

Purpose:

The purpose of this policy is to promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct, or reporting of funded research, grants or cooperative agreements will be free from bias resulting from an Investigator's financial conflicts of interest (and/or of the Investigator's spouse and/or dependent children).

This policy complies with the following federal regulations:

- Title 42 Code of Federal Regulations (CFR), Part 50, Subpart F, Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding is Sought

Scope:

This policy applies to Investigators participating in, or planning to participate in the design, conduct, reporting or proposing research funded by Public Health Service (PHS) or National Institute of Health (NIH).

If a research project involves subcontractors, subgrantees, or subawardees (collectively subrecipients), the subrecipient institution must provide written assurance that a financial conflict of interest in research policy is in effect at that institution and compliant with all applicable federal regulations. Should Public Health Service (PHS) or National Institute of Health (NIH) funds be subcontracted by ONL Therapeutics (ONL) to a subrecipient institution without a conflict of interest in research policy, a written agreement must state that this policy shall apply to the subrecipient.

Definitions:

- **Financial Interest** means anything of monetary value or potential monetary value held by the Investigator, the Investigator's spouse and/or dependent children, regardless of whether or not the value is readily ascertainable.
- **Financial Conflict of Interest** means a Significant Financial Interest (see below) related to a research program or project that could directly and significantly affect the design, conduct or reporting of research.
- **Significant Financial Interest (SFI)** means
 - A financial interest consisting of one or more of the following interests of the Investigator (and/or of the Investigator's spouse and/or dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:
 - With regard to any 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 the 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 interests includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value.
- Regarding any 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 (and/or the Investigator's spouse and/or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or
 - Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.
- For PHS-funded investigators, any reimbursed or sponsored travel related to an Investigator's institutional responsibilities, including that which is paid on behalf of the investigator so that the exact monetary value may not be readily available.
 - The term *significant financial interest* **does not include** the following types of financial interests:
 - Salary or consulting fees paid by ONL to the Investigator if the Investigator is currently employed or otherwise appointed by ONL.
 - Income from seminars, lectures, or teaching engagements sponsored by a federal, state or local agency, an Institution of higher education, an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.
 - Income from service on advisory committees or review panels for a federal, state, or local government agency, an Institution of higher education, an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.
 - Travel by a PHS-funded Investigator that is reimbursed or sponsored by a federal, state, or local government agency, an Institution of higher education, an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

Policy:

Each year any investigator who conducts research on any ONL project must disclose via the electronic system all significant financial interests (SFIs) that are relevant to an investigator's institutional research responsibilities or within 30 days after he/she becomes aware of new SFI or after a financial conflict of interest has been eliminated.

Investigators are required to complete the annual disclosure form even if they have no financial interest to report. Transactional disclosure by the PI is also required at the time a research proposal is submitted to ONL's Grants Director in order to ensure compliance with Federal disclosure and management requirements.

Procedure:

Investigator Responsibilities:

- Disclosing all significant financial interests
- Providing updates to disclosed information as needed
- If acting as the PI/PD, providing a list of individuals who meet the definition of “investigator” within the required disclosure timeline
- Completing all required training and education
- Completing the annual disclosure form even if they have no financial interests to report.
- Ensuring that an updated FCOI in Research Disclosure is on file at the time of Institutional Review Board (IRB) or the Institutional Animal Care and Use Committee (IACUC) approval for any new research proposals.

Financial Conflicts of Interest (FCOI):

A financial conflict of interest (FCOI) means a significant financial interest that could directly and significantly affect the design, conduct or reporting of research. Examples include, but are not limited to, the following:

- Investigator (and/or an Investigator's spouse and/or dependent children) entering into a paid consultancy with an outside entity that has an interest in the investigator's;
- Investigator (and/or an investigator's spouse and/or dependent children) receiving royalties or non-royalty payments related to ongoing research;
- Investigator (and/or an investigator's spouse and/or dependent children) having an equity interest (e.g., stocks, stock options, warrants) related to ongoing research;

This policy addresses individual financial conflicts of interest; however, ONL may also have conflicts of interest in research whenever the financial interests of ONL, or of an ONL official acting within his or her authority on behalf of ONL, might affect—or reasonably appear to affect— ONL processes for the conduct, review, or oversight of research. If institutional conflicts of interest are identified via the process described below, they will normally be addressed in a manner that is consistent with this policy.

Review of FCOIs:

ONL’s FCOI administrator conducts an initial review of all disclosures. If necessary, the FCOI administrator obtains additional information from the investigator and other individuals to help determine whether the SFI disclosed is related to a proposed or existing sponsored project or program. The administrator then formally identifies cases that require further review by management.

ONL’s Management and Quality Review Committee (QRC) will review the collected information to determine whether a financial conflict of interest exists by considering the following:

- Impact on integrity of research data;

- Risks to rights and safety of animal and/or human research subjects; Risks to the rights of students and trainees participating in research; and
- Appearance of conflict of interest.

If a financial conflict of interest is identified, ONL's Management and QRC will determine whether the research can be undertaken.

Management of FCOIs:

For cases that require action, a plan of action will be developed by members of ONL's Management and QRC on a case by case basis. Such a plan will include some or all of the following as deemed appropriate:

- Public disclosure of significant financial interests (e.g., when presenting or publishing the research), if appropriate;
- Disclosure of significant financial interests directly to subjects involved in human research;
- Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of research;
- Modification of 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 (e.g., sale of an equity interest);
- Severance of relationships that create the actual or potential conflict of interest;
- If it proves impossible to reach an acceptable plan of action, funds will be returned to the sponsor.

A draft of the plan of action will be provided to the Investigator for review and comment before it is finalized. The Investigator and their immediate supervisor must sign the approved plan to acknowledge their agreement to comply.

If the Institution identifies an SFI that was not disclosed or reviewed in a timely manner it will initiate the review process and an interim plan of action will be implemented when necessary.

Monitoring:

Investigator compliance with plans of action will be monitored by ONL's Management and QRC. The frequency of monitoring will be dictated by sponsor/agency requirements and action plan provisions.

Research Involving Humans:

Special consideration and scrutiny must be given to protect human subjects in research. Investigators with an identified financial conflict of interest or a significant financial interest

that could directly and significantly affect the design, conduct, or reporting of the research shall not ordinarily participate in any research involving human subjects. This presumption against the participation in human subjects' research by financially interested individuals may be rebutted by compelling circumstances. Compelling justification may include factors such as unique investigator expertise, unique institutional resources, unique access to particular patient populations, nature of the science, level of risk to human subjects and the degree to which the financial conflict of interest and the research are related.

The compelling justification and the degree of risk to human subjects must be presented and reviewed by the QRC. If compelling circumstances justify a waiver of this policy, the research will be subject to the development and implementation of an action plan to ensure the safety of human subjects and the integrity of the research. The QRC must review the research with consideration given to the requirements of the action plan. The QRC may require additional safeguards to be implemented but may not determine less stringent financial conflict of interest management requirements.

Appeals:

Investigators may appeal QRC decisions in writing within 15 days of receipt of the finalized action plan or other decision of the committee. The written appeal should include details regarding circumstances which support the request for a proposed revision to a QRC decision. An Appeals Committee will be formed for purposes of investigating the appeal and making a final decision. A meeting of the Appeals Committee will be convened to review the SFI information, the Management and Monitoring Plan, and previous meeting minutes, to make a decision. The Investigator may be invited to describe reasons for the appeal and to address further questions. The appeals process will take no more than 60 days from the date requested by the Investigator. The decision of the Appeals Committee is final and binding.

Confidentiality:

Financial and other information disclosed in compliance with this policy will be kept confidential and disclosed only on a need-to-know basis as required to perform appropriate review and evaluation required by the policy, except in the case of required public accessibility of identified financial conflicts of interest held by senior/key personnel.

Enforcement:

Failure on the part of an Investigator to comply with this policy will result in disciplinary action and/or sanctions which may include formal reprimand, non-renewal/termination of appointment or affiliation, additional training requirements, additional supervision, closing existing research or denying future research by the Investigator, and/or any other enforcement action mandated by the applicable funding agency or ONL.

Policy Revision:

ONL may modify this policy to conform to organizational changes and circumstances including revisions to federal or state law or regulations. The QRC will have 30 business days to review and comment on any proposed revisions.

The QRC is responsible for granting final approval for these policy revisions. It will review all proposed revisions, in collaboration with management, and will consider the committee's feedback during the review process. When necessary, procedures will be developed or modified to implement this policy.

Additional Requirements:

The following **additional** requirements also apply to all research funded by the PHS of the U.S. Department of Health and Human Services and any PHS Awarding Component including the NIH.

Reporting:

ONL will provide to the PHS Awarding Component a FCOI report as outlined in the regulations: 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. ONL 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 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 action plan

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

Subrecipients:

For PHS-funded research that involves subcontractors, subgrantees or subawardees (collectively subrecipients) at other Institutions, ONL requires a written agreement that includes terms that establish whether the FCOI policy of the awardee Institution or that of the subrecipient Institution will apply to subrecipient Investigators. This agreement will specifically address time periods to meet disclosure and/or financial conflict of interest reporting requirements.

Subrecipient Institutions who rely on their Financial Conflict of Interest policy must report identified financial conflicts of interests to the ONL in sufficient time to allow the ONL to report the FCOI to the PHS Awarding component.

Subrecipients who do not have such a conflict of interest policy will be required to follow the ONL FCOI in Research policy. A subrecipient's failure to promptly comply with the ONL policy will be considered grounds for immediate termination by ONL of any applicable subcontract or subaward. The written agreement terms required by ONL will contain a provision that subrecipients will report to ONL as the pass-through entity, any identified FCOI in sufficient time to allow ONL to report and manage the FCOI and meet the reporting obligations described above.

Public Accessibility:

This policy will be posted, on the ONL's public website. In addition, information concerning identified FCOIs held by senior/key personnel will be made available to requestors via **an email** response within five business days from when the Research Official receives the request. This information may be requested by **emailing info@onltherapeutics.com**

The written response will include:

- Senior/key personnel name
- Senior/key personnel's role in the research project
- Name of the entity in which the FCOI is held
- Nature of the FCOI
- Approximate dollar value of the FCOI or a statement that the value cannot be readily determined

This information will remain available for three years from the date the information was most recently updated.

Training Requirements:

PHS-funded Investigators must complete FCOI training prior to engaging in research related to any PHS-funded grant or contract and at least every four years thereafter. Training must also be completed *as soon as reasonably possible* under the following circumstances:

- This policy changes in a manner that affects Investigator requirements
- An Investigator is new to a subrecipient and will be working on PHS- funded research

- An Investigator is found to be noncompliant with this policy or their approved action plan

Investigator/Institutional Non-Compliance:

If an SFI is not disclosed or reviewed in a timely manner, ONL will review the Investigator's financial interest, and determine if it is related to PHS-funded research; determine whether an FCOI exists, and if so:

- Implement an action plan for ongoing research, at a minimum implement an interim action plan
- Complete a retrospective review of Investigator's activities and the PHS- funded research project within 120 days of a non-compliance finding to determine if bias was present in the design, conduct, or reporting of such research; and
- If bias/non-compliance is found, the Institution will promptly inform the PHS Awarding Component by submitting a mitigation report

If the retrospective review finds that the Investigator knew, or should have known about the FCOI related to his/her institutional responsibilities, but failed to disclose in compliance with this policy, the costs associated with the retrospective review and mitigation report may be pulled from the subrecipient's Indirect Cost Allocation portion. If the Department of Health and Human Services determines that a PHS-funded clinical research project 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 conflicting interest that was not managed or reported to ONL , the Investigator must disclose the FCOI in each public presentation of the results of the research and must request an addendum to previously published presentations.

NIH Reporting Requirements:

If ONL is unable to satisfactorily manage a conflict of interest involving NIH funding, it will appropriately notify NIH's Office of the General Counsel.

Responsibilities and Authorities:

Investigators participating in, or planning to participate in the design, conduct, or reporting of research including Public Health Service (PHS) or National Institute of Health (NIH) funded research at ONL have the authority and responsibility for the activities in this policy.

Records:

ONL will maintain all records related to the implementation of this policy for at least three years after:

- the date of creation;
- the date of termination or completion of a research award or contract;
- the submission of the final expenditures report; or

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- the date of final resolution of any investigation, audit, or similar action involving the records.

For additional information, please email the company at info@onltherapeutics.com