
Yale University Human Research Protection Program

500 PR.2 Procedures for Disclosing Financial and Non- Financial Interests Related to Specific Human Research Projects: Research Team Members and Departmental Chairs

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Overview

This procedure identifies the process whereby persons as required by HRPP Policy 500: *Disclosures and Management of Interests In Human Research*, who have, or may be perceived to have a protocol-specific interest make known their interest to the Principal Investigator and disclose the interest to the Yale Institutional Review Board (IRB).

Recognizing a Protocol-Specific Interest in Human Research

A protocol-specific interest in human research exists when either an individual (or his/her immediate family member) or Yale University has an external interest or relationship related to a research project.

A conflict of interest in human research exists when either an individual (or his/her immediate family member) or an institution has an external interest that affects or may provide an incentive to affect actions or decisions related to the conduct or oversight of the research. A conflict of interest may be financial or non-financial in nature. It is important to note that not all protocol-specific interests may be considered conflicts of interest. (See HRPP Policy 500, Disclosure and Management of Interests in Human Research for definitions of financial and non-financial interests.)

In order to recognize if a real or potential conflict of interest exists in human research it is important to consider the study's attributes. Such attributes include, but are not limited to:

- sponsorship of the research, including the source providing the study drug or device or other research-related materials, or,
- knowledge of the sponsor's competition as relationships with the competitor may be considered as a conflict of interest,
- the use of intellectual property in the research, such as methods of treatment, diagnosis or data analysis.

The Principal Investigator is responsible for ascertaining information regarding possible protocol-specific interests from persons listed as an investigator, consultant or study person on research protocols, when the person is ultimately responsible for designing the research project, the manner or methods through which research is performed, or reporting outcome data or results of the research project.

Disclosing a Protocol-Specific Interest

Disclosing Interests to the Principal Investigator and Principal Investigator Responsibilities

Individual protocol-specific conflicts of interest must be disclosed to the Principal Investigator by the following individuals;

- Co-investigator(s) listed on a human research protocol application or a proposal, and
- Research team member(s) deemed otherwise responsible by the PI.

The Principal Investigator is responsible for ensuring that each individual with such interest is appropriately identified and disclosed to the IRB on the IRB protocol application form, the Form 5R for reapproval, or the Request to Change Study Personnel Form. In addition, the PI should ensure that all responsible personnel have completed the annual financial interest disclosure form required by the University's Conflict of Interest and Conflict of Commitment Committee, accessible at <http://www.yale.edu/coi/>.

Such disclosure to the PI should occur when the individual is asked to take part in the research or at any time that a new interest related to the research emerges or a change occurs in a previously disclosed interest such that it now may adversely affect the protection of research participants, the credibility of the research or the community's trust in Yale as a research institution (e.g., a patent is filed by the University related to the novel methodology being tested in the research.)

The Principal Investigator is responsible for evaluating the interest to determine whether or not the interest presents a conflict. In consultation with the IRB, the Principal Investigator must subsequently decide whether or not the conflict must be managed, reduced or eliminated in order to protect the welfare of research participants or the integrity of the research.

The Principal Investigator should report to the IRB any incidents where the investigator is feeling pressure or influence not to manage the conflict of interest.

The Principal Investigator must inform the IRB of his/her actions taken to manage, reduce or eliminate the conflict of interest.

The Principal Investigator may also determine that while no management action is required related to the interest, a disclosure of the interest to potential research participants during the informed consent process may be appropriate. Such a decision may be made to promote a spirit of openness and trust in the research, or when the risk of a bad outcome is possible due to a conflicting relationship. Should this occur, the Principal Investigator is responsible for assuring that all research personnel, who conduct informed consent processes, are sufficiently knowledgeable to answer questions related to the disclosure of the interest. A decision by the Principal Investigator not to include a disclosure statement during the informed consent process may be overridden by the IRB or the University's Conflict of Interest and Conflict of Commitment Committee.

Department Chair or Designee Responsibility to Disclose Interests

The Department Chair(s) or Section Chief(s) representing the Principal Investigator's department/section must make known to the Principal Investigator any protocol-specific interests held by the Department Chair or Section Chief and any real or apparent institutional protocol-specific interest when known (e.g., Yale ownership of a sponsoring company, patents, licensure) and disclose them to the IRB.

Disclosing Research-Related Interest to the IRB

An individual with a protocol-specific interest must disclose the interest through the principal investigator to the IRB when the protocol is submitted to the IRB for initial review, continuing review, and at any time that a change in financial or other circumstances warrants. The name of each affected individual should be disclosed on the initial IRB protocol application form, the Form 5R for reapproval, or the Request to Change Study Personnel Form. Clarifications concerning relationships or compensation may be

requested of the individual disclosing the interest, the Department Chair or Section Chief or of the Office for Cooperative Research in order to obtain the information necessary for the IRB to perform a thorough review.

IRB Review of Protocol-Specific Interests

Summarization of the Disclosure

A high level IRB staff member will access the COIC financial interest disclosure system to obtain information on the individual identified by the PI as having research-related interests. This staff member will prepare a summary of the interest(s) and essential attributes of the protocol. The summary contains information that helps to identify whether or not the interest has the potential to adversely affect the rights and welfare of research participants or the integrity of the research. The information evaluated includes, but is not limited to, the type of interest or relationship involved, the type and amount of earned compensation, if any, from the past year, and the projected next twelve months, and any potential future involvement. In addition, the summary information includes the purpose of the study, whether the study is single- or multi-site, randomized and/or blinded, the total number of persons who will be enrolled across all research sites and the total number of persons who will be enrolled at Yale, and study oversight. The summary also describes the role that the individual disclosing the interest has in the conduct of the research; e.g., whether or not the individual recruits subjects or obtains informed consent, conducts study monitoring, data analysis or otherwise serves in a role that could influence or be perceived to influence subject enrollment, data integrity or study outcomes.

IRB Review of the Research Related Interest

The IRB Chair/Vice Chair is responsible for reviewing the summary and ascertaining whether or not review by the fully convened IRB is required.

The IRB Chair/Vice Chair may delegate this review to a duly qualified person knowledgeable in the area of conflicts of interest and study design.

The IRB Chair/Vice Chair or designee may use an expedited approach to review and determine the disposition of protocol-specific interests that include but are not limited to:

- a) protocol-specific interests that are *de minimis* in nature;
- b) when there has been no change in the value or relationship of the previously reported interest and previous evaluations of the interest remain in effect;
- c) when the conflict does not have nor will it ever have, the potential to influence the research outcome or the integrity of the research. Example: disclosure of a patent that will not be pursued by Yale or other holder as appropriate because publication of the method being patented has already occurred; or
- d) interests disclosed previously that are thought not to represent conflicts.

Review of Interests by the Fully Convened IRB and Reporting Management Plans

The fully convened IRB will review protocol-related interests when the Chair/Vice Chair or designee determines that the interest may adversely impact the rights and welfare of the research participants or the integrity of the research or trust in the research relationship.

Review by the fully convened IRB will be required for any reported interest considered a significant financial interest. The IRB may defer the review of the protocol until the Conflict of Interest and Conflict of Commitment Committee has considered the factors as described in the following section.

IRB members will be informed of the protocol-specific interest, study attributes and other factors described in the summary when the interest is referred to the fully convened IRB for review and determination. The IRB members should consider the following, with the aid of Checklist 500 CH.1: Determining Financial and Non-Financial Interests Related to Human Research:

- whether or not the protocol-specific interest will or has the potential to adversely affect the protection of participants in terms of the criteria for IRB approval (e.g., whether, due to the conflict, risks to subjects are made greater, rather than minimized);
- whether or not risks associated with the interest compared to benefits remain reasonable;
- whether or not the interest permits subject selection to remain equitable and unbiased;
- whether or not subjects should be informed of the interest; and
- whether or not the interest will adversely affect the integrity of the research.

When an interest is identified by the IRB as impacting or having the ability to adversely affect the protection of research participants or the integrity of the research, the IRB must determine whether or not the interest needs to be managed, reduced or eliminated. The IRB may also require disclosure of the interest in the study consent form and additional information when, in the judgment of the IRB, the information would meaningfully add to the protection of the rights and welfare of subjects. Alternatively, the IRB may determine that the interest does not adversely impact human research protections or integrity but that disclosure of the interest during the consent process is necessary to promote openness and trust in the research.

The IRB can determine that a protocol-specific interest needs to be managed or reduced. Such management “plans” can vary depending on the nature of the interest and the research aims and objectives. Management plans can include:

- limiting the researcher’s role in the study; for example, prohibiting recruitment of, or obtaining consent from potential research volunteers;
- restricting data collection or analysis activities’
- requiring that a consent monitor be present during the initial consenting of potential research volunteers;
- requiring an independent Data and Safety Monitoring Board to oversee the conduct of a study, or evaluate study outcomes or adverse events; and/or
- requiring elimination of the conflict either by removing the individual with the conflict from the study or requiring the individual to reduce the interest to a permissible level.

The full IRB will vote on the management plan and determine that it sufficiently protects participants in terms of the criteria for IRB approval, and that the integrity of the research remains intact. IRB meeting minutes will include the full discussion and votes taken on the management plan.

The determinations and management plans instituted during the expedited review of protocol-specific interests will be shared with the fully convened IRB at the discretion of the IRB Chair.

All management plans resulting from the IRB review of protocol-specific interests will be shared with the Committee on Conflict of Interest and Conflict of Commitment for inclusion in the financial interest disclosure system.

Referral of Conflict to Conflict of Interest/Conflict of Commitment Committee (COIC)

The IRB Chair and/or the fully convened IRB can defer a disclosed protocol-specific interest to the COIC for their review when it is a significant financial or non-financial interest. The IRB may review the interest concurrently with the COIC, but the IRB will not approve the conflicted individual’s participation in the research until receiving the COIC’s determination. The COIC may impose a stricter management plan than the IRB, but may not impose a lesser requirement than the IRB. The IRB retains the final authority to determine whether the research with the financial interest and the management plan, if any, are permissible and approvable.

Newly Discovered Protocol-Specific Interests

There are several circumstances that warrant reporting of a protocol-related interest that had not previously existed on an approved protocol. For example, the addition of a new member to the research team requires the individual to inform the Principal Investigator of any protocol-specific interest as soon as it is identified, preferably at the time the new member joins the research team, and the PI should identify this individual as having a protocol-related interest on the Request to Change Study Personnel Form. Similarly, an addition to, or change in, the sponsorship of the protocol requires all members of the research team to ascertain whether or not they have an interest with the new sponsor and make the interest known to the Principal Investigator. Finally, a change in an individual's circumstances, such as his/her spouse is newly employed by the sponsor, or the individual has begun a consulting or other relationship with the sponsor, requires prompt reporting to the Principal Investigator and the IRB.

References:

45 CFR 46.107(e)

21 CFR 56.107(e)

Accreditation Council for Continuing Medical Education Report on Standards for Commercial Support accessed March 12, 2005 at http://www.accme.org/dir_docs/doc_upload/68b2902a-fb73-44d1-8725-80a1504e520c_uploaddocument.pdf

American Medical Association. Opinion of the Council on Ethical and Judicial Affairs, E-8.061 <http://www.ama-assn.org/ama/pub/category/4001.html>> Accessed January 20, 2005.

Department of Health and Human Services, Office for Human Research Protections; Conflict of Interest Final Guidance <http://www.hhs.gov/ohrp/humansubjects/finreltn/fguid.pdf>

Department of Health and Human Services, Office of Inspector General. OIG Compliance Program Guidance for Pharmaceutical Manufacturers. Fed Regist 2003;68:23731-43.

Food and Drug Administration Regulation 21 CFR 54.2 and Guidance: <http://www.fda.gov/default.htm>

Investigator Conflicts of Interest and Review; Stanford University
<http://humansubjects.stanford.edu/hrpp/manual.html>

Investigator Conflicts of Interest and Review; University of California San Francisco
http://www.research.ucsf.edu/CHR/Guide/chrCOI_CHR.asp

Public Health Services Regulation 42 CFR 50.603

Yale University HRPP Policy 500 Disclosures and Management of Personal Interests In Human Research

Yale University 500 FR 2: Financial and Non Financial Interests in Human Research Disclosure: Researchers and Department Chairs

500 CH.1 Determining Financial and Non-Financial Interests Related to Human Research

Yale University Policy on Conflict of Interest and Conflict of Commitment
<http://www.yale.edu/provost/html/coi.html>