FRIENDS RESEARCH INSTITUTE, INC.
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Subject: Conflict of Interest
Division: IRB
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IRB Policy 102.1: CONFLICT OF INTEREST

Policy

1. In the research environment, openness and honesty are characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts of interest (COIs) should be eliminated wherever possible, and effectively managed and disclosed when they cannot.

2. COIs may reduce the objectivity of research by affecting the design, conduct, or reporting of research, or the analysis and interpretation of data. If research is designed or conducted improperly, its value is limited. It is not ethical to involve human subjects in research that is of no, or very limited, value. COIs may also directly affect subject safety. For example, an investigator with a COI may, even if unwittingly, color the consent discussion by minimizing the risks or overstating the benefits, or dismissing the value of alternative treatments. An investigator's willingness to report adverse reactions possibly related to the study article may also be affected. Investigators with a COI may also improperly include or exclude subjects.

Disclosure Requirement

1. **Investigator:**

   a) Investigators must disclose any significant financial interest with a research sponsor, and any other significant financial interest that may reasonably appear to affect or be affected by the research to FRI's COI Officer. The Officer will then send the IRB a report of his assessment of the real or perceived COI, and a remediation plan regarding any real COI.
   b) Investigators should disclose any COI to the IRB at the time of the initial application for a research protocol review, its renewal, or whenever the status of the COI changes.

2. **IRB Member:**

   a) No IRB member may participate in the initial or continuing review of any research project in which the member has a conflict of interest, except to provide information as requested. It is the responsibility of each member of the IRB to disclose any COI in a study submitted to the IRB, and recuse himself or herself from deliberations and voting.
   b) A conflict of interest is defined as a close personal or professional association with the submitting Investigator(s); direct participation in the research (e.g., protocol development, Principal or Sub-investigator); or any significant financial interest in the sponsoring company.

3. **Employees:**

   Institutional staff whose job status or compensation is affected by research that is reviewed by the IRB must recuse themselves from any meeting at which such a protocol is reviewed.

Definitions of a COI (21 CFR 54.2)

1. **Compensation** affected by the outcome of clinical studies means compensation that could be higher for a favorable outcome than for an unfavorable outcome, such as compensation that is explicitly greater for a favorable result or compensation to the Investigator in the form of an equity interest in the Sponsor of a covered study or in the form of compensation tied to sales of the product, such as a royalty interest.

2. **Significant equity interest** in the sponsor of a covered study means any ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices (generally, interests in a nonpublicly traded corporation), or any equity interest in a publicly traded corporation that exceeds $50,000 during the time the Clinical Investigator is carrying out the study and for 1 year following completion of the study.

3. **Proprietary interest** in the tested product means property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement.

4. **Clinical Investigator** means only a listed or identified Investigator or Sub-investigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the Investigator.

5. **Covered clinical study** means any study of a drug or device in humans submitted in a marketing application or reclassification petition subject to this part that the applicant or FDA relies on to establish that the product is effective (including studies that show equivalence to an effective product) or any study in which a single Investigator makes a significant contribution to the demonstration of safety. This would, in general, not include phase l tolerance studies or pharmacokinetic studies, most clinical pharmacology studies (unless they are critical to an efficacy determination), large open safety studies conducted at multiple sites, treatment protocols, and parallel track protocols. An applicant may consult with FDA as to which clinical studies constitute "covered clinical studies" for purposes of complying with financial disclosure requirements.

6. **Significant payments** of other sorts means payments made by the Sponsor of a covered study to the Investigator or the institution to support activities of the Investigator that have a monetary value of more than $25,000, exclusive of the costs of conducting the clinical study or other clinical studies, (e.g., a grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria) during the time the clinical Investigator is carrying out the study and for 1 year following the completion of the study.

7. **Applicant** means the party who submits a marketing application to FDA for approval of a drug, device, or biologic product. The applicant is responsible for submitting the appropriate certification and disclosure statements required in this part.

8. **Sponsor** of the covered clinical study means the party supporting a particular study at the time it was carried out.

Financial Conflict of Interest (FCOI) under Public Health Services regulations (42 CFR Part 50, Subpart F)

1. A FCOI exists when the Institution, through its designated official(s), reasonably determines that an Investigator's Significant Financial Interest (SFI) is related to a NIH-funded research project and could directly and significantly affect the design, conduct or reporting of the NIH-funded research.

2. An "Investigator" is defined as 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 (e.g., NIH), or proposed for such funding, which may include, for example, collaborators or consultants. FRI will consider the role, rather than the title, of those involved in research and the degree of independence with which those individuals work.

3. Investigators are required to disclose to a designated FRI official(s) a listing of SFIs (and those of his/her spouse and dependent children) that: (1) would reasonably appear to be affected by the research for which funding is sought, and (2) includes those entities whose financial interests would reasonably appear to be affected by the research.

4. PHS FCOI regulation defines a "Significant Financial Interest" as follows:

   (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. 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.

(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;
- any ownership interests in the Institution, if the Intuition is an applicant under the SBIR and STTR programs;
- 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;
- 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;

Determining the Existence and Nature of a COI

The IRB should consider the following to evaluate whether any of the disclosed interests are COIs that might affect subject safety or research objectivity:

1. Does the research involve financial relationships that could create potential or actual conflicts of interest?

    - How is the research supported or financed?
    - Where and by whom was the study designed?
    - Where and by whom will the resulting data be analyzed?

2. What interests are created by the financial relationships involved in the situation?
    - Do individuals or institutions receive any compensation that may be affected by the study outcome?
    - Do individuals or institutions involved in the research;
        - have any proprietary interests in the product, including patents, trademarks, copyrights, or licensing agreements?
        - have an equity interest in the research sponsor and, if so, is the sponsor a publicly held company or non-publicly held company?
        - receive significant payments of other sorts? (e.g., grants, compensation in the form of equipment, retainers for ongoing consultation, or honoraria)
        - receive payment per participant or incentive payments, and are those payments reasonable?

3. Given the financial relationships involved, is the institution an appropriate site for the research?

4. How should financial relationships that potentially create a conflict of interest be managed?

Eliminating, Managing, or Reducing COIs

1. COIs should be eliminated if possible. The IRB will review the Investigators' disclosures and the COI Officer's assessment of any COI, taking particular note of the impact of the COI on research integrity

and risks to research participants.

2. The IRB will assess whether the rights and welfare of human subjects would be better protected by any or a combination of the following:

   - reduction of the financial interest?
   - disclosure of the financial interest to prospective subjects?
   - separation of responsibilities for financial decisions and research decisions?
   - additional oversight or monitoring of the research?
   - an independent data and safety monitoring committee or similar monitoring body?
   - modification of role(s) of particular research staff or changes in location for certain research activities, e.g., a change of the person who seeks consent, or a change of investigator?
   - elimination of the financial interest?

3. The IRB will make the final decision about the COI and may require the following:

   a) Prohibition of the Investigators' participation in the research
   b) Management of the COI through:
      (i) Disclosure to subjects in the consent form of the COI
      (ii) Public disclosure in articles and presentations
      (iii) Limiting the role of the Investigators
      (iv) External oversight of the study
      (v) Other remediation, as required

4. The IRB will not approve research until it is satisfied that COIs have been or will be eliminated, managed, or reduced.

Disclosure to Subject in Consent Form

1. If the IRB believes that a COI cannot be eliminated, and that the COI could be considered material to a potential subject's decision-making process (i.e., when subject is assessing risks and benefits or the merits of the research itself), the investigator must inform the subject in the consent process and the form of the existence and nature of the COI. The consent process and form should also document how the COI is being managed, and what additional protections have been put in place.

2. Subject must be informed in easily understandable language.

3. Investigators should disclose to subjects only COIs, not other financial interests.

4. The dollar amount of the COI should not be disclosed to the subject.

Confidentiality of Financial Disclosure Statements

To the extent permitted by law, the IRB will maintain the confidentiality of all records of financial disclosure (see 42 CFR 50.606). For example, if any such records are sought under the Freedom of Information Act (FOIA), the custodian of the records will seek legal counsel and request that all applicable exemptions to disclosure under FOIA are asserted.

Education and Training in COI

IRB members and staff are encouraged to participate in available education and training activities related to financial conflict of interest issues including those required by the institution.

Responsibility

1. Questions regarding COI should be referred to the IRB Department.

2. IRB Administrator (or equivalent) is responsible for monitoring the COI status and disclosures of IRB members. The IRB will maintain records of financial disclosures and actions taken with respect to each COI for at least one year from the date of completion of research (see 42 CFR 50.604).

3. IRB Chairperson (or designee) is responsible for identifying COI disclosures before beginning every IRB meeting. If a member has a COI, s/he will recuse him/herself from the discussion and vote of the protocol.

4. The IRB may suspend research if they believe that an existing COI is not being reduced or managed in accordance with their directions, or a new COI is deemed to threaten the safety of the subject or the objectivity of the research, or upon discovery that the investigator failed to disclose a COI.

Applicable Regulations and Guidelines

21 CFR 56.107(e)
21 CFR 54
42 CFR 50, Subpart F
42 CFR 50.604, 606
FDA Information Sheets, FAQs, Section II, question 12