

Protagonist Therapeutics, Inc. Financial Conflict of Interest Policy

Introduction

Protagonist Therapeutics, Inc. (hereafter “Protagonist”) is committed to the design, conduct, and reporting of research in an objective manner, free from bias or undue influence as a result of financial conflicts of interest.

This Financial Conflict of Interest Policy (this “Policy”) implements U.S. federal requirements pertaining to “Objectivity in Research” disseminated by the Public Health System (“PHS”) 2011 Financial Conflict of Interest (“FCOI”) requirements, related to PHS Organization-funded research, and published in U.S. regulations 42 CFR Part 50, Subpart F (and 45 CFR Part 94).

Purpose

The intent of this Policy is designed to promote objectivity in Protagonist’s PHS-funded research by establishing standards and procedures that provide a reasonable expectation that the design, conduct, and reporting of research performed will be free from bias resulting from Investigator financial conflicts of interest.

Applicability

As such, this Policy is applicable to each Investigator who is planning to participate in, or is participating in, such research.

Definitions

Disclosure of Significant Financial Interests: An Investigator’s disclosure of Significant Financial Interests to an Institution (in this instance, Protagonist).

Financial conflict of interest (“FCOI”): A Significant Financial Interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

FCOI report: Protagonist’s report of an FCOI to a PHS Awarding Component.

Financial interest: Anything of monetary value, whether or not the value is readily ascertainable.

HHS: The United States Department of Health and Human Services (HHS), and any components of the Department to which the authority involved may be delegated.

Institution: Generally, any domestic or foreign, public or private, entity or organization (excluding a Federal agency) that submits a proposal, or that receives, PHS research funding. For purposes of this Policy, Protagonist is the “Institution.”

Institutional Official: The individual, or individuals designated by Protagonist to be responsible for enforcing this Policy, reviewing disclosures of Significant Financial Interests, determining whether disclosures constitute FCOI, and managing such conflicts.

Institutional responsibilities: An Investigator’s professional responsibilities performed on behalf of Protagonist.

Investigator: The 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.

Key Personnel: The PD/PI (program director/principal investigator) and other individuals who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not they receive salaries or compensation under the grant.

Manage: Taking action to address an FCOI, which can include reducing or eliminating the FCOI, to ensure, to the extent possible, that the design, conduct, and reporting of research will be free from bias.

PHS: 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”).

PHS Awarding Component: The organizational unit of the PHS that funds the research.

Research: 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. As used in this part, the term includes any such activity for which research funding is available from PHS.

Significant Financial Interest: A financial interest consisting of one or more of the interests set forth below.

Significant Financial Interests include:

A financial interest consisting of one or more of the following interests of the Investigator (including those of the Investigator’s spouse/domestic partner and/or dependent children) that reasonably appears to be related to the Investigator’s institutional (i.e., Protagonist) responsibilities:

1. 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 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. With regard to 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 holds any equity interest (e.g., stock, stock option, or other ownership interest); or
3. Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

Investigators must disclose the occurrence of any reimbursed or sponsored travel over \$2,500 (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 (i.e., Protagonist) 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. Such disclosure will include, at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. The Institutional Official 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. In addition, Investigators must disclose reimbursed or sponsored travel received from a foreign institution of higher education or the government of another country (which includes local, provincial, or equivalent governments of another country).

The term Significant Financial Interest does not include the following financial interests:

1. Salary, royalties, or other remuneration paid by Protagonist to the Investigator if the Investigator is currently employed or otherwise appointed by Protagonist, including intellectual property rights assigned to Protagonist and agreements to share in royalties related to such rights;
2. Any ownership interest in Protagonist held by the Investigator; 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;
3. 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
4. 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.

Responsibilities of Protagonist

Protagonist shall maintain, update, and enforce this Policy, and make it available via a publicly accessible website.

Protagonist shall inform each Investigator of:

1. This Policy,
2. The Investigator's responsibilities regarding disclosure of Significant Financial Interests, and
3. The relevant regulations, 42 CFR 50 Subpart F (and 45 CFR Part 94).

Protagonist shall:

1. Assign a designated Institutional Official to review financial disclosure documents, make determination of potential conflicts of interest and execute a management plan as appropriate.
2. Require that each Investigator who is participating in its PHS-funded research complete mandatory training on both Federal and Institutional policies. This is detailed in the mandatory training section.
3. Require that each Investigator who is participating in Protagonist's PHS-funded research submit a disclosure of Significant Financial Interest form, within the timeframe below, to the designated Institutional Official disclosing the Investigator's Significant Financial Interests (and those of the Investigator's spouse/domestic partner and/or dependent children).
 - a. No later than at the time of application for NIH-funded research;
 - b. Within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new Significant Financial Interest; and
 - c. At least annually, in accordance with the specific time period prescribed by the Institution, during the period of award.
4. Provide guidelines for the designated Institutional Official to determine whether an Investigator's Significant Financial Interest is related to PHS-funded research and, if so

related, whether the Significant Financial Interest is an FCOI.

5. Take such actions as necessary to manage financial conflicts of interest. Establish adequate enforcement mechanisms to ensure Investigator compliance.
6. 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 an FCOI), and all actions under the this Policy for at least three years from the date of the submission of the final expenditures report.

Responsibilities of the Investigator

Investigators are responsible to:

1. Read the National Institute of Health ("NIH") Regulations and Code of Federal Regulations ("CFR") on FCOI.
 - a. NIH Financial Conflict of Interest Overview:
<https://grants.nih.gov/grants/policy/coi/index.html>
 - b. Federal Register Notice for 45 CFR Part 50 Subpart F (and 45 CFR Part 94):
https://grants.nih.gov/grants/policy/coi/fcoi_final_rule.pdf
 - c. FCOI Frequently Asked Questions: <https://grants.nih.gov/faqs#/financial-conflict-of-interest.html>
2. Complete the NIH tutorial on FCOI:
https://grants.nih.gov/grants/policy/coi/tutorial2018/story_html5.html.
3. Read this Policy

Mandatory Training Requirements

1. All Investigators will be required to complete FCOI training on both Federal and Protagonist policies. This training must be completed prior to engaging in research related to any PHS-funded grant and at least every four years, and immediately if any of the following circumstances apply:
 - a. The FCOI Policy or procedures contained within or the PHS Financial Disclosure Form are revised in any manner that affects the requirements of Investigators;
 - b. An Investigator joins Protagonist; or
 - c. Protagonist is made aware of an Investigator who is not in compliance with this FCOI Policy.
2. To fulfill Protagonist's training requirements, all relevant Protagonist personnel will be required to read through this FCOI Policy.
3. To fulfill the Federal training requirement, all Investigators must complete the NIH tutorial on FCOI (https://grants.nih.gov/grants/policy/coi/tutorial2018/story_html5.html).

Policy application to subawardees, subcontractors and Affiliates

Subawardees, subcontractors, and other Protagonist affiliates collaborating on PHS funded research will be required to confirm that they have their own FCOI policy in place that conforms to PHS FCOI 2011 Regulations prior to collaboration, or will be required to comply with this Policy.

Management of FCOIs

Prior to the Institution's expenditure of any funds under a PHS-funded research project, Protagonist's designated Institutional Official shall review all Investigator disclosures of Significant Financial Interests; determine whether any Significant Financial Interests relate to PHS-funded research; determine whether

an FCOI exists; and, if so, take action to manage such FCOI.

Whenever Protagonist implements a management plan pursuant to this Policy, Protagonist shall monitor Investigator compliance with the management plan on an ongoing basis until the completion of the PHS-funded research project.

Whenever, in the course of an ongoing PHS-funded research project, an Investigator who is new to participating in the research project discloses a Significant Financial Interest or an existing Investigator discloses a new Significant Financial Interest to the Institution, the designated Institutional Official(s) shall, within sixty days: review the disclosure of the Significant Financial Interest; determine whether it is related to PHS-funded research; determine whether a financial conflict of interest exists; and, if so, implement, on at least an interim basis, a management plan that shall specify the actions that have been, and will be, taken to manage such financial conflict of interest.

Depending on the nature of the Significant Financial Interest, an Institution may determine that additional interim measures are necessary with regard to the Investigator's participation in the PHS-funded research project between the date of disclosure and the completion of the Institution's review.

Retrospective Review

Whenever an FCOI is not identified or managed in a timely manner (including: any failure by an Investigator to disclose a Significant Financial Interest that is determined by Protagonist to constitute a FCOI; any failure by Protagonist to review or manage such an FCOI; or any failure by an Investigator to comply with an FCOI management plan), Protagonist shall, within 120 days of Protagonist'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. Protagonist will document the retrospective review; such documentation shall include, but not necessarily be limited to, all the following key elements:

1. Project number;
2. Project title;
3. PM/PD/PI or contact PM/PD/PI if a multiple PM/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 a retrospective review, if appropriate, Protagonist will update the previously submitted FCOI report, specifying the actions that will be taken to manage the FCOI going forward. If bias is found, Protagonist 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 Protagonist'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, the Institution will submit FCOI reports annually. Depending on the nature of the FCOI, Protagonist 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 financial conflict of interest or the Investigator's noncompliance is determined and the completion of Protagonist's retrospective review.

Reporting

Per PHS FCOI Regulations, Protagonist will submit to the NIH through the eRA Commons FCOI Module both initial and ongoing FCOI reports:

1. Prior to the expenditure of funds;
2. Within 60 days of identifying a new FCOI;
3. Annually during the progress report submission.

Prior to Protagonist's expenditure of any funds under a PHS-funded research project, Protagonist shall provide to the PHS Awarding Component the FCOI report regarding any Investigator's Significant Financial Interest found by Protagonist to be conflicting, at the time of filing, and ensure that Protagonist has implemented a management plan in accordance with this Policy. In cases in which Protagonist identifies a financial conflict of interest and eliminates it prior to the expenditure of PHS-awarded funds, Protagonist shall not submit an FCOI report to the PHS Awarding Component.

Any FCOI report required shall include information to enable the PHS Awarding Component to understand the nature and extent of the financial conflict, and to assess the appropriateness of the Institution's management plan.

Elements of the FCOI report shall include, but are not necessarily limited to the following:

1. Grant number;
2. PD/PI;
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 be readily 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 the Institution's determination that the financial interest conflicts with such research; and
8. A description of the key elements of the Institution'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.

For any FCOI previously reported by Protagonist with regard to an ongoing PHS-funded research project, Protagonist shall provide to the PHS Awarding Component an annual FCOI report that addresses the status of the FCOI and any changes to the management plan for the duration of the PHS-funded research project. The annual FCOI report shall specify whether the FCOI still being managed or explain why the FCOI no longer exists.

For any Significant Financial Interest that Protagonist identifies as conflicting subsequent to Protagonist's initial FCOI report during an ongoing PHS-funded research project (e.g., upon the participation of an Investigator who is new to the research project), Protagonist shall provide to the PHS Awarding Component, within sixty days, an FCOI report regarding the FCOI and ensure that the Institution has implemented a management plan in accordance with this Policy. Where such FCOI report involves a Significant Financial Interest that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed or managed by the Institution (e.g., was not timely reviewed or reported by a subrecipient), the Institution also is required to complete a retrospective review to determine whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the FCOI was biased in the design, conduct, or reporting of such research. In addition, if bias is found, the Institution is required to notify the PHS Awarding Component promptly and submit a mitigation report to the PHS Awarding Component.

Enforcement

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, Protagonist shall 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 the Institution for further action, which may include directions to Protagonist on how to maintain appropriate objectivity in the PHS-funded research project. 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 SFI related to federally sponsored projects.

In any case in which the HHS determines that a PHS-funded 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 Protagonist as required by this subpart, Protagonist 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.

Public Availability of FCOI Disclosures

Protagonist shall ensure public accessibility, via written response to any requestor within five business days of a request, of information concerning any Significant Financial Interest disclosed to Protagonist that meets the following three criteria:

1. The Significant Financial Interest was disclosed and is still held by Key Personnel;
2. Protagonist determines that the Significant Financial Interest is related to the PHS-funded research; and
3. Protagonist determines that the Significant Financial Interest is an FCOI.

The information that Protagonist makes available via written response to any requestor within five business days of a request, 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.

More Information

If you have, or believe you may have, a financial conflict of interest or if you have a question to discuss, contact the Institutional Official.

This Policy is available at the Protagonist Therapeutics, Inc. publicly available website.

For more information, visit the following:

42 CFR Part 50 Subpart F, 45 CFR Part 94 https://grants.nih.gov/grants/policy/foi/fcoi_final_rule.pdf

NIH FCOI <https://grants.nih.gov/grants/policy/foi/index.html>

NIH FCOI FAQs <https://grants.nih.gov/faqs#/financial-conflict-of-interest.html>

NIH FCOI Tutorial https://grants.nih.gov/grants/policy/foi/tutorial2018/story_html5.html