Financial Conflict of Interest Policy

Last Update: July 25, 2022

Rationale/Purpose of the Policy

It is the policy of Neurosetta to ensure that research is not biased in its design, conduct, or reporting, and to ensure especially the protection of human subjects, by requiring disclosure and review of certain outside activities, and where appropriate, by managing and reporting significant financial interests that might present a real or perceived conflict of interest with an individual's institutional responsibilities in such a manner as to appear to directly and significantly compromise the integrity of research.

Definitions

The following definitions apply solely to the use of the terms in this policy and its attendant guidelines.

Business entity
: Any corporation, partnership, proprietorship, firm, enterprise, franchise, association, trust, or legal entity other than an individual or body politic. This term also includes any entity acting as the agent of a business entity (e.g., a contract research organization). Business entities include both nonprofit and for-profit entities.

Fiduciary
: A person holding the character of a trustee, or a character analogous to that of a trustee, in respect to the trust and confidence involved in it and the scrupulous good faith and candor which it requires. A person having duty, created by his undertaking, to act primarily for another's benefit in matters connected with such undertaking.

Financial conflict of interest (FCOI)
: A significant financial interest that could directly and significant affect the design, conduct, or reporting of federally funded research or research involving human subjects.

Human subject
: A living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information. (For definitions of intervention, interaction, and private information, see the Common Rule, 45 CFR 46.102).

Immediate family
: An investigator's spouse and dependent children.

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.

Institutional responsibilities
: An investigator's professional responsibilities on behalf of Neurosetta, including research, research consultation, instruction, professional practice, extension/outreach, administrative activities, and institutional committee memberships.

Investigator
: The principal investigator or project director and any individual (e.g., company employee or as determined by inter-institutional agreements, collaborators or subrecipient awardees not employed by Neurosetta) who is responsible for the design, conduct, or reporting of research involving human subjects, federally funded research, or research proposed for federal funding.

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

Minimal risk

The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Research

A systematic investigation designed to develop or contribute to generalizable knowledge. The term encompasses basic and applied research (e.g., that which results in a published article, book or book chapter) and product development (e.g., a diagnostic test or a drug).

Senior/key personnel

For the purposes of this policy, refers to the individuals engaged in federally funded research and means the Principal Investigator and any other person identified as senior/key personnel by Neurosetta in the grant application, progress report, or any other report submitted to the Public Health Service by Neurosetta under 42 C.F.R. Part 50, Subpart F.

Significant financial interest (SFI)

Any financial interest held by an investigator (and/or his or her immediate family), or by a business entity controlled or directed by the investigator or a member of his or her immediate family, that has monetary value, whether or not the value is readily ascertainable, including:

- *Remuneration*
  - Publicly traded companies: (e.g., salary, consulting fees, honoraria, paid authorship, etc.) received from a publicly traded entity, including any foreign entities, in the twelve months preceding disclosure, and the value of any equity interest (stock, stock option, or other ownership interest) in the entity at the date of disclosure that, when aggregated, exceed $5,000.
  - Privately held companies: Remuneration, (e.g., salary, consulting fees, honoraria, paid authorship, etc.) received from a non-publicly traded entity, including any foreign entities, of greater than $5,000 in the twelve months preceding the disclosure.
- *Any equity interest* (e.g., stock, stock option, or other ownership interest) in a non-publicly traded entity, including any foreign entities.
- *Royalty income* from intellectual property rights not arising out of Neurosetta employment, which are not assigned to organizations created to manage such rights on behalf of the Neurosetta.
- *Reimbursed or sponsored travel* related to **institutional responsibilities** that is not reimbursed or sponsored by a U.S. government agency, a U.S. university, or an academic teaching hospital, medical center, or research institute that is affiliated with a U.S. university.
- *Service in positions with fiduciary responsibility*, including senior managers (e.g., presidents, vice presidents, etc.) and members of boards of directors, whether or not the **investigator** receives compensation for such service.

Subrecipient

An entity or individual named on a subcontract from Neurosetta on a federally funded award or human subjects research proposal.

Technology

Any diagnostic, therapeutic, medical, or surgical procedure and any process, method, compound, drug, or device.

Financial Conflict of Interest Policy

Last Update: July 25, 2022

Scope

This policy applies to investigators engaging in - or proposing to engage in - federally funded research or any research involving human subjects. Generally, the Neurosetta Conflict of Interest Committee does not review or manage outside activities of individuals who are not employeed by Neurosetta. However, in accord with Federal regulations, when Neurosetta carries out federally funded research through subcontractors, subrecipients, or collaborators, the terms of the agreement between the parties will dictate whether this policy or the policy of the other party applies to the subrecipient investigator(s).

Policy

I. Relationship to Similar Policies and Documents

Neurosetta has adopted this policy and its attendant guidelines to incorporate the requirements set forth in the regulations promulgated by the US Department of Health and Human Services (42 C.F.R. § 50, Subpart F and 45 C.F.R. § 94) and the National Science Foundation (NSF 510) to promote objectivity in research.

II. Background

Neurosetta encourages its employees to engage in research that furthers its mission of reducing the prevalence of neurodevelopmental disorders by ensuring chemical and drug safety and enabling precision medicine drug discovery. This includes research funded through federal grants that make use of Neurosetta’s proprietary technology or by developing novel technologies. Since these activities may result in financial gain to investigators, Neuroestta has the responsibility to identify those interactions that create potential conflicts of interest and to manage those conflicts in a way that ensures the integrity of Neurosetta's core activities and values.

According to the National Institutes of Health, a potential financial conflict of interest exists when an investigator has significant financial interests that could lead an independent observer to reasonably question whether the design, conduct, or reporting of research might be influenced by the possibility of personal gain to the individual or to his or her immediate family. Others define conflict of interest situations in terms of obligations. Two activities may interact such that judgment in one activity may be, or may seem to be, influenced by the other activity. Together, these two definitions identify important elements of conflicts of interest. Conflicts of interest:

A. represent a state of affairs, not behavior,
B. frequently involve perceptions, and
C. are judged by others, not by those directly involved.

Significant financial gains are considered to be of ultimate relevance in the current context for understanding conflicts of interest because money is recognized by the general public to be a potent motivator -- one that is easily understood, easily quantified, and discretionary. While the focus of conflict of interest considerations is financial gain, other relevant interests inherent in the biotechnology industry, including prestige, promotion, grants, and publications, can also potentially exert influence over research activities.

Because financial conflicts of interest could contribute to bias in research reporting, influence judgment, reduce free exchange of research findings, pose a threat to research integrity, and compromise the protection of human subjects, Neurosetta has

legal and ethical responsibilities to review and manage potential financial conflicts of interest in research.

III. Requirements

A. Training

A. Investigators must undergo training on conflict of interest regulations, as well as Neurosetta's policy, prior to the expenditure of funds in any federally funded research or participation in human subjects research. Training must be renewed at least every four years thereafter. Investigators newly hired to Neurosetta must undergo Neurosetta's training prior to the expenditure of funds on a federally funded research project or participation in human subjects research. Retraining will be necessary should Neurosetta revise its policy concerning conflicts of interests in a manner that impacts the requirements of investigators, or in instances of noncompliance with this policy or a management plan.

B. Disclosure

A. Investigators engaging in, or proposing to engage in, federally funded research or research involving human subjects are required to report all significant financial interests held by themselves or their immediate families that reasonably appear to be related to the investigator's institutional responsibilities.

B. Significant financial interests are to be reported on Financial Conflict of Interest (FCOI) Activities Reports annually, and must be completed no later than the time of application for federally funded research. In addition, investigators must update their FCOI Activities Reports within 30 days of acquiring or discovering a new significant financial interest.

C. Principal Investigators conducting research involving human subjects must submit information to IRBs in accordance with the guidelines.

D. Investigators receiving funding from the federal agencies must also disclose the occurrence of travel reimbursed or sponsored by an outside organization, including all foreign entities. Per NIH Guide Notice NOT-OD-13-004, Investigators' initial disclosures must include all reimbursed and sponsored travel over the previous twelve-month period. After the initial disclosure, Investigators are required to update FCOI Activities Reports within 30 days of such travel. As with other significant financial interests, this travel disclosure requirement also applies to reimbursed or sponsored travel by members of an Investigator's immediate family. This disclosure requirement includes all foreign entities, including academic institutions, but does not apply to travel that is reimbursed or sponsored by a U.S. Federal, state, or local government agency, a U.S. institution of higher education, a U.S. academic teaching hospital or a medical center, or a research institute that is affiliated with a U.S. institution of higher education.

C. Review and Management of Relationships with External Entities

A. Neurosetta has an obligation to manage any financial conflicts of interest as part of ensuring the integrity of research and protection of human subjects. To meet this obligation, Neurosetta directs the COI Committee to review all annual FCOI Activities Reports, updates to such reports, and any protocol-specific FCOI Activities Reports made by researchers conducting or proposing to conduct federally funded research or conducting research involving human subjects, to implement

management plans, and to recommend appropriate actions to manage any financial conflicts of interest to reviewing IRBs. If an activity meets the definition of SFI, the COI Committee makes a recommendation of management or no management and assigns a Committee member to conduct a review. During the review, the assigned COI Committee member (1) determines whether there is a nexus between an investigator's research and the significant financial interest; (2) determines whether a financial conflict of interest (FCOI) exists; and (3) make a management recommendation. The full committee then votes by simple majority to confirm the recommendation or suggest a change. If it is determined by the committee that an FCOI exists, a management plan is assigned to an investigator that specifies actions that have been, or will be, taken to manage the FCOI. A significant financial interest is a financial conflict of interest when the significant financial interest could directly and significantly have a material effect on the design, conduct, or reporting of research. Reviewers may consider the stage of the research, its commercial potential, magnitude of risk to participants in studies, and other factors when making a determination about the existence of a financial conflict of interest.

B. An individual with a management plan for an external entity cannot serve as an investigator on a human subjects protocol considered by a reviewing IRB to pose greater than minimal risk to research participants if the managed entity (a) sponsors the study, or (b) owns or licenses a technology used in the study.
   i. An investigator may apply to the COI Committee for an exception to this prohibition based on compelling circumstances.
   ii. If a reviewing IRB determines that a study poses no greater than minimal risks to subjects, investigators will generally be permitted to participate in the study subject to limitations set forth in the conflict of interest management plan.
   iii. A reviewing IRB has the authority to impose additional requirements that the IRB determines necessary to protect research participants.

D. Payments from Business Entities

A. Neurosetta prohibits payments to individuals from company accounts or directly or indirectly from business entities for particular research results or for research outcomes related to human subject protocols conducted at or through Neurosetta. Further, neither investigators nor their immediate families may receive any personal incentives from company accounts or directly or indirectly from business entities, such as recruitment incentives, performance incentives, fellowships, or other research support, except through an agreement entered into by the company for sponsored research. Neurosetta only permits payments for subject enrollment, or for the referral of potential subjects to human subjects studies, when all of the following are present:
   i. The payment reasonably relates to costs incurred, as specified in research agreements between the sponsor and the Neurosetta.
   ii. The payment reflects the fair market value of services performed.
   iii. The payment is commensurate with the efforts of the investigator(s) performing the research.

E. Public accessibility of information concerning individuals receiving funding from the Public Health Service

A. In accordance with Federal regulations, certain information about identified conflicts of interest of investigators who are named as senior/key personnel on research funded by the Public Health Service must be made available to the public.

F. Reports to Funding Agencies

A. As a condition of eligibility to receive grants or cooperative agreements for research from the Public Health Service, Neurosetta must provide reports on financial conflicts of interest to the appropriate PHS Awarding Component in the time and manner specified in the regulations and outlined in the Guidance Document.

G. Reconsideration of COI Committee Decisions

A. An investigator may request reconsideration of any COI Committee determination that affects his or her ability to participate, or conditions of participation, in federally funded or human subjects research. Investigators have twenty (20) business days from receipt of notification from the COI Committee or a Neurosetta IRB conveying the determination to request reconsideration. Individuals must make requests in writing.

H. Ongoing Monitoring

A. Neurosetta monitors compliance with management plans on an ongoing basis.

I. Noncompliance

A. Deliberate misrepresentation of information to the COI Committee or an IRB or failure to comply with the terms of this policy or a management plan may result in sanctions including disciplinary actions up to and including termination and/or loss of privilege to serve as an investigator on federally funded research projects or human subjects research protocols.

B. In the case of research funded by the Public Health Service, instances of noncompliance require Neurosetta to conduct a retrospective review. The review will determine whether any PHS-funded research conducted during the period of noncompliance was biased in its design, conduct, or reporting. If the review makes a determination of bias, Neurosetta will notify the PHS of its findings, along with a mitigation report that includes: (1) the key elements documented in the retrospective review; (2) a description of the impact of the bias on the research project; and (3) UW–Madison's plan of action for eliminating and mitigating the effects of the bias.

C. In any case in which the Department of Health and Human Services determines that a PHS-funded project of clinical research whose purposes 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 as required by federal regulations, the Investigator shall be required to disclose the FCOI in each public presentation of the results of the research and to request an addendum to previously published presentations to indicate the existence of the FCOI.

J. Records Retention

A. UW–Madison must maintain records of all financial disclosures and all actions taken with respect to any conflict of interest covered by this policy 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. § 74.53(b) and 92.42(b) for different situations.

IV. Financial Interests Arising from Ordinary Professional Activities

A. Significant financial interests do not include the following:
   A. Salary, royalties, or other remuneration received from Neurosetta
   B. Royalty income from intellectual property rights arising out of Neurosetta employment that are assigned to organizations created to manage such rights on behalf of the Neurosetta.
   C. Income from investment vehicles, such as mutual funds and retirement accounts, as long as the investigator does not control the investment decisions made in these vehicles.
   D. Income from seminars, lectures, or teaching engagements sponsored by a domestic government agency, a university, an academic teaching hospital, a medical center, or a research institute that is affiliated with a university.
   E. Income from service on advisory committees or review panels for a domestic government agency, a university, an academic teaching hospital, a medical center, or a research institute that is affiliated with a university.
   F. Travel related to institutional responsibilities that is reimbursed or sponsored by a domestic government agency, a university, an academic teaching hospital, a medical center, or a research institute that is affiliated with a university.