

Praevium Research, Inc.

Financial Conflict of Interest Policy

I. Introduction:

Federal regulations require that Praevium Research, Inc. have a written and publicly accessible financial conflict of interest policy before engaging in or applying for funds for Public Health Service sponsored research. This Financial Conflict of Interest Policy is intended to satisfy this requirement, and to instruct Praevium Research, Inc. employees in applying and complying with Praevium requirements regarding financial conflicts of interest in research. This policy is to be in full compliance with Financial Conflict of Interest (FCOI) Regulation 42 CFR Part 50 Subpart F (grants and cooperative agreements) and 45 CFR Part 94 (research contracts), including the 2011 revised FCOI regulations. These regulations promote objectivity in research by establishing standards for institutions and Investigators, that provide a reasonable expectation that the design, conduct, and reporting of research funded under PHS grants, contracts, or cooperative agreements will be free from bias resulting from Investigator financial conflicts of interest.

Praevium Research requires that Investigators disclose any Significant Financial Interests. While full and accurate disclosure is required, Praevium Research recognizes that the existence of a conflict of interest or appearance of conflict does not necessarily constitute wrongdoing on the part of the Investigator. Furthermore, the appearance of conflicts or actual conflicts may be acceptable if appropriately managed and monitored.

To address FCOI, Praevium Research has established a process by which Investigators disclose potential conflicts and are evaluated on a case-by-case basis. This policy describes procedures for disclosure, review, and oversight when necessary.

II. Guiding Principles

1. Praevium Research and its Investigators must conduct research with the utmost integrity. Praevium and its researchers have a responsibility to conduct research that is free of bias, free of influence by outside financial interests, and free of the appearance of non-objectivity or outside financial influence. Failure to do so may jeopardize future and current funding. It may also damage the reputation of Praevium Research, its employees, and its collaborators.
2. Investigators working with and for Praevium have a responsibility to disclose to Praevium Research, Inc. financial interests that conflict with or appear to conflict with their responsibilities at Praevium Research, Inc.
3. Praevium Research has the responsibility to promptly review all disclosures of financial interests and take measures to identify, manage, reduce, or eliminate any FCOI that may exist, to ensure that the design, conduct, and reporting of research will remain free from bias resulting from Investigator financial conflicts of interest.

III. Definitions

Investigator: 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 NIH, or proposed for such funding, which may include collaborators or consultants. Graduate students, interns, some consultants, and others whose work is regularly and closely scrutinized by a senior investigator, and who are not responsible for design, conduct, and reporting of research, may not necessarily be considered Investigators in this sense. Praevium Research may, at its discretion and as a matter of due diligence, place the same requirements on these individuals as it places on Investigators as described in this policy.

Significant Financial Interest (SFI):

(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:

(i) 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;

(ii) 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 (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or

(iii) 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 (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. Praevium's FCOI policy requires disclosure of at a minimum, the purpose of the trip, the identity of the sponsor/organizer, the destination, and the duration. In accordance with Praevium's FCOI policy, the COI 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.

(3) 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.”

Investigators must disclose all foreign financial interests (which includes income from seminars, lectures, or teaching engagements, income from service on advisory committees or review panels, and reimbursed or sponsored travel) received from any foreign entity, including foreign Institutions of higher education or a foreign government (which includes local, provincial, or equivalent governments of another country) when such income meets the threshold for disclosure (e.g., income in excess of \$5,000).

IV. Investigator Training Requirements

FCOI training includes a thorough review of Praevium Research’s financial conflict of interest policy on its website and completion of the 2018 NIH FCOI Tutorial Webinar

(https://grants.nih.gov/grants/policy/coi/tutorial2018/story_html5.html). Upon completion of training, Investigators must sign a Praevium Research completion of training certificate.

Every new Investigator must be provided a copy of this policy and training materials within 7 business days of hire date. The Investigator must complete training and submit the training certificate to the designated institutional official within 30 days, and prior to engaging in any PHS funded research or submitting proposals for such research. This certificate must be filed in the company’s records until an updated certificate is received. Training must be renewed at least every 4 years after initial training or more frequently if required by NIH regulations (see below).

Additionally, training must also be completed, and a new training certificate filed at the following times:

- Institutional FCOI policies change in a manner that affects Investigator requirements.
- An Investigator is new to the institution.
- An institution finds an Investigator to be noncompliant with the institutions FCOI policy or management plan.

V. Disclosure, Review, and Monitoring Requirements

Disclosure Form (Annual and Updated)

1. An annual disclosure form for each federally funded project is required from an employee considered an Investigator, including:
 - Praevium Research employees responsible for the design, conduct, and reporting of PHS funded research (deemed “Investigators”).
 - Investigators and other individuals identified on PHS funded grants and responsible for the design, conduct, or reporting of research.

- Investigators and other individuals identified on IRB applications and responsible for the design, conduct, or reporting of research.
2. Those individuals required to provide an annual reporting form must disclose any SFI greater than \$5,000 (for themselves, spouse, or dependent children).
 3. Annual disclosure forms will be provided by December 1 and are required to be completed and returned by December 31.
 4. Investigators are responsible for maintaining a current accurate disclosure form. If a new relationship or change in a current relationship could be perceived as a FCOI, Investigators must update their disclosure form to reflect such conflicts within 30 days. They may do so by contacting the Conflict of Interest official.
 5. Investigators are required to disclose all SFI/FCOI at time of application for PHS funds (i.e. complete a disclosure form for proposed research).

Review

The Praevium Research, Inc. CEO will appoint a conflict of interest (COI) official to review disclosure of all SFIs. The current COI official is Christopher Burgner. After disclosure forms are returned to Praevium Research's COI official, the official will review them to determine whether or not an overlap with research and external interests might exist. In more complex cases, the COI official may appoint an internal committee or seek outside counsel to determine whether an FCOI exists, or to establish procedures for managing the FCOI. The relevant Investigator will be notified if a COI exists such that it could directly and significantly affect the design, conduct, and reporting of PHS funded research. This Investigator will then work with the COI official to mitigate the conflict (by managing, reducing, or eliminating it).

Retrospective Review and Mitigation Report

Whenever a Financial Conflict of Interest is not identified or managed in a timely manner, including:

- Failure by the Investigator to disclose a Significant Financial Interest that is determined by Praevium Research to constitute a Financial Conflict of Interest;
- Failure by Praevium Research to review or manage such a Financial Conflict of Interest; or
- Failure by the Investigator to comply with a Financial Conflict of Interest management plan;

Praevium Research shall, within 120 days of the Institution's determination of noncompliance, complete a "retrospective review" of the Investigator's activities and the NIH-funded research project to determine whether any NIH-funded research, or portion thereof, conducted during the time period of the noncompliance was biased in the design, conduct, or reporting of such research.

The Institution shall document the retrospective review which must include at least the following key elements:

- A. Project number;
- B. Project title;
- C. PD/PI or contact PD/PI if a multiple PD/PI model is used;
- D. Name of the Investigator with the FCOI;
- E. Name of the entity with which the Investigator has a financial conflict of interest
- F. Reason(s) for the retrospective review;

- G. Detailed methodology used for the retrospective review (e.g., methodology of the review process, composition of the review panel, documents reviewed, etc.);
- H. Findings of the review; and
- I. Conclusions of the review.

Praevium policies must be followed regarding maintenance of records as long as they are in compliance with the PHS regulation. Under the regulation, Praevium is required to keep all records of all Investigator disclosures of financial interests and the Institution's review of, or response to, such disclosure (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, as follows:

- Records of financial disclosures and any resulting action must be maintained by the Institution for at least three years from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 C.F.R. 75.361 for different situations.

Monitoring

Acceptable strategies for managing, reducing, or eliminating FCOIs include but are not necessarily limited to:

- Withdrawal of an Investigator from a grant application or from participation in the conflicting research effort.
- Severance of financial relationships that create the FCOIs.
- Modification of the research plan.
- Appointment of an independent committee to monitor the research and prevent bias.
- Disclosure of FCOI when publishing or presenting research findings: Investigators will disclose relevant financial interests to all journals where this research will be published and in all public presentations of this research. Investigator must also request an addendum to previously published presentations, if an FCOI needs to be disclosed.
- Disclosure of FCOI to potential human subjects: If deemed necessary by the COI official, any FCOIs will be disclosed to all potential research participants in the consent process.
- Oversight and monitoring of research and decisions by a Praevium Research or non-conflicted member of the research team.

VI. Reporting Requirements to NIH

If it is determined that a FCOI exists, initial, annual (ongoing), and revised FCOI reports will be submitted to NIH (via eRA Commons):

- Prior to expenditure of funds.
- Within 60 days of identification for an Investigator who is new to the project.
- Within 60 days for new, or newly identified, FCOIs for existing Investigators.
- At least annually (in conjunction with annual progress reports or at the time of an extension).
- Following a retrospective review to update a previously submitted report.

NIH will be notified within 30 days if bias is found with the design, conduct, or reporting of research and will include a Mitigation Report outlining the management plan.

NIH will be notified within 30 days if an Investigator fails to comply with this policy or if the FCOI management plan appears to have biased the design, conduct, or reporting of research.

VII. Maintenance of Records

All FCOI records (training certificates, disclosures, management plans, retrospective reviews) will be held for three years after the final report is submitted to NIH. If any of the situations specified in 45 CFR 75.361 apply, the timelines specified in these sections will be adhered to.

VIII. Enforcement, Non-Compliance, and Disciplinary Action

Compliance with Praevium Research's FCOI policy for PHS research is a condition of employment with Praevium Research.

Federal regulations require Praevium Research to impose sanctions where appropriate. Failure to disclose SFIs and abide by this policy may be cause for termination of employment, or restriction of future research submissions or participation in certain research efforts. Other disciplinary actions in proportion to the offense may be taken.

If it has been determined that an Investigator or the Institution is in noncompliance with this policy (e.g. SFIs not disclosed, reviewed or managed in a timely or appropriate manner), then Praevium Research must complete and document a retrospective review within 120 days. The retrospective review should be conducted by the SFI disclosure review committee as designated by the CEO. The results of the retrospective review shall be documented and attached to the disclosure documents. If bias is found, Praevium Research must immediately notify the NIH by submitting a mitigation report.

Praevium Research must enforce any sanctions or actions required by the Department of Health and Human Services pertaining to a PHS-funded research project involving clinical research. If an FCOI was not reported or managed according to regulations, then Praevium Research must require the Investigator to disclose the FCOI in each public presentation of the results or research and request an addendum to previously published results or presentations.

IX. Sub-recipient Requirements

Sub-recipients with an FCOI policy that is compliant with current regulations cited in section I above, may comply with their institution's FCOI policy provided they supply Praevium Research with the necessary disclosure information to meet all reporting obligations and deadlines. If the subrecipient's institution does not have a suitable FCOI policy in place, then they shall adhere to the Praevium Research policy described in this document. A written agreement must exist with the sub-recipient certifying its own policy meets regulations, and that it will provide the required information to Praevium Research, or that the sub-recipient will adhere to the Praevium FCOI policy.

X. Public Accessibility

Praevium Research's FCOI policy will be publicly available on its website at www.praevium.com.

In the event that FCOIs are identified, information regarding the COI and the Investigator will also be publicly available on www.praevium.com. Publicly available information will be:

- Updated annually at a minimum.
- Made available within 5 calendar days of a written request.
- Updated within 60 days of newly identified FCOIs.
- Remain available for 3 years from the most recent update.
- Information to be made publicly available is to include, but is not limited to:
 - Investigator's name.
 - Investigator's title and role with respect to the research project.
 - Name of the entity in which the SFI is held.
 - Nature of the SFI.
 - Approximate dollar value of SFI (or a statement that the interest is one whose value cannot be readily determined through references to public prices or other reasonable measures of fair market value).