

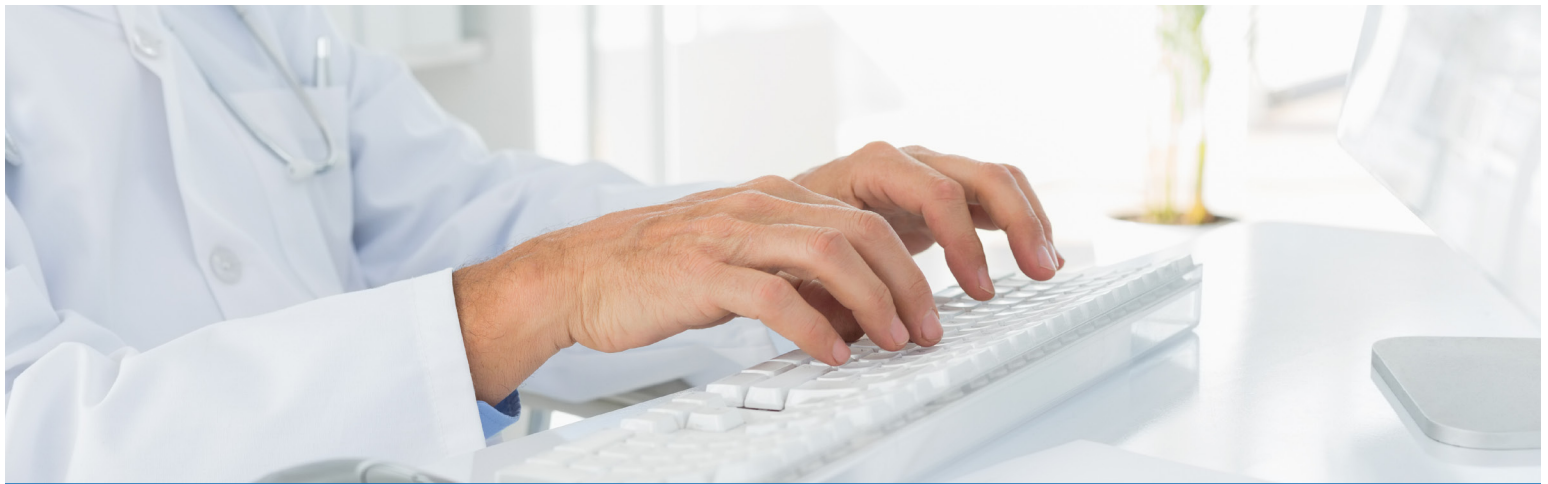


Managing Conflicts of Interest: Why an Independent IRB Should be Part of an Institution's Policy

Stuart Horowitz, PhD, MBA

Introduction

Reliance on independent Institutional Review Boards (IRBs) can often be a matter of choice – a decision made by institutions seeking to maximize their opportunities to participate in industry-funded multicenter clinical trials. Biopharma and medical device industries strongly encourage independent IRB review, and preferentially select clinical sites so that the number of IRBs used for multicenter studies can be minimized. In addition to the effort to gain more sponsored research, there is another rationale for forward-thinking institutions to consider relying on independent IRBs: research involving institutional and IRB member conflict of interest.



Conflict-of-Interests

A conflict of interest (COI) arises when two or more different interests are at odds with one another.

A financial conflict of interest (FCOI) arises when one of those interests involves a financial incentive of any kind (e.g. gift, payment, ownership interest). In research, a problem arises when a COI leads to bias, or even the appearance of bias. FCOI may involve individual investigators, or may involve the entire institution, as when an institution owns a patent, creates or partially-owns a company, or otherwise has a business interest in the successful development of a product discovered at, or licensed by, the institution.

To help reduce the possibility of bias and to promote objectivity in research,¹ the US Public Health Service (PHS) has promulgated a rule for FCOI in research. But the rule is limited to investigator FCOI, and does not address institutional COI (ICOI). The rule also does not address COI that is relevant to IRB members involved in the research approval process.



IRB Member Conflict of Interest

The Code of Federal Regulations states that no IRB may have a member participate in the IRB's initial or continuing review of research in which the member has a conflict of interest, except to provide information requested by the IRB.² Therefore, an IRB member with a conflict of interest may neither participate in deliberations nor vote on IRB actions taken for research in which the member has a conflict of interest. Often, the conflict is obvious, involving the participation of an IRB member who is an investigator or a sub-investigator on a study he or she has reviewed. Even so, it is not unusual for IRBs to accidentally or intentionally allow the participation of these researchers in the approval process. For example, as shown in a recent Warning Letter from FDA:³

The minutes of the IRB's February 11, 2013, meeting indicate that Dr. (b)(6), who was either a principal investigator or a subinvestigator for three FDA-regulated studies ((b)(4)), attended the meeting and voted to approve these studies during the meeting. However, in letters dated April 6 and April 30, 2015, which were included in the IRB's response to the Form FDA 483, Dr. (b)(6) stated he had abstained from voting on these studies.

The potential conflict of interest in an investigator voting on whether his/her own study should be approved is clear. All IRBs should have and follow written procedures for ensuring that investigators are not involved in the review of their own research, except to provide information requested by the IRB, and to be absent from subsequent deliberations and voting. It is unclear whether this was also a FCOI, and it should be emphasized that the regulation for IRB members does not specifically mention FCOI.

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IRB Member Conflict of Interest

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Not every instance of COI is clear. For example, is there a conflict if...

- the IRB member is related to the investigator?
- the IRB member is in the same department as the investigator?
- the IRB member is a subordinate to, or supervisor of, the investigator?
- any of the income from a clinical trial is allocated directly or indirectly to the IRB member or their department (for example, bringing in more research increases the department budget) ?

If there is a real or perceived conflict and the IRB member is recused, does the IRB still have the requisite expertise to review the research? If, for example, the department chair is a member of the IRB and recuses his or herself from the deliberation of a protocol in the therapeutic area, does anyone with that therapeutic expertise remain in the discussion?

Depending on the institution's answers to these questions, it is useful to consider reliance on an outside, independent IRB to ensure that the research is reviewed swiftly in the absence of bias or the potential for bias.



Institutional Conflicts of Interest (ICOI)

There are currently no federal regulations on ICOI, and thus, there is no legal or statutory definition of an ICOI. However, through the Institute of Medicine, scholars and research leaders have met and published the following operating definition:⁴

Institutional conflicts of interest arise when an institution's own financial interests or those of its senior officials pose risks of undue influence on decisions involving the institution's primary interests. For academic institutions, such risks often involve the conduct of research within the institution that could affect the value of the institution's patents or its equity positions or options in biotechnology, pharmaceutical, or medical device companies. Conflicts of interest may also arise when institutions seek and receive gifts or grants from companies, for example, a gift of an endowed university chair or a grant for a professional society to develop a clinical practice guideline.

In addition, institutional conflicts of interest exist when senior officials who act on behalf of the institution have personal financial interests that may be affected by their administrative decisions. In situations like these, an individual's financial relationship also implicates the institution's interests.

The report by the Institute of Medicine describes how institutions can identify ICOI, and offers ideas for how potential ICOI should be managed. Part of the suggested management plan involves review by an outside IRB, because review and continuing research oversight by the local IRB – which is captive to the institution, inasmuch as it is overseen, administered and managed by the institution which has a conflict of interest – does not adequately reduce the presence, potential, or appearance of bias in decisions being made about that study. The outside IRB can be the local IRB that is captive of a peer institution, but such an arrangement, especially if reciprocal, can also appear to be biased. Thus, it is ideal to rely on an independent IRB, rather than on the IRB captive of a peer institution.

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Complex and Multi-Factor Components

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Although there is no regulatory standard for ICOI, other organizations have addressed this in their policies and practices. The Association for the Accreditation of Human Research Protection Programs (AAHRPP), includes a standard related to ICOI for accreditation:⁵

Standard I-6: The Organization has and follows written policies and procedures to ensure that research is conducted so that financial conflicts of interest are identified, managed, and minimized or eliminated.

Element I.6.A. The Organization has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the Organization that could influence the conduct of the research or the integrity of the Human Research Protection Program.

Element I.6.B. The Organization has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and Research Staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. The Organization works with the Institutional Review Board or Ethics Committee in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate.

Note that Element I.6.A specifically refers to the interests of the organization (i.e. institution), in contrast to I.6.B, which addresses researchers. In both cases, the Human Research Protections Program has a role to play in managing or eliminating FCOI.



Management of Identified Institutional Conflict of Interests

How can an institution best manage IRB review when it has an identified ICOI? Although a central tenet of all IRBs – including local IRBs – is that they make “independent” decisions, they are not financially independent of their parent organization. It is reasonable to conclude that when the institution has an FCOI, the IRB within that institution also has an FCOI related to the research. Therefore, even in the absence of a specific rule related to ICOI, a reasonable interpretation of the available standards and guidelines is that a local institutional IRB should not review research involving an ICOI. At the very least, within institutions that have (or seek) AAHRPP accreditation, the local IRB should consider a policy specifying that the local IRB not review research when there is an ICOI.

Major research institutions recognize this and have chosen to adopting best practices by adopting a policy that requires reliance on independent IRB review as part of a Management Plan when an ICOI is identified (e.g. MD Anderson Cancer Center).⁶ The two initial challenges are to first identify the ICOI, and then to manage it. By choosing to rely on independent IRB review, your institution can ensure that real or perceived bias in IRB review of this research is eliminated.

References

- ¹ The Final Rule on Financial Conflict of Interest Regulations - Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding is Sought and Responsible Prospective Contractors (Federal Register / Vol. 76, No. 165 / Thursday, August 25, 2011 / Rules and Regulations, pp. 53256-53293
- ² 21 CFR 56.107(e), 45 CFR 46.107(e).
- ³ <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm484164.htm>
- ⁴ Conflict of interest in medical research, education, and practice. 2009. Bernard Lo and Marilyn J. Field, Eds. The National Academies Press, Washington, DC.
- ⁵ https://admin.share.aahrpp.org/Website%20Documents/AAHRPP_Accreditation_Standards.PDF
- ⁶ <https://www.mdanderson.org/content/dam/mdanderson/documents/about-md-anderson/about-us/conflict-of-interest/Institutional%20Conflict%20of%20Interest-2016%20OncoResponse.pdf>

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