

Texas Health Resources



Corporate Policy Conflicts of Interest in Research Involving Human Subjects

Chapter 1.

The Ethical Mandate to Manage Conflicts of Interest

“Conflict of interest” can be defined as any situation in which financial, professional, or personal obligations may compromise or present the appearance of compromising an investigator’s professional judgment in designing, conducting, analyzing, or reporting research. Financial incentives may negatively impact the recruitment of subjects; collection, analysis and interpretation of data; or scientific objectivity and integrity — all of which ultimately affect public trust in the research enterprise.

- a. Public Trust in the Research Enterprise.** The public, whose members will be recruited to volunteer to test new theories, interventions, and products, must be assured that their interests and welfare will be protected to the fullest extent possible. The principle of justice, as articulated in the Belmont Report, demands that the benefits and the burdens of research be distributed equitably.

- b. Purpose of this System-Wide Policy.** THR endorses the principle that all research should be conducted with the highest degree of ethical conduct and integrity and should not be negatively impacted by financial or other Conflicts of Interest.

This System-Wide Conflict of Interest Policy for research involving human subjects is intended to help THR investigators, IRB members, and the THR Institutional Official effectively reduce, eliminate, and manage any financial interests they may have in the research they conduct, review, or sponsor. In addition, it promulgates THR policies and procedures relative to disclosing, reporting, and investigating Conflicts of Interest related to research activities.

Chapter 2.

The Regulatory Mandate to Manage Conflicts of Interest

Currently, three different regulations address Conflicts of Interest in research involving human subjects.

Regulations issued by the Public Health Service (PHS) in 1995 address how *institutions* receiving PHS support should handle Conflicts of Interest. Institutions receiving support from the National Science Foundation (NSF) must meet identical requirements.

Regulations issued by the Food and Drug Administration (FDA) govern *individual* investigator disclosure of Conflicts of Interest to Sponsors of FDA regulated research.

Finally, the Federal Policy (Common Rule) for the Protection of Human Subjects in Research impacts the issue of Conflicts of Interest in research for members of Institutional Review Boards (IRBs).

- a. Public Health Service (PHS) Agencies.** Institutions receiving research support from Public Health Service (PHS) Agencies (such as the National Institutes of Health, the Centers for Disease Control and Prevention, and the Indian Health Service) must comply with the PHS regulations at 42 CFR Part 50, Subpart F.

These regulations require that institutions establish policies and procedures relating to Conflicts of Interest and appoint a Conflict of Interest Official or Conflict of Interest Committee to manage and report Conflicts of Interest.

According to the PHS regulations, a designated institutional official or committee is responsible for reviewing all financial disclosures, and determining if a Conflict of Interest exists. At THR, the designated Institutional Conflict of Interest mechanism involves disclosure of all financial conflicts to the THR Research Conflicts of Interest Committee. This Committee is appointed by the THR Institutional Official as a subcommittee of the IRB and is responsible for receiving and reviewing disclosures of any Conflicts of Interest and determining what actions should be taken to manage, reduce, or eliminate the conflicting interest.

A detailed summary of the PHS requirements and copies of the relevant regulatory provisions are provided via links on the THR electronic IRB system (eIRB system) which is available to all researchers

As indicated above, Institutions receiving support from the National Science Foundation (NSF) must meet identical requirements.

- b. Food and Drug Administration (FDA) Regulations.** FDA regulations at 21 CFR Part 54 apply to investigators conducting research regulated by the FDA. These regulations require that investigators disclose information related to Conflicts of Interest to the research sponsor so the sponsor can inform the FDA. THR requires investigators to provide copies of any such disclosures provided to sponsors to the THR Institutional Official for review by the THR Research Conflict of Interest Committee.

A detailed summary of the FDA requirements and copies of the relevant regulatory provisions are provided via links on the THR eIRB system.

- c. Federal Regulations for the Protection of Human Research Subjects.** The Federal Policy for the Protection of Human Subjects in Research, commonly called the Common Rule and codified at 56 FR 28003 and 45 CFR 46.107(e), prohibits IRB members who have a conflicting interest from participating in the IRB's initial or continuing review of research, except to provide answers to questions from the IRB. FDA IRB regulations include exactly the same provision at 21 CFR 56.107(e).

THR applies this restriction to all research regardless of funding source. An IRB member who (i) has a financial stake in the research or (ii) plays a substantive role in the research (including, for example, enrolling subjects in the protocol) would be considered to have a Conflict of Interest.

THR abides by all three regulatory requirements. In all cases, the THR guidelines meet or exceed the standards set by the federal regulations, so investigators who adhere to the THR guidelines also adhere to applicable federal standards.

Chapters 4 and 5 provide detailed guidance concerning THR and investigator responsibilities and mechanisms for managing, reducing, or eliminating Financial Conflicts of Interest in human subject research.

Chapter 6 provides guidance on how the THR IRB and IRB members should strive to eliminate, reduce, or manage Conflicts of Interest during their reviews and other deliberations.

Chapter 3. Types of Conflicts of Interest

Conflicts of Interest can take many forms. They can be straightforward, such as consulting fees, education subsidies, stock ownership, honoraria, or salary from entities with a role in the research. Alternatively, they may include what some may view as more subtle kinds of Conflict, such as intellectual property rights, royalties, financial incentives offered by pharmaceutical or biotech companies to researchers or physicians for conducting trials or enrolling subjects, or financial relationships due to spousal employment.

Examples of individuals and possible Conflicts of Interest follow.

- a. Research Personnel.** For researchers (investigators, co-investigators and other research personnel), financial incentives may negatively impact the conduct of the research or the collection, analysis, or interpretation of data, thereby damaging scientific objectivity and the integrity of the research enterprise. In addition, a research investigator who is also the subject's treating physician (or other clinician) may unwittingly, or even purposely, exert coercion or undue influence on patients (or clients) to participate in research.

Conflict of interest may also occur where other incentives (for example, enrollment bonuses, the pressure to publish, desire for career advancement, or professional rivalries) negatively affect one's standards for the appropriate conduct of the research or the appropriate collection, analysis, or interpretation of data.

Chapter 5 details the responsibilities of THR research personnel in disclosing and managing Financial Conflicts of Interest.

- b. THR as an Institution and THR Leadership.** Officials and staff of THR and THR entities must also refrain from involvement in decisions affecting research in which they have personal financial or professional interests, or in which the institution or institutional leadership have significant financial or other interests that may influence research conduct or outcomes.

In recognition of such potential conflicts, THR leadership who participate in the decision-making process regarding the approval or disapproval of research funding may not serve as voting members of any THR designated IRB.

- c. IRB Chairperson and Members.** The IRB chairperson and IRB members may find themselves in situations that present Conflicts of Interest, such as the following:

- Where the IRB Chairperson or IRB member is listed as a principal investigator or co-investigator on the research.
- Where the IRB Chairperson or IRB member plays any substantive role in planning or conducting the research, including enrolling subjects in the research or obtaining subjects' informed consent.
- Where any investigator must report to, or is under the supervision of, an IRB Chairperson or IRB member or vice versa.
- Where the IRB Chairperson or IRB member competes for research support in the same field, or a similar field, as an investigator whose research is scheduled for review.

In these instances, individuals with a Conflict should absent themselves from participating in any deliberative IRB discussion or vote in connection with the relationship or transaction related to the Conflict. Chapter 6 provides detailed guidance on Managing Conflict of Interest in IRB Review.

Chapter 4. Institutional Responsibilities for Managing Conflicts of Interest

THR has specific institutional responsibilities under current regulations governing Conflicts of Interest for research involving human subjects.

THR has a responsibility to manage, eliminate, or reduce any Conflicts of Interest in accordance with applicable regulations.

- a. THR Conflicts of Interest Official.** US Public Health Service (PHS) regulations require that THR appoint an official to implement and ensure compliance with Conflicts of Interest policies, procedures, and requirements on behalf of the organization. The THR Institutional Official for Human Subject Protections serves in the role of Corporate Conflicts of Interest Official for all THR entities involved in the conduct or support of human subject research.

The THR Institutional Official also serves as the Corporate Conflicts of Interest Official to assist in implementing THR's Research Conflicts of Interests policies, procedures, and requirements at the entity level.

Activities and records of the THR Research Conflicts of Interest Committee shall be subject to review and monitoring by the THR Institutional Official and the THR Chief Compliance Officer.

The THR Chief Compliance Officer has full authority to investigate possible Conflicts of Interest and to enforce THR's Conflict of Interest policies, procedures, and requirements in human subject research at all THR entities and by all THR personnel involved in the conduct or support of human subject research.

- b. Conflicts of Interest Committee(s): Function.** The THR Research Conflicts of Interest Committee reviews information submitted by THR investigators and research personnel and determines whether particular investigators or research personnel have Conflicts of Interest. Where Conflicts of Interest (or the appearance of Conflicts of Interest) are identified, the Committee recommends how best to manage or eliminate such conflicts and reports its findings and recommendations to the THR IRB and to relevant officials of the entity involved in the research, as warranted.
- c. THR Research Conflicts of Interest Committee: Composition.** The THR Research Conflicts of Interest Committee shall be appointed by the THR Institutional Official/Conflicts of Interest Official. Although representatives of the research community may be appointed to the Committee, a substantial majority of the members shall be persons not

involved with research or research-related activities. The THR Chief Compliance Officer and a THR staff attorney will serve as non-voting members of the Committee.

Members of the Conflicts of Interest Committee shall not be regular members or alternate members of any THR Institutional Review Board (IRB).

- d. Research Conflicts of Interest Committee: Quorum and Voting.** The presence of a simple majority (e.g., five of nine members, or four of seven members) shall constitute a quorum of members necessary to conduct business. Decisions of the Committee shall require at least a majority of the attending Committee members.
- e. Research Conflicts of Interest Committee: Procedures.** The following procedures will govern the operation of the Committee:

Receipt and Storage of Information

- The Committee will receive and review disclosures relating to the financial interests of investigators and research staff.
- The Committee recognizes that such information may be sensitive and highly confidential and will treat such information in a confidential manner.
- Forms for disclosing interests and all associated documentation and files will be kept in a locked filing cabinet.

Basis for Findings and Determinations

- The Committee will consider the information submitted on a case-by-case basis and render a reasonable decision as to whether the financial interest of the affected investigator or research staff person could significantly affect the research activities directly or indirectly.
- The Committee may seek consultation from any source necessary to help in making its findings or determination or in the design, implementation, and monitoring of any mechanism or plan for managing Conflicts of Interest.

Notification of Findings and Determinations

- If the Committee reaches a decision that no Conflict of Interest exists, it will notify the appropriate IRB and the affected investigator or research staff person of such a determination.
- If the Committee reaches a decision that a Conflict of Interest exists, the Committee will recommend a mechanism or management plan to the THR IRB for the specific conflict.

- The IRB will also notify the affected investigator or research staff person of its determination and of the proposed plan to manage the conflict.

Examples of Management Plans

The Committee has discretion and authority in designing and recommending a management plan for IRB approval.

Examples of management plans include, but are not limited to, the following:

- Public disclosure of financial interests.
- Monitoring of the research by independent reviewers.
- Modification of the research plan.
- Complete divestiture of interests in the sponsor, product, or entity under study.
- Selection of another investigator or research staff person to perform the research or research-related function.
- Disclosure of the conflicting interest in the informed consent document and any manuscripts or oral presentations based upon the research in question.
- Severance of relationships that create actual or potential conflicts

Implementation and Monitoring of the Management Plan

- The affected investigator or research staff person will be asked to acknowledge the determination of the IRB and to agree to abide by the terms of the mechanism or plan for managing the conflicting interest.
- If the affected individual does not accept the plan, the IRB will notify the individual that he/she can request an appeal. The IRB will review the disclosure, the proposed management plan and any other information presented by the affected individual. The IRB will determine if the proposed management plan should be revised and communicate the final proposed management plan to the affected individual.
- Disapproval by the IRB constitutes organizational disapproval, and the research may not be initiated until a plan that is satisfactory to the IRB has been accepted by the affected individual.
- THR as an institution has the right to deny implementation of any IRB approved research project that is inconsistent with THR institutional conflict of interest policies and procedures.
- The Conflict of Interest Committee requires that investigators and research staff provide disclosure updates to the Committee at

least on an annual basis or concurrently as possible conflicting interests are identified during the course of the research and for 1 year after completion of the research.

- The Committee will periodically update (at least annually) the IRB of the status of compliance with the management plan.

Reporting Relationships

- The THR Conflict of Interests Official, the THR Chief Compliance Officer, or the THR General Counsel may take Conflict of Interest matters directly to the THR Board of Directors should the need arise.
- The Conflicts of Interest Committee is a sub-committee of the THR IRB..
- The THR Chief Compliance Officer, periodically reviews and monitors the Committee activities and may, if warranted, take matters regarding any Conflicts of Interest Committee activities directly to the THR Board of Directors or to the THR Audit and Compliance Committee should the need arise.
- The Committee will report findings to the IRB, the affected research investigator or research staff person.

Chapter 5. Responsibilities of Research Investigators and Other Personnel for Disclosing Conflicts of Interest in Human Subject Research

Research investigators and other personnel involved in the conduct or support of human subject research (e.g., study planning and design, conduct of the study, data analysis, subject recruitment, subject consent, authorship) at THR entities or research in which THR is engaged, as defined in the THR Corporate Policies for the Protection of Human Research Subjects, must disclose all possible Financial Conflicts of Interest to the Conflicts of Interest Committee.

Conflict of Interest Disclosures must be made prior to the submission of an application or proposal for external funding or at the time of application for IRB review, whichever comes first.

A plan to manage identified Conflicts of Interest must be prospectively approved by both the Conflicts of Interest Committee and the Institutional Review Board (IRB), and must be in place, before any research activities involving human subjects are initiated.

- a. **Financial Interests Defined.** It is THR policy that all personnel are required to disclose to the Conflicts of Interest Committee **any Financial Interest** (regardless of the dollar value) in any human subject research in whose conduct or support they are involved (e.g., study planning and design, conduct of the study, data analysis, subject recruitment, subject consent, authorship).

Financial Interest means (i) anything of monetary value that could reasonably appear to affect, or to be affected by, the research; or (ii) anything of monetary value in entities whose interests could reasonably affect, or be affected by, the research. The latter includes membership in partnerships or group practices that could reasonably affect, or be affected by, the research.

Financial Interest includes, but is not limited to, the following:

- Any financial arrangement whereby compensation paid to the investigator could influence, or be influenced by, the outcome of the study.
- Salary and other payments for services (e.g., consulting fees, honoraria, speaker's bureau, etc.).
- Payments of other sorts from the sponsor of the research (e.g., a grant to fund other ongoing or additional research, compensation in the form of equipment, retainer for on-going consultation, etc.).

- Equity interests (e.g., stocks, stock options, or other ownership interests).
- Proprietary interests or intellectual property rights (e.g., patents, trademarks, copyrights, licensing agreements, royalties, etc.).
- Non-cash items such as travel expenses, business gifts or educational subsidies.

However, **Financial Interest does not include** the following:

- Salary, royalties, or other remuneration from THR for purposes unrelated to the research in question.
- Income from seminars, lectures, or teaching engagements sponsored by public or nonprofit entities.
- Income from service on advisory committees or review panels for public or nonprofit entities.

- b. Disclosure Standards for Family Members.** Investigators and other personnel involved in the conduct or support of human subject research must submit a listing of any Financial Interests, as defined in Section (a) above, for **themselves, their (i) parents, (ii) ancestors, (iii) spouse, (iv) child, grandchild or great grandchild, (v) siblings, whether related by whole or half blood, or (vi) the spouse of an individual described in clause (iv) or clause (v)** prior to the submission of an application or proposal for external funding or at the time of application for IRB review, whichever comes first.

Thereafter, **disclosure must be made at least annually** (typically in conjunction with the application for continuing IRB review) **and as new Financial Interests are obtained or as other changes occur.**

- c. Disclosure Mechanism.** Disclosure of Financial Interests is made through filing the Disclosure Forms provided via links on the THR eIRB system which is available to all researchers and staff. .

A current, up-to-date Conflict of Interest Disclosure Form must be on file with the Conflict of Interests Committee (i) before a proposal or application for external support can be submitted to the funding agency, organization, or sponsor; and (ii) before any application for initial or continuing IRB review can be processed.

Chapter 6.

Managing Conflicts of Interest in IRB Review

IRBs are required to manage Conflicts of Interest of their members. Regulatory guidance dictates broad consideration of what constitutes a Conflict of Interest for IRB members.

The Office for Human Research Protections (OHRP) interprets the DHHS regulations to prohibit IRB members from participating in the deliberative discussion or vote relative to any research in which they participate in any way, including but not limited to study planning and design, conduct of the study, data analysis, subject recruitment, subject consent, and authorship. IRB members are likewise prohibited from participating in the deliberative discussion or vote relative to any research in which they have, or may appear to have, a financial, personal, or professional conflict.

If the IRB member believes that a conflicting interest might impact, or appear to impact, IRB deliberations or the protection of human subjects, the member must declare the presence of the conflict to the IRB and absent himself or herself from any deliberative IRB discussion or vote on the research. There are no exceptions from this requirement

In most cases, it is not necessary for the IRB member to disclose to the Conflicts of Interest Committee or to the IRB the details of any Conflict of Interest for which the member voluntarily absents herself or himself from the IRB's deliberative discussion and vote, and limits herself or himself to answering questions posed by the IRB.

However, there may be circumstances in which it is in the best interests of the individual, the institution, and/or the human subjects involved for the member to make a complete, written disclosure to the Conflicts of Interests Committee. IRB members are expected to use their best judgment to ensure that all IRB deliberations take place without any appearance or possibility of conflict of interest.

- a. Disclosure of Conflicts of Interest by IRB Members.** IRB members must complete the IRB Member Conflict of Interest Declaration before each meeting. This form addresses both financial and non-financial conflicts of Interest. IRB members who declare a possible Conflict of Interest will leave the meeting during the IRB's final deliberative discussion or vote on the relevant action.

- b. Solicitation of Disclosure of Conflicts of Interest by IRB Chair During the Meeting.** At the beginning of every meeting, the IRB Chairperson will review the agenda and request Declaration of any possible Conflicts of Interest that have not already been identified to the Chair or the IRB staff.

- c. Recusal of IRB Members from Participation or Voting.** Members found to have any (financial or non-financial) interest in the research under consideration will be recused from participation in or voting on the initial or continuing review of research. The member may be present to answer questions posed by the IRB, but any other IRB activity — including the final discussion in which a determination is made as to how the IRB will vote on the protocol — must be conducted without the presence or participation of the conflicted IRB member.
- d. Recusal of IRB Member Documented in IRB Minutes.** All recusals/absences of IRB members for conflict of interest must be noted as such in the official IRB minutes, and a determination must be made as to whether the recusal affects quorum requirements or other such issues.

Two different scenarios may adversely affect the requirement of a quorum:

- If the absence of the conflicted member results in a majority of the IRB members no longer being present at the meeting, no IRB actions or determinations can take place until a majority of IRB members have again joined the meeting.
- If the (now-absent) conflicted member was the only non-scientist member present at the meeting, no IRB actions or determinations can take place until an additional non-scientist member has joined the meeting.