



Financial Conflict of Interest (FCOI) Policy

1. Policy Statement

- 1.1. Cyclopure, Inc. (Cyclopure) is committed to protecting the integrity and objectivity of its research activities by ensuring that the design, conduct, and reporting of research funded under PHS grants, cooperative agreements or contracts will be free from bias resulting from an Investigator's financial conflicts of interest (FCOI). Cyclopure has implemented this policy to identify, manage, reduce or eliminate financial conflicts of interest. Although this policy was created and designed primarily to comply with the specific regulatory requirements it is also intended to provide a basic framework and standards for identifying, evaluating, and managing potential financial conflicts of interest relating to Cyclopure's other research activities. For non-PHS research, the specific steps, timing, determinations, documentation, and notifications may be tailored as appropriate but will remain focused on maintaining Cyclopure's high standards for research integrity.
- 1.2. The Signing Official is the person responsible for the procedures under this FCOI Policy and is responsible for informing Investigators of their obligations under this Policy and any related regulations. The Signing Official may designate one or more individuals to assist in any or all of these responsibilities, and/or may delegate any or all of these responsibilities to one or more individuals.

2. Definitions

- 2.1. **Financial Conflict of Interest (FCOI)** means a significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.
- 2.2. **Institutional Responsibilities** means an Investigator's professional responsibilities on behalf of Cyclopure, and as defined by Cyclopure 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.
- 2.3. **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 research funded by the PHS, or proposed for such funding, which may include, for example, collaborators or consultants.
- 2.4. **PHS** means the Public Health Service of the U.S. Department of Health and Human Services and any components of the PHS to which the authority involved may be delegated, including the National Institutes of Health (NIH).

- 2.5. 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 (e.g., a published article, book or book chapter) and product development (e.g., a diagnostic test or drug). As used in this subpart, the term includes any such activity for which research funding is available from a PHS Awarding Component through a grant or cooperative agreement, whether authorized under the PHS Act or other statutory authority, such as a research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or research resources award.
- 2.6. Senior/key personnel** means the project director or principal Investigator and any other person identified as senior/key personnel in the grant application, progress report or any other report submitted to the PHS.
- 2.7. Significant Financial Interest (SFI) means:**
- 2.7.1** A **financial interest** consisting of one or more of the following interests 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:
- 2.7.1(i) Publicly traded entity**, a significant financial interest exists if the value of any remuneration received from the entity in the twelve 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
- 2.7.1(ii) Non-publicly traded entity**, 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
- 2.7.1(iii) Intellectual property rights and interests** (e.g., patents, copyrights), upon receipt of income related to such rights and interests.
- 2.8.** Significant financial interests also include any reimbursed or sponsored travel (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 Institution's FCOI policy will specify the details of this disclosure, which will include, at a minimum, the purpose of the

trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with the Institution's FCOI policy, the institutional official(s) will determine if further information is needed, including a determination or disclosure of monetary value, in order to determine whether the travel constitutes an FCOI with the PHS-funded research.

- 2.9.** The term significant financial interest does not include the following types of financial interests: salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution, including intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for-profit organization; income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles; 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.

3. Researchers Covered

- 3.1.** Each Investigator who will participate or is participating in research conducted with PHS must follow this Policy, disclose to Signing Official the Investigator's significant financial interests and complete the required training. Subcontractors and consultants who perform services within the definition of an Investigator must either maintain a policy that complies with the requirements of 42 CFR Part 50, Subpart F or comply with Cyclopure's Policy.

4. Mandatory Investigator Training Requirements

- 4.1.** Each Investigator must complete training regarding this policy and the applicable regulations prior to engaging in research related to any PHS-funded grant and at least every four years. In addition immediate training is required when any of the following circumstances apply:
- 4.1.1** Cyclopure revises the FCOI policies or procedures in any manner that affects the requirements of Investigators
 - 4.1.2** Investigator is new to Cyclopure
 - 4.1.3** Cyclopure finds an Investigator noncompliant with Cyclopure's FCOI policy
- 4.2.** "Immediately" shall mean the training is provided or made accessible and the Investigators participate in the training expeditiously following the event that triggers the immediate training requirement.

5. Disclosure Requirements

- 5.1** Prior to submission to PHS of an application for a research grant, the Principal Investigator shall:
- identify to the Signing Official all Investigators anticipated to be participating in the research,
 - those who are senior/key personnel and
 - those who are subrecipients
- 5.2** Also prior to submission of the application Investigator shall submit a listing of his/her known significant financial interests and those of his/her spouse and dependent children that reasonably appear to be related to the Investigator's institutional responsibilities, if any. The Signing Official shall ensure that subrecipient Investigators either comply with this FCOI Policy or that their institution(s) provides assurances to enable Cyclopure, to fulfill the requirements of this FCOI Policy.
- 5.3** All disclosures must be updated annually during the period of the award or within 30 days of discovering or acquiring (e.g., through purchase, marriage, inheritance, or expansion of responsibilities) a new significant financial interest. Each Investigator is responsible for submitting disclosure forms within 30 days of discovering or acquiring a new significant financial interest. Disclosures shall be provided by an Investigator at any other time upon request.

6. Review of Disclosures and Monitoring and Reporting FCOI

- 6.1.** The Signing Official shall solicit and review disclosures of significant financial interests from each Investigator who is planning to participate in or is participating in the PHS-funded research, make the requisite determinations, and take any subsequent action.
- 6.2.** Prior to the expenditure of funds or, with respect to an ongoing PHS-funded project, within 60 days of the disclosure or discovery of a significant financial interest of an Investigator who is new to participating in the research project, or of a new significant financial interest disclosed by an existing Investigator, the Signing Official shall:
- 6.2.1** review all disclosure forms and determine whether (a) an Investigator's significant financial interest is related to PHS-funded research and (b) if so related, whether the significant financial interest is a financial conflict of interest (FCOI); and
 - 6.2.2** in the case of a FCOI, develop and implement a management plan specifying actions that have been and shall be taken to manage the FCOI; and
 - 6.2.3** submit initial and ongoing FCOI reports to the PHS Awarding Component as required under the FCOI Regulations [42 CFR 50.605(b)].

7. Reporting Requirements to NIH

- 7.1.** Prior to the expenditure of any funds under a PHS-funded research project, Cyclopure shall provide the PHS Awarding Component an FCOI report regarding any Investigator's SFI found by Cyclopure to be conflicting and ensure that Cyclopure has implemented a management plan in accordance with 42 CFR §50.605(b). In the case of a FCOI, Signing Official shall submit an Initial Report and annual report and revised FCOI reports as required pursuant to 42 CFR §50.605(b). If the FCOI is identified and eliminated prior to the expenditure of any PHS-awarded funds, no FCOI report need be submitted.
- 7.2.** Initial Report: Prior to expenditure of any funds under the NIH-funded research project, the Institution will provide a FCOI report regarding any SFI found to be a FCOI. Cyclopure will also provide a FCOI report within 60 calendar days from the date of a new SFI disclosure determined to be a FCOI, a new Investigator with an identified FCOI becomes engaged in the project or when the Institution identifies a FCOI not previously disclosed. This report will include the following information:
- Grant/Contract Number
 - PD/PI
 - Name of Investigator with the FCOI
 - Nature of the FCOI (e.g., equity, consulting fees, travel reimbursement or honoraria)
 - Value of the financial interest 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
 - Description of how FCOI relates to PHS-funded research and the basis for the determination that the financial interest conflicts with such research
 - Key elements of the FCOI management plan
- 7.3.** Annual updates to this report will be submitted to the PHS Awarding Component for the duration of the research project. The annual report will include:
- Status of the FCOI Changes to the action plan
 - Justification that an FCOI no longer exists
- 7.4.** An Investigator's significant financial interest is related to PHS-funded research when the Signing Official reasonably determines that the significant financial interest could be affected by the PHS-funded research or is in an entity whose financial interest could be affected by the research. In determining whether an Investigator's significant financial interest is related to PHS-funded research the Signing Official will consider all relevant factors and information, including but not limited to whether there is an ongoing relationship between the Investigator and the payer.
- 7.5.** A financial conflict of interest (FCOI) exists when the Signing Official reasonably determines that the significant financial interest could directly and significantly affect the design, conduct,

or reporting of the PHS-funded research. In determining whether there is an FCOI, the Signing Official will consider all relevant factors and information, including but not limited to the nature of the research, the magnitude of the financial interest and degree to which it is related to the research, the extent to which the interest could be directly and substantially impacted by the research, and the degree of risk to the human subjects, if any, that is inherent in the research protocol.

- 7.6. Prior to making the decision whether an FCOI exists, the Signing Official may impose interim measures, may ask the Investigator to submit additional information and may meet or communicate with the Investigator. The Investigator may be encouraged to suggest procedures, protocols, or other measures designed to manage the FCOI.
- 7.7. “Manage” means taking action to address an FCOI, which can include reducing or eliminating the financial conflict of interest to ensure, to the extent possible, that the design, conduct and reporting of research will be free from bias.
- 7.8. Examples of conditions or restrictions that might be imposed to manage an FCOI include, but are not limited to:
 - Public disclosure of financial conflicts of interest (e.g., when presenting or publishing the research);
 - Monitoring of the research by independent reviewers;
 - Modification of the research plan;
 - Change of personnel or personnel responsibilities or disqualification from participation in all or a portion of the research;
 - Reduction or elimination of the financial interest; and/or
 - Severance of relationships that create financial conflicts.
- 7.9. For all management plans, the Signing Official shall (1) monitor ongoing Investigator compliance and (2) submit annual updates to the PHS Awarding Component at the time and in the manner specified by the PHS Awarding Component, both until the completion of the PHS-funded research project to which the FCOI relates.
- 7.10. With respect to FCOI related to research sponsored by NIH, annual FCOI reports will be submitted through the eRA Commons FCOI Module for the duration of the project period (including extensions with or without funds) at the same time annual progress reports are required to be submitted and at the time of extension (if any).
- 7.11. If the financial conflicts of interest report involves a significant financial interest that was not disclosed by an Investigator or not previously reviewed or managed by Cyclopure, (e.g., not reviewed or reported by a subrecipient in a timely manner), Cyclopure, will within 120 days undertake a retrospective review in accordance with 42 CFR §50.605(a)(3). Such retrospective review will determine whether there was bias in the design, conduct, or reporting of the PHS-funded research, or portion thereof, conducted prior to the identification and management of the conflict. If bias is found, Cyclopure, will promptly notify the PHS Awarding Component and submit a mitigation report.

8. Noncompliance and Remedies

- 8.1.** If an Investigator knowingly fails to comply with this policy (e.g., fails to identify an actual or potential financial conflict of interest), the Signing Official within 120 days of the determination of noncompliance, conduct a retrospective review of the Investigator's activities and the research project to determine whether any PHS-funded research or portion thereof conducted during the period of noncompliance was biased in design, conduct or reporting.
- 8.2.** Cyclopure, may take appropriate disciplinary action, which may include, without limitation, termination of the Investigator's participation in the research. In addition, for PHS-funded research, failure to comply with this policy or the applicable regulations shall result in the following:
 - 8.2.1** If the Investigator's failure to comply with this policy or a financial conflicts of interest management plan has biased the design, conduct, or reporting of the PHS-funded research, Cyclopure, shall promptly notify the PHS Awarding Component of the corrective action taken or to be taken;
- 8.3.** Cyclopure will make available to PHS Awarding Component all records pertinent to financial conflicts of interest and the management of such conflicts.

9. Maintenance of Records

- 9.1.** The Signing Official shall maintain all disclosure forms and related records of determinations made and actions taken for a period of three (3) years from the date of submission of the final expenditures report to the PHS (or, where applicable, from other dates specified in 45 CFR 75.361).

10. Enforcement Mechanism and Sanctions

- 10.1.** All researchers to whom this FCOI Policy applies are expected to fully and promptly comply with it. The Signing Official may impose sanctions for noncompliance which may include, but is not limited to, the following:
 - Failure to make timely, full or accurate disclosures;
 - Failure to provide information requested;
 - Failure to update a disclosure form as necessary; or
 - Failure to comply with a management plan.
- 10.2** For Cyclopure employees, sanctions may include suspension or dismissal, denial of eligibility to engage in the research at issue or other appropriate penalties. Such sanctions may require giving notice of relevant information to funding agencies, professional bodies or journals, or the public. The Signing Official will determine what sanctions, if any, are to be applied.

11. Sub-recipients

- 11.1.** The Signing Official will have the responsibility to take reasonable steps to ensure that Investigators for subrecipients (e.g., subgrantees, subcontractors, or collaborators) fully comply with this policy by:
- 11.2.** Incorporating as part of a written agreement with the subrecipient terms that establish whether Cyclopure's or the subrecipient's financial conflicts of interest policy will apply to the subrecipient's Investigators.
- 11.3.** If the subrecipient's Investigators must comply with the subrecipient's financial conflicts of interest policy, the subrecipient shall:
- Certify as part of the agreement that its policy complies with Cyclopure's FCOI policy.
 - If subrecipient cannot provide such certification, the agreement shall state that subrecipient Investigators are subject to Cyclopure's FCOI policy for disclosing significant financial interest that are directly related to the subrecipient's work
 - The agreement shall also specify time period(s) for the subrecipient to report all identified financial conflict of interest to Cyclopure. Such time period(s) shall be sufficient to enable Cyclopure to provide timely FCOI reports, as necessary, to the PHS as required
- 11.4.** If Cyclopure's policy will apply to the subrecipient Investigators, the agreement shall specify time period(s) for the subrecipient to submit all Investigator disclosures of significant financial interest to Cyclopure. Such time period(s) shall be sufficient to enable Cyclopure to comply timely with its review, management and reporting obligations.

12. Public Accessibility Requirements

- 12.1.** This FCOI Policy will be posted on Cyclopure's publicly accessible website, as required by the FCOI Regulations.
- 12.2.** Prior to expending any funds under a PHS-funded grant or cooperative agreement, Cyclopure, shall ensure public accessibility to information concerning an FCOI held by a senior/key personnel member by providing a written response to any written request, such response to be postmarked or dated (if replying by electronic means) within five (5) business days of the receipt of the written request. Such information shall consist of that required to be provided under the FCOI Regulations [42 CFR 50.605(a)(5)(ii),(iii)], shall be updated at least annually and within 60 days of the receipt or identification of information concerning an additional significant financial interest, and shall remain available for three years from the date the information was most recently updated.