

CONFLICTS OF INTEREST: WHAT'S HOT AND WHAT'S NOT

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Conflicts of interest concerns for Board Members, executives, faculty and staff have become more prominent in recent years due to intermediate sanctions, Sarbanes-Oxley, and anti-kickback laws.

Definition of Conflicts of Interest

A Conflict of Interest is a situation in which financial or other personal considerations have the potential to compromise or bias professional judgment and objectivity.

Conflicts of Interest involve the use of a person's authority for personal and/or financial gain.

Conflicts may involve both individuals and institutions

Why Are Conflicts of Interest a problem?

May endanger human subjects' safety

May jeopardize public's faith in findings and/or lead them to question whether the investigator is acting in their best interest or merely using them as a vehicle for conducting research

May reduce the public's willingness to participate in studies

May inhibit future discoveries if less support for research

Who Can Have a Conflict of Interest?

Individuals

- Clinical Investigators
- Study Coordinators
- Research technicians
- IRB members
- Anyone else involved in technology transfer

Institutions

- Financial holdings of the institution
- Allocation of resources for research

Examples of COI Headlines

Welsinger v. University of Pennsylvania (2000)

- University sued after 18 year old with rare metabolic disorder died while volunteering for a gene transfer clinical trial. The principal investigator failed to disclose the relationship between the investigator, the University of Pennsylvania and Genovo, Inc., maker of the therapy.

Examples of COI Headlines (cont'd)

Right v. Fred Hutchinson Cancer Center (March 2001)

- Patients in two separate studies brought suit against the Center for research improprieties, much of which grew out of researchers' and the institution's alleged failure to disclose their financial interests in a collaborating research company.

Examples of COI Headlines (cont'd)

House of Representatives Investigation

- Rep. Billy Tauzin (R-La.) and James Greenwood (R-Pa.) launched a broad investigation into NIH grant-making decisions after discovering alleged improprieties in how grants were distributed by former NCI Director. House Committee sought full accounting of industry payment to NIH employees.

Institutional Conflicts of Interest

Institutional Conflicts of Interest can occur in a variety of ways. This includes when interests of the institution might affect or appear to affect institutional processes including the conduct, review, or oversight of human research. If an institution owns a financial interest in a company that holds a patent to a new drug or device, a conflict and/or a perception of a conflict can arise.

IRB Conflict of Interest

An IRB member can have a conflict of interest if he/she has a stake of any kind in a protocol being considered by the IRB.

Above all, conflicts arise when career and personal advancement desires interfere, or appear to interfere, with research objectives.



Public Health Service Regulations

Regulations are found in: 42 CFR Part 50, Subpart F

Under the regulations, an investigator must disclose:

- Any “significant financial interest” in entities whose financial interests might be affected by the research, and require the institution to designate an “institutional official(s)” to solicit and review the financial disclosure statements made by investigators
- Applies to any institution who has signed a Federal Wide Assurance with the Department of Health and Human Services. May apply to all research if entity has agreed to apply the Assurance to all its research.

HS Definition

PHS regulations define a significant financial interest as:

- Income (salary, royalties and other payments) which when aggregated for the investigator, an investigator's spouse or dependent children exceeds \$10,000 over twelve months OR
- An equity interest (including spouse and dependent children) in excess of \$10,000 or 5% ownership in a single entity

IH Grant Policy Statement

Applies to any entity that gets funding from the NIH

States that COIs might be handled by:

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

Limits to Disclosure

PHS regulations demand reporting of financial interests only.

They do not require recusal by the researchers with a conflict of interest

There is no requirement for notification to research subjects

IRBs and Conflict of Interest

IRB conflict of interest issues are regulated under:

- 45 CFR 46.107(e)
- 21 CFR 56.107(e)

Under these regulations, “No IRB member may participate in initial or continuing research in which they have a conflicting interest except to provide information requested by the IRB.”

If a conflict is found, an IRB member must recuse him or herself.

How Should An Institution Respond to the Problem of COIs?

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Objective:

The goal of an institution's conflict of interest/conflict of commitment policy should be to:

- Protect the institution
- Protect those who volunteer to participate in the research
- **Managing** financial relationships that create the potential for conflicts of interest

Management of COIs

The Institution, not PHS, selects the method for gathering information from investigators, determining if a COI exists, and if any COI that exists is properly managed

If an institution determines that an investigator has a conflict, it must report that conflict to the “PHS awarding component and explain whether the conflict has been managed, reduced or eliminated’.”

Management Techniques

Create a precise definition as to what constitutes a financial COI

- Determine what standard will be used in evaluating what should be done with a conflict (i.e., “rebuttable presumption of not doing the research vs. “compelling circumstances”)
- Articulate what is allowed in terms of investments, fees and honoraria, consulting fees, intellectual property rights, enrollment bonuses, payments coupled to results, and spouse/dependent finances
- Establish enforcement mechanisms/sanctions

Management Techniques (continued)

Establish a standing COI committee. The committee should be responsible for:

- Reviewing any financial interests that may pose a conflict and determine whether disclosure, management, elimination, or another course of action is appropriate.
- Documenting the committee's decisions
- Monitoring procedures and conditions surrounding research involving a financially interested individual.
- Communicating, on a regular basis with the IRB
- Developing a process by which COI committee or IRB decisions may be appealed by investigator

Management Techniques (continued)

Require that all faculty, key employees, and board members of the Institution should annually complete and submit a Conflict of Interest Disclosure Form.

Designate an institutional official(s) to solicit and review financial disclosure statements from investigators, and a separate body to review institutional disclosure statements

Allocate space and personnel for maintaining records of investigator and institution disclosures and COI and IRB committee decisions

Management Techniques (continued)

Other important methods for dealing with COIs:

- Ensure representation of public on COI committee
- Design educational programs for all researchers, data managers, IRB members, institutional officials with research and finance decision-making responsibilities
- Establish a firewall between offices responsible for financial decisions and those responsible for research decisions
- Ensure that that scientists and other institutional personnel never accept gifts or favors of more than nominal value from a company with which the Institution has or may have a sponsored-research, licensing or other relationship without the express permission of the Vice President of Research Administration or other member of Senior Management.

Other Issues to Consider

Points to Consider When Evaluating Financial Interests:

How is the research supported or financed?

Where and by whom was the study designed?

Where and by whom will the resulting data be analyzed?

Do individuals or institutions involved:

- Have any proprietary interests in the product including patents, trademarks, copyrights, and licensing agreements?
- Have an equity interest in the research sponsor and is it a publicly held or closely held company?
- Receive significant payments of other sorts (grants, equipment, honoraria, retainers, etc.)
- Receive payment per participant or incentive payments

Given the financial relationships involved, is the institution an appropriate site for the research?

Where is the Issue of Conflict of Interest Going From Here?

Greater focus on the issue from Congress

Increased regulation and guidance

Institutions will need more precise policies and procedures which lay out not only a definition of conflict of interest, but also structures, policies and procedures for identifying, eliminating, disclosing, and managing conflicts of interest, such as:

- Clear recognition of institutional conflicts
- Clear separation of research administration and financial administration (e.g., technology licensing) within the institution
- More detailed reporting
- Disclosure of conflicts on informed consent
- Delegation of conflicts review function to IRB or a separate conflicts committee

How do you support institutions dealing with COI issues?

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Conflict of Interest review includes:

- Assessing an institution's compliance with related regulatory requirements on reporting financial interests
- Identifying potential individual conflicts of interest (board members, executives, faculty, staff)
- Identifying potential institutional conflicts of interest
- Identifying potential Institutional Review Board conflicts of interest
- Evaluating procedures to manage or eliminate conflict of interest scenarios
- Recommending changes to internal policies and procedures relating to conflicts of interest
- Providing training to board members, executives, faculty, and/or staff on current conflict of interest issues, regulatory requirements, and industry best practices

Conflict of Interest Case Study

Case Study 1

Dr. Smith is an investigator in several studies testing drugs in human subjects. The sponsors of each individual study are large pharmaceutical companies.

During the trial period, Dr. Smith agrees to be a consultant for BigPharm to evaluate and assess their current protocols as well as give insight on recent research developments with other pharmaceutical companies. For these services she has been paid \$5,000.

Is this a potential conflict of interest?

So, how should this potential conflict of interest be addressed?

Conflict of Interest Case Study (cont.)

Discussion

Assume that the investigator would do nothing that would compromise the integrity of the research but is willing to take steps to manage the potential conflict anyway in order to reduce the risk? If so, what would you choose?

- . Require that the investigator disclose his/her financial interest in publications or in public discussions of the research?
- . Require that the investigator terminate all consulting activities during the course of the study?
- . Remove the investigator from any or all of the following: patient recruitment and selection, treatment, data analysis?
- . Require the investigator be removed from the study?