PATH Investigator Conflict of Interest Policy

(Public Health Service (PHS)-Funded Research)

Background

The Department of Health and Human Services (HHS) and the Public Health Service (PHS) published the *Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding Is Sought*, as outlined in the regulations 42 CFR Part 50, Subpart F for Grants and Responsible Prospective Contractors as outlined in the regulation 42 CFR Part 94 for Contracts, as revised in 2011 (collectively, the “Regulations”). The intent of the Regulations is to address the increasing complexity of the financial interests held by investigators and to set standards to ensure that the design, conduct, and reporting of research funded under PHS grants, cooperative agreements and contracts will not be biased by any conflicting financial interest of those investigators (including the investigator’s immediate family) involved in the research.

Some of the major PHS funding components are the Centers for Disease Control (CDC) and National Institutes of Health (NIH), including all divisions of NIH such as NIDA, NINDS, NIAID, NIA, and so forth. As outlined in the PHS policy statement, the Regulations require that the Institution certify at the time of proposal submission that it has a written and enforced administrative process to identify and manage, reduce, or eliminate conflicting interests with respect to all research projects for which funding is sought. By the time an application/proposal submission is submitted, each Investigator who is planning to participate in the research must have submitted to the designated official a listing of her/his known Significant Financial Interests (and those of his/her spouse and dependent children) that could reasonably appear to be related to the Investigator’s institutional responsibilities (including the conduct of research). Prior to spending any funds under an award, PATH must report to the PHS awarding component the existence of any conflicting financial interests and assure that the interest has been managed, reduced, or eliminated in accordance with the Regulations.

The goal of managing investigator conflicts of interest is to minimize the extent to which the design and conduct of research is influenced – consciously and unconsciously – by financial and other considerations. In order to comply with these requirements, and also in furtherance of PATH’s mission and principles, including PATH’s Code of Ethics, Governance and Responsibility and PATH’s Guiding Principles for Managing Conflict of Interest, PATH has adopted this policy on investigator conflict of interest and disclosure.

This policy is in addition to PATH’s *Employee Conflict of Interest Policy* and PATH’s *REC Conflicts of Interest in Research Reviewed by the IRB Policy*.

Policy

PATH complies with the PHS regulations governing Investigator conflict of interest. This policy applies to all Investigators, as that term is defined in the Appendix, who apply for or receive funds from PHS funding components (also defined in the Appendix), by grant or subgrant, by contract or subcontract, or by cooperative agreement, with regard to PHS-funded Research that is sponsored, conducted, administered or funded in part or in whole by PATH. This policy applies
to Phase II SBIR/STTR applications, but not to Phase I SBIR/STTR applications. Some of the major PHS funding components are the Centers for Disease Control (CDC) and National Institutes of Health (NIH), including all divisions of NIH.

Required Practices

1. **Disclosure of Significant Interests**

   **1.1 At Initial Application**
   - For each PHS-funded research project, all Investigators are required to complete a disclosure form (the “Assurance Form”) describing any Significant Interests for themselves and their Immediate Family Members prior to submitting applications for PHS funds. (Note: This is a project-specific filing that is in addition to the PATH Employee Conflict of Interest disclosure requirements.)
   
     - The PATH RPM or designee is responsible for identifying all Investigators under this policy and to ensure that an Assurance Form and any accompanying material is submitted to the Designated Official for each of them, as well as a list of all Investigators for each Research project.
   
     - All Assurance Forms must be completed in full and in detail, with sufficient information to determine if the interests meet the definition of “Significant Interest,” as outlined in the appendix and must be signed by the Investigator.
   
     - If Human Subjects Research, any conflict of interest issues must be resolved prior to REC/IRB submission. If a Management Plan is implemented, the Investigator must include a copy of it and the Assurance Form with the protocol submitted for REC/IRB review.

   **1.2 Updated Disclosures; Investigators added to Project after Proposal Submission**
   
     - Adding or changing Investigators after proposal submission requires prior approval from the Research sponsor. The RPM or designee must submit completed and signed Assurance Forms for each subsequently-added Investigator(s) to the Designated Official as soon as such Investigators are approved by the sponsor and assigned to the project. The RPM or designee is also responsible for updating the list of all Investigators for each Research project.
   
     - Investigators must submit updated Assurance forms as follows:
       - within thirty (30) days of acquiring or discovering (e.g., through purchase, marriage or inheritance) a new Significant Interest; and
       - annually, on a timetable as specified by the Designated Official
The RPM or designee is responsible for collecting the initial and any updated Assurance Forms and submitting them to the Designated Official and, for notifying PATH’s REC of any updates in writing.

2. Collaborator and Subcontractor Compliance. For PHS-funded research, collaborators from other institutions, subcontractors and subgrantees must either comply with this policy or provide a certification or assurance that their institutions are in compliance with the PHS regulations regarding Investigator Conflict of Interest and that their portion of the project is in compliance with their institutional policies.

3. Designated Official Review

- If Significant Interests are disclosed, either on initial Assurance Form or on an annual or revised or updated Assurance Form, the Designated Official will forward the Form and any supporting documentation to the Conflict of Interest Committee (“COIC”) for its review and determination as to whether the disclosure(s) constitutes a Significant Interest, with notice to the Investigator. The Designated Official or COIC may ask the Investigator to provide additional information and may also consult with individuals such as PATH department heads or employees (such as country and program leaders), Legal Affairs, financial experts, patent and licensing experts, or others.

- Assurance Forms that reveal no Significant Interests will remain file in the office of the Designated Official.

- If an Investigator already has a Management Plan in place, but there are unresolved or new issues as to the Investigator’s Significant Interests in light of the proposed Research to be conducted, the Designated Official may refer the Plan, Forms and any supporting documentation to the COIC.

4. Conflict of Interest Committee (COIC) Review. The Conflict of Interest Committee (COIC) will review the Assurance Form(s), Research plan or protocol and any supporting documentation, as appropriate. The COIC will make the following determinations:

- Whether the Significant Interests disclosed constitute or appear to constitute a Conflict of Interest. A Conflict of Interest will be deemed to exist when the COIC reasonably determines that the Significant Interest is related to PHS-funded Research and could directly and significantly affect the design, conduct or reporting of the Research, or have the appearance of doing so. Not all Significant Interests constitute or appear to constitute a conflict of interest.

- Institute a Management Plan, i.e., which conditions or restrictions, if any, should be imposed upon the Investigator prior to the expenditure of any funds under the award in order to manage, reduce or eliminate such conflict of interest or appearances of conflict of interest. In reviewing the information, the COIC will consider the role and responsibilities of the individual with the conflict in regard to the design, conduct and
reporting of the Research. The Management Plan will include the following key elements:

- The role and principal duties of the conflicted Investigator in the Research project;
- Conditions of the Management Plan;
- How the Management Plan is designed to safeguard objectivity in the Research project;
- Confirmation of the Investigator’s agreement to the Management Plan;
- How the Management Plan will be monitored to ensure Investigator compliance; and
- Other information as needed.

The Management Plan may propose that one or more of the following actions be taken in order to manage, reduce, or eliminate a conflict of interest:

- Public disclosure of Significant Interests (e.g., when presenting or publishing the Research; to staff members working on the Research project; to the reviewing IRB);
- For Research projects involving human subjects research, disclosure of conflicts of interest directly to participants;
- Monitoring plan with independent reviewers, such as a data safety; monitoring board, routine on-site study review, and/or consent process with an independent subject advocate/representative;
- Audits of the informed consent and subject enrollment process;
- Modification of the Research plan;
- Disqualification of those with Significant Interests from participation in all or a portion of the Research activity;
- Reduction or divestiture of Significant Interests;
- Severance of relationships that create conflicts of interest or the appearance of such conflicts; and/or
- Other as it deems appropriate.

Modify an existing Management Plan in light of the proposed research to be conducted, making changes as it deems appropriate given the particular research project, which may include one or more of the measures specified above, in order to manage, reduce, or eliminate actual or perceived conflicts of interest.

Determine whether Significant Interests constitute a Conflict of Interest or appearance of a Conflict of Interest that cannot be managed, reduced or eliminated. In these cases, the Research cannot proceed.

5. Notifications. The COIC will notify the Investigator, the RPM or designee, the Designated Official, Office of Sponsored Research and the Research Support Services Department Head (if Human Subjects Research is involved) regarding its determination. If the final decision includes a Management Plan, the Investigator will acknowledge his or her
acceptance of the Management Plan in writing to the COIC, and in cases of Human Subjects Research, the REC or other reviewing IRB (such as WIRB), prior to the expenditure of any funds under the award or contract. The same notification process will apply to any Management Plans that are modified after initial approval. The Designated Official may redact confidential information as appropriate.

6. Reconsiderations. Investigators may make a request to the COIC for a reconsideration of its determinations and/or Management Plan. Additional information may be provided to the COIC for its consideration. The investigator may appear before the COIC in person or via teleconference, if desired.

7. COIC Consultations. In making its determinations, the COIC may ask the Investigator, employee or PATH staff involved in the determination to provide additional information. This may be done in person, in writing, or by audio/visual means, at the COIC’s discretion. The COIC may also consult with individuals such as the Designated Officer, other PATH department heads or employees (such as country and program leaders), Legal Affairs, financial experts, patent and licensing experts, REC members or others from within or outside of PATH.

8. Relationship between COIC and the REC and other external IRBs

- For Human Subjects Research, the Research Support Services Department Head will inform the PATH REC of determinations made by the COIC with regard to disclosed Significant Interests, including, if applicable, the terms of any Management Plan. The REC may impose additional requirements or restrictions, such as whether the conflict and management methods should be disclosed in the consent form, or whether additional modifications in the consent form process are indicated.

- The COIC and REC shall maintain open lines of communication regarding the review of financial interests related to Human Subjects Research.

- The Research Support Services Department Head or designee will be the liaison between PATH and any external IRBs concerning Investigator conflicts of interest, and will be communicate the terms of Management Plans and related issues, such as non-compliance with the terms of a Management Plan, to those entities.

9. Reporting to PHS Awarding Components; HHS Access to Records

- Prior to the expenditure of any PHS funds under a PHS-funded research project, PATH will provide to the PHS Funding Component a report regarding any Investigator Significant Interest found to be a Conflict of Interest, in accordance with the Regulations. The report will include, without limitation, the name of the Investigator, the name of the entity with which the Investigator has a Conflict of Interest, the nature of the interest, and the value of the interest.

- PATH will submit a report within sixty (60) days after its determination that a Conflict of Interest exists for an Investigator who is newly participating in an ongoing project or for
an existing Investigator who discloses a new Significant Interest to PATH during the period of an award.

- If an Investigator does not timely disclose a previously existing Significant Interest, or if PATH fails to review a previously existing Significant Interest disclosure during the ongoing PHS-funded project, PATH shall, within sixty (60) days: review the Significant Interest; determine whether it is related to the PHS-funded research; and determine whether a Conflict of Interest exists. If so, PATH must implement, on at least an interim basis, a Management Plan that shall specify the actions that have been, or will be, taken to manage such Conflict of Interest going forward, and PATH shall submit a Conflict of Interest report to the PHS Funding Component. In addition to the report, the Institution will take the steps as specified in Section 10 “Sanctions and Remedies for Violation of this Policy.”

- For any Conflict of Interest previously reported by PATH, PATH shall provide an annual Conflict of Interest report that addresses the status of the financial interest and any changes to the Management Plan. Annual reports shall specify whether the Conflict of Interest is still being managed or explain why the Conflict of Interest no longer exists. Annual reports will be submitted for the duration of the project period (including extensions with or without funds) at the same time as when PATH is required to submit the annual progress report or at the same time as the extension.

- Pursuant to Section 50.606 of the PHS Regulations, upon request and to the extent required by law, PATH will make available to HHS PATH’s procedures and actions regarding conflicts of interest in PHS-funded Research.

10. Sanctions and Remedies for Violation of Policy

- Non-compliance of this policy must be reported by any knowledgeable individual to the Designated Official, and to the REC if it involves Human Subjects Research. The COIC, and the REC if applicable, will investigate the allegation, reach a conclusion and recommend sanctions or dismissal of the charges to the Office of the President, who will have the final decision.

- When an Investigator is found to have failed to comply with this policy or the management plan, PATH will, within 120 days of the determination of noncompliance:

  a) Complete a retrospective review of the Investigator’s activities and the PHS-funded research project to determine any bias in the design, conduct or reporting of research;
  b) Document the retrospective review consistent with the Regulations;
  c) Document PATH’s determination as to whether any PHS-funded research, or portion thereof, conducted during the period of time of the Investigator’s non-compliance with this policy or a management plan, was biased in the design, conduct, or reporting of such research.
If bias is found, PATH will notify the PHS Awarding Component promptly and submit a mitigation report to the Awarding Component that addresses the following: 1) impact of the bias on the Research project and 2) PATH’s plan of action or actions taken to eliminate or mitigate the effect of the bias.

Thereafter, PATH will submit Conflict of Interest reports annually, in accordance with the Regulations. Depending on the nature of the Conflict of Interest, PATH may determine that additional interim measures are necessary with regard to the Investigator’s participation in the PHS-funded Research project between the date that the Conflict of Interest is identified, and the completion of PATH’s independent retrospective review, in accordance with 42 CFR 50.605(a) and 42 CFR 50.605(b)(3).

- Noncompliance with any provision of this policy will be subject to sanctions up to and including termination of employment for PATH employees, and institutional suspension or termination of an ongoing Research project. Recommendations may also involve the notification of the sponsor and/or journal editors if non-compliance may have resulted in compromise of the integrity of the Research and/or resulting publications or other communications.

- If HHS determines that a PHS-funded Research project, whose purpose was to evaluate the safety or effectiveness of a drug, device or treatment, was designed, conducted, or reported by an Investigator with a conflicting interest that was not managed or reported by PATH, PATH must require the Investigator involved to disclose the conflicting interest in each public presentation of the results of the Research, and to request an addendum to previously published presentations.

11. Records Retention. Records of and related to financial interest disclosures and COIC determinations will be retained by PATH no less than six years from the date of submission of the final expenditures report. Such records will be maintained by the office of the Designated Official. Such records are considered confidential and will be shared only with PATH staff and individuals who have a need to know (such as COIC members or consultants), HHS upon request (see below), or as otherwise required by law or regulation.

12. Training. Investigators, including Subrecipient Investigators, must complete training upon submission of the proposal or within thirty (30) days thereafter. Training must be repeated at least every four years, and immediately in the following situations: PATH’s Investigator Conflict of Interest policy changes in a manner that affects Investigator requirements; an Investigator is new to PATH; PATH finds that an Investigator is not in compliance with PATH’s policy or management plan.

13. Required Certifications. In each PHS application for funding, PATH will certify the following:

- PATH has in effect a written and enforced process to identify and manage, reduce, or eliminate conflicting interests.
• Prior to expending any funds under the award, PATH will report to the PHS Awarding Component the existence of a conflicting interest and assure that it has been managed, reduced, or eliminated, and, for any interest identified as conflicting subsequent to PATH’s initial report, a report will be made and the conflicting interest managed, reduced, or eliminated, least on an interim basis, within 60 days; and

• Upon request, PATH agrees to make information available to HHS regarding all conflicting interests and how those interests have been managed, reduced, or eliminated.


• PATH will make this policy publicly accessible on its website, pursuant to the requirements of 42 CFR 50.604(a).

• Within five (5) calendar days of a written request, PATH will make available information concerning identified Conflicts of Interest held by senior or key personnel. The information will include the minimum elements as required by the Regulations.

15. Contact for Questions. Questions concerning this policy should be directed to the Designated Official at phscoforms@path.org.
APPENDIX

Definitions

Assurance Form: means the disclosure form completed by all Investigators on a project-by-project basis, disclosing Significant Interests.

Conflict of Interest (“COI”): means a divergence between in an Investigator’s financial or other personal interests and the obligation to abide by principles of the ethical conduct of Research, especially the obligation to protect the rights and welfare of human subjects (for Human Subjects Research), such that considerations of personal gain, financial or otherwise, may influence or create the perception of influencing that Investigator and compromise the objectivity or appropriate conduct of the Research. A Conflict of Interest exists when PATH, through its Designated Official and, where applicable, its Conflict of Interest Committee, reasonably determines that an Investigator’s Significant Interest is related to a PHS-funded research project and could directly and significantly affect the design, conduct or reporting of the PHS-funded research.

Conflict of Interest Committee: means the PATH committee whose role is to review disclosures of Significant Interests and determine if these constitute a Conflict of Interest and, if so, to decide how such conflicts will be managed, reduced or eliminated. The Conflict of Interest Committee (“COIC”) is comprised of the following individuals or their designees: Research Support Services Department Head, General Counsel, and the Director, Donor Compliance and Sponsored Programs, and other such members as may be appointed by the Office of the President at his or her discretion.

Designated Official(s): The individual(s) designated by PATH, pursuant to the PHS regulations, to be responsible for the management of this Conflict of Interest policy. The Director, Donor Compliance and Sponsored Programs will serve as the Designated Official.

Financially Interested Entity: means any domestic or foreign, public or private, organization (excluding a Federal agency) from which an Investigator (or his or her Immediate Family Member) receives remuneration or in which the Investigator (or his or her Immediate Family Member) has an ownership or equity interest. This term includes, without limitation, companies that sponsor or conduct the Research, agents of the sponsor (for example, contract research organizations), are the manufacturers, licensees or licensors of an investigational product, or the investment industry (e.g., stockbrokers and analysts, investment bankers, venture capital firms and investment firms).

Human Subjects Research: means all “research” performed with “human subjects” as these terms are defined in 45 CFR Part 46 and 21 CFR Part 56.

Immediate Family Member: means spouse/domestic partner, and dependent children.
Institutional Responsibilities: means an Investigator’s professional responsibilities on behalf of PATH, which includes activities such as research, research consultation, and service on panels such as institutional review boards (IRBs) or Data and Safety Monitoring Boards.

Investigator: means the project director or principal investigator and any other person, regardless of title or position, who is responsible for the design, conduct or reporting of the Research funded by the PHS, or proposed for such funding, which may include, for example, consultants or collaborators. This definition will typically include the principal investigator, but may also include co- and sub-investigators, study staff and inventors of investigational products if such individuals are responsible for the design, conduct or reporting of the Research.

Management Plan: means conditions, restrictions or other actions approved by the Conflict of Interest Committee in order to manage, reduce or eliminate Investigator conflicts of interest or the appearance of conflicts of interest.

PHS: means the Public Health Service, an operating division of the U.S. Department of Health and Human Services (“HHS”).

PHS Awarding Component: means the organizational unit of the PHS that funds the Research.

Research: means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge relating broadly to public health, including behavioral and social-sciences research. The term encompasses basic and applied research (e.g., a published article, book or book chapter) and product development (e.g., a diagnostic test or drug). Activities which meet this definition constitute “research” for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Research Ethics Committee (REC): The PATH committee that conducts prospective ethical review of Human Subjects Research engaged in or supported by PATH or PATH employees.

Senior/Key Personnel: means the project director or principal investigator and any other person identified as senior/key personnel by PATH in the grant application, progress report, or any other report submitted to the funding agency by PATH.

Significant Interest: means anything of monetary value, aggregated for the Investigator and his/her Immediate Family Members, or other interests of the Investigator (and his or her Immediate Family), that reasonably appear to be related to the Investigator’s Institutional Responsibilities (as defined in this policy), as follows:

1. Any financial interests such as salary, directors’ fees, consulting payments, paid authorship, teaching or lecture fees, advisory board fees, honoraria, royalties, gifts, dividends or other payments from a Financially Interested Entity, whether for consulting, lecturing, travel, service on an advisory board, or for any purpose not directly related to the reasonable costs of conducting the Research (as specified in the
clinical trial or research agreement), in the 12 months preceding the disclosure or reasonably expected in the 12 months following the disclosure.

2. Any equity interests such as stocks, stock options or other ownership interests in a Financially Interested Entity.

3. Intellectual property rights (for example, patents, pending patent applications, licenses or copyrights) involving a Financially Interested Entity or that would reasonably appear to affect or be affected by the Research being conducted;

4. Service by an Investigator or Immediate Family Member as an officer, director, partner, trustee, consultant, advisor or other management role in a Financially Interested Entity, whether or not compensation is received for such service;

5. Any payments or entitlements to payments in connection with the Research that are not directly related to the reasonable costs of the Research (as specified in the research agreement). This includes any bonus or milestone payments to the investigators in excess of reasonable costs incurred, whether such payments are received from a Financially Interested Entity or from PATH;

6. Any reimbursed or sponsored travel (ie, that which is paid on behalf of the Investigator and not reimbursed to the Investigator so that the exact monetary value may not be readily available), related to their institutional responsibilities; provided, however, that this disclosure requirement does not apply to travel that is reimbursed or sponsored by excluded sources provided in the Regulation (i.e., federal, state or local government agencies, an institution of higher education, an academic teaching hospital, a medical center, or a research institute affiliated with an institution of higher learning);

7. Other personal or professional interest or involvement of the Investigator, or an Immediate Family Member, that could reasonably affect the Investigator’s conduct or behavior with regard to the Research.

The term “Significant Interest” does NOT include:

1. Salary or compensation from PATH or from the Investigator’s employer, unless such compensation could be affected by the conduct or outcome of the research (for example, a bonus payment for reaching a study recruitment target);

2. Payments to PATH, or via PATH to the Investigator, including salary, that are directly related to reasonable costs incurred in the conduct of Research as specified in the clinical trial or research agreement; and

3. Publicly-traded diversified mutual funds or pension funds in which the Investigator or Immediate Family Member do not exercise control over the investments.

4. Income from seminars, lectures, or teaching engagements sponsored by a federal, state or local government agency, an Institution of higher education as defined at 20
U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education; or

5. Income from service on advisory committees or review panels for a federal, state or local government agency, Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education.

A Significant Interest does not necessarily constitute a Conflict of Interest or the appearance of a Conflict of Interest.
References

Part 50, Subpart F of Title 42 of the Code of Federal Regulations (CFR) “Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding is Sought” and the corollary regulation for NIH contractors, 45 CFR Part 94 “Responsible Prospective Contractors” (the “PHS Regulations”)

PATH’s Personnel Policy and Procedures Manual, Conflict of Interest and Conflict of Interest Disclosure

PATH’s Code of Ethics, Governance and Responsibility

PATH’s Guiding Principles for Managing Conflict of Interest

PATH’s REC policy “Conflicts of Interest in Research Reviewed by the IRB”


FDA regulations, 21 CFR parts 50 and 56

HHS regulations, 45 CFR part 46