

Purpose

This document describes the policy implemented to comply with the requirements of 42 CFR 50 Subpart F, including the requirements and responsibilities associated with identifying and managing financial conflicts of interest to safeguard the integrity of RareCyte research funded under Public Health Service (PHS) grants, such as those awarded by the National Institutes of Health (NIH).

Scope

This policy applies to all individuals who plan to participate in, or are participating in, research funded by PHS grants or cooperative agreements.

Definitions

Designated Company Official (DCO) – the individual within RareCyte that is responsible for the solicitation and review of disclosures of significant financial interests related to an Investigator's Company responsibilities. The DCO is Jim Cooper/the VP of Finance.

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 – an Institution's report of financial conflict of interest 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, and any components of the Department to which the authority involved may be delegated.

Institution - any domestic or foreign, public or private, entity or organization (excluding a Federal agency) that is applying for, or that receives, PHS research funding. A Company, such as RareCyte.

Institutional/Company responsibilities - an Investigator's professional responsibilities on behalf of RareCyte, which may include for example: activities such as research, research consultation, or professional practice.

Investigator - the project director (PD) or principal Investigator (PI) and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the PHS.

Manage - taking action to address a financial conflict of interest, 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.

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 that is subject to this subpart.

Senior/key Personnel - he PD/PI and any other person identified as senior/key personnel by RareCyte in the grant application, progress report, or any other report submitted to the PHS.

Significant Financial Interest (SFI) –

(a) 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:

1. With regard to any publicly traded entity, when the value of any remuneration (salary and any payment for services not otherwise identified as salary, for example consulting fees, honoraria, paid authorship) received from the entity in the twelve (12) months preceding disclosure of the interest aggregated with the value of any equity in the entity (for example, stock, stock options, or other ownership interests as determined through reference to public prices or other reasonable measure of fair market value) in the entity as of the date of the disclosure exceeds \$5,000.
2. With respect to any non-publicly traded entity, when the aggregated value of any remuneration received from the entity in the twelve (12) months preceding disclosure of the interest exceeds \$5,000, or any equity in the entity; or
3. Intellectual property rights and interests (e.g., patents, copyrights) upon receipt of income related to such rights and interests.

(b) Any travel that is reimbursed (i.e., the Investigator is made whole for the financial outlay required) or sponsored (i.e., the costs are paid on behalf of the Investigator such that the exact monetary value may not be readily available) other than by RareCyte, 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.

Exclusions: The term Significant Financial Interest does not include the following types of financial interests: salary, royalties or any 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; 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.

Training Requirements

Investigators involved with PHS funded research must complete training on this Policy, the investigator's disclosure responsibilities, and the federal regulations prior to engaging in research related to any PHS-funded grant, and at least every four years following the initial training. Training may consist of completing the FCOI Training tutorial provided on the NIH FCOI website and acknowledgment of this Policy.

Immediate training will be required to be completed (in a reasonable period of time, as determined by the DCO) if:

- The Company revises this Policy in a manner that affects requirements of the Investigators;
- The Investigator is new to the Company; or
- The Company determines an Investigator is not in compliance with this policy or a management plan related to their activities.

Disclosure, Review, and Monitoring Requirements**Disclosure**

All investigators must disclose their Significant Financial Interests, SFIs, (and those of their spouse and dependent children) as defined herein, that are related to the Investigator's Company responsibilities as described below.

Reimbursed or sponsored travel (as defined above under SFI) related to an Investigator's Company responsibilities must also be disclosed. Information required for such a disclosure includes, at minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, the duration, and, if known, the monetary value. Additional information may be requested by the DCO in order to determine whether the travel constitutes an FCOI with the PHS-funded research.

Disclosure Frequency

- Disclosures shall be made no later than at the time of application for PHS -funded research
- Disclosures must be made at least annually to the Company, during the period of the award(s). If no SFI is present a Disclosure must still be submitted that states "none". The due date of annual Disclosure shall be set by the DCO and communicated company wide.
- All Investigators must disclose their SFI to the Company, through the DCO (or designee), within 30 days of their initial appointment, employment, or discovery/acquiring of a new SFI.

Review of Disclosures

General Review: Prior to the Company's expenditure of any PHS-awarded funds and annually during the award period, the DCO shall solicit and review the disclosures of applicable Investigators for a determination of FCOI related to the sponsored research; and if a FCOI is determined to exist, take action to manage the FCOI.

An Investigator's SFI is related to PHS -funded research when the Company/DCO reasonably determines that the SFI could be affected by the sponsored research or is in an entity whose financial interest could be affected by the research. The Investigator may be involved in the determination of whether a SFI is related to the sponsored research.

A FCOI exists when the DCO (or designee) determines that SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded research.

New SFI Disclosure Review: The DCO shall review, within 60 days, SFI disclosures and determine if they are a FCOI when required for an Investigator who is new to participating in the research project or for an existing Investigator who discloses a new SFI.

If and SFI is identified that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the DCO during an ongoing PHS-funded research project, the DCO shall within 60 days:

- Review disclosures of SFIs;
- determine whether the SFI is related to PHS-funded research;
- determine whether an FCOI exists; and
- if so, implement at least on an interim basis, a management plan that specifies the actions that have been, and will be taken to manage such FCOI going forward.

Management of Identified FCOIs

For any identified FCOI, The DCO will take appropriate action to manage the conflict including reduction or elimination of the conflict, as appropriate, to ensure the safety or validity of the research. The DCO may seek input from the Investigator to implement a suitable action plan ("Management Plan") consistent with the objectives of this policy. The Management Plan shall provide for periodic review and updating. In the event there is no reasonable way to manage a FCOI, then the Investigator may be prohibited from participating in the related research until such a time as the FCOI is eliminated.

Examples of conditions or restrictions that might be imposed to manage a FCOI include, but are not limited to:

- Public disclosure of financial conflicts of interest (e.g., when presenting or publishing the research);
- For research projects involving human subjects research, disclosure of financial conflicts of interest directly to participants;
- 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;
- Modification of the research plan;
- Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;
- Reduction or elimination of the financial interest (e.g. sale of an equity interest); or
- Severance of relationships that create financial conflicts

Company management personnel shall review the proposed Management Plan and can approve, modify and approve, or return to the Members for additional work. Final review and determination must be completed prior to the expenditure of any PHS funds for the applicable Research.

Investigators have an on-going obligation to comply with implemented management plans and non-compliance may be grounds for sanctions under this policy. The Company will monitor Investigator compliance with imposed management plans on an ongoing basis until the completion of the sponsored research project.

Subrecipient Requirements

The Company, through the DCO, shall require subrecipient compliance with pertinent FCOI requirements as mandated by regulation.

- If applicable, obtain a certification from the subrecipient that its FCOI policy complies with the regulation.
- If applicable, include in the written subrecipient agreement a requirement for the subrecipient to report identified FCOIs for its Investigators in a time frame that allows the awardee Institution to report identified FCOIs to the PHS as required by the regulation.
- Alternatively, if applicable, include in the written agreement a requirement to solicit and review subrecipient Investigator disclosures that enable the awardee Institution to identify, manage and report identified FCOIs to the PHS.

Noncompliance

Retrospective Review

For PHS-funded research, in the event of a failure to meet regulations, including failure by the Investigator to disclose timely a SFI that that is determined to constitute an FCOI, the Company's failure to review or manage such an FCOI, or Investigator failure to comply with an FCOI management plan, the Company will conduct retrospective review.

Within 120 days of the Company's determination of noncompliance, complete a retrospective review of the Investigators activities and the PHS-funded research projects to determine whether any of the research, or portion thereof, conducted during the time period of the noncompliance, was biased in the design, conduct, or reporting of such research.

The Company shall document the retrospective review, which shall include at minimum the following:

- Project Number
- Project Title
- PD/PI or contact PD/PI if multiple PD/PI model is used
- Name of the Investigator with the FCOI
- Name of the entity with which the Investigator has an FCOI
- Reasons for the retrospective review

- Detailed methodology used for the retrospective review (e.g., methodology of the review process, composition of the review panel, documentation reviewed)
- Findings of the review
- Conclusions of the review

Clinical Research

In any case in which the HHS determines that 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 and Investigator with a FCOI that was not managed or reported by the Company as required by this policy, the DCO shall require the Investigator involved to disclose the FCOI in each public presentation of the results of the research and to request an addendum to previously published presentations.

Enforcement and Sanctions

Violations of Company policies, including failure to avoid prohibited activity or disclose a SFI in a timely manner, will be dealt with in accordance with applicable policies and procedures that may include disciplinary actions or suspension of relevant activities until the matter is resolved or other action deemed appropriate by the Company is implemented.

Reporting Requirements

The DCO, or designee, will provide initial, ongoing, and revised reports to the PHS Awarding Component in accordance with the PHS regulation.

- FCOI reports shall be sent prior to the expenditure of funds, annually during the award period, and within 60 days of identifying any subsequent FCOIs for existing or newly participating Investigators.
- Annual FCOI reports will address the status of previously reported FCOI with regard to an ongoing PHS funded research project and any changes to the management plan until the completion of the project.
- Revised reports will be provided following retrospective review to update a previously submitted report, if new information is discovered following completion of the review.

The PHS awarding component shall be notified if bias is found with the design, conduct, or reporting of the research. Information regarding whether Investigator failure to comply with this FCOI policy or management plan may have caused such bias should be included.

- When bias is found, a Mitigation Report will be submitted in accordance with the regulation. The mitigation report shall include the entity name, name of the Investigator with the FCOI, nature of SFI(s), value of the SFI(s), and a description of the impact of the bias on the research project and the plan of action or actions taken to eliminate or mitigate the effect of the bias.

Maintenance of Records

The Company will maintain all FCOI-related records relating to Investigator disclosures of financial interests and the review of, and response, to such disclosures (whether or not a disclosure resulted in a determination of a FCOI) and all actions under this Policy or retrospective review, for a minimum of three years from the submission of the final expenditure reports for the applicable PHS funding or longer as required by other policy or regulation.

Public Accessibility Requirements

The Company shall make this FCOI policy publicly accessible via the Company public website, as required by the regulation.

Prior to the expenditure of funds, the Company will publish on a publicly accessible website or provide to any requestor, within five business days of the request, information concerning any identified FCOIs held by senior/key personnel. The information to be made available shall be consistent with the requirements of the PHS regulation. Any information posted to the Company's website shall be:

- Updated at least annually;
- Updated within 60 days of a newly identified FCOI; and
- Available for 3 years from the date the information was most recently updated.