

ISA ASSOCIATES POLICY ON FINANCIAL CONFLICTS OF INTEREST IN PUBLIC HEALTH SERVICE-FUNDED RESEARCH

I. Policy and General Principles

As a steward of the public trust, ISA is committed to the principle that its research be carried out with integrity, open inquiry, and rigorous analysis, free from outside conflicts of interest that might compromise, or give the appearance of compromising, the sound professional judgment of its investigators. This policy sets forth that position and provides a mechanism for ensuring the integrity of ISA's research when such conflicts arise.

This policy implements federal disclosure requirements pertaining to objectivity in research promulgated by the U.S. Public Health Service (PHS) in 42 CFR Part 50 and 45 CFR Part 94. These federal regulations require ISA Associates (herein, ISA) to maintain an appropriate written policy on financial conflict of interest disclosure as a condition for receiving PHS grants. These federal requirements, as implemented in this Policy, are applicable to all proposals for PHS funding with the exception of SBIR Phase I projects.

II. Purpose and Scope of Policy

A. Purpose

The goal of this Policy is to assure the objectivity with which Research projects are designed, conducted or reported by managing financial conflicts of interest that occur between an Investigator's personal financial interests and his professional Research interests.

This Policy establishes a process of disclosure and independent review when an Investigator (as defined below) has Significant Financial Interest(s). When ISA determines that such an interest might reasonably appear to affect the Research directly and significantly, ISA will take steps to manage or to eliminate the conflict.

B. Scope

This Policy applies to Research projects for which ISA submits a proposal to, or receives research funding from PHS. This Policy sets forth requirements that each Investigator who is planning to participate in, or is participating in such Research, must follow; provided, however, that this Policy does not apply to SBIR (Small Business Innovation Research) Program Phase I applications.

III. Disclosure of Financial Interests

When an Investigator has a Significant Financial Interest, a written Significant Financial Interest Disclosure Form (Disclosure Form; located in Appendix A) detailing that interest is required. When an Investigator does not have a Significant Financial Interest, the Investigator must still complete the Disclosure Form but can check the box stating that no Significant Financial Interest exists.

Each investigator must also update his or her financial disclosures by completing a new Disclosure Form. This update must occur either annually or as new Significant Financial Interests are obtained throughout the period of the award (see Section IV, Part F of this Policy).

IV. Definitions

A. Investigator

An Investigator is any individual responsible for the design, conduct, or reporting of Research funded by the PHS. This includes the Principal Investigator, Co-Investigators, and any other individual, regardless of title or position, who is responsible for designing, conducting, or reporting of this Research.

B. Research

Research means a systematic investigation, study or experiment 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 and product development.

C. Reviewing Officer

An official designated by ISA to solicit and review completed Disclosure Forms from each Investigator who is planning to participate in, or who is participating in, PHS-funded Research and to determine whether any reported Significant Financial Interest is a Financial Conflict of Interest.

D. PHS Awarding Component

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

E. Significant Financial Interest

Significant Financial Interest means either of the following:

1. Any interest of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities, including follows: that including, but not limited to, one or more of the following:
 - a. With regard to any publicly traded entity (outside of ISA), a Significant Financial Interest exists if the value of any remuneration received from the entity in the twelve (12) months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds \$5,000. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;
 - b. With regard to any non-publicly traded entity (outside of ISA), a Significant Financial Interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds \$5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or
 - c. Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.
2. Investigators also must disclose the occurrence of any reimbursed or sponsored travel that is receive in the previous twelve (12) months (i.e., 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 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. The term Significant Financial Interest does not include the following types of financial interests: salary, royalties, or other remuneration paid by ISA to the Investigator if the Investigator is currently employed by ISA, including intellectual property rights assigned to ISA and agreements to share in royalties related to such rights; income from investment vehicles, such as mutual funds and retirement accounts, 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 income from service on advisory committees or review panels for 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.

Significant Financial Interest **does not** include:

1. An Employee's salary or royalties received from ISA,
2. Income from seminars, lectures or teaching engagements sponsored by a federal, state or local government agency or an institution of higher education, or
3. Income from service on panels for a federal, state or local government agency or institution of higher education.

F. Financial Conflict of Interest (FCOI)

A Financial Conflict of Interest (FCOI) is a **Significant Financial Interest that could directly and significantly affect the design, conduct or reporting of PHS funded Research**. That is, situations where an Employee's Financial Interest (including an Investigator's Significant Financial Interest, where applicable) compromises, or could appear to compromise, his or her judgment or ability to carry out the Institutional Responsibilities associated with his or her employment at ISA. When applied to an Investigator, Financial Conflicts of Interest occur in situations in which such Investigator's Financial Interest (including Significant Financial Interest) compromises, or could appear to compromise, his or her professional judgment regarding the design, conduct or reporting of research or if such Financial Interest could directly and significantly affect the design, conduct or reporting of research. The bias such

conflicts may conceivably impart not only affects collection, analysis and interpretation of data, but also the hiring of staff, procurement of materials, sharing of results, choice of protocol, involvement of human participants and the use of statistical methods.

G. Update of Disclosure of Financial Interests

Each Investigator must complete a new Disclosure Form either annually or whenever he or she acquires a new Significant Financial Interest that was not listed in the original Disclosure Form, whichever occurs first.

H. Institutional Responsibilities

Institutional responsibilities means an Investigator's professional responsibilities on behalf of the Institution, and as defined by the Institution in its policy on financial conflicts of interest, which may include for example: activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards.

I. Senior/Key Personnel

Senior/key personnel means the PD/PI and any other person identified as senior/key personnel by the Institution in the grant application, progress report, or any other report submitted to the PHS by the Institution under this subpart.

V. Disclosure Requirement

Each Investigator who is planning to participate in PHS-funded Research is required to disclose to the ISA Reviewing Official the Investigator's Significant Financial Interests (and those of the Investigator's spouse and dependent children) no later than the time of application for PHS-funded Research. Each Investigator must do so by completing the Disclosure Form. Each Investigator who is participating in PHS-funded Research is required to submit an updated Disclosure Form either within 30 days of discovering or acquiring a new Significant Financial Interest, or at least on an annual basis (yearly at the close of the fiscal year, December 30th), during the period of the PHS funding award.

VI. Review of Disclosures and Management of FCOIs

- A. Initial review and management:** Prior to ISA expenditure of any funds under a PHS-funded Research project, the ISA Reviewing Official will review all Investigators' Disclosure Forms; determine whether any Significant Financial Interests relate to PHS-funded Research; determine whether a FCOI exists; and, if so, develop and implement a management plan that specifies the actions that have been, and will be, taken to manage such FCOI.
- B. Review and management in the course of a PHS-funded Research project:** Whenever, in the course of an ongoing PHS-funded Research project, (1) an Investigator who is new to participating in the Research project discloses a Significant Financial Interest; (2) an existing Investigator discloses a new Significant Financial Interest; or (3) ISA identifies a Significant Financial Interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by ISA during an ongoing PHS-funded Research project, the ISA Reviewing Official will, within sixty days: review the disclosure of the Significant Financial Interest; determine whether it is related to PHS-funded Research; determine whether a FCOI exists; and, if so, implement, on at least an interim basis, a management plan that specifies the actions that have been, and will be, taken to manage such FCOI. Depending on the nature of the Significant Financial Interest, ISA 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 ISA's review.
- C. Examples of management:** Examples of conditions or restrictions that may be imposed to manage an FCOI include, but are not limited to:
 - 1. Public disclosure of the FCOI;
 - 2. For Research projects involving human subjects, disclosure of the FCOI directly to participants;
 - 3. Appointment of an independent monitor capable of taking measures to protect the design, conduct and reporting of the Research against bias resulting from the FCOI;
 - 4. Modification of the research plan;
 - 5. Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the Research;
 - 6. Reduction or elimination of the financial interest; or
 - 7. Severance of relationships that create financial conflicts.

- D. Additional requirements for Retrospective Review: In addition to the above requirements, whenever an FCOI is not identified or managed in a timely manner including failure by the Investigator to disclose a Significant Financial Interest that is determined by ISA to constitute an FCOI; failure by ISA to review or manage such an FCOI; or failure by the Investigator to comply with an FCOI management plan, ISA will, within 120 days of ISA'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.

ISA is required to document the retrospective review, including all of the following key elements: (1) Project number; (2) Project title; (3) PD/PI or contact PD/PI if a multiple PD/PI model is used; (4) Name of the Investigator with the FCOI; (5) Name of the entity with which the Investigator has an FCOI; (6) Reason(s) for the retrospective review; (7) Detailed methodology used for the retrospective review (e.g., methodology of the review process, composition of the review panel, documents reviewed); (8) Findings of the review; and (9) Conclusions of the review.

Based on the results of the retrospective review, if appropriate, ISA will update the previously submitted FCOI report, specifying the actions that will be taken to manage the FCOI going forward. If bias is found, ISA will notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component. The mitigation report must include, at a minimum, the key elements documented in the retrospective review above and a description of the impact of the bias on the Research project and ISA's plan of action or actions taken to eliminate or mitigate the effect of the bias (e.g., impact on the Research project; extent of harm done, including any qualitative and quantitative data to support any actual or future harm; analysis of whether the Research project is salvageable). Thereafter, ISA will submit FCOI reports annually. Depending on the nature of the FCOI, ISA 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 FCOI or the Investigator's noncompliance is determined and the completion of ISA's retrospective review.

- E. Monitoring: Whenever ISA implements a management plan, ISA will monitor Investigator compliance with the management plan on an ongoing basis until the completion of the PHS-funded Research project.

VII. Reporting of Financial Conflicts of Interest

- A. Initial FCOI Report: Prior to ISA's expenditure of any funds under a PHS-funded Research project, ISA will provide to the PHS Awarding Component an FCOI report regarding any Investigator's Significant Financial interest found by ISA to be an FCOI and ensure that ISA has implemented a management plan in accordance with Section VI of this Policy. In cases in which ISA identifies an FCOI and eliminates it prior to the expenditure of PHS-awarded funds, ISA does not need to submit an FCOI report to the PHS Awarding Component.
- B. Annual Reporting: For any financial conflict of interest previously reported by the Institution with regard to an ongoing PHS-funded research project, the Institution shall provide to the PHS Awarding Component an annual FCOI report that addresses the status of the financial conflict of interest and any changes to the management plan for the duration of the PHS-funded research project. The annual FCOI report shall specify whether the financial conflict is still being managed or explain why the financial conflict of interest no longer exists. The Institution shall provide annual FCOI reports to the PHS Awarding Component for the duration of the project period (including extensions with or without funds) in the time and manner specified by the PHS Awarding Component, that is, at the same time as when the Institution is required to submit to NIH the annual progress report, multi-year progress report, if applicable, or at time of extension.
- C. Subsequent FCOI Reports: For any Significant Financial Interest that ISA identifies as conflicting after ISA's initial FCOI report during an ongoing PHS-funded Research project, ISA will provide to the PHS Awarding Component, within sixty days, an FCOI report regarding the FCOI and ensure that ISA has implemented a management plan in accordance with Section VI of this Policy and, if required, a retrospective review and a mitigation report according to section VI of this Policy.
- D. Contents of an FCOI report: Any FCOI report required under paragraphs A or B of this Section VII will include sufficient information to enable the PHS Awarding Component to understand the nature and extent of the financial conflict, and to assess the appropriateness of ISA's management plan. Elements of the FCOI report will include, but are not necessarily limited to the following:
1. Project number;
 2. PD/PI or Contact PD/PI if a multiple PD/PI model is used;

3. Name of the Investigator with the FCOI;
 4. Name of the entity with which the Investigator has an FCOI;
 5. Nature of the financial interest (e.g., equity, consulting fee, travel reimbursement, honorarium);
 6. Value of the financial interest (dollar ranges are permissible: \$0–\$4,999; \$5,000–\$9,999; \$10,000–\$19,999; amounts between \$20,000–\$100,000 by increments of \$20,000; amounts above \$100,000 by increments of \$50,000), or a statement that the interest is one whose value cannot readily be determined through reference to public prices or other reasonable measures of fair market value;
 7. A description of how the financial interest relates to the PHS-funded Research and the basis for ISA's determination that the financial interest conflicts with such Research; and
 8. A description of the key elements of ISA's management plan, including:
 - a. Role and principal duties of the conflicted Investigator in the Research project;
 - b. Conditions of the management plan;
 - c. How the management plan is designed to safeguard objectivity in the Research project;
 - d. Confirmation of the Investigator's agreement to the management plan;
 - e. How the management plan will be monitored to ensure Investigator compliance; and
 - f. Other information as needed.
- E. Public request:** The Institution will provide a written response to any public FCOI Informational requests within five (5) business days as provided for under the applicable regulations. The information provided with applicable shall include, at a minimum, the following: the Investigator's name; the Investigator's title and role with respect to the research project; the name of the entity in which the significant financial interest is held; the nature of the significant financial interest; and the approximate dollar value of the significant financial interest (dollar ranges are permissible: \$0-\$4,999; \$5,000-\$9,999; \$10,000-\$19,999; amounts between \$20,000-\$100,000 by increments of \$20,000; amounts above \$100,000 by increments of \$50,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value. Information concerning the significant financial interests of an individual shall remain available, for responses to written requests for at least three years from the date that the information was most recently updated.
- F. Disclosure with Regards to Drugs, Medical Devices or Treatment:** In any case in which the HHS determines that a PHS-funded research project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment has been designed, conducted, or reported by an Investigator with a financial conflict of interest that was not managed or reported by the Institution as required by this regulation, the Institution shall require the Investigator involved to disclose the financial conflict of interest in each public presentation of the results of the research and to request an addendum to previously published presentations.

VIII. Training

Prior to engaging in any PHS-funded research project, all Investigators must complete training on the Investigator obligations under this policy. This training must be repeated at least every four (4) years. Immediate training is required if 1) this policy is revised so as to affect the Investigator obligations, 2) an investigator is new to the Institution, or 3) the Institution finds that an Investigator is not in compliance with the Institution's financial conflict of interest policy or management plan.

Training can be found at <http://grants.nih.gov/grants/policy/coi/tutorial2011/fcoi.htm>. Once the Investigator completes the training, the certificate should be printed and provided to the Reviewing Officer.

IX. Enforcement

Failure to comply with this Policy, including failure to file a complete or timely Disclosure Form or update or to comply with any conditions or restrictions imposed on the conduct of the project under this Policy, including a management plan, will be grounds for discipline up to and including termination.

In addition, if the failure of an Investigator to comply with this Policy or an FCOI management plan appears to have biased the design, conduct, or reporting of the PHS-funded Research, ISA is required to promptly notify the PHS Awarding Component of the corrective action taken or to be taken. The PHS Awarding Component will consider the situation and, as necessary, take appropriate action, or refer the matter to ISA for further action, which may include directions to ISA on

how to maintain appropriate objectivity in the PHS-funded research project. In addition, federal regulations may require reports to the federal sponsor of any information which may show a violation of ISA policy. Sponsors may impose special award conditions or may suspend or terminate the award and/or debar an Investigator from receiving future awards in the event of failure to comply with applicable federal regulations on disclosure, review, and management of Significant Financial Interests related to federally sponsored projects.

X. Records

ISA will maintain records relating to all Investigator disclosures of financial interests and the Institution's review of, and response to, such disclosures (whether or not a disclosure resulted in the Institution's determination of a financial conflict of interest) and all actions under the Institution's policy or retrospective review, if applicable, for at least three years from the date of the final expenditures report is submitted to the PHS or, where applicable, from other dates specified in 45 CFR 74.53(b) and 92.42(b) for different situations.

XI. Sub-recipients

The Institution shall require sub-recipient compliance with the Financial Conflict of Interest Requirement as mandated by the PHS regulation.

**Appendix A:
Significant Financial Interest Disclosure Form**

This Disclosure Form is to be completed by each Investigator pursuant to the ISA Policy on Financial Conflicts of Interest in Public Health Service-Funded Research. Please refer to that Policy for detailed requirements and definitions. Complete this form and submit it to the Rebekah Hersch, ISA's Reviewing Officer.

I. Research Project Title and number:

II. Project Director/Principal Investigator or Contact PD/PI if a multiple PD/PI model is used:

III. Name of Investigator making this report about his/her financial interest(s):

IV. Check which of the following you are submitting:

- A. _____ Initial Disclosure Form: Before the time of application for PHS-funded Research
- B. _____ Update Disclosure Form: Within 30 days discovering or acquiring a new Significant Financial Interest during a PHS-funded Research award
- C. _____ Update Disclosure Form: Required Annual Update during a PHS-funded Research award

V. Indicate whether you, the Investigator, have any Significant Financial Interests related to the work to be conducted under the PHS-funded Research project(s):

- A. _____ I have no Significant Financial Interest as that term is defined in the Policy (stop completing this Disclosure Form here and submit it).
- B. _____ I do have Significant Financial Interest(s) to report (continue completing rest of this Disclosure Form)

VI. For each Significant Financial Interest (use additional pages if necessary):

- A. Provide the name of each entity in which the Investigator has a Significant Financial Interest:

- B. Provide the nature of the financial interest (for example, equity, consulting fee, travel reimbursement, or honorarium):

- C. Indicate the value (dollar amount) of the Significant Financial Interest:

D. For Reimbursed or Sponsored Travel required to be reported by the Policy, indicate all of the following:

1. The purpose of the trip:

2. The identity of the sponsor/organizer:

3. The destination:

4. The duration:

E. Describe how the Significant Financial Interest relates to the PHS-funded Research:

F. Do you believe that the Research project(s) could directly and significantly affect the Significant Financial Interest(s) you are reporting?

VII. For further information about the Policy and how to complete this information, you may contact the Rebekah Hersch, ISA's Senior Vice President, and Review Officer.