
GUIDANCE: CONFLICT OF INTEREST (COI) REVIEW PROCESSES FOR SINGLE IRB REVIEW



Conflict of Interest Working Group of the
SMART IRB Harmonization Steering Committee

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REGULATORY AND ETHICAL JUSTIFICATION FOR IRBS REVIEWING COI

A conflict of interest (COI) exists when an individual or institution has two or more obligations or interests that may compete with each other. Conflicts can be financial or non-financial. For the purposes of this document COI refers to an individual's financial COI (institutional COI is briefly discussed in [FAQ #5](#)). The NIH defines a financial COI as "when the recipient's designated official(s) reasonably determines that an investigator's significant financial interest could directly and significantly affect the design, conduct, or reporting of the [Public Health Service (PHS)]-funded research." (See <https://grants.nih.gov/grants/policy/coi/index.htm> and [NIH FAQs](#) for additional information.)

From a practical standpoint, COIs in research occur when an investigator has a significant financial interest or relationship that could be impacted by the outcome of the research. Examples of such significant financial interests include: holding stock or other forms of equity; being an inventor entitled to royalty payments or licensing fees related to a product being evaluated in the research; receiving speaker fees or other honoraria for promoting a company's product(s) or consulting for them; or having a fiduciary relationship with the company sponsoring the research, such as serving as an advisor or on the board of directors.

Concern over the impact of financial conflicts of interest led to the promulgation of regulations [42 CFR 50, subpart F](#), "Promoting Objectivity in Research." These regulations require institutions that are recipients of NIH (or PHS) funds to have policies in place to identify and manage any financial conflicts of interest. Investigators must disclose to the institution their financial interests and institutions must determine whether these interests create a financial conflict of interest related to the research. If such a conflict exists, the institution must put into place a plan to mitigate or manage the conflict.

Conflicts of interest directly affect an institutional review board's (IRB's) ability to approve research. Conflicted investigators' questionable objectivity may (intentionally or subconsciously) incentivize them to enroll subjects that do not meet eligibility requirements or to incorrectly attribute the causality of adverse events, or may bias the presentation of risks and benefits when obtaining informed consent or insert bias into the analysis of the data or reporting of the research. Any of these directly impact the criteria for IRB approval, in particular, 45 CFR 46.111(a)(1) requiring that risks to subjects are minimized and 46.111(a)(2) that risks be reasonable in relation to anticipated benefits.

Given the potential for a COI to affect human subjects protections, IRBs must be aware of any investigator COI and determine that adequate measures are in place to manage the conflict. An adequate management strategy is one that minimizes the risk of potential harm caused by a conflicted investigator's actions and preserves the scientific integrity of the data, yet does not unduly interfere with the ability of the research to be conducted. In assessing the adequacy of any management plan, the IRB will need to understand the role of the conflicted investigator in conducting the research, as well as how actions taken by that investigator in the research process might either increase the risk of harm to subjects or impact scientific integrity of the research. In fact, the Association for the Accreditation of Human Research Protection Programs ([AAHRPP](#)) requires that accredited IRBs review COI management plans and have the authority to require additional actions, if deemed necessary to protect human subjects.

When IRB review is performed at an investigator's own institution, there are developed processes and communication to integrate the disclosure and management of COI with IRB review. However, when IRB review is performed at an institution separate from the COI review process, as may occur in single IRB review for multisite research, a number of challenges emerge. The purpose of this document is to provide a framework for both Relying Institutions and Reviewing IRBs and their institutions to handle this important component of human subjects protections, regardless of whether the research is PHS-funded.

WHO IS RESPONSIBLE FOR DETERMINING WHETHER AN INVESTIGATOR COI EXISTS?

The current version of the [SMART IRB Agreement \(v2.0\)](#) requires Relying Institutions to “[m]aintain policies regarding the disclosure and management of Research Personnel conflicts of interest related to Research and to share those policies with the Reviewing IRB, as requested.” The default position is that Relying Institutions are responsible for performing a COI review of their investigators under their own policies to determine whether there are any conflicts and, if so, whether they require management, and for providing that information to the Reviewing IRB. However, the Relying Institution and Reviewing IRB can agree to an alternate approach, if for example, the Relying Institution does not have a COI review process established or its policy does not conform to the PHS policy, if the research is NIH funded. In instances where an IRB reliance agreement other than the SMART IRB Agreement is used, the reliance agreement should clearly delineate the institutions’ responsibilities for COI assessment and management.

The guidance below addresses Relying Institution and Reviewing IRB/Reviewing IRB Institution responsibilities in two scenarios: 1) when a Relying Institution has a PHS-compliant COI policy (necessary for NIH-sponsored research) and 2) when a Relying Institution does not have a PHS-compliant COI policy and must rely on the COI policies of the Reviewing IRB Institution. This is followed by specific guidance to assist in determining whether there is a COI, and if so, management strategies that can be used to manage the COI, as well as frequently asked questions regarding COI.

If a Relying Institution has a COI policy compliant with 42 CFR 50, subpart F for PHS-funded research

In this scenario, the Relying Institution will review for COI and will develop a management plan when COI is identified.

Roles and responsibilities of the Relying Institution

- Have policies that define which interests require disclosure and which are considered a significant financial interest (SFI).
 - The policies should either apply the PHS regulations (42 CFR 50, subpart F) to all sponsored research or describe that only NIH/PHS-sponsored research must follow the PHS regulations.
- Have processes and policies to identify conflicts of interest at initial review as well as during a study (for example when additional personnel are added to the study team, or when an investigator gains a new financial interest).
- Have a process through which any identified COI is resolved, either by elimination of the conflict (for example by divestiture) or by development of a management plan for the identified COI, as per institutional policy. (See [“Identifying COI and Management Strategies”](#) below.)
- Communicate the presence of any COI and associated management plan to the Reviewing IRB at initial review and if a new COI is subsequently identified.
 - If consent disclosure language is required, provide the disclosure language to the Reviewing IRB.
 - Non-federal Relying Institutions will provide information about the managed conflict of interest as well as the management plan to the Reviewing IRB upon request.
 - Federal Relying Institutions will provide assurance to the Reviewing IRB that they have completed conflict of interest analyses under existing relevant federal policies and that the participation of agency Research Personnel is permissible and consistent with federal law. See [guidance from the NIH regarding Federal COI requirements](#).
 - Monitor its investigators’ adherence to the management plan.

Roles and responsibilities of the Reviewing IRB/Institution

- Have a process to receive information about COI and associated management plans from Relying Institutions at initial review and if a new COI is subsequently identified.
 - This information may be shared as part of the local context information provided by the Relying Institution, or through a document such as the SMART IRB [Protocol-Specific Document](#).
- Determine if the management plan is sufficient or if additional management strategies are needed to protect human subjects (see “[Identifying COI and Management Strategies](#)” below).
- If additional changes or strategies are needed, communicate with the Relying Institution to come to an agreement on what additional strategies are required (see “[Identifying COI and Management Strategies](#)” below).
- Accept the assurance from a federal Relying Institution that all federal investigator COI policies have been met and that participation of federal investigators in the research is permitted.

If a Relying Institution does not have a COI policy compliant with 42 CFR 50, subpart F for PHS-funded research or has no COI policy at all

In this scenario, the Relying Institution will rely on the Reviewing IRB/Institution or the primary recipient of federal funds (if applicable) to review for and manage COI.

Roles and responsibilities of the Relying Institution

- Make clear when coordinating the reliance arrangement that it does not have a COI policy and process or that it does not have a COI policy that is adherent to 42 CFR 50, subpart F, for instances in which the research is PHS-funded.
- Ensure that its investigator(s) understands that they will be working with the Reviewing IRB’s COI review entity for disclosure and review of their financial interests according to the policy of the Reviewing IRB Institution.
- Upon receipt of a COI disposition and management plan for one or more of its investigators, disseminate the management plan to its investigators and institutional officials, as per its policy.
- Monitor and ensure adherence of the conflicted investigator with the COI management plan and provide such follow-up information to the Reviewing IRB upon request. The Relying Institution is responsible for sanctions should conflicted investigators not adhere to the COI management plan.

Roles and responsibilities of the Reviewing IRB/Institution

- Have a process for investigators associated with the Relying Institution to confidentially disclose financial interests to the Reviewing IRB /Institution.
- Review the disclosed financial interests of investigators from the Relying Institution according to its own policy.
- Determine whether investigators at the Relying Institution have a COI in the context of the delineated research responsibilities. (see “[Identifying COI and Management Strategies](#)” below)
- If it is determined that a COI exists for investigators from the Relying Institution, mitigate or manage the COI according to the Reviewing IRB Institution’s policy and process. (see “[Identifying COI and Management Strategies](#)” below)
- Pending no disagreement over the COI management plan, ask the conflicted investigator at the Relying Institution to agree to or accept the management plan, depending on the process and terminology utilized by the Reviewing IRB/Institution.

- Implement aspects of the management plan within its purview, such as ensuring disclosure information in the informed consent form. As a courtesy, communicate to the Relying Institution as to how the COI management plan was implemented.
- If affiliated with the institution that is the prime recipient of PHS funding, report all COIs and their management to the NIH eRA Commons.

IDENTIFYING COI AND MANAGEMENT STRATEGIES

Financial interests that may constitute COI within a study context

- Consulting for a company* associated with the study (payment > \$5,000 over the past 12 months), includes scientific advisory board membership
- Paid speaking for a company associated with the study (> \$5,000 over the past 12 months)
- Travel paid or reimbursed by a company associated with the study (> \$5,000 over the past 12 months)
- Serving in a paid or unpaid fiduciary role for an entity associated with the study, i.e., board of directors, chief scientific officer
- The conflicted investigator's investigational product being evaluated in the study is licensed to the company sponsoring the research or providing the investigational product
- The conflicted investigator's investigational product utilized in the study is patented, but not licensed
- Founder and/or equity owner of a non-public company associated with the study
- Holding a > \$5,000 equity interest over the past 12 months in a public company associated with the study

* "Company" means a for-profit or not-for-profit entity, public, private, or start-up, that is related to the study such as, but not limited to, serving as a study sponsor or an industry partner or providing investigational product or in-kind support.

Considering the impact of the COI

- Is the nature of the conflict something that a participant would want to, or should, know about in order to make an informed decision?
- Could the conflict result in decisions that adversely affect participant safety and welfare?
- Could the conflict bias the conflicted investigator's judgement so that decision-making about eligibility, adverse event reporting, clinical care, etc., is not objective?
- Could the conflict impact the data collection?
- Could the conflict impact analysis of data?
- Is the conflicted investigator's participation essential for the conduct of the research (e.g., unique knowledge, skill, access to patient population)?
- Could the outcome of the research impact the financial interest?

If the answer to any of the above questions is yes, consider whether COI management should be implemented. COI management is context-dependent. Also consider the following additional questions.

- Is the research single-site or multi-site? (Single-site research may be more greatly impacted by investigator COI.)
- Is the study adequately designed to minimize bias and thus prevent the need for certain types of COI management?
- What is the risk of the research? (Minimal risk research may require a lower level of management than greater than minimal risk research.)

COI management strategies

- In most cases, Reviewing IRBs should make every effort to defer to COI management put in place by the Relying Institution. The COI management strategies below are most relevant if the Reviewing IRB/Institution is responsible for COI assessment and management plans.
- The strategies below are organized from minimal to more restrictive management. Because management strategies beyond #1 may impact the Relying Institution's ability to conduct the study, unilateral application of COI management by the Reviewing IRB without communication with the Relying Institution is discouraged.

COI Management Strategies: Implement one or more.

- 1) Disclose (if legally permissible) the conflict in the informed consent form and in any publications or presentations related to the research.
- 2) Restrict the conflicted investigator's access to identifiable data. (Communicate with the Relying Institution.)
- 3) Restrict the conflicted investigator's ability to determine eligibility status of prospective subjects. (Communicate with Relying Institution.)
- 4) Restrict conflicted investigator from obtaining informed consent. (Communicate with the Relying Institution.)
- 5) Restrict the conflicted investigator from adjudicating adverse events, serious adverse events, or unanticipated problems. (Communicate with the Relying Institution.)
- 6) Restrict the conflicted investigator's participation in data analysis and interpretation. (Communicate with the Relying Institution.)
- 7) Remove the conflicted investigator as PI, but allow them to retain a co-investigator role. (This requires significant dialogue with the Relying Institution.)
- 8) Remove the conflicted investigator from involvement in the conduct of the study. (This is a last-resort consideration that requires significant dialogue with the Relying Institution.)

FREQUENTLY ASKED QUESTIONS

1. How should a Reviewing IRB handle a situation where the management plans for similar COIs differ greatly among the institutions involved in the study?

Many factors impact what constitutes a conflict of interest at an institution and which methods an institution uses to manage those conflicts. Differences in interpretation of conflict and, importantly, differences in how conflicts are managed, are acceptable and even expected in the single IRB (sIRB) model. See Section 5.8 in the [SMART IRB Agreement v2.0](#).

Generally, the Reviewing IRB should defer to the COI management plans developed by the Relying Institutions, even if management plans for similar COIs differ across institutions or differ from the policies of the Reviewing IRB. An exception to this would occur if, when coordinating the reliance arrangement, the Reviewing IRB and Relying Institution document that the Reviewing IRB will take on the responsibility for identifying and managing conflicts of interest. See [“Who is responsible for determining whether an investigator COI exists?”](#) above for a discussion of the responsibilities of the Reviewing and Relying IRBs in determining whether a COI exists.

2. For PHS-funded research, who is responsible for ensuring that an institution’s COI policy adheres to the PHS regulation 42 CFR 50, subpart F—Promoting Objectivity in Research?

Ensuring adherence to 42 CFR 50, subpart F is the responsibility of the institution who receives a PHS award. The Reviewing IRB is not responsible for reviewing the policies of and/or assessing compliance of the Relying institution(s) with this regulatory requirement. This could be included as part of the collection of Relying Institution information, for example through use of the SMART IRB [“Protocol-Specific Document,”](#) which captures information about conflict of interest determinations for protocols reviewed under the SMART IRB Agreement.

3. If the Reviewing IRB has follow-up questions regarding an investigator’s COI, who should they contact?

If a Reviewing IRB has questions regarding a conflict of interest issue, the query should be made directly to the conflicted investigator at the Relying Institution and to the HRPP point of contact at the Relying Institution (i.e., the [SMART IRB POC](#)). If the investigator is not able to answer or respond to the Reviewing IRB’s questions, it is the investigator’s responsibility to contact the appropriate individuals within their institution to address the question from the Reviewing IRB.

4. What kind of information about COI and its management should be conveyed to the Reviewing IRB?

The Relying institution may supply the management plan or the following specific information:

- a) Name of investigator with conflict of interest*
- b) Role of the investigator on the study*
- c) Name of the entity(ies) with which the investigator has a financial relationship (e.g., study sponsor and/or research-related company)*
- d) The nature of the conflict of interest (services provided, e.g., consulting, speaking, equity, royalty income, scientific advice, etc.)*

- e) Amount of remuneration at issue in the COI (i.e., when aggregated exceeds \$5000 received in the past 12 months as defined in 42 CFR 50, subpart F).*
- f) Safeguards implemented by the Relying Institution to mitigate the COI (e.g., disclosure statement, divestment, independent oversight, removal from research processes such as determining eligibility, obtaining informed consent, performing intervention, evaluating adverse events, conducting data analysis, etc.)*

* A federal Relying Institution(s) will provide assurance to the Reviewing IRB that they have completed conflict of interest analyses under existing relevant federal policies and that the participation of agency Research Personnel is permissible and consistent with federal law. See [guidance from the NIH regarding Federal COI requirements](#).

5. How is organizational or institutional COI dealt with by both Relying Institutions and Reviewing IRB Institutions?

Each engaged organization or institution should perform its own institutional conflict of interest (ICOI) analysis under its relevant institutional policies and/or practices. Once an ICOI is identified, the management plan should be provided, as applicable, to the Reviewing IRB. Often these types of conflicts are managed by having the research reviewed by an external IRB, and/or disclosure of the conflict in the consent form. It is the responsibility of the Relying Institution to ensure that the terms of the ICOI management plan are being carried out at the local site.

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