

# Institutional Review Board (IRB) Policies & Procedures Manual



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## Institutional Review Board (IRB) Conflict of Interest

### Purpose

This policy applies to all investigators at Boston Children's Hospital (BCH) who submit proposals for human subject research to the Institutional Review Board (IRB). BCH is compliant with the Food and Drug Administration and the Office of Human Research Protections Guidance in reviewing, evaluating, and managing conflicts of interest in human subject research.

To fulfill its obligations, the IRB must address the impact of financial interests and other relationships on human subject protection. Financial interests may be held by an investigator, an IRB member, or the Institution.

### Policy

#### Definitions

**Investigator Conflict of Interest.** In addition to the general definitions set forth in The Conflict of Interest Policy, the following are definitions of certain conflicts as they relate to human subject research:

**Investigator Conflict of Interest** is defined as those circumstances in which an investigator's personal interest conflicts with, may affect, or has the appearance of affecting human subjects or the integrity of human subject research. Personal interests include not only the individual's own interest but also those of a member or his or her family or those with whom he or she maintains living arrangements approximating a family relationship.

**IRB Member Conflict of Interest** is defined to include the interest of an IRB member and his or her immediate family (i.e., spouse, children, persons with whom he or she maintains living arrangements that approximate a family relationship) which may affect, or has the appearance of affecting the human subjects or the integrity of human subject research.

**Organizational Conflict of Interest** is defined as a financial interest of Children's or its Senior Leadership that may result in inappropriate influence, or the perception of such influence over human subjects and human subject research.

#### Disclosure Requirements

##### 1. Investigator Conflict of Interest

In addition to the annual and situational disclosures set forth in **Conflict of Interest Policy**, the **Institutional Statement on Disclosure and Reporting of Conflicts of Interest**, as well as the

research disclosures set forth in the **Public Health Service Investigator Public of Interest Policy**, all investigators submitting protocols to the IRB for review must submit a conflict of interest disclosure statement. An investigator must disclose financial relationships or investment interests in a research sponsor. Investigators must also disclose any intellectual property interest in technology that is the subject of the research (whether or not the technology is licensed), certain positions of responsibility with the sponsor, and certain other interests that could affect the research. Investigators must also update the protocol anytime there is a significant change.

## 2. IRB Member Conflict of Interest

IRB Members must notify the IRB should any conflicts of interest arise when they are reviewing a protocol.

## 3. Organizational Conflict of Interest

In addition to the disclosure requirements set forth for Children's and its Senior Leadership in the **Conflicts of Interest Policy**, Children's will ensure disclosure to the IRB of potential Institutional conflicts in the following manner: The Technology Transfer Development Office ("TIDO") and the Investment Office maintain lists of entities in which Children's has equity. These lists will be provided to the IRB on an annual basis in order to identify whether any of the entities in which Children's has equity is sponsoring a study before the IRB. Further, The Children's Hospital Trust, which maintains a database of donations made to Children's will provide the IRB with a list of all significant donations on an annual basis, in order to identify whether any entities providing the donations sponsor human subject research.

## Procedure

### Management of Conflicts

#### 1. Investigator Conflict of Interest

In many cases, investigator's conflicts of interests will be barred or managed independently of IRB review through institutional policies of Children's or Harvard Medical School (See: **Institutional Statement on Disclosure and Reporting of Conflicts of Interest**). However, in certain situations, regulations or other standards that govern human subject protection may treat a financial interest or relationship as potentially affecting human subjects, even though Children's and HMS institutional policies do not prohibit it.

For example, compensation for serving as a company consultant to design a protocol, particularly where company payments to the investigator will depend on the outcome of the clinical research, raises special concerns for the protection of human subjects. Those concerns require IRB attention even though such consulting may be permitted under Harvard Medical School and Children's conflict of interest policies.

Similarly, from time to time, the IRB reviews protocols in which an investigator wishes to test, in children, a device the investigator has invented. In some of these cases the device is not licensed to any company, Children's owns all or some of the patent rights, and the investigator wishes to collect data that might ultimately support licensing and development. This may not violate HMS and Children's policies and guidelines, which are instead directed to regulating the financial and equity relationships between the investigator and a company that is sponsoring

research or to which the device is licensed or "contractually committed." Nonetheless, this is an issue for IRB review, since the design, conduct, and results of the research protocol, and its effect on children, are intertwined with the investigator's interest in developing and licensing the invention, its regulatory approval, and (if the results of the trial are favorable) the financial terms a company would offer the investigator to license his or her patent rights.

Additional management strategies the IRB may impose include the following:

- a. Where the investigator, as an interested party, is also the primary source of information contained in the protocol (for example, concerning the risks and benefits to subjects of a drug or device to be tested) and in other circumstances as appropriate, the IRB may require that independent scientific review verify the investigator's representations of risks and benefits, assess the impact of the research design on subject burdens and benefits, and identify any critical points in the protocol in which the conflict of interest, if acted upon, could have a material adverse impact on the clinical care of the subject. The precise form of scientific review may vary. The independent review may occur as part of the departmental review, if the reviewers are appropriately aware of the nature of the conflict, or it may occur in other ways, including referral to the clinical research support office.
- b. Where the investigator, as an interested party, also has significant clinical involvement in the care of subjects under the protocol, the IRB may require that an independent data safety monitoring process be established for reviewing adverse events, validating the application of inclusion and exclusion criteria, performing interim analyses of the integrity of the data, and assessing any potential effects on the clinical care of subjects. In this context, or for purposes of later reporting on continuing review, the IRB may consider requiring the collection of additional data that would document whether a conflict of interest has had any effect on subjects or the research.
- c. Where applicable, the informed consent must disclose that the investigator is the inventor of or has an interest in a related patent, that the investigator and /or Children's Hospital, as applicable, may receive financial benefits from development of the invented technology, and that the financial benefit may depend on the outcome of the trial.

The following language is recommended for cases in which an investigator has an intellectual property interest:

*As [an inventor of the technology], Dr. Z has a financial interest in \_\_\_\_\_ technology that is used in this research study. In the future it is possible that this technology will be sold commercially, and that the results of this trial will be important in securing government approval or contracting with a business to manufacture or develop the technology. If this were to occur, Children's Hospital and/or the investigator might receive financial benefits in the form of royalties or other compensation. As in all research studies, the Hospital has taken steps designed to ensure that this potential for financial gain does not endanger research subjects, or undercut the validity and integrity of the information learned by this research.*

In other cases, the IRB may require the informed consent to state the general nature of the interest.

- d. The IRB may require that someone other than an investigator who has a financial relationship, intellectual property interest, or investment interest, serve as the principal investigator (PI), perform certain of the functions otherwise designated for the investigator (such as enrollment), or engage in supplementary oversight roles,

particularly where subject safety would otherwise depend solely on clinical judgments made by an investigator with a conflict of interest.

- e. In treatment protocols where the risks are significant and medical circumstances warrant, the IRB may request that the investigator, the sponsor, or the department provide a mechanism for the ongoing monitoring of the clinical care of the subjects against the effects of any potential conflict of interest, through peer reviewed or other concurrent clinical processes not triggered simply by reported adverse events, and may condition approval on implementation of such a process as approved by the pertinent Chief. This may take the form of an enhanced data safety monitoring plan, which includes broader review of clinical data pertinent to risks; or, where the conflict may raise or appear to raise significant questions about whether clinical care of subjects may be subordinated to research objectives to the detriment of patients, the IRB may condition its approval on periodic reporting of the results, or sufficiently concurrent departmental or other clinical review.
- f. As part of the IRB deliberations, the committee will consider the particular protocol, associated risks, and the potential for risks and benefits, and determine whether any or all of the above mentioned safeguards, or any others appropriate under the particular circumstances, should be required as part of the approval process. The IRB may, for example, consider any other remedies it would ordinarily have available, such as conditioning approval on a process to manage or eliminate other effects of a conflict, requiring consent monitoring, or requesting information about how sponsors or their agents will mitigate or monitor for risks presented.

## 2. IRB Member Conflict of Interest

Any IRB member, voting or nonvoting, with a conflict of interest in a study, must leave the room during the final discussion and vote on the protocol. A member with a conflict may be asked questions about the content of the protocol, and issues concerning the study, but must not be present beyond the questions and answers, and, other than to provide information, must not seek, inside or outside the meeting, to influence or affect the voting of no conflicted members. The minutes must document the fact that the member left the meeting room during the final discussion and vote because of a conflict of interest. Members are expected to advise the Director of Clinical Research Compliance if they are assigned a protocol, continuing review or amendment as a reviewer so that the protocol may be reassigned. Members are also expected to notify the Chair during a meeting if they have a conflict of interest for an initial review, continuing review, modification, adverse event, unanticipated problem or review of non-compliance.

## 3. Institutional Conflict of Interest.

Organizational Conflicts of Interest are reviewed, evaluated and managed in accordance with the **Conflict of Interest Policy**. This Policy further focuses on the resolution of such conflicts to ensure that they do not influence Children's clinical operations, the conduct of clinical research or the integrity of the IRB or its operations. The following describes the evaluation and management of Organizational Conflicts as they relate to human subject research.

- a. Children's Equity or Financial Interest in Entities Sponsoring Clinical Research

Children's will from time to time acquire equity or a financial interest or relating to licensing, technology transfer and patents.

Children's will not generally participate in clinical trials sponsored by a company in which the Hospital holds equity except in extraordinary situations, as demonstrated by the presence of *all* of the following circumstances: (1) there is no other venue that is appropriate for the study, or there are other compelling reasons why Children's must be a possible venue, such as ensuring access for vulnerable or affected populations; (2) the test article, whether a drug or device, is of significant potential benefit for the public or Children's patients; (3) there is independent verification and monitoring of all significant aspects of the study relevant to human subject protection and scientific integrity, including protocol design, description of risks and benefits, implementation of exclusion and inclusion criteria, securing informed consent, criteria and procedures for subject withdrawal, reporting and addressing adverse events, maintaining research subjects' awareness of their rights, and reporting of data; and (4) the Children's Institutional Review Board, in its sole discretion, has approved the study, and whatever additional conditions Children's Institutional Review Board has imposed are satisfied.

In deciding whether to participate in a clinical trial sponsored by a company in which Children's owns equity, the IRB will independently evaluate whether the criteria above have been met; the requirements and standards of regulatory and accrediting bodies, and its own policies; the adequacy of the Children's and the clinical department's steps to ensure that impacts of a potential conflict have been and will be effectively mitigated; the conflict's impact on the validity and integrity of the data generated from the clinical trial, to the extent such data contributes to the potential benefit of the study; how to implement full disclosure of Children's equity interest to subject patients and others; and how to ensure that there is no inappropriate preferential access to patient populations for companies in which the Hospital owns equity.

It is expected that confirmatory clinical trials (typically Phase II and Phase III studies) will be conducted as multi-center studies and directed by principal investigators who have no affiliation with the hospital.

When Children's holds equity with a Company that sponsors the research, the following statement should be included in the informed consent:

Informed Consent Statement if Children's Hospital Owns Equity:

*Children's Hospital licenses certain of its research discoveries to companies for research and/or commercial development. From time to time, Children's Hospital receives equity, either as capital stock or as options to buy capital stock, as partial consideration for a license. In keeping with Children's Hospital policy, you are advised that Children's Hospital has equity in the company that is sponsoring this research and may gain financial (monetary) benefits if the drug/device/technology being studied in this trial proves to be of benefit. As in all research studies, the Hospital confirms that it has taken, and will continue to take, all necessary steps to ensure research subject safety, and the validity and integrity of the information obtained by this research.*

b. Charitable Donors

As set forth above, the Compliance Office and IRB will review charitable donations against sponsors of human subject research to identify and evaluate potential conflicts.

Any conflict of interest will be assessed by the Office of General Counsel, which will report them as necessary to the Chief Executive Officer. The Chief Executive Officer may refer any or all disclosure statements to the Board of Trustees, 2) appoint an ad hoc committee to review and resolve any conflicts of interest issues, or 3) review and resolve any conflict of interest personally or through a designee(s) and draft a management plan.

## Review of Conflicts

In addition to the general review process set forth in **Procedures for Reviewing Conflicts of Interests**, the following review processes shall be in place for conflicts as they pertain to humans subject research.

### Investigator Conflicts of Interest

Investigator Conflict of Interest shall be reviewed by Compliance, and if necessary, the Office of General Counsel, and/or the Research Conflicts of Interest Committee. These bodies will make recommendations to the IRB for management of any conflicts. The Research Conflicts of Interest Committee may require and approve a management plan for an investigator's conflict; The Office of General Counsel and Compliance will support the Committee in reviewing any conflicts and will work with the investigator to draft a management plan. The Compliance Office will maintain all management plans in its electronic system and will provide the IRB with the key elements of any such management plan. All recommendations and management plan elements will be communicated to the IRB by Compliance or the Office of General Counsel through the IRB's electronic system and will be saved in such. The IRB will have the ultimate decision-making authority of whether to accept the recommendations for management or put in place any further management requirements. The IRB may require any additional action as it deems appropriate to ensure the protection of human subjects.

### Organizational Conflict of Interest

Organizational Conflict of Interest shall be reviewed by the Compliance and/or the Office of General Counsel. When necessary, such conflicts may be referred to the Chief Executive Officer, who may refer any or all disclosure statements to the Board of Trustees, 2) appoint an ad hoc committee to review and resolve any conflicts of interest issues, or 3) review and resolve any conflict of interest personally or through a designee(s) and draft a management plan. Recommendations for management as it relates to human subject research will be made to the IRB through the electronic system. The IRB may require any additional action as it deems appropriate to ensure the protection of human subjects.

Additional management strategies the IRB may impose include the following:

1. If an individual conflict, recusing oneself from relevant decision making.
2. If an individual conflict, reduce, modify or eliminate the financial interest.
3. If a conflict related to the institutional ownership of equity, the decision that the institution will not conduct clinical trials on the technology of the company.
4. If a conflict related to a major donation, a separation from those involved in soliciting/managing the gift and those involved in any related research or clinical care.

5. Disclosure of the financial interest in publications, presentations, future grant applications and other communications.
6. Disclosure of the financial interest to trainees and supervisees.
7. If involving human subject research, establishing a monitoring process to protect the integrity of the research and the well-being of human subjects.
8. Not proceeding with the activity related to the financial interest.

Violation of this policy may result in disciplinary or other remedial action, including termination of employment and removal from office.

## Related Content

IRB and Other Policies

*Conflict of Interest*

*Conflict of Interest Procedures Guidance*

*Harvard Medical School Policy on Conflicts of Interest and Commitment*

*Institutional Statement on Disclosure and Reporting of Conflicts of Interest*

*Public Health Service Investigator Conflict of Interest Policy*

## Document Attributes

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<b>Author</b>	Suzanne Tannenbaum Business Conflicts Manager	<b>Dates Reviewed/ Revised</b>	4/29/15
<b>Reviewed/ Revised by</b>	Timothy Hogan Chief Compliance Officer		
<b>Copyright</b>	©Boston Children's Hospital, 2020	<b>Last Modified</b>	2/11/2020
<b>Approved</b>	Timothy Hogan Chief Compliance Officer  August Cervini, MBA Vice President for Research Administration  Susan Kornetsky Director of Clinical Research Compliance		