For Internal Use Only

Phoenix Children's Hospital

Scope: Department-specific
Research Policy

Identifying and Managing Conflicts of Interest in Research

Effective Date: November 21, 2017

RELATED FORM(S)

1. PCH CITI Training Instructions and Guidelines
2. PCH Financial Disclosure/ Conflict of Interest Form
3. Potential Conflict of Interest Worksheet

RELATED POLICIES

1. PCH Research Policy: Education and Training Requirements for Human Research Protections at PCH.
2. PCH Research Policy: Role of the IRB at PCH.
3. Phoenix Children's Hospital Code of Conduct.
4. Phoenix Children's Hospital IRB Standard Operating Procedures.
5. Phoenix Children's Hospital Institutional Conflict-of-Interest (place holder as in process)

REASON FOR POLICY

This policy is intended to provide guidance identifying and managing potential conflicts of interest that may arise during the conduct of research, clinical and non-clinical, at Phoenix Children's Hospital ("PCH").

DEFINITIONS

1. Conflict of Interest (COI):
   A divergence between an individual's private interests and his/her professional obligations to PCH, other medical staff, patients, and employees, such that an independent observer might reasonably question whether the individual's professional actions or decisions are influenced by considerations of direct or indirect personal gain or advantage, financial or otherwise. Conflicts of interests can be an actual or potential conflict of interest, and the perception/appearance of a conflict is considered a conflict of interest for purposes of this policy. No "presumption of guilt" is created by the mere existence of a relationship between an Investigator and a Third-Party that may benefit from the conduct of research at PCH and its outcome. Conflict of interest situations are analyzed on a case by case basis.

2. Third-Party:
   Any individual, entity, or organization that currently, or in the future, conducts business transactions with PCH. Third Party includes entities where an investigator owns a substantial interest in public corporations or non-publicly held entities, (Substantial interest is defined as

owning at least five percent (5%) of a class of the outstanding securities for a publicly held corporation).

3. Family member:
   Family is defined broadly as any person who is related by blood or marriage, such as spouses, parents, children, grandchildren, brothers, sisters, sons/daughters-in-law, brothers/sisters-in-law, fathers/mothers-in-law, step parents, step siblings, step children, step grandchildren, or whose relationship with the investigator is similar to that of person(s) who are related by blood or marriage. This policy also may apply to individuals who are not legally related but who reside with the Investigator.

4. Research Compliance Committee (RCC):
   Committee charged with the review of real or perceived conflicts of interest on behalf of the Phoenix Children's Hospital Office of Research Administration.

5. Investigator:
   Principal investigator, co-principal investigators, and any other person who is responsible for the design, conduct or reporting of clinical research.

6. Key Administrators:
   Institutional officials and members of the Research Compliance Committee.

7. Research:
   Research includes a systematic investigation and/or contribution of generalizable knowledge through the conduct of a clinical research project or non-clinical research project, program or quality project

8. Significant Financial Interest (SFI):
   A Significant Financial Interest occurs when an individual has, directly and indirectly, through business, investment or family, the following financial interests, including:

   A. Payments from a Financially Interested Person or Company that exceeded or are expected or have the potential to exceed $5,000 over a period of 12 months, beginning one year before the Research Application is submitted and extending up to one year following the expected conclusion of the research project. These payments may include salary, consulting fees, honoraria, gifts, in-kind donations, equipment, income from seminars, lectures, advisory committees or review panels, or other payments that exceed the costs of the clinical research.
   B. Equity interest or an entitlement to equity (including options or warrants) of more than $5,000 or more than 5% ownership interest in a Financially Interested company, not including any interest arising solely by reason of investment by a mutual, pension, or other institutional investment fund over which the person has no control.
   C. Equity interests or an entitlement to equity (including options or warrants) of any value in a corporation or company, with a value that cannot be readily determined (usually because the company is privately held).
   D. Equity interests or an entitlement to equity (including options or warrants) of any value in the investigational item subject of the clinical or nonclinical research.
   E. Intellectual property rights (patents, copyrights, royalties, or licensing fees) in the investigational item subject of the clinical or nonclinical research.
   F. Compensation with value that may be affected by the outcome of the clinical or nonclinical research.
   G. For clinical research, payments for enrollment of study subjects, or any bonus, or milestone payments in excess of reasonable costs incurred.
   H. Any other financial interest that may interfere with the ability to protect participants in the

clinical research.

I. For Non-Clinical research, any basic research, or quality or programmatic research any compensation with value that may be affected by the outcome of the research undertaking.

9. Project Team Members:
   Project Team Members include the investigator and other individuals who may perform, but are not limited to, the following tasks for a specific protocol:
   A. Screening
   B. Enrollment and Randomization
   C. IRB Submission
   D. Regulatory Document Preparation
   E. Informed Consent Process
   F. Prescribing Privileges for the Test Article
   G. Subject Assessment
   H. Form Completion and Data Management

10. Research Staff: PCH Office of Research personnel

POLICY

Investigators must conduct their affairs with third parties so as to avoid or minimize potential conflicts of interest, and must respond appropriately when conflicts of interest do arise. A conflict of interest depends on the situation and not on the character of the individual. Such behavior calls into question the professional objectivity and ethics of the individual and it carries the potential to reflect negatively on PCH. PCH is an institution of public trust and PCH researchers should respect this status, and conduct their affairs in ways that will not compromise the integrity or reputation of PCH. PCH investigators must, where appropriate, disclose material financial, business or personal interest relationships in accordance with this policy. **PCH must also disclose, in writing, any potential conflict to the Federal awarding agency in accordance with applicable Federal awarding agency policy, where applicable.**

Copies of this policy are available to any requesters within 5 business days. At any time that the PCH IRB obtains a publicly accessible website, the policy will be posted within 30 days.

PROCEDURE - CLINICAL RESEARCH

1. POTENTIAL CONFLICTS OF INTEREST BY INVESTIGATOR, STUDY TEAM MEMBERS, AND RESEARCH STAFF INVOLVED IN HUMAN SUBJECTS RESEARCH:

   A. As part of the initial research application process for each research project, each Investigator, Team Member, and all Research Staff will submit to the Research Office a Financial Disclosure/ Conflict of Interest Form (FD/COI), which asks for the disclosure any Financial Interest related to the proposed clinical research. These forms will be submitted annually at Continuing Review.
   B. At the time of IRB submission, the IRB Office will review the Financial Disclosure/ Conflict of Interest Form to ensure that the form for each Investigator, Team Member and Research Staff is complete and signed.
   C. The IRB staff, once in receipt of the FD/COI declaration, will forward a copy of the forms stating there is a conflict of interest to the Director – Research Ethics & Governance for review and submission to the RCC for review and management plan development.
   D. If the applicable research team member does not agree with the COI management plan, the RCC will provide an opportunity to the individual to explain the Significant Financial Interest

or other potential COI, taking such information into consideration when developing a final management plan.

E. In developing the COI management plan, the RCC will consider options that will mitigate or eliminate the impact of the COI on the design, conduct, reporting or integrity of the clinical research and will alleviate or eliminate any circumstances that would cause an independent observer to reasonably question whether an individual's professional actions or decisions are determined by consideration of personal gain, financial or otherwise, and will promote the protection of research subjects. The RCC will consider the nature of the research, the magnitude of financial interest, the degree to which it is related to the research, the extent to which the research could be directly and substantially affected by the interest, and the degree of risk to the human subjects that is inherent in the research protocol.

F. The RCC will consider the following options for the COI management, and will adopt a course of action most appropriate for the individual circumstances presented. One or more of these options may be adopted, or the RCC may choose to adopt another option not listed here as appropriate:
   i. Monitoring of research by independent reviewers, such as a data and safety monitoring committee or other similar monitoring body;
   ii. Negotiation of the clinical research contract with the sponsor by a disinterested person within the Institution;
   iii. Modification of the clinical research protocol or safeguards in the study to prevent the introduction of bias, such as randomly selected research subjects or independent corroboration of research results;
   iv. Recommend to the IRB that a person other than the Investigator, Team Member, or their employees to collect informed consent from the clinical research participants;
   v. Recommend monitoring of the informed consent and enrollment process to the IRB;
   vi. Disclosure of the financial interest to the clinical research subjects during the informed consent process as well as in the informed consent document , noting, however, that where a COI may affect the protection of research subjects; disclosure may not be the sole method of managing a conflict;
   vii. Disclosure of the financial interest to the public;
   viii. Requiring the Investigator or Team Member, the immediate family member, or affiliated entity to divest the Significant Financial Interest as a condition for approving the clinical research;
   ix. Requiring that a non-interested party to hold or administer the Significant Financial Interest (e.g. blind trust);
   x. Requiring the Investigator or Team Member or the immediate family member to sever the relationship(s) that create the COI (such as resignation from the Board of Directors);
   xi. Disapproval of the proposed research or termination of research if already underway
   xii. Modification of study staff role(s), such as a change in Investigator; and/or
   xiii. Disclosure to the editors of journals publishing the results of the research.

G. The RCC will forward a copy of the completed Potential Conflicts Worksheet to the Research Administration

H. At the time of continuing review by the IRB, each Investigator, Team Member, and Research Staff will provide any amendments, deletions or additions to the original Financial Interests Disclosure Form to Research Administration

I. If the information in the original Financial Interests Disclosure Form changes at any time during the course of research, updated information must be provided to the Research Administration Office within 30 days of discovering or acquiring (e.g. through purchase, marriage, or inheritance) a new significant financial interest.

J. In response to any amendments, deletions, or additions to the Financial Interest Disclosure Form, the Research Office will forward this information to the RCC for reconsideration of the COI management plan.

If an individual does not disclose a Financial Interest, fails to complete the Financial

Disclosure of Interests form in an accurate and truthful manner, or fails to update the Financial Interests Disclosure Form as required by this Policy, the RCC may recommend appropriate sanctions, including but not limited to: limitations on the investigator's conduct of research at the Institution, referral to the appropriate body for initiation of actions related to medical staff privileges, or employment-related discipline.

Whenever PCH identifies a SFI that was not disclosed timely by an investigator or was not previously reviewed by the Institution during an ongoing PHS-funded research project, (e.g. was not timely reviewed or reported by a sub recipient), the PCH designated official(s) shall, within sixty days: review the disclosure of the significant financial interest; determine whether it is related to PHS-funded research; determine whether a financial conflict of interest exists; and, if so, implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest. Depending on the nature of the significant financial interest, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date of disclosure and the completion of the Institution's review.

In addition, whenever a financial conflict of interest is not identified or managed in a timely manner including failure by the Investigator to disclose a significant financial interest that is determined by the Institution to constitute a financial conflict of interest; failure by the Institution to review or manage such a financial conflict of interest; or failure by the Investigator to comply with a financial conflict of interest management plan, the Institution shall, within 120 days of the Institution's determination of noncompliance, complete a retrospective review of the Investigator's activities and the PHS-funded research project to determine whether any PHS-funded research, or portion thereof, conducted during the time period of the noncompliance, was biased in the design, conduct, or reporting of such research.

K. If an Investigator, Team Member, or Research Staff member wishes to appeal this decision, he/she should appeal in writing to the Chief Research Officer.

PROCEDURE - BASIC AND NON-CLINICAL RESEARCH

2. POTENTIAL CONFLICTS OF INTEREST BY INVESTIGATOR, PROJECT TEAM MEMBERS, AND RESEARCH STAFF INVOLVED IN NON HUMAN SUBJECTS RESEARCH:
   A. As part of the research application process, each Investigator, Team Member, and all Research Staff will submit to the Research Administration Office a Financial Disclosure/ Conflict of Interest Form, which asks for the disclosure any Significant Financial Interest related to the proposed research. These forms may be submitted at the time of project submission, at the time of award, during the project renewal, when added as an Investigator to an ongoing Public Health Service (PHS) project, and prior to participation in any PHS-funded research at least annually. .
   B. The Research Administration will review the Financial Disclosure/ Conflict of Interest Form to ensure that the form for each Investigator, Team Member and Research Staff is complete and signed.
   C. If the Financial Disclosure/ Conflict of Interest Form do not reveal a Financial or other potential COI, the Research Administration will fill out the Potential Conflicts of Interest Worksheet notating the absence of COI.
   D. If the Financial Disclosure Form reveals a Financial Interest or other potential COI, the Research Administration will complete the Potential Conflicts of Interest Worksheet and will forward a copy of the Financial Disclosure/ Conflict of Interest Form and the Potential Conflicts of Interests worksheet to the Research Compliance Committee (RCC). A

designated member of the RCC will contact the Investigator, Team Member, or Research Staff Member with the potential COI to gather additional information and to attempt to develop a mutually agreeable COI management plan that eliminates the COI. This plan will be presented, discussed, and voted on by the RCC.

E. If the RCC does not approve the COI management plan, the RCC will provide an opportunity to the Investigator, Team Member, or Research Staff to explain the Financial Interest or other potential COI, to make suggestions on an appropriate management plan, and to explain why the research should be permitted at the Institution if the COI cannot be eliminated.

F. In developing the COI management plan, the RCC will consider options that will alleviate or eliminate the impact of the COI on the design, conduct, reporting or integrity of the research and will alleviate or eliminate any circumstances that would cause an independent observer to reasonably question whether an individual's professional actions or decisions are determined by consideration of personal gain, financial or otherwise, and will promote the responsible conduct of research. The RCC will consider the nature of the research, the magnitude of financial interest, the degree to which it is related to the research, the extent to which the research could be directly and substantially affected by the interest, and the degree of risk that is inherent in the research protocol.

G. The RCC will consider the following options for the COI management, and will adopt a course of action most appropriate for the individual circumstances presented. One or more of these options may be adopted, or the RCC may choose to adopt another option not listed here as appropriate:
   i. Monitoring of research by independent reviewers, such as a data and safety monitoring committee or other similar monitoring body;
   ii. Negotiation of the research contract with sponsoring agency by a disinterested person within the Institution;
   iii. Modification of the research protocol or safeguards in the study to prevent the introduction of bias;
   iv. Disclosure of the financial interest to the public;
   v. Requiring the Investigator or Team Member, the immediate family member, or affiliated entity to divest the Significant Financial Interest as a condition for approving the research project;
   vi. Requiring that a non-interested party to hold or administer the Significant Financial Interest (e.g. blind trust);
   vii. Requiring the Investigator or Team Member or the immediate family member to sever the relationship(s) that create the COI (such as resignation from the Board of Directors);
   viii. Disapproval of the proposed research or termination of research if already underway
   ix. Modification of project staff role(s), such as a change in Investigator; and/or
   x. Disclosure to the editors of journals publishing the results of the research.

H. The RCC will forward a copy of the completed Potential Conflicts Worksheet to the Research Administration.

I. At the time of project renewal, each Investigator, Team Member, and Research Staff will provide any amendments, deletions or additions to the original Financial Interests Disclosure Form to the Research Administration.

J. If the information in the original Financial Interests Disclosure Form changes at any time during the course of research, updated information must be provided to the Research Administration within 30 days of discovering or acquiring (e.g. through purchase, marriage, or inheritance) a new significant financial interest.

K. In response to any amendments, deletions, or additions to the Financial Interest Disclosure Form, the Research Administration will forward this information to the RCC for reconsideration of the COI management plan.

L. If an individual does not disclose a Financial Interest, fails to complete the Financial Disclosure of Interests form in an accurate and truthful manner, or fails to update the Financial Interests Disclosure Form as required by this Policy, RCC will recommend appropriate sanctions, including but not limited to: limitations on the Investigator's conduct of

research at the Institution, referral to the appropriate body for initiation of actions related to medical staff privileges, or employment-related discipline. Whenever PCH identifies a significant financial interest that was not disclosed timely by an investigator, or, for whatever reason, was not previously reviewed by the Institution during an ongoing PHS-funded research project, (e.g. was not timely reviewed or reported by a subrecipient), the designated official(s) shall, within 60 days, review the significant financial interest, determine whether it is related to PHS-funded research, determine whether a financial conflict of interest exists. If such a conflict is determined to exist, implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest going forward.

M. If an Investigator, Team Member, or Research Staff member wishes to appeal this decision, he/she should appeal within 60 days in writing to the Chief Research Officer.

PROCEDURE - KEY ADMINISTRATORS AND COMMITTEE MEMBERS

3. POTENTIAL CONFLICTS OF INTEREST BY KEY ADMINISTRATORS
   A. In the event that COIs arise that involve key administrators, the Office of Research Administration will submit a letter and appropriate documents to the Institutional Official/CEO of PCH. Attachments will include the original Financial Disclosure and Conflicts-of-Interest forms that were submitted as well as findings and recommendations by the Research Compliance Committee. to determine if any Key Administrators have a real or perceived financial interest in the sponsor or other known Third-Party. For each new research project considered, the Director of Research Operations will request Research Compliance Committee members to disclose any personal COI that exists or has potential for conflict
   B. Potential Conflicts of Interest will be noted in the minutes and then forwarded to the Research Administration Office.
   C. If no Financial or other potential COI is identified by Research Compliance Committee the Research Administration Office will fill out the Potential Conflicts of Interest Worksheet noting the lack of COI.
   D. If the response indicates Key Administrators have a potential COI, the Research Administration Office will bring the potential COI to the attention of the Chief Executive A designated member of the RCC will contact the individual with the potential COI to gather additional information and to attempt to develop a mutually agreeable COI management plan that eliminates the COI. This plan will be presented to the RCC for approval or disapproval.
   E. If the If the affected individual does not approve the COI management plan the RCC will provide an opportunity to the individual to explain the Financial Interest or other potential COI, to make suggestions on an appropriate management plan, and to explain why the research should be permitted at the Institution if the COI cannot be eliminated.
   F. In developing the COI management plan, the RCC will consider the options set forth in Section).
   G. The RCC will forward a copy of the completed Potential Conflicts Worksheet to the Research Administration Office.

4. POTENTIAL CONFLICTS BY IRB MEMBERS
   A. In addition to having a Financial Interest as defined in, an IRB member has a potential Conflict of Interest if:
   B. The IRB member is an Investigator, employee of the Investigator, or member of the clinical research team for the proposed clinical research.
   C. The IRB member has an interest that the IRB member believes may conflict with his or her ability to objectively review a clinical research protocol. This may include a close personal or professional relationship with the Investigator.
   D. Initially each IRB member will fill out a Financial Disclosure form that will be accompanied by a list of Sponsors currently conducting Research at PCH. IRB members will be asked to submit a new FD/COI form at reappointment to the IRB.

E. Sponsors and protocol titles for new studies being reviewed will be listed on the IRB meeting attendance rosters to determine whether any new COI exists.
F. An IRB member or IRB consultant with a COI may provide information to the IRB, as requested by the IRB, but may not be present during IRB deliberations unless the member or consultant is providing information. The IRB member or IRB Consultant with a COI may not be present during the voting. An IRB member may not vote on a research protocol with which the IRB member has a COI. The member's name must be recorded for each applicable vote indicating the member was not present for the vote. The member cannot count toward quorum.

ADMINISTRATIVE DOCUMENTATION, RETENTION AND DISCLOSURE

5. RETENTION OF DOCUMENTATION
   A. The Institution will maintain all documentation noted in this Policy, all other documentation related to potential conflict of interest, and a record of all actions taken for at least seven years from the termination of the research or from resolution of any government action involving those records, whichever is longer. The institution will maintain all records as required by law, if a retention period longer than seven years is required. The institution will make available all records related to the identification of any conflict of interest and the manner in which it was managed, reduced, or eliminated to the Department of Health and Human Services and the National Science Foundation upon request.

6. CONFIDENTIALITY
   A. All documentation noted in this policy, all other documentation produced during evaluation of and response to a potential COI, and any recordings or interviews will be marked confidential. These documents will be used by the Finance Committee, MEC, Research Administration, and other appropriate individuals only to determine whether there is a COI of interest exists and how to manage the COI. Such documents will only be disclosed as required by law or with the permission of the subject of the form.

7. TRAINING
   A. The Institution will provide this policy, supporting documents and other educational guidelines as appropriate to each Investigator, Team Member, personnel employed in the Research Office and members of the IRB.
   B. All investigators conducting research at PCH are required to complete Conflict of Interest training via the CITI Training website. Proof of training must be provided to the PCH IRB office.

8. INSTITUTIONAL REPORTING OBLIGATIONS
   A. Public Health Service ("PHS") Funding
      i. Before expenditure of PHS funds, the Institution must report to the PHS organizational unit that funds the research, the existence of an investigator's COI (although no details of the conflict are required) and assurance the COI has been managed, reduced or eliminated. If the institution identifies a COI after the submission of the report to PHS, the institution must manage, reduce or eliminate the COI and file an interim report within 60 days of identifying the COI.
      ii. The institution must promptly notify the PHS of an Investigator's noncompliance with this policy if the noncompliance was based on the design, conduct or the report of research. The notification should include a statement of the corrective action taken or proposed to remedy the situation.
   B. National Science Foundation ("NSF") Funding
      i. If an institution is unable to satisfactorily manage a COI relating to research funded by NSF, the institution will inform the NSF's office of General Counsel. Grantee

notifications of a COI that cannot be managed, reduced or eliminated must be submitted electronically via the NSF Fast Lane System.

C. Obligations as Research Sponsors
   i. Research sponsors have additional obligations to report to the FDA financial relationships between the sponsors and investigators. This policy does not cover the obligations if the Institution is also acting as the sponsor because it is funding a clinical study that will be submitted in support of a marketing application or reclassification petition for a human drug, biological product or device.

REFERENCES

42 C.F.R. Part 50, Subpart F

45 C.F.R. Part 94)

PCH IRB Standard Operating Procedures
PCH Research Education Policy
45 CFR 46
21 CFR 50
21 CFR 56
2 CFR 200.112
2 CFR 200.113