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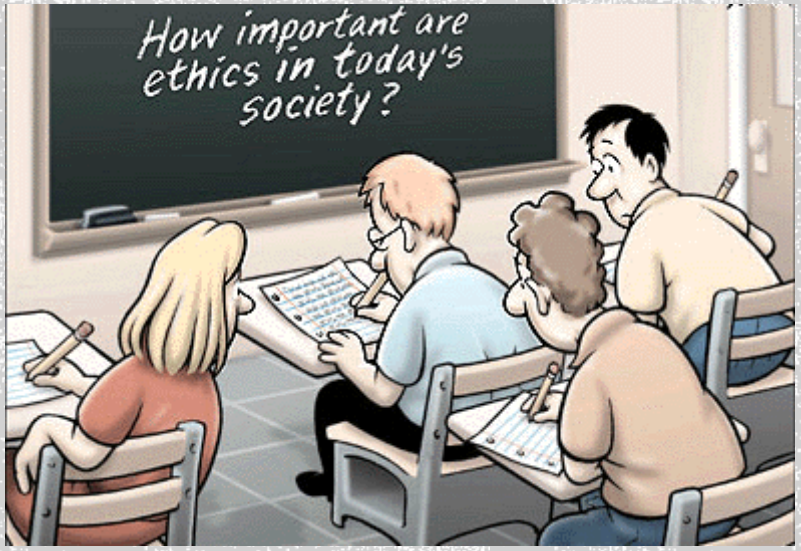
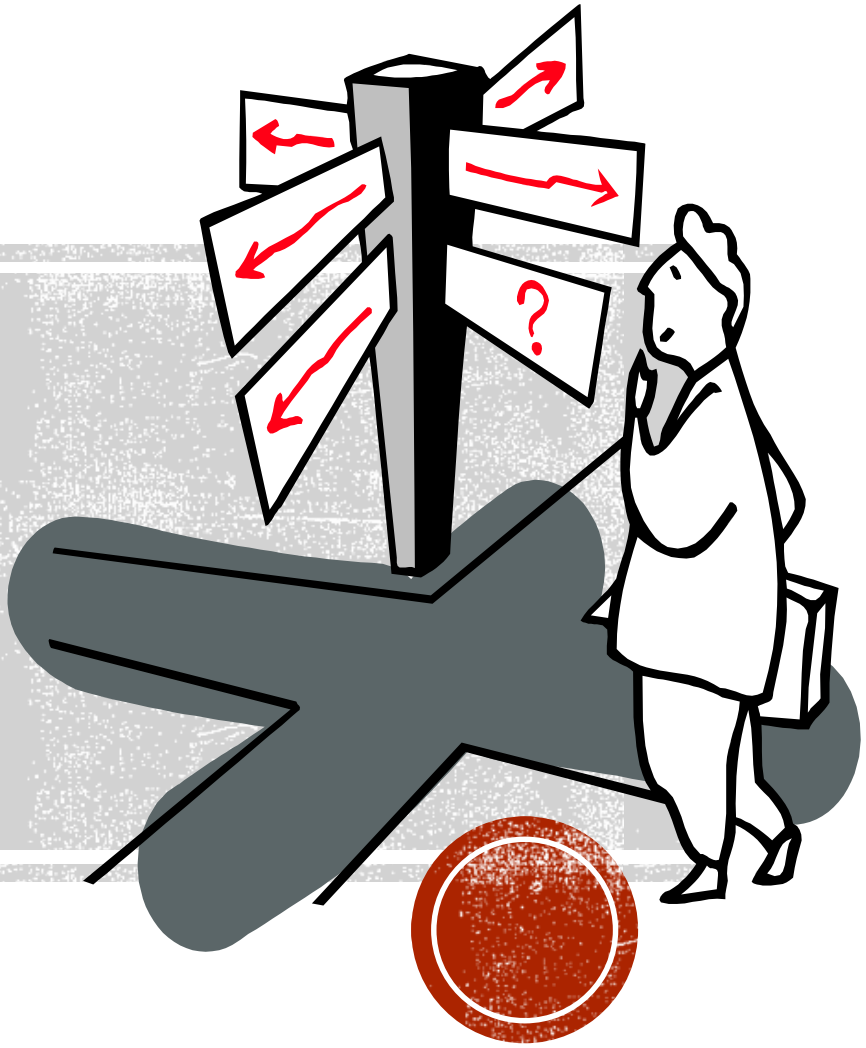
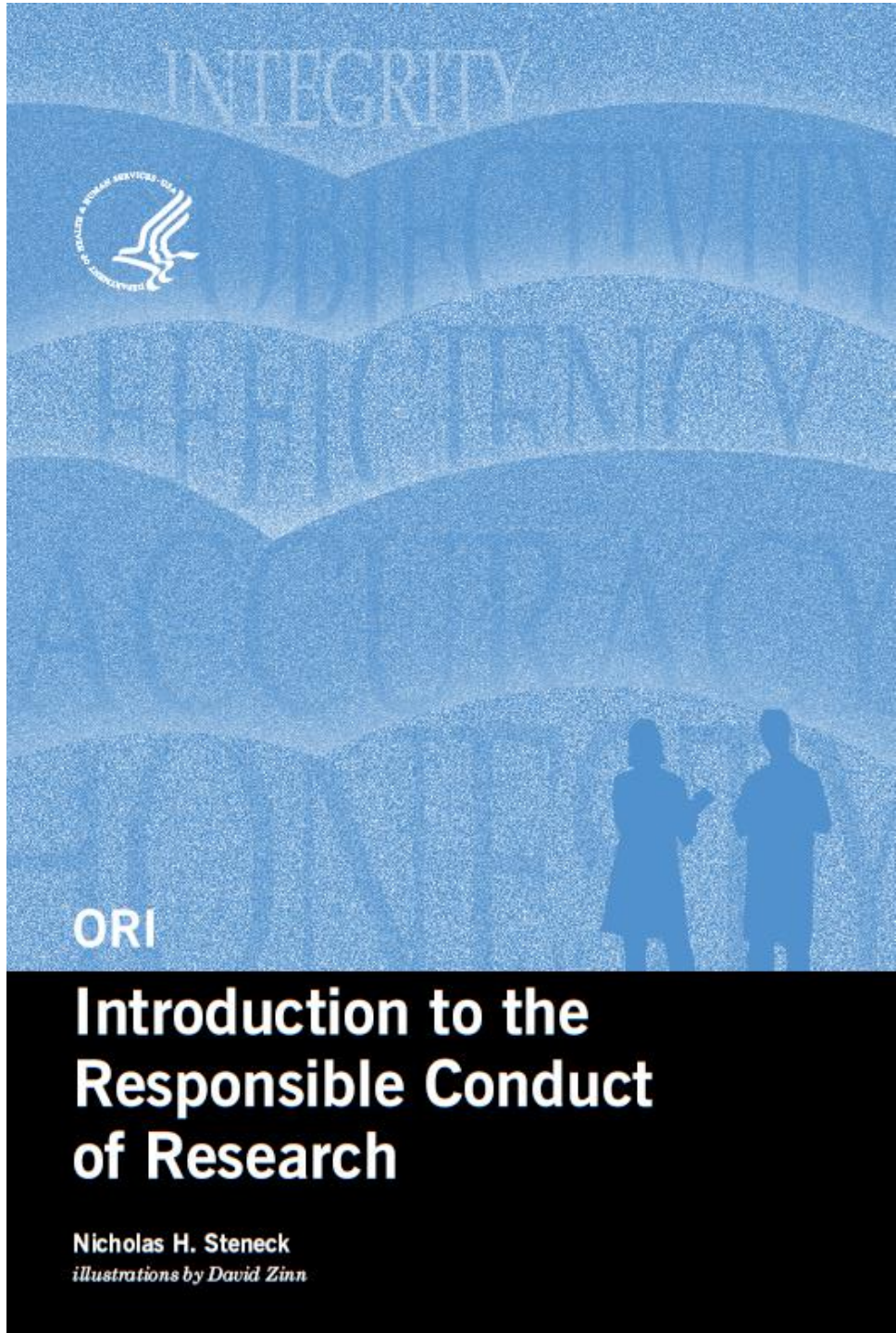




RESPONSIBLE CONDUCT OF RESEARCH

INTRODUCTION TO THE RESPONSIBLE CONDUCT OF RESEARCH

- **Nicholas H. Steneck**
- *illustrations by David Zinn*
- **Revised Edition**
- **August 2007**



OUTLINE

- Definitions
- What brought research ethics to the surface?
- Brief history
- Why research ethics?
- Basic concepts in ethical research
- IRBs/RECs
- Ethical Guidelines Governing Research

DEFINITIONS: ETHICS

- The discipline concerned with what is morally good & bad, right & wrong
- Societal norms adopted by a group (small vs. large)
- Universality vs. Relativity

- Is a way of understanding & examining what is “right” & what is “wrong” in research

DEFINITIONS: RESEARCH ETHICS

IS RESEARCH ABOVE ETHICS & MORALITY?

EXPERIMENTS IN THE PAST

- Tuskegee: 1932-1974
- Nazi's: World War II

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE FREE PREVIEW ARCHIVE

Ethics and Clinical Research

Henry K. Beecher, M.D.†

This article has no abstract; the first 100 words appear below.

HUMAN experimentation since World War II has created some difficult problems with the increasing employment of patients as experimental subjects when it must be apparent that they would not have been available if they had been truly aware of the uses that would be made of

June 16, 1966
N Engl J Med 1966; 274:1354-1360
DOI: 10.1056/NEJM196606162742405

HISTORY

- The Nuremberg Code – 1947
- The Declaration of Helsinki - World Medical Association - (1964, 1975, 1983, 1989, 1996, 2002)
- The Belmont Report – 1978
- Council for International Organizations of Medical Science (CIOMS) Guidelines – (1993, 2002)

WHY RESEARCH ETHICS – MAJOR GOALS

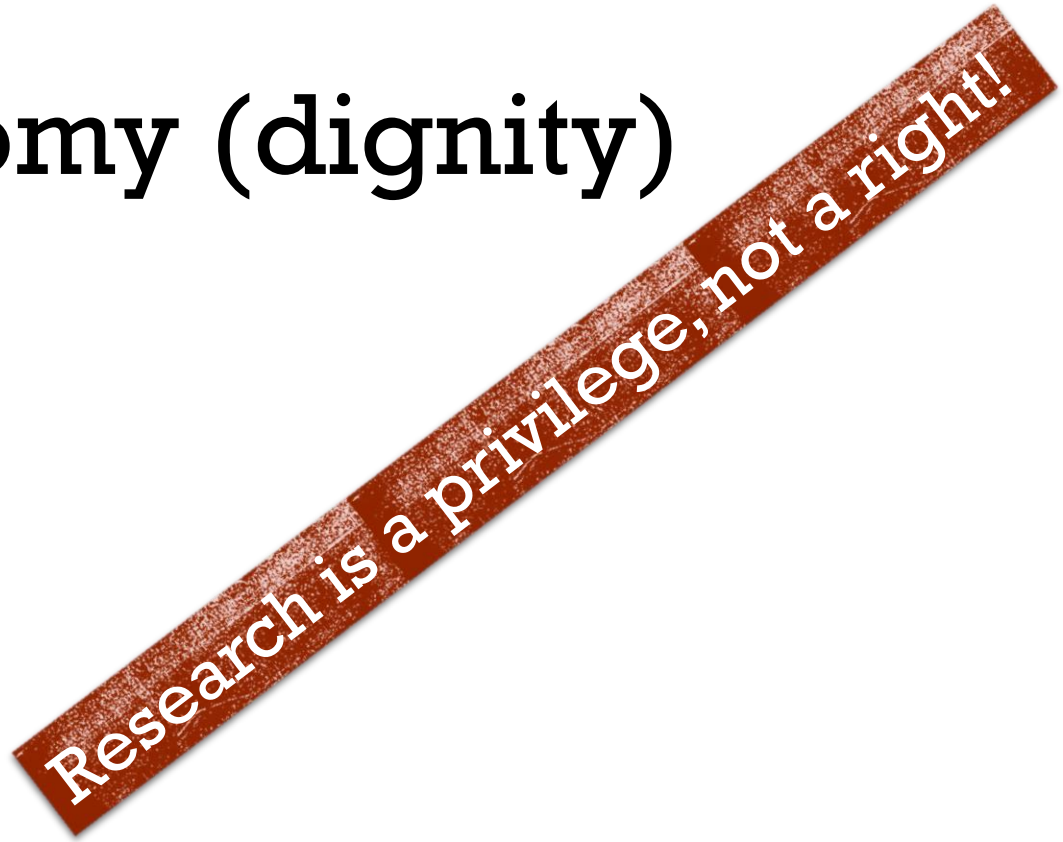
- To protect participants /society /resources /researcher?
- To ensure accuracy of scientific knowledge
- To protect intellectual and property rights

WHY RESEARCH ETHICS – HIDDEN GOALS

- Establish trust
- Establish an environment of open communication
- Promote best practices
- Share ideas
- Increase understanding
- Establish a culture of concern

BASIC CONCEPTS FOR ETHICAL RESEARCH

- ✓ Respect for autonomy (dignity)
- ✓ Beneficence
- ✓ Justice



RESPECT FOR AUTONOMY - INFORMED CONSENT

- Fully explain
- Answer questions
- Give time
- Give a copy
- Asses understanding

- Voluntariness
- Vulnerable participants
- Incapability (Assent)
- Verbal
- Open
- Deception
- Withdrawal

RESPECT FOR AUTONOMY – ANONYMITY & CONFIDENTIALITY

- Anonymity: refers to concealing the identity of participants/places in all documents resulting from the research

- Confidentiality is concerned with who has the right of access to the data provided by participants

BENEFICENCE VS. NON-MALEFICENCE

- Participation in research is associated with a favorable balance of potential benefits and harms
- Maximize possible benefits, minimize potential harm
- Humans, animals

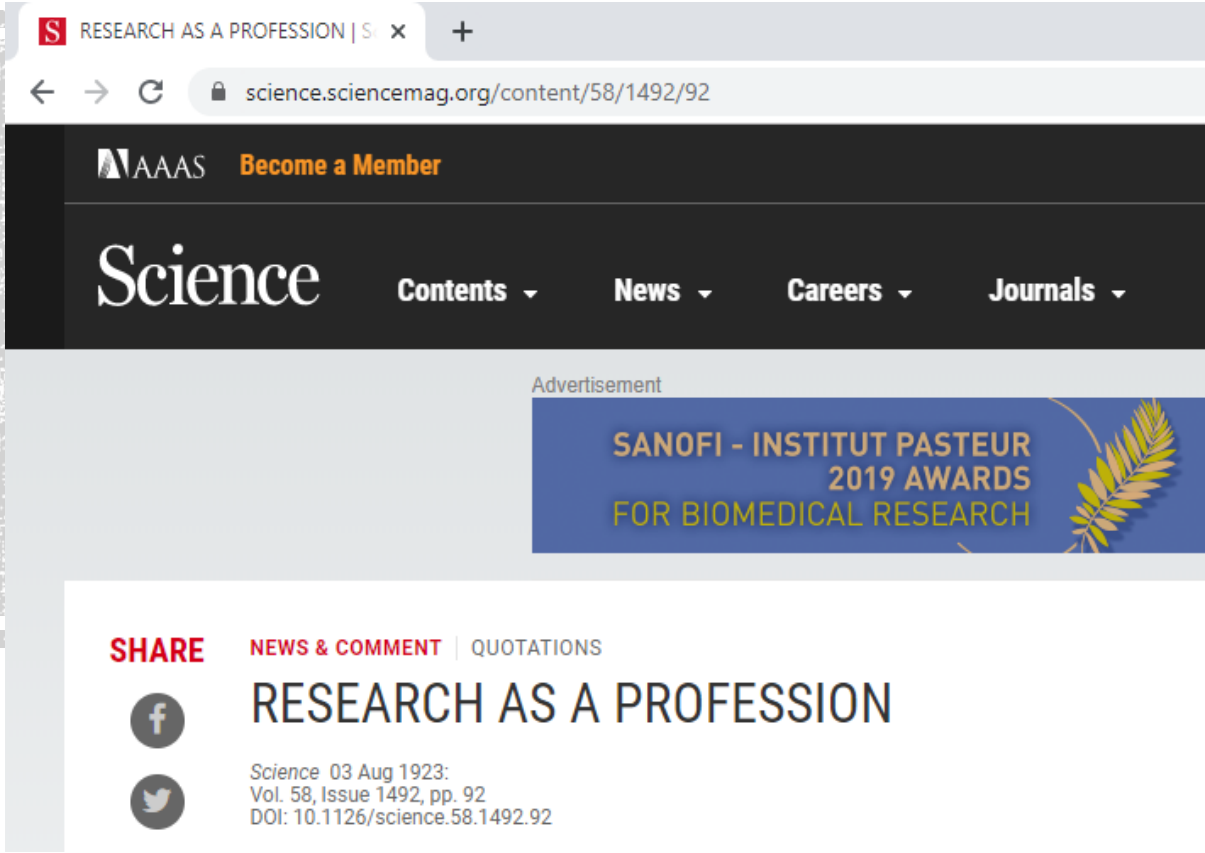
"Personally, I wouldn't have signed it."

JUSTICE

- Participation in research is associated with a favorable balance of potential benefits and harms
- May not exploit or exclude vulnerable individuals who may benefit without good reason
- Distribute benefits and risks equally (medicine and placebo use)

IS RESEARCH A PROFESSION?

1. **How is integrity in research monitored?**
2. **Is self-regulation of integrity in research effective?**



WHAT ARE THE MAIN CONCERNS WHEN CONDUCTING RESEARCH?

- Well-being & privacy of participants
- Well-being of the researcher(s)
- Integrity of the research
- Compliance with University & other policies
- Reputational issues

IRB OR RECS – ROLE

- To protect the welfare and rights of research participants

- To review ethical aspects of research – at which state?

IRB OR RECS – WHO SHOULD BE THERE?

- ≥ 5 members, experience, expertise, various backgrounds!
- (training & education, race, gender, culture)
- Scientist, non-scientist, unaffiliated… directed toward research proposal under discussion
- Must meet all! Replacement…

Physician	Nurse	Ethicist
Lawyer	Any regular person (lay person)	Philosopher

LEVELS OF IRB REVIEW

- Exempt Review (~2 weeks): minimal risk
  - Category 1 – Educational Practices
  - Category 2 - Educational Tests, Surveys, Interviews, or Observation of Public Behavior
  - Category 3 - Benign Behavioral Interventions
  - Category 4 - Existing (Secondary) Data
  - Category 5 – Public Benefit and Service Program Research
  - Category 6 – Taste & Food Quality Evaluation
  - Categories 7 & 8: Broad Consent for Storage or Maintenance of Data for Secondary Use
- Expedited Review (~3 weeks)
- Full Board Review (~1 month or more)

ETHICAL GUIDELINES GOVERNING RESEARCH

ETHICAL GUIDELINES GOVERNING RESEARCH

- Investigator
- Mentor/Trainee Relationship
- Conflict of Interest & Commitment
- Collaborative Research
- Data Management, Sharing, & Ownership
- Research Misconduct
- Publication Practices & Authorship

ETHICAL GUIDELINES: INVESTIGATOR

- Usually a group - Rarely conducted by a single person
- The PI:
  - A qualified person
  - Is responsible for the proper scientific conduct
  - Ensures compliance with the financial & administrative aspects
  - Ensures that those working under him are doing good science
  - Should hold regular meetings
  - Has no choice but to be honest with students, postdoctoral fellows, & staff about possible lapses in funding

Mentor

- Helps the new researcher to excel his skills
- Actively serves the trainee in dealings with the University
- Also, with contacts outside the institution
- Helps the trainee to evolve (with time) into an independent investigator
- Should be accessible to the trainee

Trainee

- Must learn the basic methods of scientific investigation
  - Exploring & evaluating the literature in their field
  - keeping good records, & examining, analyzing, & interpreting data frequently

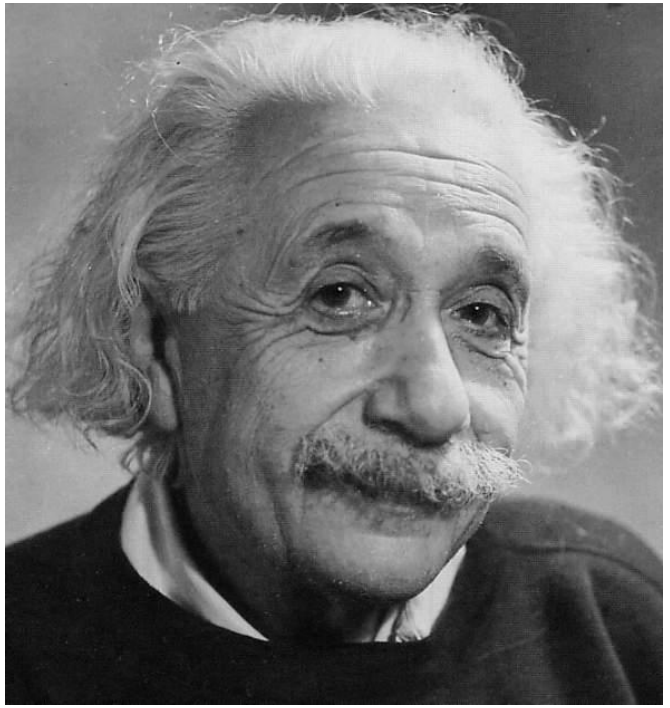
» Should take an increasingly independent role in selecting, conceptualizing, & executing research projects

» Sustain a relationship of mutual respect & cooperation

ETHICAL GUIDELINES: MENTOR/TRAINEE RESPONSIBILITIES

WORKING WITH FACULTY

- Expect to be treated with **respect but not equally**
- Expect to work hard & do **menial jobs**
- Choose a professor who **shares like interests**
- Personality **conflicts do occur**
- Ultimately **YOU are in charge of your future**



ETHICAL GUIDELINES: CONFLICT OF INTEREST & COMMITMENT

- Conflicts of interest or commitment are not necessarily good or bad

- What is important is how they are acted on

ETHICAL GUIDELINES: CONFLICT OF INTEREST & COMMITMENT

- For financial conflict of interest; researchers should:
  - Report significant ($? per year) financial conflicts before any research is undertaken
  - Manage, reduce, or eliminate significant financial conflicts (accomplished by disclosure to the Conflict of Interest Committee)

ETHICAL GUIDELINES: CONFLICT OF INTEREST & COMMITMENT

- Conflicts of commitment occur from the competing demands on a researcher's time & loyalties:
  - Working on more than one funded project
  - Preparing proposals for new projects
  - Teaching & advising students
  - Attending professional meetings
  - Serving as a peer reviewer

ETHICAL GUIDELINES: COLLABORATIVE RESEARCH

- Researchers collaborate with colleagues who have expertise &/or resources to contribute to a project
- Agencies & universities seek to foster interdisciplinary science
- Collaboration or competition?

ETHICAL GUIDELINES: COLLABORATIVE RESEARCH

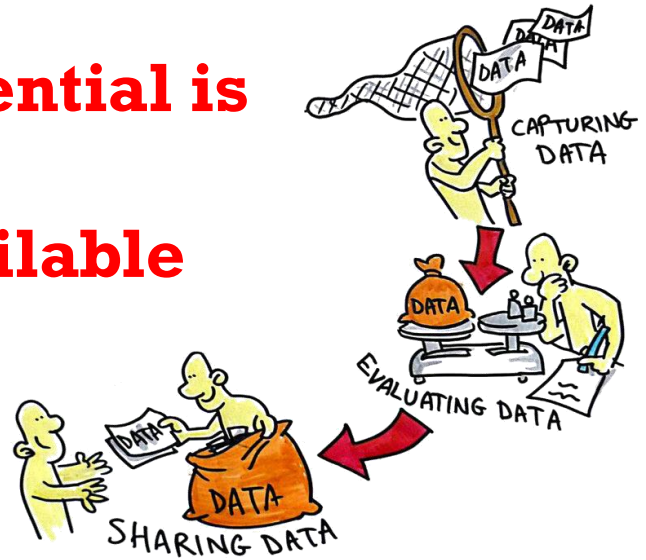
- Effective collaboration begins with a clear understanding of the following of roles:
  - **Goals & anticipated outcomes**
  - **Roles of each partner**
  - **Data collection, storage, & sharing**
  - **Agreeing to changes in research design**
  - **Who will draft publications**
  - **Criteria to rank authors**
  - **Authority to speak publicly**
  - **Intellectual property rights & ownership**
  - **How the collaboration can be changed**
  - **When the collaboration will end**

ETHICAL GUIDELINES: DATA MANAGEMENT

- Data must be protected for later use
- Data Storage: Lab notebooks; backed up; samples saved so as not to degrade (if applicable)
- Confidentiality: human subjects or confidential business information
- Retention: at least for 3 years

ETHICAL GUIDELINES: DATA SHARING

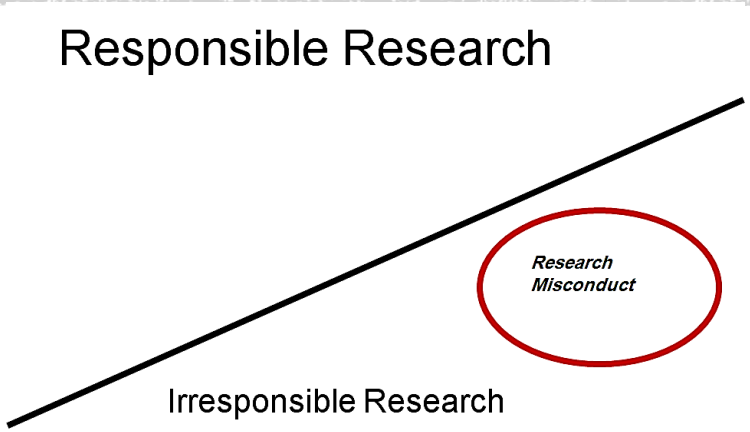
- Although there is a general agreement that research data must be shared there are some considerations:
  - **Preliminary data**
  - **Confirmed or validated data: confidential is widely accepted**
  - **Published data: should be freely available**



ETHICAL GUIDELINES: DATA OWNERSHIP

- **Student, researcher, PI, School, funding agency?**
- In general for the funding agency represented by the institution
- Support for research institutions is awarded to the research institution, not to individual researchers

RESEARCH MISCONDUCT



RESEARCH MISCONDUCT

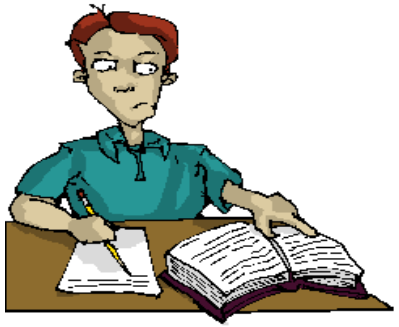
- **Eight Areas of Dishonesty:**

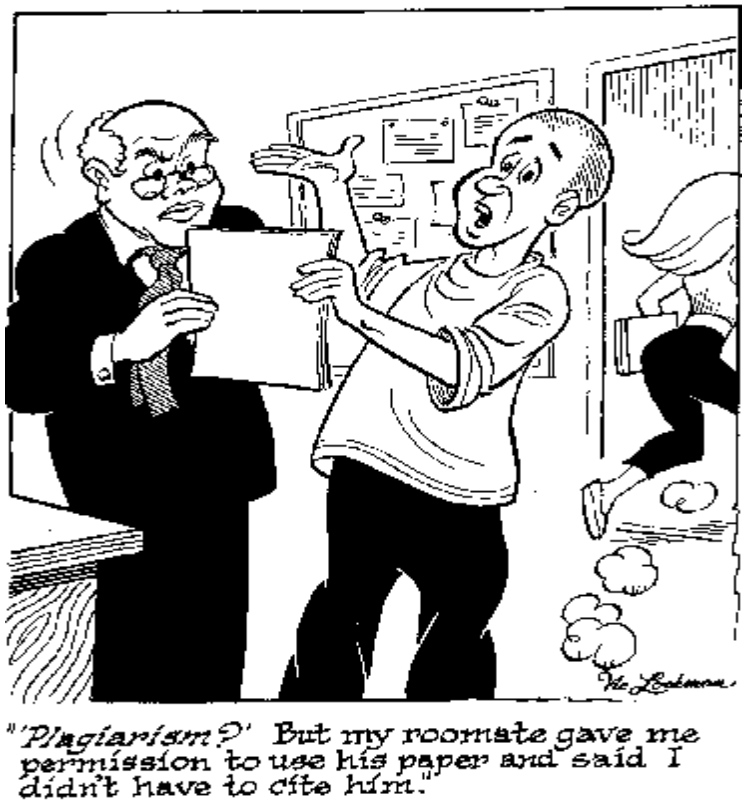
1. Plagiarism
2. Fabrication
3. Falsification
4. Non-publication of data
5. Faulty data-gathering procedures
6. Poor data storage & retention
7. Misleading authorship
8. Sneaky publication practices

RESEARCH MISCONDUCT : PLAGIARISM

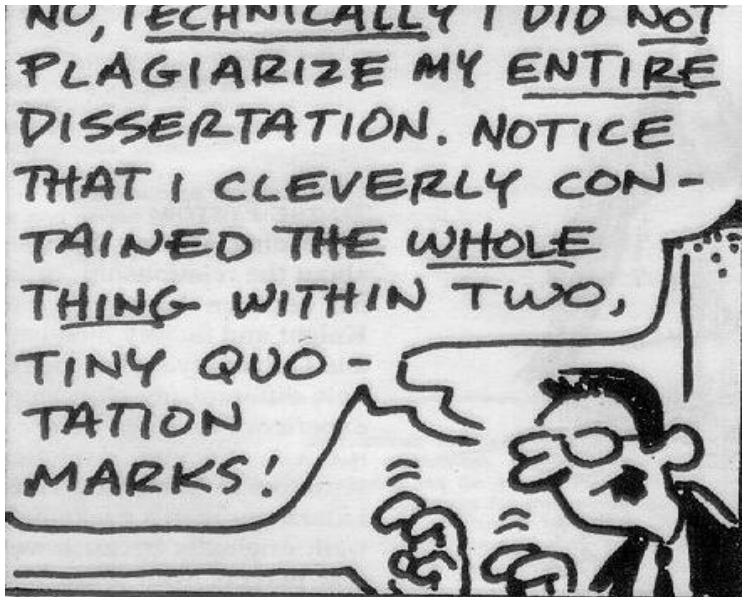
- **The intentional use of ideas, writings, & drawings of others as your own**

- **Also includes "self-plagiarism"**





"'Plagiarism?' But my roommate gave me permission to use his paper and said I didn't have to cite him."



RESEARCH MISCONDUCT: FABRICATION

- Intentionally **creating records that do not exist** & for which there is no truth with the intent to mislead or deceive
  - **Interviewer completing a questionnaire for a fictitious subject that was never interviewed**
  - **Preparing records for follow-up calls or contacts to subjects who were really lost to follow-up**
  - **Creating notes for a subject visit that never took place**

ERIC POEHLMAN, PHD

- **UVM** College of Medicine – fabricated data in 17 grant applications for federal funding as well as in journal articles
- Barred for life from receiving any federal funds for research – plead guilty to fraud –sentenced in 6/06 to a year & one day in prison
- Letters of retraction published
- Also see **NY Times** article "An Unwelcome Discovery" (10/22/06)

RESEARCH STAFF – HELD TO THE SAME STANDARD

- Jessica Grol, Research Project Coordinator at **University of Pittsburgh** – 11/05
- Fabricated study research records for 15 subjects, including interview data – research funded by NIH
- For 3 years – debarred from contracting or subcontracting w/ any US Gov't agency

RESEARCH MISCONDUCT: FALSIFICATION

- Alteration of data collected
- Omission/deletion/suppression of conflicting data without scientific justification
  - > Back-dating interviews to fit within the timeline provided in protocol
  - > Changing a subject's age in data records by an unimportant amount to fit enrollment criteria

CRAIG GELBAND, PH.D.

- Published in 11/03 Federal Register
- Falsified data in different manuscripts or publications citing NIH support & NIH grant applications
- 10-year Voluntary Exclusion Agreement
- 2 papers retracted, 1 paper withdrawn, figures retracted from 3 papers

JOY BRYANT & DIANA LAYMAN

- Published in 7/07 Federal Register
- Phlebotomists at **University of Oklahoma** Health Sciences Center
- Falsified research in study by substituting their own blood for the 10-15 blood samples of child study participants as required by the protocol
- Entered into Voluntary Exclusion Agreement for 3 years

KRISTIN ROOVERS, PH.D.

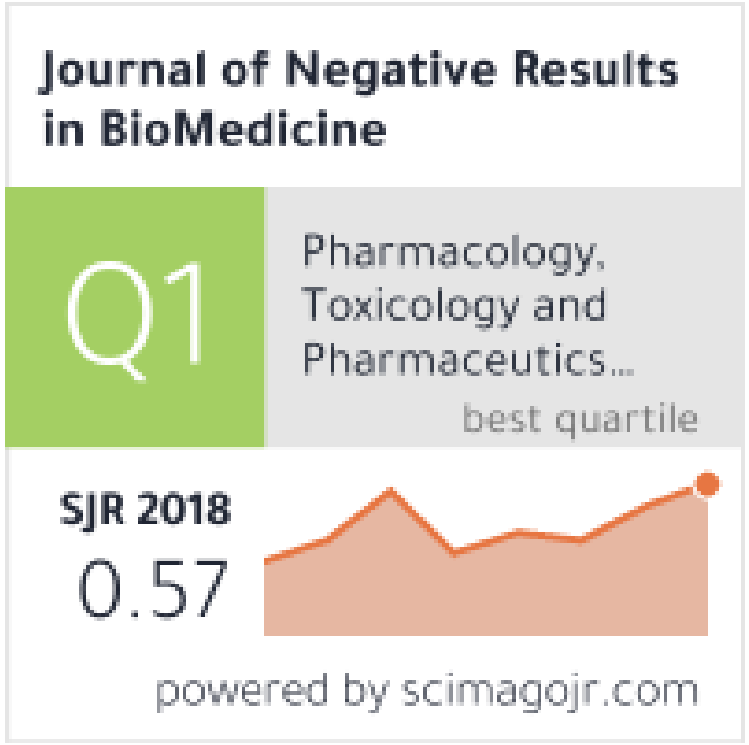
- Published in Federal Register in 7/07
- **University of Pennsylvania** researcher
- Falsified data by duplicating & reusing data to misrepresent results as data from different experiments
- ORI Action: For 5 years – cannot contract or subcontract w/ U.S. government agency or serve in any advisory capacity to PHS

ANDREW FRIEDMAN, MD

- Brigham & Women's Hospital physician
- Between 1992 & 1995, altered & fabricated data in permanent medical records
- Also falsified & fabricated research data in 80% of his publications (retractions published)
- 1996 - 3 year Voluntary Exclusion Agreement; for 2 years following 3-year period, employer must submit a plan detailing how he will be supervised for any PHS proposals
- Now researcher at Ortho-Mcneil Pharmaceutical

RESEARCH MISCONDUCT: NON-PUBLICATION OF DATA

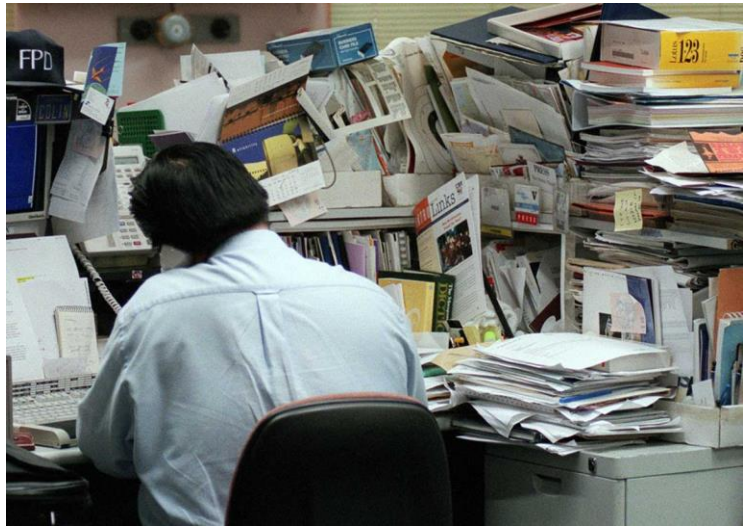
- Data not included in results because they don't support the desired outcome
- Some data are "bad" data
- **Bad data** should be recognized while it is being collected or analyzed
- **Outlier** – unrepresentative score; a score that lies outside of the normal scores
- How should outliers be handled?



RESEARCH MISCONDUCT: FAULTY DATA GATHERING

- Collecting data from participants who are not complying with requirements of the study
- Using faulty equipment
- Treating participants inappropriately
- Recording data incorrectly

RESEARCH MISCONDUCT: POOR DATA STORAGE & RETENTION



- Data should be stored in its original collected form for **at least 3 years** after publication
- Data should be **available for examination**
- **Confidentiality** of participants should be maintained

ETHICAL GUIDELINES: PUBLICATION PRACTICES & AUTHORSHIP

- Elements of a responsible publication
  - **Abstract**
  - **Introduction**
  - **Methods**
  - **Results**
  - **Discussion**
  - **Notes, bibliography, & acknowledgements**
  - **References**
- Results of publication should meet some minimum standards
  - **A full & fair description of the work**
  - **An accurate report of the results**
  - **An honest & open assessment of the findings**

RESEARCH MISCONDUCT: SNEAKY PUBLICATION PRACTICES

- Publication of the thesis or dissertation (it is the student's work)
  - Committee chair & members may be listed as secondary authors
- Dual publication – a manuscript should only be published in a single journal
  - What about studies which include a huge amount of data?
- Salami: dividing one significant piece of research into a number of small experiments (least publishable units or LPUs)

RESEARCH MISCONDUCT: AUTHORSHIP

- Who should be an author?
  - Intellectual contribution vs. technical one
  - Always discuss authorship before the project!
- The following qualifies you to be an author:

  - Statistical expertise

» Manuscripts with more than 6 authors!

RESEARCH MISCONDUCT: MISLEADING AUTHORSHIP

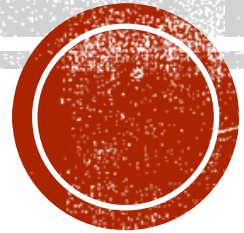
- Practices that should be avoided:
  - Honorary & gift authorship (limited to individuals who make significant contributions & listed according importance – 1st vs. last)
  - Ghost Authorship

WHISTLE-BLOWING

- Clear and proper channels
- Protection
- Future career status
- Effectiveness

THE END OF PART 1

ETHICAL CASE STUDIES



CASE STUDY 1. INFORMED CONSENT
DEVELOPMENT OF A NEW MICROBICIDE
SOURCE: FAMILY HEALTH INTERNATIONAL - MODIFIED

- **Question**

In this case the REC should:

1. Recommend that the study be terminated (not allowed to continue).
2. Retrain the site investigator and the study staff in the informed consent process.
3. Rely on the site investigator's knowledge of the study population.
4. Take no action. Signed consent forms for each participant are on file.

CASE STUDY 2.
THE MILGRAM EXPERIMENT

- Is deception allowed here?
  - Milgram also interviewed participants afterward to find out the effect of the deception. Apparently, 83.7% said that they were "glad to be in the experiment," and 1.3% said that they wished they had not been involved
- Protection of participants
  - In his defense, Milgram argued that these effects were only short-term. Once the participants were debriefed (and could see the confederate was OK) their stress levels decreased. Milgram also interviewed the participants one year after the event and concluded that most were happy that they had taken part
- Right to Withdrawal
  - Milgram argued that they are justified as the study was about obedience so orders were necessary. Milgram pointed out that although the right to withdraw was made partially difficult, it was possible as 35% of participants had chosen to withdraw

CASE STUDY 3. CHILD STUDIES - NATURE'S THUMBPRINT: THE NEW GENETICS OF PERSONALITY

RECORDS FROM CONTROVERSIAL TWIN STUDY SEALED AT YALE UNTIL 2065

- In the depths of Yale's library collections, records from a controversial study that separated twins and triplets at birth remain sealed, despite demands from the study's participants to see their own files.
- The study, conducted by child psychiatrist **Peter Neubauer** throughout the 1960s and 70s, involved at least eight twins and a set of triplets who had been separated at birth at the now-defunct New York City adoption agency Louise Wise Services.
- In 1990, a decade after abruptly ending the confidential study, **Neubauer and the Child Development Center of the Jewish Board of Family and Children's Services arranged to house the locked records at Yale.** The Jewish Board set forth terms that gave the organization the power to approve or deny any requests to access the records for the next 75 years.
- The records will remain sealed until Oct. 25, 2065. The study came into the spotlight after this summer's documentary "**Three Identical Strangers**" and 2017 documentary "**The Twinning Reaction**" highlighted the stories of the participants and explored the study.
- **What ethical issues are there?**

CASE STUDY 4. INDIVIDUAL VERSUS COMMUNITY CONSENT

SOURCE: HARVARD SCHOOL OF PUBLIC HEALTH, USA - MODIFIED

- **Questions**

1. How should the reseacher handle this problem?
2. How critical is signed informed consent in this setting?
3. Is it acceptable to obtain consent from the village chief or is individual consent necessary?
4. Is informed consent culturally bound or is it a universal principle?
5. Are there circumstances when informed consent is unnecessary?
6. Can the IRB waive informed consent in such instances?

Case Study 5. Intervention
QUESTIONNAIRE ON DEPRESSION

- University students
- Informed consent
- Confidentiality vs. anonymity
- Should you intervene?

Case Study 6. Politics
INTERVIEWING POLITICAL FIGURES

- Political figures
- Informed consent
- Confidentiality vs. anonymity
- Should you reveal?

Case Study 7. Informed Consent
STUDENTS' INVOLVEMENT IN RESEARCH

- Students' that you teach
- Informed consent
- Withdrawal?

Case Study 8. Authorship Authorship dispute

- What is the story?

Case Study 9. Authorship Honorary authorship

- Colleague
- Should you agree?
- What to write in contributions? To lie?
- How friction it might create?

Case Study 10. Collaboration Contribution is not just right!

- Colleague
- Should you agree and continue?
- What you should do? What options do you have?
- How friction it might create?

Case Study 11. Collaboration Contribution is not just right!

- Colleague
- Should you agree and continue?
- What you should do? What options do you have?
- How friction it might create?

Case Study 12. Whistleblowing Authorship is in exchange!

- Colleague
- Should you agree and continue?
- What you should do? What options do you have?
- How friction it might create?

THE END OF PART 2