CONFLICT OF INTEREST IN HUMAN SUBJECT RESEARCH

COI IN THE MEDIA
• Financial conflict of interest frequently appear in the media, but particularly subject to public scrutiny are those high profile adverse events involving human subject research and conflict of interest, or allegations of failure to disclose conflict of interest along with failure to disclose conflict of interest along with failure to disclose risk to research participants.

HIGH PROFILE CONFLICT OF INTEREST CASES INVOLVING HUMAN SUBJECTS
• 1990 Moore v. University of California
• 1999 Gelsinger v. University of Pennsylvania
• 2001-2004 Fred Hutchinson Cancer Center cases
COI IN HUMAN SUBJECTS RESEARCH

- “to the extent financial interests may affect the rights and welfare of human subjects in research, IRBs, institutions, and investigators need to consider what actions regarding financial interests may be necessary to protect those subjects.”
  – The 2004 OHRP COI guidance
  http://www.hhs.gov/ohrp/humansubjects/finreltn/fguid.pdf

THE BELMONT REPORT AND COI

THE BELMONT PRINCIPLES

I. Respect for Persons
II. Beneficence
III. Justice

The Belmont Report
The National Commission for Protection of Human Subjects of Biomedical and Behavioral Research (1978)
I. RESPECT FOR PERSONS

• Autonomy
• Voluntariness
• Informed Consent

Disclosure of the investigator’s significant financial interest allows the IRB to approve and informed consent process in which potential research participants are apprised of the financial interest.

II. BENEFICENCE

• Risks justified by potential benefits
• Risks minimized
• Optimal study design, conduct, reporting

A Data Safety Monitoring Board or independent reviewer may be mandated to assess data integrity and the safety of research participants in the presence of a conflict of interest.

III. JUSTICE

• Distribute risks and potential benefits equitably among those who may benefit from the research

Subject selection should be conducted in an equitable manner and not biased to enhance the investigator’s financial interest.
REGULATIONS

DEFINITION OF COI IN SPONSORED RESEARCH
“Situations in which financial considerations may compromise, or have the appearance of compromising, an investigator’s professional judgement in conducting or reporting research”

NIH COI REGULATIONS
• “The Federal government… (requires that) recipients of PHS and NSF funding identify and manage potential financial conflicts of interest when funds from those two agencies are involved. The stated purpose of these requirements is to ensure a reasonable expectation that the design, conduct or reporting of research will be unbiased by any conflicting financial interest of the investigator.”
**NIH: MANAGE, REDUCE, ELIMINATE**

- Institutions and individuals receiving research assistance through the secretary (of Health and Human Services) must abide by the regulations that establish standards for managing, reducing or eliminating the existence of the financial conflict
  - 1995 NIH Financial COI Workgroup Report

**PHS, FDA COI REGULATIONS**

- 1995: PHS (for NIH – NSF adopts these regulations)
  - 42 CFR 50 Subpart F “Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought”
  - 45 CFR 94 “Responsible Prospective Contractors”
- 1998: FDA, DHHS
  - 21 CFR 54 “Financial Disclosure by Clinical Investigators”
HSRO POLICIES

UM-JHS COI POLICY AND PROCEDURES

“The University, the IRB and investigators must consider whether specific financial relationships or other considerations create conflicts of interest in research that may bias judgment and affect the rights and welfare of subjects and, if so, to determine what actions must be taken to protect those subjects. ... It is within the discretion of the IRB to decide whether such conflicts of interest are manageable, and if so, to devise a management plan for the protection of human subjects participating in the study.”

– UM Policies & Procedures – HSRO/IRB, Section 4.1

CONFLICTS OF INTEREST

• Significant financial interests exceeding $10,000 in any preceding or anticipated 12 month period
• Serving in a management position such as director, officer, partner or trustee
• Ownership equity interest equal to or exceeding $10,000 or a 5% or greater ownership interest
• Intellectual property rights such as patents, licensing agreements or a copyright or royalties
• Drug, device or other invention created at the University or by an employee who is not the PI or key personnel of the study
**HUMAN SUBJECT CONFLICT OF INTEREST (HSCOI) COMMITTEE**

“A Human Subject Conflict of Interest (HSCOI) Committee... shall be composed of the chairs and vice-chairs of the UM IRB panels with the exception of the chairs and vice-chairs of panels employed by an extramural, commercial IRB. Membership on this committee shall also include a community representative and the Assistant Provost for IRB Affairs who shall chair this Committee.”

– UM Policies and Procedures – HSRO/IRB, Section 4.4

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**WHEN IN DOUBT, DISCLOSE!**

- Mechanisms for disclosure
  - Outside consulting form – annual Faculty Affairs
  - HSRO/IRB application and notifications – disclosure is required on a per study basis
  - Contracts and Compliance Committee / CRIS
- Updates if a new conflict arises or an existing conflict changes within 10 days after onset
  - Submit notification to the HSRO with COI disclosure form

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**HSRO PROCEDURES FOR COI**

- COI disclosures submitted by all study team members
- PI recommendation on managing the COI
- Reviewed by the HSCOIC
  - Includes community representative
- HSCOIC recommendation sent to the IRB
- Final conflict management plan
  - Determined by the IRB
- Communication to the PI and Department Chair
**CONFLICT MANAGEMENT PLANS**

- Disclosure of the financial interest
  - COI ICF template language
- Independent external monitoring
- Modification of the study
- Divestiture of the financial interest
- Severance of conflicting relationship

**MANAGEMENT OF COI IN NON-HUMAN SUBJECT RESEARCH**

- Data Integrity
  - Results are not manipulated to enhance the investigator’s financial interest
- Transparency
  - Disclosure to all stakeholders – to the funding agency (NIH), research staff/advisees, regulatory agencies (e.g. IACUC); on publications and presentations

**INSTITUTIONAL CONFLICTS OF INTEREST**
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• “An institution may have a conflict of interest in human subjects research whenever the financial interests of the institution, or of an institutional official acting within his or her authority on behalf of the institution, might affect – or reasonably appear to affect – institutional processes for the conduct, review, or oversight of human subjects research.”

SITUATIONS THAT CAN CREATE INSTITUTIONAL COIs

• Royalties to Institution from licensed IP
• Equity held by institution in company
• Institutional Official has significant financial interest in company
• Gift from company (Development Office)
• Purchasing decisions by institutional officials
• Equipment utilized by institution

MANAGING INSTITUTIONAL COI IN SPONSORED RESEARCH

• Disclosure of institutional COI to IRBs, IACUC, potential research participants, staff, on publications
• Set up independent DSMB with individuals outside the university/hospital
• Fairness and firewalls in lab use agreements, purchasing agreements
CASE STUDY #1

• Dr. Ritche has invented a chemotherapy and implant delivery system for throat cancer and UM has licensed the technology to a start-up company, Laryngogen. Dr. Ritche also has stock in and consults for Laryngogen, which now wants to sponsor a feasibility study. Investors are waiting for the clinical trial to begin. The IRB has tabled the protocol pending COIC review of the COI disclosed by Dr. Ritche, a co-investigator on the IRB application. She asks the IRB Director if the process can be accelerated.

INFORMED CONSENT DISCLOSURE #1

• "A co-investigator on this study, Dr. I.M. Ritche, has a significant financial interest in this research, consisting of stock in the company sponsoring the study as well as salary as a consultant. Dr. Ritche’s invention licensed to Laryngogen could generate royalty income for her and for the University of Miami (the owner of the patent for the invention)"
**CASE STUDY #2**

- Dr. Young in Biomedical Engineering has invented a portable imaging device that research subjects receiving Dr. Ritche’s chemotherapy implant can wear to monitor subtle tumor changes. UM filed a patent application for the invention, but Laryngogen declined to license the product. Dr. Young is a co-investigator on Dr. Ritche’s protocol.

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**INFORMED CONSENT DISCLOSURE #2**

- “Dr. Young, a co-investigator, has applied for a patent for technology he invented that is being used in this research. At this time, neither Dr. Young nor the University of Miami is receiving any income from this invention. However, it is possible that, in the future, if the technology is patented and licensed to a company, Dr. Young and the University could gain royalty income.”

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**COINS STUDY**
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(COI NOTIFICATION, 2006)
- Research: Sixteen focus groups in 3 cities, including healthy adults and those with illnesses of varying degrees
- Received wisdom is that disclosure promotes: informed decision-making, trust, reduction of legal liability
  - Views of Potential research Participants on Financial Conflicts of Interest

NINE TYPES OF COI “DISCLOSURE” IN THE COINS SURVEY
- Salary Support
- Money received outside the study
- Per capita payments to cover costs
- Finders’ fees for professional uses
- Unrestricted finders’ fees
- Patent ownership by researcher
- Patent ownership by the university
- Equity holdings by researcher
- Equity holdings by university

“COINS” PARADOXICAL RESPONSES
- Some study participants believed that the financial interest was indicative that researchers are committed, ethical, confident of the effectiveness of the experimental therapy
- Some study participants stated they would not participate, their trust level would diminish, they believed scientific quality would decrease or they did not understand the disclosure language
**CONCLUSIONS**

- Many had not thought about financial interests in research
- Media attention highlights the topic
- Terms such as “equity” and “patent” confusing
- Description of financial interest and name of sponsor important
- Opportunity for discussion very difficult logistically, but important
- Potential research participants felt they had a “right to know”
- Disclosure promotes trust in the investigator

**KEY POINTS**

**COI MANAGEMENT PLAN**

- Broad disclosure (IRB’s, IACUC, staff/students, publications, human subjects)
- Independent data safety monitoring
- Recusal from as PI and form aspects of research (e.g. subject selection, informed consent, preliminary data analysis)
- Staff report to PI who has no conflict
- Agree to recuse as investigator on future validation studies
CONCLUSION

• Conflicts of Interest in research are not illegal but they can influence decisions and actions
• Let’s be proactive and address these situations in a collaborative manner as they arise
• Protect the rights and well being of our research subjects – disclose!