Conflicts of Interest in Clinical Research

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Overview
DO YOU KNOW WHAT YOU DON’T KNOW ABOUT CONFLICTS OF INTEREST IN RESEARCH?

• Pop Quiz
• 10 Questions
• True or False?

INTRODUCTION: WHAT WE WILL COVER

• How to identify a potential FINANCIAL conflict of interest;
• How to determine what action to take; and
• How to decrease the possibility of situations arising that present these conflicts of interest.
DISCUSSION: WHAT ARE WE TALKING ABOUT HERE?

• What is a **CONFLICT OF INTEREST** pertaining to the design, conduct, or reporting of research? Although answers may vary, the U.S. Department of Health and Human Services (HHS) defines this term for purposes related to Public Health Service (PHS) agency funded research or FDA marketing application procedures.

THE PHS REGULATIONS

• The regulations at 42 CFR, Part 50, Subpart F (grants) and 45 CFR Part 94 (contracts), were promulgated to promote objectivity in research. These regulations are applicable to each institution that applies for HHS Public Health Service grants, research contracts, or cooperative agreements.
THE STANDARD

• The regulation establishes standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research funded under PHS grants or cooperative agreements will be biased by any conflicting financial interest of an Investigator participating in this research.

THE TERMS

• RESEARCH means a systematic investigation designed to develop or contribute to generalizable knowledge relating broadly to public health. The term includes any activity for which research funding is available from a PHS awarding component, including basic and applied research and product development.
WHO IS COVERED BY THE RULE?

- For reporting purposes, “Investigator” means the PI and any other person who is responsible for the design, conduct, or reporting of research funded or proposed for funding by PHS. This can include a post-doctoral fellow or graduate student meeting the definition, and key personnel under a grant.
- Reportable interests include those of the Investigator, spouse, and dependent children.

ANYONE ELSE?

- If the institution carries out the research through subgrantees, contractors, or collaborators, it must take steps to ensure that Investigators working for such entities comply with the regulation, and it is responsible for reporting their conflicting interests, either by complying with the institution’s policy or by providing assurances that will enable the institution to comply.
WHAT IS EXPECTED?

• Each grantee institution must have a written enforced policy for identifying financial conflicts of interest, informing Investigators, and ensuring that conflicts will be managed, reduced, or eliminated.

FIRST STEPS

• A designated institutional official must solicit financial disclosure statements from each Investigator planning to participate in PHS-funded research before application submission.
WHAT IS INCLUDED IN THE DISCLOSURE?

• These statements list (1) known Significant Financial Interests of the Investigator that would reasonably appear to be affected by the research for which PHS funding is sought and (2) such interests in entities whose financial interests would reasonably appear to be affected by the research.

WHAT IS THE SCOPE OF THE INTEREST?

• A Significant Financial Interest means anything of monetary value, including but not limited to salary or other payments for services (e.g. consulting fees or honoraria), equity interests (e.g. stocks, stock options, ownership interests), intellectual property rights (e.g. patents, copyrights, royalties).
WHAT AMOUNTS TRIGGER DISCLOSURE?

• An equity interest is a Significant Financial Interest when, aggregated over 12 months for the Investigator, spouse, and dependent children, it exceeds $10,000 (as referenced in public prices or other reasonable measures of FMV) or represents more than a five percent ownership interest in a single entity.

WHAT ELSE?

• Salaries, royalties, or other payments for the Investigator, spouse, and dependent children (not from the applicant institution) when aggregated which are reasonably expected to exceed $10,000 in the next twelve months.
WHAT ABOUT SBIR?

• Significant Financial Interest does not include:
  – Ownership in the institution if the institution is an applicant under the Phase I Small Business Innovation Research Program (SBIR) or the Small Business Technology Transfer (STTR) Program.

WHAT CREATES A CONFLICT?

• A CONFLICT OF INTEREST exists when the designated official reasonably determines that a Significant Financial Interest could directly and significantly affect the design conduct, or reporting of the PHS-funded research. The institution may require the management of other conflicting financial interests, as it deems appropriate.
RELATIONSHIP ISSUES

• Research
  – Sponsorship funds
  – Investigators’ fees
  – Equity, joint ventures
  – Paid consultants, clinical advisors
  – Boards, officers

• Educational Grants
  – CME, Medical School
  – Drug samples
  – Gifts to individuals
  – Industry program
  – Writing, speaking

WHAT DO WE DO ABOUT IT?

• Grantees must CERTIFY on the grant application that they have a process to identify conflicting interests, and that existing conflicts (but not their nature or other details) will be reported to the PHS awarding component prior to expenditure of any funds under that award, with assurance that conflicts have been managed, reduced or eliminated.
HOW DO WE MANAGE CONFLICTS?

• Conditions may be imposed by the institution through the designated official to manage or reduce conflicts of interest, such as public disclosure of significant financial interests, modification or the research plan, disqualification from participation in part of the research, or independent monitoring of research.

IF THAT DOES NOT WORK?

• Conditions may be imposed by the institution to eliminate conflict, such as divestiture of the interest or severance of the relationships that create the actual or potential conflict.
WHAT HAPPENS NEXT?

- During the award period, the Investigator must **update** the disclosures annually or as new reportable interests arise. The institution must report any **new conflicting interests** within 60 days of identification, and those interests must have been managed, reduced, or eliminated by that time, at least on an interim basis.

DO WE KEEP RECORDS?

- The institution must **maintain records of all financial disclosures and all actions taken** by the institution with respect to each conflicting interest for at least three years from the date of submission of the final expenditures report (or other specified dates for situations as specified in 45 CFR 74.53(b)).
WHAT IF THERE IS NONCOMPLIANCE?

• Each institution must establish an adequate enforcement mechanism and provide for sanctions where appropriate. The PHS awarding component must be notified in such a case and must be told of the corrective actions that will be taken by the institution. PHS may take action also.

IS THERE HHS OVERSIGHT?

• HHS may inquire into institutional procedures and actions at any time. The PHS awarding component (1) may decide that a conflict of interest that will bias the objectivity of the research has not been remedied and may order further corrective action or (2) may determine that suspension of funding is necessary until the matter is resolved.
ANY SPECIAL CIRCUMSTANCES?

- If HHS determines that research whose **purpose** is to evaluate the safety or effectiveness of a drug, medical device, or treatment is associated with a conflicting interest that was not properly disclosed or managed, the institution **must require the Investigator(s) to disclose the interest in all public presentations of the research results.**

WHAT DO NIH GRANTEES NEED TO KNOW NOW?

- In October 2007, **NIH** began a Pilot Compliance Program to assess institutional compliance with the financial conflict of interest regulations applicable to NIH grants and cooperative agreements. The program review of twelve (12) institutions is not yet complete. This is an outgrowth of the NIH Targeted Site Reviews of eighteen (18) institutions conducted by the Division of Grants Compliance and Oversight, OPERA, OER that focused on this topic.
WHAT DO NIH GRANTEES NEED TO KNOW NOW, CONT’D

- See Observations document @ http://grants.nih.gov/grants/compliance/compliance.htm
- The most common compliance issued centered around the appropriate definition of “Investigator” or around institutional reporting requirements (implementation issues).

DOES FDA HAVE ITS OWN RULES?

- Under 21 CFR Part 54, the Food and Drug Administration (FDA) requires anyone who submits a marketing application of any drug, biologic, or device to submit Form 3454 and 3455 to the FDA concerning compensation to and financial interests of any clinical investigator (including spouse and dependents) conducting clinical studies covered by the rule.
WHO HAS THE FDA RESPONSIBILITY?

- At the time the marketing application is submitted to FDA, Applicants must certify to the absence of certain financial interests, (interests in or payments by the “sponsor” providing study support, certain compensation or proprietary interests) or disclose those interests and steps taken to minimize the potential for bias. If the applicant does not comply, FDA may refuse to file the marketing application.

WHAT IS THE PURPOSE OF DISCLOSURE TO FDA?

- The purpose of disclosing these certain financial arrangements (which are identified on the disclosure form and higher than the NIH monetary thresholds), is to ensure that financial interests of Clinical Investigators that could affect the reliability of data submitted to FDA are identified and disclosed by the party who submits a marketing application to FDA for approval.
FDA ACTIVITY

- FDA announced on August 4th, 2008 that it has issued Guidance Documents imposing stricter limits on financial conflicts of interest for its Advisory Committee members. The cap will be $50,000 in financial interest in all companies that may be affected by a particular meeting.

ARE THERE DISTINCT RULES FOR IRB MEMBERS?

- Regulations for HHS conducted or supported human subject research at 45 CFR 46.107(e) and for FDA supported research at 21 CFR 56.107(e) prohibit an IRB member with a conflicting interest in a project from participating in the IRB’s initial or continuing review (i.e. recusal), except to provide information as requested by the IRB.
IS THIS ISSUE WIDESPREAD?

- Conflicts of interest may influence judgment decisions for anyone in your institution. Last year, a researcher at an institution was serving as a peer reviewer for an article for a medical journal. It was a pooled analysis of studies of the marketed drug and suggested that the drug increased the risk of heart attack. He faxed a draft to the drug manufacturer whose drug was the subject of the article.

WHAT WAS THE CONFLICT?

- This researcher had received consulting fees and honoraria from the drug company in the past and had conducted research for the company. Did this researcher’s financial relationship with the company affect his judgment and his actions? His actions have become the subject of a Senate investigation.

IS THIS ISSUE WIDESPREAD?

• “Three prominent psychiatrists at the Harvard Medical School and its affiliated Massachusetts General Hospital have been caught vastly underreporting their income from drug companies whose fortunes could be affected by their studies and their promotional efforts on behalf of aggressive drug treatments.”

NY Times, Sunday June 8, 2008: Hidden Drug Payments at Harvard

WHAT ABOUT INSTITUTIONAL CONFLICTS OF INTEREST?

• The AAMC and AAU issued a joint report recently calling on all medical schools and major research universities to develop institutional financial conflict of interest policies within the next two years.

WHAT DOES THE AAMC-AAU REPORT RECOMMEND?

• The report reflects the concern as academic institutions expand their relationships with industry. The report recommends development of policies that cover the financial interests of faculty, institutions and their officials. For example, one recommended action is to separate the institutional research and financial decision-making processes and agents.

DOES HHS OFFER SUGGESTIONS FOR MANAGING HUMAN SUBJECT RESEARCH?

• OHRP recommends, e.g., disclosure to prospective subjects, additional oversight or monitoring of the research, modification of roles of research staff or changes in location for certain research activities.

DO WE KNOW WHAT WE DID NOT KNOW THEN?

• THE ANSWERS TO THE TRUE/FALSE QUESTIONS PRESENTED TO YOU AT THE BEGINNING OF THIS SESSION ARE AS FOLLOWS:

• (ANSWERS WILL BE GIVEN ORALLY)

• QUESTIONS?

RESEARCH Compliance Conference
October 20–22, 2008
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Conflicts of Interest in Clinical Research

Lawsuits and Enforcement Actions
LAWSUITS/ENFORCEMENT ACTIONS

*Moore v. Regents of University of California*

- Patient undergoes treatment for leukemia
- Physician recognizes commercial possibilities of patient’s rare cells
- Physician recommended removal of spleen, some of which was sent to lab for commercial development
- University later received a patent used to negotiate agreements for commercial development of cell line

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LAWSUITS/ENFORCEMENT ACTIONS

*Moore v. Regents of University of California, cont’d*

- Patient sues physician and University
- Alleges conversion and breach of physician disclosure obligations
- California Supreme Court finds that a physician must disclose personal interests that may affect professional judgment
- Failure to disclose results in failure to obtain informed consent and breach by physician of fiduciary duty
LAWSUITS/ENFORCEMENT ACTIONS

• **Gelsinger** – Jesse Gelsinger was an 18 year old with a genetic disorder that interfered with the ability of certain liver enzymes to remove ammonia (a byproduct of processing proteins) from the body. His condition was controlled by diet and medication. He agreed to participate in a clinical trial involving gene transplantation to treat the disorder, and died from multiple organ failure four days after receiving a high dose of the viruses used to carry the genetic material.

LAWSUITS/ENFORCEMENT ACTIONS

• **Gelsinger, cont’d**
  – Director of University’s Institution for Human Gene Therapy owned a 30% equity interest in biotech company that produced product being evaluated in study
  – Ownership interest later valued at $13.5 million
**LAWSUITS/ENFORCEMENT ACTIONS**

- **Gelsinger, cont’d**
  - University had agreement with biotech company to receive rights to gene research discoveries that occurred at University
  - Same biotech company contributed 20% of the budget for the Institution for Human Gene Therapy

- **Gelsinger, cont’d**
  - Family claimed adverse reactions in other studies were not disclosed to research participants, and that COIs led to acceptance of Jesse Gelsinger as research subject when he failed to meet protocol criteria
  - DOJ files lawsuit against University, alleging false statements in documents submitted to NIH and FDA
LAWSUITS/ENFORCEMENT ACTIONS

• Gelsinger, cont’d
  – University and associated hospital paid $1 million to resolve FCA suit
  – Director of research institute and PIs and could not play a significant role in clinical trials for a number of years

LAWSUITS/ENFORCEMENT ACTIONS

• Gelsinger, cont’d
  – University and Hospital agreed to:
    • Increase IRB oversight
    • Increase in budget and size of IRB
    • Mandatory ethics/COI training for all investigators and clinical coordinators
    • Established Office of Human Research
LAWSUITS/ENFORCEMENT ACTIONS

• Gelsinger, cont’d
  – University and Hospital hired Physician Research Subject Advocate to:
    • Observe consent process periodically
    • Assist investigators
    • Monitor adverse event reporting

Fred Hutchinson Cancer Research Center

• Involved study to prevent graft-versus-host disease in leukemia patients who received bone marrow transplants. To prevent GVHD, synthetic proteins were added to bone marrow prior to transplantation. Researchers and cancer institute had financial ties (equity interests, consulting fees and research funding) to biotech company that produced the proteins.
Fred Hutchinson Cancer Research Center, cont’d

• Seattle Times published story suggesting that financial ties were basis for continuing study for 12 years despite multiple problems
• Higher rate of graft failure and cancer relapses
• Lawsuit filed on behalf of 82 patients

Fred Hutchinson Cancer Research Center, cont’d

• Claimed financial ties and significant risks of procedure were not disclosed to research subjects
• Trial resulted in jury verdict in favor of defendants
  – Jury found that information omitted from informed consent process would not have prevented subjects from participating in trial
LAWSUITS/ENFORCEMENT ACTIONS

Fred Hutchinson Cancer Research Center, cont’d

• Court found no private right of action for violation of federal regulations protecting human research subjects
• Constitutional rights not implicated by failure of informed consent, unless subjects did not know that they were participating in experimental treatment

LAWSUITS/ENFORCEMENT ACTIONS

Cleveland Clinic/AtriCure

• Cleveland Clinic obtains indirect interest in maker of cardiac medical devices

• Physician CEO of Clinic
  – Held seat on Board of Directors for AtriCure for a time
  – Negotiated with AtriCure for royalties for a medical device he developed
  – Along with other Clinic physicians, actively promoted cardiac device and received consulting fees from AtriCure
LAWSUITS/ENFORCEMENT ACTIONS

Cleveland Clinic/AtriCure, cont’d

- Device used off-label at Clinic
- Wall Street Journal article discloses financial relationships and use of device in clinical trials at Clinic
- COI Committee at Clinic revises consent forms to disclose existence of financial ties and that Clinic could benefit if research is successful
- Wall Street Journal points out that only 16 out of 1247 patients saw the new consent form

Darke v Eisner

- Patient with chronic heart disease referred to experimental gene therapy program
- Died 24 hours after receiving gene therapy
- Principal investigator and hospital each owned 20% interest in biotech company that produced gene therapy
- Patient’s wife sues PI and hospital for failure to disclose financial COI
- Courts finds that Massachusetts informed consent law implicated, and denies MSJ filed by defendants
LAWSUITS/ENFORCEMENT ACTIONS

Continuing Themes

- Bad outcomes in clinical trials attributed to poor judgment resulting from conflicts of interest
- Lawsuits, investigations
  - Lack of informed consent
  - Fraud
  - False Claims Act
  - Constitutional violations
  - Failure to comply with applicable regulations

LAWSUITS/ENFORCEMENT ACTIONS

Continuing Themes

- Negative PR, tarnished reputations
- Calls for disclosure of COI to research subjects
LAWSUITS/ENFORCEMENT ACTIONS

Continuing Themes

• Negative PR, tarnished reputations
• Calls for disclosure of COI to research subjects

OIG January 2008 Report

• National Institutes of Health: Conflicts of Interest in Extramural Research
  – NIH could not provide an accurate count of financial conflict-of-interest reports received from grantees during 2004 - 2006
  – NIH is not aware of the types of financial conflicts of interest that exist within grantee institutions because details do not have to be reported and most reports do not state the nature of the conflict
LAWSUITS/ENFORCEMENT ACTIONS

OIG January 2008 Report, cont’d

• Primary method of oversight is reliance on grantee institutions’ assurances that financial conflict-of-interest regulations are followed

• Oversight of grantee institutions should be increased to ensure compliance with Federal financial conflict-of-interest regulations

• Reports should require more information regarding the nature of financial conflicts of interest and how they are managed, reduced, or eliminated

LAWSUITS/ENFORCEMENT ACTIONS

OIG 2008 Workplan

• Review of NIH’s Monitoring of Extramural Conflicts of Interest.

“Conflicts of interest in the scientific community pose serious risks to clinical trial subjects and consumers, because a risk of bias can affect the quality of treatment decisions. We will focus on financial conflicts of interest that grantee institutions report to NIH, as well as the extent to which NIH oversees grantees’ monitoring and management of potential financial conflicts of interest.”
FDA Warning Letters

- West Jefferson Medical Center IRB (Feb. 25, 2008) (Division of Scientific Investigations)
  - IRB failed to excuse an IRB member from participating in the initial review of a project in which the member had a conflicting interest
- Brookhaven Memorial Hospital Medical Center (July 8, 2008) (Center for Devices and Radiological Health)
  - IRB minutes reflected that physician participated in review of studies for which physician served as PI, and no indication that physician abstained from voting

FDA Warning Letters, cont’d

- Synthemed, Inc. (Feb. 19, 2008) (Center for Devices and Radiological Health)
  - Failed to observe protocol that physician who performed patient assessment could not also perform surgery
Conflict of Interest in Clinical Research

Conflict of Interest Policies

Harvard COI Policy

- Researcher cannot participate in research on a technology owned by or contractually obligated to a Business in which the researcher has a financial relationship unless -
Conflict of Interest Policies

*Harvard COI Policy, cont’d*

- Ownership interest is in a publicly traded company and does not exceed $30,000 (for recipients of PHS/NSF funds, no more than $10,000 and no more than 5% ownership of business)

- Acquisition was independent of research (must be arms length or by family gift before research begins)

Conflict of Interest Policies

*Harvard COI Policy, cont’d*

- Income from business through honoraria, consulting or participation on advisory boards may not exceed $20,000 ($10,000 for recipients of PHS/NSF funds)

- Receipt of university or hospital-supervised sponsored research support or royalties under institutional royalty sharing is excepted
Conflict of Interest Policies

Harvard COI Policy, cont’d

• Disclosure of financial relationship for purposes of publications, presentations or providing expert commentary is required
  – No reference to disclosure to research subjects

Conflict of Interest Policies

Harvard COI Policy, cont’d

• Full time faculty may not serve in executive position in for-profit business engaged in bio-medical research

• Faculty serving as Director of business may not
  – Participate in clinical research on technology owned by or obligated to business or received sponsored research funding from the business
Conflict of Interest Policies

Harvard COI Policy, cont’d

• Faculty member may participate in clinical research on a technology developed by faculty member or family unless ownership interest or financial relationship exceeds permitted amounts
  – Disclosure in publications, presentations required
  – Oversight “where necessary”

Conflict of Interest Policies

Harvard COI Policy, cont’d

• Researcher serving as mentor must disclose to students and trainees
  – Source of funding
  – Any personal financial interest held by researcher
  – Any restrictions on scientific communication of data
Conflict of Interest Policies

Duke COI Policy

- Annual reporting form for each faculty member posted on website
- Lists 200 companies
- Report form lists seven types of financial relationships for each company

Conflict of Interest Policies

Duke COI Policy, cont’d

- “A research grant or contract from this company partially supports my university salary”
- “A research grant or contract from this company supports my research projects”
- “I have equity in this company” (designate if greater than $10,000 or 1%)
- “I receive significant personal royalties from this company”
Conflict of Interest Policies

Duke COI Policy, cont’d

- “Educational activities or lectures for this company generates revenue for Duke” (less than $10,000 or greater than $10,000)

- “Consulting or other services for this company generates personal income” (less than $10,000, between $10,000-$25,000 or greater than $25,000)
  – Different categories for CME Services/non-CME services

Duke COI Policy, cont’d

- Analysis of forms by computer software, COI staff and COI Committee

- Standard management plan
  – Follow-up with IRB, and Office of Research Administration
  – Disclosure of conflict to research subjects, academic journals, manuscript reviewers, audiences and sponsors
Conflict of Interest Policies

Duke COI Policy, cont’d

- Options for custom management plan
  - Public disclosure
  - Monitoring of research by independent reviewers
  - Modification of research plan
  - Disqualification from participation in all or part of research
  - Divestiture of significant financial interests
  - Severance of relationships that create actual/potential conflicts

Conflicts of Interest in Clinical Research

Case Studies from Report “Protecting Patients, Preserving Integrity, Advancing Health” by AAMC-AAU Advisory Committee on Financial Conflicts of Interest in Human Subjects Research
Case Study #1: Consulting

- Dr. Smith proposes to be the local site principal investigator (PI) of a large Phase III multi-center trial to test a new statin in human subjects.
- CardioX, manufacturer and publicly-traded company, is the sponsor.
- University receives a fixed fee for each subject enrolled.
- CRO will administer study, and DSMB has been established.
- Dr. Smith’s site is one of 50, enrolling 2-3% of subjects.

Case Study #1: External Interests

- Dr. Smith is a member of CardioX’s scientific advisory board, earning $8,000 to attend four meetings a year.
- The work of the advisory board is not directly related to the subject of the study.
- CardioX asks Dr. Smith to continue acting as an advisor, while also serving as site-based PI of the study.
Case Study #1: Conflict of Interest?

- The research could proceed:
  - Dr. Smith’s compensation falls under the threshold often designated as de minimus.
  - Dr. Smith does not hold a leadership position on the scientific advisory board.

- However, some institutions require disclosure of all external financial interests and have a “rebuttable presumption” prohibiting an investigator with a financial interest from conducting research without compelling justification for an exception.

Case Study #1: Risk-benefit analysis

- Increased risk to human subject safety?
  - Dr. Smith’s relationship with CardioX could be enhanced by a favorable outcome, but a COI committee could find risks are not likely to be increased.

- Risk to data integrity?
  - Dr. Smith has no control over the study protocol. A CRO is monitoring the data collection practices, and the DSMB reviews the data quarterly.

- Appearance of conflict of interest?
  - Dr. Smith may consider $8,000 modest, but the public could have a different view. Perception of a COI could be enhanced by adverse events, and the university may not get to present mitigating facts.

- Could the outcome of the study benefit the public?
  - Yes, assuming any actual and perceived conflicts of interest are effectively managed.
Case Study #1: Risk-benefit analysis

• Should Dr. Smith pursue the research while a paid consultant to CardioX?

• The university could consider one or more of the following management conditions:
  – Dr. Smith must disclose he is paid by the research sponsor as a consultant in all publications, presentations, and consent forms.
  – All publications and presentations must be written by investigators, not by CardioX ghost writers.
  – Dr. Smith may not participate in selecting, recruiting, and obtaining consent from research participants.
  – Dr. Smith must inform the CRO and DSMB of his conflict of interest.

Case Study #2: Licensing, Leadership

• In animal laboratory studies, Dr. Rose, Professor and Chief of the Division of Gastroenterology, identifies a biomarker that may be important in identifying precancerous intestinal lesions.

• Dr. Rose has developed a method to “light up” the biomarker so it can be detected by imaging.

• Preliminary work suggests an association between the marker and cancer.

• Dr. Rose proposes to be the PI on an NIH grant to test his hypothesis.
Case Study #2: Licensing, Leadership

• Under protocol, surgeon will remove sample of intestinal tissue from patients undergoing GI surgery for diagnoses other than cancer.

• Dr. Rose will test samples for the biomarker and over next 3 years will follow clinical progress of patients.

• If there is a correlation between presence of biomarker and diagnosis of cancer, predictive value of assay will be established.

• Consent will be obtained from patients by a research coordinator, and Dr. Rose will have no role in surgery.

Case Study #2: External Interests

• The University has licensed Dr. Rose’s assay to Diagnocorp, a large company that develops diagnostic kits.

• License terms include modest annual fees and post-marketing royalty payments of 4% of sales.

• Under University’s intellectual property policy, Dr. Rose is entitled to 35% of the University’s income, and his division is entitled to 30%.
Case Study #2: Conflict of Interest?

- Existence of conflict depends in part on whether project is considered clinical research.
- National higher education associations recommend prohibiting clinical research in the presence of an investigator’s significant financial interests.
- Federal regulations recognize royalties as potentially significant financial assets.
- Is it clinical research?
  - No. Clinical research must involve experimental procedures performed in vivo; IRB can determine if benefit justifies any risk associated with removal of tissue sample.
  - Yes. COI exists, and committee will undertake risk-benefit analysis.

Case Study #2: Risk-benefit analysis

- Increased risk to human subject safety?
  - Risk is very low. Dr. Rose will not participate in selection, recruitment, consent, or surgery. Risks to subjects are distinct from risks that might result from Dr. Rose’s financial interests.
- Risk to data integrity?
  - Potential risk that potential sales of diagnostic kits could influence Dr. Rose’s judgment in analyzing data. However, diagnosis of cancer will be handled by an objective third-party over a period of 3 years.
- Appearance of conflict of interest?
  - A potential risk, but can be mitigated through public disclosure.
- How does Dr. Rose’s role at the University affect the COI review?
  - Administrative decisions could be influenced by research and royalties.
  - Might be tempted to involve faculty, staff, and students inappropriately.
  - Division’s royalties could be channeled to advantage of Dr. Rose.
- Benefits to public?
  - There is a benefit to producing a potentially valuable diagnostic tool.
Case Study #2: Risk-benefit analysis

• Should Dr. Rose forego revenue to conduct the study?
  – Even if Dr. Rose does not forego revenue, his ability to manipulate the results will be limited, especially if there is oversight.

• Institution should:
  – Require Dr. Rose to disclose his financial interest in future fees and royalties in relevant publications and consent forms, and to department chair, other division faculty, trainees participating in the project, and others on the study and surgical teams.
  – Require the chair/designee to review Dr. Rose’s administrative decisions affecting the division and his laboratory.
  – Require a disinterested person to oversee the collection, analysis, and reporting of study data.
  – If royalties accrue to the division, the use of these funds should be reviewed to ensure compliance with purchasing and ethics requirements.
  – Designate a disinterested person as a “safe haven” for any faculty and staff who have concerns about the arrangement.

Case Study #2: Variation

• What if Dr. Rose’s protocol also requires injecting a radioactive compound into the intestine for later imaging to detect biomarker?
  – Risk to human subject safety?
    There is more risk. However, the risk that Dr. Rose’s conflict would influence the protocol is unchanged.
  – Risk to data integrity?
    No significant change. The image analysis will be done by an independent radiologist.
  – Appearance of Conflict of Interest?
    Yes. The increased risk to human subjects could heighten the appearance of a COI.
  – Risk of supervisory Conflict of Interest?
    Unchanged.
Case Study #2: What if…?

• Should Dr. Rose still be allowed to conduct the study?
  – If the research is prohibited by university policy, but the policy recognizes “rebuttable presumption”, the COI Committee could allow Dr. Rose to serve as PI. Factors to consider:
    • Does Dr. Rose have unique skills/qualifications needed in the protocol?
    • Is the University the only place the study can be conducted?
    • Could an independent, unconflicted investigator be appointed as PI?
    • Could Dr. Rose serve as co-investigator?

Case Study #3: Start-Up Company

• Dr. Sellers, Assistant Professor of Medicine in Hematology/Oncology Division, is a clinical investigator of ovarian cancer. She discovers a protein in ovarian cancer cells and shows that a monoclonal antibody (MAB) can reduce progression of cancer in mouse xenograft model.
  • NIH declined to fund a proposal for Phase I studies in humans.
  • Dr. Sellers raises local venture capital to fund a small biotech company to develop the project.
  • The University approves establishment of the biotech company, and licenses the MAB technology to the company.
  • The company proposes to sponsor a Phase I clinical trial in which Dr. Sellers will inject the MAB into human subjects with ovarian cancer to study its effect on progression of cancer.
Case Study #3: External Interests

- Dr. Sellers was only minimally involved in license negotiations between the biotech company and the University.
- Dr. Sellers obtained 100,000 shares of founders stock.
- She receives $30,000/year as a member of the company’s advisory board, but is not an officer or member of the board of directors.

Case Study #3: Conflict of Interest?

- As founder of the company using technology generated in her laboratory under a license from the University, Dr. Sellers has a significant financial and intellectual interest in the outcome of the study.
- National associations of higher education and many institutional policies would prohibit her participation as a PI, unless the “rebuttable presumption” test is overcome.
Case Study #3: Risk-benefit analysis

• Increased risk to human subject safety?
  – Dr. Sellers' financial interests could influence her judgment in selection, recruitment and consent process.
  – She could assign patients to experimental groups in ways that enhance her financial interests.
  – She might obtain patient consent without full disclosure of the scientific facts or her personal financial interests.

• Risk to data integrity?
  – Dr. Sellers could influence the outcome of the trial by selecting patients who are not eligible, or interpreting the data in favor of effectiveness of MAB.

• Appearance of conflict of interest?
  – Dr. Sellers and the University are at risk for damage to reputation, especially should an adverse event occur.

• Could the outcome of the study benefit the public?
  – Possibly, but the project lacks important peer endorsement. Preliminary results have not provided sufficiently strong evidence for the NIH to support further research.

Case Study #3: Risk-benefit analysis

• Should Dr. Sellers conduct the study, in light of her conflict of interest?
  – The COI Committee most likely will restrict or prohibit Dr. Sellers’ involvement in the trial.
    • Dr. Sellers could eliminate the COI by reducing or eliminating her financial interests.
    • Under rebuttable presumption, the University could determine an exception. However, unique skills are not needed to conduct the trial or to assess the results, so key indicators of rebuttable presumption would not be met.
Case Study #3: Risk-benefit analysis

• The Committee could recommend that the trial go forward at the University, but without Dr. Sellers as PI. In this case, the following should be done:
  – Appoint an independent faculty investigator as PI.
    • “Independent” = not a close friend or relative of Dr. Sellers, no reporting line to her, not subject to her approval authority.
  – All members of the project team must disclose financial interests in all verbal presentations and written publications.
  – Restrict Dr. Sellers’ role to co-PI or collaborator.
  – Preclude Dr. Sellers’ role in selection, recruitment, or consent process and interaction with human subjects.
  – Restrict Dr. Sellers and her laboratory staff to the analysis of blinded data.
  – University should address institutional COI possibly by eliminating its holdings in the company before the trial.

Case Study #4: Stock Option Ownership

• Dr. Roberts, Professor of Pediatrics, proposes to be the PI on a multi-site Phase II clinical trial to test an inactivated vaccine for RSV in a pediatric population.

• The proposed sponsor and maker of the vaccine is SuperVax, a small publicly-traded biotech company.

• Dr. Roberts is the PI for a study of RSV that is funded by NIH. He plans to analyze specimens generated from the SuperVax trial as part of the larger project.
Case Study #4: External interests

• Dr. Roberts has stock options in SuperVax.
• The company is currently trading below the exercise value of his options.

Case Study #4: Conflict of Interest?

• Ownership of equity in the company that manufactures the drug/devise is a significant financial interest.
• Conflict is more significant when the company also sponsors the research. If the study proves the vaccine is safe and effective, Dr. Roberts’ equity could increase considerably.
• The need for specimens for the larger project could motivate Dr. Roberts to conduct the trial to benefit the NIH sponsored research.
Case Study #4: Risk-benefit analysis

- Increased risk to human subject safety?
  - Dr. Roberts' stock ownership and desire for the company's success could influence his clinical assessment of patients to favor the vaccine's success.
  - Dr. Roberts might receive revenue from the commercial licensing of the vaccine before the long-term effects of the vaccine are properly understood.

- Risk to data integrity?
  - Dr. Roberts' financial interest could influence how he records and interprets data.

- Appearance of conflict of interest?
  - A risk is present, and is greater because the subjects are infants and children.
  - The integrity of the institution and the investigator could be questioned.

- Could the outcome of the study benefit the public?
  - An effective vaccine would prevent serious illness and economic loss for many children and adults.

Case Study #4: Risk-benefit analysis

- In view of his conflicts, could Dr. Roberts be allowed to pursue this research as PI?
  - If he does not divest his stock options, AAMC guidelines and institutional policies would prohibit Dr. Roberts' participation in the trial as PI.
  - The circumstances do not overcome the "rebuttable presumption" – It is a multi-site study, so Dr. Roberts' qualifications are not unique.

- Because of the public benefit, the institution could impose one or more of the following conditions to allow the trial to proceed:
  - Require an independent PI.
  - Allow Dr. Roberts to participate as a co-investigator if he discloses his financial interests in the research sponsor and manufacturer of the vaccine in publications, consent forms and to others on study team.
  - Require all publications and presentations to be written by investigators, rather than a SuperVax ghost writer.
  - Prohibit Dr. Roberts from participating in patient selection, recruitment, consent, or assessment process, and no interaction with subjects.
  - Any data analysis by Dr. Roberts or his lab would be blinded data.
Case Study #4: Adding a junior colleague

• Dr. Roberts proposes that a colleague who is an assistant professor, Dr. Brill, serve as PI.

• The SuperVax grant includes 10% support of Dr. Brill’s University salary based on her effort devoted to research.

• Dr. Brill does not have a consulting or equity relationship with SuperVax.

• Conflict of Interest?
  – No direct conflict.

• Could Dr. Brill participate in the research?
  – Yes, if she does not report to Dr. Roberts and is not influenced by him in the conduct of the trial.

Case Study #5: Stock and Patent

• Drs. Weiss and Gruen (Pulmonary Division faculty) and Dr. Jones (Pharmacology Professor) propose to conduct a Phase II, randomized, double-blinded, placebo-controlled trial funded by the Cystic Fibrosis Foundation.

• Study will test efficacy of a drug to reduce lung inflammation in Cystic Fibrosis (CF) patients.

• Drs. Weiss and Gruen will administer drug, extract blood samples and send to Dr. Jones for analysis, which must be performed within one hour of collection.

• Dr. Jones’ lab has developed new protocols that facilitate analysis of the samples.
Case Study #5: External interests

- Dr. Jones has stock in the privately-held start-up company that will supply the drug. It is the only reputable company that makes the drug.

- The University has filed a patent for use of the drug in CF, with Drs. Weiss, Gruen, and Jones as inventors.

- In return for providing the compound, the company requires an agreement licensing the University’s patent to the company.

- If the trial is successful, the University and the inventors will share a royalty stream.

Case Study #5: Conflict of Interest?

- All three researchers stand to benefit from potential royalty revenues.

- Dr. Jones also owns stock in the company that makes the drug.
  - AAMC guidelines recommend investigators with equity in a start-up company closely involved in clinical research should be prohibited from engaging in the research, unless “rebuttable presumption” can be overcome.
  - Since the researchers are involved in procurement of the drug, there may be a conflict created by Dr. Jones’ interest in the company that makes the drug. However, as the company is the only reputable vendor of the drug, there should not be a procurement-related conflict.
Case Study #5: Risk-benefit analysis

• Increased risk to human subject safety?
  – The judgment of Drs. Weiss and Gruen in selection, recruitment, and consent process could be influenced by their expectation of potential royalties.

• Risk to data integrity?
  – Dr. Jones could be influenced in his data analysis by his financial interests. Drs. Weiss and Gruen could be influenced in how they record their clinical assessments.
  – Risks are reduced because study is double-blinded and placebo-controlled.

• Appearance of conflict of interest?
  – All three investigators have financial interests in outcome of trial.

• Could the outcome of the study benefit the public?
  – It could measurably improve patient health and quality of life.

Case Study #5: Risk-benefit analysis

• Could Drs. Weiss, Gruen, and Jones be allowed to pursue this research proposal?
  – First, request all three to reduce/eliminate financial interests.
  – Is rebuttable presumption overcome?
    • Drs. Weiss and Gruen do not appear uniquely qualified to conduct the trial. However, the University likely only has one or two CF specialists.
    • Dr. Jones could be uniquely qualified because his laboratory has special methods for analyzing samples.
Case Study #5: Risk-benefit analysis

• Committee could find that there are compelling reasons to allow the trial to be conducted at the University, with these conditions:
  – Require researchers to fully disclose their financial interests in all relevant publications, presentations, and consent forms.
  – If Drs. Weiss and Gruen are uniquely qualified, require an unconflicted, independent person to obtain the consents.
  – Require formation of an oversight committee to address integrity of the recruitment, selection, and consent process, evaluate the raw data, and review manuscripts.
  – Require the hospital pharmacy to “blind” the drug/placebo for administration to patients, and to maintain the code until the study is complete.
  – Require all data from Dr. Jones’ laboratory be stored immediately after collection in a secured form.
  – Require preliminary data analysis be carried out with the investigators remaining “blind” to patient treatment assignment groups.

Case Study #6: Licensed Intellectual Property

• Dr. Lief, Professor of Human Genetics and Medicine, has developed a new vector (the IP) for gene therapy for various types of cancers.
• The University’s research foundation has licensed the IP to Dr. Lief’s start-up company.
• Dr. Martin, faculty in the same department, and independent of Dr. Lief, proposed to be PI on a Phase I safety trial.
• Dr. Lief’s company plans to sponsor the research by issuing a grant to Dr. Martin.
Case Study #6: Licensed Intellectual Property

- Dr. Martin will subcontract the assay analysis to Dr. Lief’s laboratory at the University, with Dr. Lief as PI.
- Dr. Lief will devote 5% effort on the project, but will not charge his salary to the grant.
- University department will cost-share Dr. Lief’s effort on the project.
- Dr. Lief’s postdoctoral fellow will be reimbursed for 85% effort and his research specialist for 50% effort.

Case Study #6: External interests

- Dr. Lief, his spouse, and several colleagues are investors in the start-up company. Dr. Martin has no affiliation with the company.
- Dr. Lief is VP for Scientific Affairs, and his spouse is Treasurer of the start-up company.
- Dr. Lief, his spouse, colleagues, and the University Research Foundation hold equity in the start-up company, and will receive royalties from license agreement.
- The department chair has no association with the company, but the department would benefit from the distribution of royalties.
### Case Study #6: Conflict of Interest?

- Dr. Lief has a COI, since he has founder’s equity in the start-up company.
- The University/University Research Foundation’s equity and the chairman’s share in future royalties constitute institutional conflicts of interest.
- Dr. Lief has conflicting fiduciary duties to the University and his company. Even if he stepped down from the company, the COI regulations include his spouse.
- Dr. Martin does not have a personal COI.

### Case Study #6: Risk-benefit analysis

- Increased risk to human subject safety?
  - Dr. Martin has no financial interest that would influence her judgment as PI.
- Risk to data integrity?
  - Dr. Lief’s equity in the sponsoring company and expectation of future royalties could influence conduct of assays and data collection and interpretation.
- Appearance of conflict of interest?
  - Yes, the institutional COI probably can not be managed for this gene therapy trial.
- Could the outcome of the study benefit the public?
  - Subjects of trial have recurrent cancer, and the treatment may result in significant tumor shrinkage or stabilization.
Case Study #6: Risk-benefit analysis

• In light of their COI’s, could the investigators be allowed to pursue this research proposal?
  – Dr. Lief’s financial interests cannot be managed, and he should be prohibited from participating in the trial.
  – The University could eliminate the institutional conflict by divesting its equity in the start-up company.
  – If a laboratory independent of Dr. Lief conducted the assays, Dr. Martin could conduct the trial at the University without any COI. She should not consult with Dr. Lief regarding the trial or discuss the results.

Case Study #7: Administrative Conflict

• Dr. Wilson, Chair of the Neurology Department, has developed a new drug to slow development of Alzheimer’s. The drug was developed in her laboratory in collaboration with Dr. Weiss, a non-tenured assistant professor in the department.

• In compliance with University policy, Dr. Wilson seeks approval to form a start-up company to sponsor clinical trials in which she will be PI and Dr. Weiss will be co-PI.

• Dr. Wilson proposes that the University license the new drug to the start-up company in which she will be President and CEO, and Dr. Weiss will be VP for Research.
Case Study #7: External Interests

- Dr. Wilson proposes she will own 80% of the equity in the start-up company, with Dr. Weiss and the University each owning 10%. No venture capital has been secured.

- Dr. Wilson will be paid $40,000/year for her duties as Chair of the Board and Scientific Advisory Committee.

- Per University policy, royalties from marketing the drug will be distributed to Drs. Wilson and Weiss privately, to their research accounts, to their department, to the medical school, and to the University.

Case Study #7: Conflict of Interest?

- As department chair, Dr. Wilson makes decisions affecting Dr. Weiss, including salary, promotions, tenure, and teaching duties.

- Dr. Wilson also can allocate resources to her own research projects.

- Dr. Wilson’s proposed role in the company could distort her commitments to the institution and her colleagues.

- Even if not a department chair, the institution could conclude Dr. Wilson’s fiduciary duty to the University precludes her serving as an officer or board member in the company sponsoring her research.

- Dr. Wilson and Dr. Weiss have individual COI’s, since both will have financial interest in the company that might influence the research and data analysis.
Case Study #7: Risk-benefit analysis

• Increased risk to human subject safety?
  – Both physicians benefit if they select subjects, administer the drug, or explain the risks to subjects in ways that positively influence the outcome of the research.
  – The University’s equity ownership could influence its oversight. But, individuals who make decisions about University investment are usually not in close contact with research administration, IRB and investigators.

• Risk to data integrity?
  – The physicians’ conflicts could influence how they design and conduct the protocol and how they collect, analyze and report data.

• Appearance of conflict of interest?
  – Both the University and the investigators have substantial financial interest, so the appearance of a COI may persist even if the COI is managed.

• Could the outcome of the study benefit the public?
  – The drug has potential to give extended quality of life to patients. However, without divesture or conflict management, the validity of the research will be questioned.

Case Study #7: Risk-benefit analysis

• Should Drs. Wilson and Weiss be allowed to conduct clinical trials sponsored by the company?
  – The University should seek an independent expert opinion on whether the license should be pursued with the start-up or another company.
  – The company should have a separate CEO or attorney with whom the University would negotiate, rather than Dr. Wilson signing on behalf of her company.
  – Most universities would not allow Dr. Wilson to serve in the company if it plans to sponsor research conducted by Dr. Wilson.
  – Dr. Weiss’ equity in the company could bias his judgment in the conduct and interpretation of the research.
  – The conflicts are so unmanageable that neither the formation of the start-up company nor the University’s and investigator’s participation in the clinical trials should be allowed.
**Case Study #7: Risk-benefit analysis**

- Possible solutions:
  - Another institution could sponsor the research
  - The University sponsors the research with different investigators:
    - New investigators must be independent of Drs. Wilson and Weiss
    - Drs. Wilson and Weiss may not hold management positions in the company, but could serve as consultants.
    - Drs. Wilson and Weiss may participate in the trials, but have no contact with subjects or data collection.
    - Data analysis will be reviewed by unbiased experts.
    - If Drs. Wilson and Weiss serve as consultants, full disclosure of interests must be required.

**Case Study #8: Controversial Funding Source**

- Dr. Cho, Professor of Radiology, is approached by a well-known soap company that proposes to sponsor a human subjects research study at the medical school, with Dr. Cho as PI.
- Dr. Cho is an expert in MRI technology, and has a national reputation for his work in mapping the parts of the brain that “light up” during day-to-day activities.
- Dr. Cho has created a body of evidence that under certain circumstances, knowing which parts of the brain “light up” can allow prediction about the choices an individual will make.
- In the study, Dr. Cho will ask subjects about the soap product and different advertising strategies. The company will use the results for improving its marketing.
Case Study #8: Controversial Funding Source

- The company demands exclusive rights to the study results, which Dr. Cho has refused.
- Dr. Cho proposes to use the medical school’s MRI equipment and reimburse the University with part of the research funds from the soap company.
- Dr. Cho believes that the study will allow him to test new aspects of choice, and that the research is valid regardless of how the results are used.

Case Study #8: External interests

- Dr. Cho has no financial relationship with the soap company.
- No patentable technology is expected to result.
- The soap company is not a vendor to the University.
- The University and its officers have no investments in the company.
Case Study #8: Conflict of Interest?

- There is no financial COI.
- At issue is whether the project constitutes valid research.
  - Are basic academic values upheld? Is the research appropriate to the institution's mission?
- Possible conclusions by COI Committee:
  - The project conflicts with the University's mission, and pursuing the research would place the reputation of the University and the investigator at risk.
  - The study evaluates human behavior and is allowed.
  - The study is for marketing purposes and is denied.
  - The study is valid but the controversial funding source and intent constitute a COI. Risk-benefit analysis will determine if the study should be allowed.

Case Study #8: Risk-benefit analysis

- Increased risk to human subject safety?
  - Since the study is not invasive, there are minimal physical safety concerns.
- Risk to data integrity?
  - The possible COIs are not likely to influence Dr. Cho’s judgment in conducting or publishing the study.
- Appearance of conflict of interest?
  - No financial COI.
  - High risk the research will be construed as a conflict with what the University should be doing, or if it is even “research”.
  - Risk to the reputations of Dr. Cho and the University, since University equipment purchased for patient care would be used in the study.
- Could the outcome of the study benefit the public?
  - It might, but Dr. Cho could address the scientific questions more effectively in other studies with different funding sources.
CONCERNS OF RESEARCH SUBJECTS


- Found greater willingness to participate in trial when researcher received per capita payments instead of equity interests
- Disclosure deemed more important when researched owned equity interests
- 67% not surprised that researcher or institution might benefit from clinical trial
- 36% of subjects trust was diminished as a result of disclosure
- General perception that quality of science was decreased by financial interests

Case Study #9: License, Consulting, Equity

- Drs. Jefferson and Suarez, tenured Professors of Neurosurgery, have invented an implantable chemotherapy wafer to treat brain tumors.
- The doctors propose to be co-PIs of a Phase I safety study in a group of ten patients.
- NeuroX has obtained a license from the University and will sponsor the study.
- NeuroX was founded by Dr. Jefferson with University approval.
Case Study #9: External Interests

• Terms of license include up-front payments, 3% royalty on sales, 10% royalty on sales by sub-licensees and a 10% equity stake to inventors.

• Under University policy, inventors receive and split 40% of proceeds from sale of University’s stock, and their labs would split 30%. Fees and royalties are subject to same distribution schedule.

• At the time of the licensing, Dr. Jefferson bought out all future financial interest of Dr. Suarez in the implantable wafer.

• NeuroX’s investors have offered Dr. Jefferson an extra 10% equity interest, and requested that he serve as chair of the company’s scientific advisory board at $50,000/year.

Case Study #9: Conflict of Interest?

• Dr. Suarez has no financial interest.

• Dr. Jefferson’s financial interests substantially exceed permitted thresholds.

• Dr. Jefferson argues that as a highly-skilled brain surgeon and co-inventor of the wafer, he is uniquely qualified to conduct the study.

• Dr. Jefferson says he does not intend to participate in larger-scale studies, but his expertise is needed to fine-tune surgery for placement of the wafer in the Phase I study.
Case Study #9: Risk-benefit analysis

- Increased risk to human subject safety?
  - Risk of bias in recruiting and obtaining consent due to Dr. Jefferson’s financial interest.
  - Dr. Jefferson proposes to hand off the recruiting and consent to Dr. Suarez, who has no financial conflict of interest.

- Risk to data integrity?
  - High risk due to potential benefit of over-stating results (no DSMB), which would enhance NeuroX’s value.

- Appearance of conflict of interest?
  - Dr. Jefferson has significant financial conflicts of interest.
  - Risk to reputation of Dr. Jefferson and the institution if the study is allowed to proceed as proposed.
  - Dr. Suarez has an intellectual investment, but disinterested peer review process should neutralize this type of interest.

- Could the outcome of the study benefit the public?
  - If successful, there could be tremendous medical benefits.

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Case Study #9: Risk-benefit analysis

- Should Drs. Jefferson and Suarez be allowed to conduct clinical trials sponsored by the company?
  - COI Committee may conclude Dr. Jefferson should be excluded, since Dr. Suarez has equal experience and expertise.
  - If COI policy prohibits the participation of a conflicted investigator, Dr. Jefferson will have to forego the study or reduce his financial interests to acceptable level.
  - Even with management plan, any bad outcome attributed to the clinical research would bring questions, criticisms, and potential litigation.
Case Study #9: Risk-benefit analysis

• If Dr. Jefferson presented convincing evidence that his participation in the trial is essential, the COI Committee should impose provisions:
  – Disclosure of financial interest on consent forms, to prospective subjects, to other members of the study team, to any collaborators, and in any oral presentations and written publications.
  – Allow only Dr. Suarez or another individual who does not report to Dr. Jefferson to solicit and obtain consent. Dr. Jefferson may only explain the study procedures to subjects.
  – Due to the close relationship between Drs. Jefferson and Suarez, disinterested individuals should oversee data collection and analysis.
  – Dr. Jefferson is allowed a co-investigator role, with the majority of responsibility resting with Dr. Suarez.
  – Dr. Suarez and an independent reviewer should assure the COI Committee the design of the study is valid.
  – Dr. Jefferson should reduce his consulting fee below $10,000. He should relinquish his position of chair of the scientific advisory board, but may remain one of its members.
Recommendations in AAMC/AAU Report

• The audience for disclosure of potential individual financial COI in human subjects research should be extended to:
  – State, federal officials, as required by law
  – Research sponsors/funding sources
  – Researchers, students, trainees on the project
  – Editors of publications to whom research is submitted
  – Public communication of research results
  – Human subjects

Recommendations in AAMC/AAU Report

• Scope of disclosure of potential COI should be expanded to:
  – Describe nature of financial interest (consulting fees, royalties, stock or other equity, inventor’s share, position of advisory or fiduciary (e.g., board) duties)
  – IRB determines wording of consent forms
  – Convey that conflicting financial interest has been reviewed and approved by a COI committee, subject to committee oversight, and that conflict poses no significant risk to the welfare of research subjects
Recommendations in AAMC/AAU Report

- Institutions should have clear policies, consistent with applicable regulations, that address conflicts of interest of IRB members
  - No de minimis threshold
  - Update annually and as circumstances change
  - Specify how COIs will be identified and evaluated
  - Require recusal from IRB deliberations

Recommendations in AAMC/AAU Report

- Institutions’ COI policies should cover both the institution and its representatives (board, deans, department chairs)
  - Implement COI process
  - Require reporting, evaluation, management
  - Establish standing committee
    - Include at least one community member without institutional affiliation
  - Complete policy development and implementation within 2 years of issuance of report
Recommendations in AAMC/AAU Report

- Separate research and financial decision making within the institution
  - Rebuttable presumption against doing research at conflicted institutions
  - Assure that institutional COI is addressed consistently throughout the institution to protect the integrity of research and human subjects
  - Standing COI committee to address institutional conflicts (or use one committee for both individual and institutional COIs)

Recommendations in AAMC/AAU Report

- Monitoring of COI Program
  - Oversight of education, conflict management plans
  - Establish comprehensive, institutional database (integrate information relating to IRB, technology transfer, grant administration, gifts, education)
  - Monitor conflict management plans
  - Self-certification + institutional monitoring
  - Review oversight committee reports, disclosures, publications, communications with trainees, data analysis plans, financial records
Recommendations in AAMC/AAU Report

• Report contains helpful information to use as a starting point:
  – Appendix A: Model Policy on Institutional Conflict of Interest in Human Subjects Research
  – Appendix B: Analyzing Cases Involving Potential Conflicts of Interest in Human Subjects Research -- Template and Compendium of Cases
  – Appendix C: Definition of Financial Interests in Research
  – Appendix D: Institutional Policies and Practices on Consulting -- Topics and Questions to Consider

Where is an Institution to Begin?

• Adapt policy to your setting --
  – Define COI and covered persons under the policy
  – Identify your areas of vulnerability for COI
  – Designate systems for collecting an accessible database of COI disclosures, monitoring management plans
  – Determine COI committee membership and jurisdiction
  – Develop COI management plan ideas, monitoring techniques
  – Bring together needed participants: who do you need at the table?
  – Educate all stakeholders
Conclusion

• Given the spotlight placed on COI, every institution involved in human subject research must develop and implement policies and procedures for identifying, disclosing, managing and monitoring COI

• The particular plan adopted may vary depending on the size, resources and risk-profile of the institution, but institutions who delay the inevitable are at risk
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