	2003
Citations, MEDLINE	463,014	502,056	526,338
Citations, Index Medicus	445,041	459,558	492,911
Journals, Medline/PubMed		4,538	4,697
Journals, Index Medicus	3,707	3,834	3,994
Abstracts entered	345,624	398,885	465,975

## Estimate of the number of duplicate publications

- ✓ Studies estimate at 10=20%
- ✓ 500,000 x 1 in 10 x 1/2 scholarly = 25,000/year

## \$\$\$ / article ?

- ✓ Review, publish, process, purchase, read ...
- ✓ Plus cost of inaccurate scientific record!
- ✓ \$100/article = \$2.5 M/year; \$1,000/article = \$25 M/year

## Are QRPs more important the FFP?

# Conclusions

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- ☛ **Responsible conduct is essential in research**
  - ✓ Widespread professional commitment
  - ✓ Agreement that standards should be set high
- ☛ **Current practices fall short of ideals**
  - ✓ Serious misconduct more common than recognized
  - ✓ Researchers are aware of but fail to report misconduct
  - ✓ Other QRPs have been shown to occur at unacceptably high rates and seriously undermine the integrity of science
- ☛ **Failure to respond will harm research/science**
  - ✓ Undermine public support
  - ✓ Risk of over-regulation (e.g. NIH conflict of interest policy)
  - ✓ Reduced interest in science careers ...

# Recommended Professional Response

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## ☛ Realistic assessments

- ✓ What situations are researchers confronting?
- ✓ Problem areas?

## ☛ Useful guidelines and resources

- ✓ Codes (set tone but do not provide practical advice)
- ✓ Field-specific research guidelines
- ✓ More detailed journal policies
- ✓ Recommended RCR curricula
- ✓ Checklists for measuring response

## ☛ Clear professional commitments

- ✓ Make RCR a prominent feature of national meetings
- ✓ Encourage more substantive RCR publications
- ✓ Encourage researchers to take RCR seriously

# What constitutes RCR?

