

Instructions and rules for financial conflicts of interest in PHS funded projects at Karolinska Institutet (“FCOI-Policy”)

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**Karolinska
Institutet**



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1. Introduction

In the U.S., the National Institutes of Health (NIH) provides research grants through the federal governmental authorities within Public Health Services (PHS). The PHS comprises various agencies, including, but not limited to:

- Agency for Healthcare Research and Quality (AHRQ)
- Agency for Toxic Substances and Disease Registry (ATSDR)
- Centers for Disease Control and Prevention (CDC)
- Food and Drug Administration (FDA)
- Health Resources and Services Administration (HRSA)
- Indian Health Service (IHS)
- Office of Global Affairs (OGA)
- Substance Abuse and Mental Health Services Administration (SAMHSA)
- Office of the Assistant Secretary for Preparedness and Response (OASPR)
- Office of the Assistance Secretary for Health (OASH)

In cases where researchers at Karolinska Institutet (KI) receive PHS funding, there are strict requirements enforced that involve the objectivity and independence of researchers' financial ties to businesses that could influence the design, conduct or reporting of research. As KI is the recipient of PHS grants, the institution has established instructions, rules and procedures in compliance to U.S. federal regulations that require KI principal investigators (including the PI's spouse and/or dependent children) to disclose compensation and paid incentives for their financial investments. KI has developed the respective rules and instructions for identifying, managing, and reporting financial conflicts of interests that comply to U.S. federal regulations stipulated in the "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought (Title 42 CFR 50, Subpart F).

This is done specifically for PHS funded projects in parallel to other KI reporting requirements for conflicts of interest.

2. Purpose

The purpose of these rules and instructions are to promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct, or reporting of funded research, grants or cooperative agreements will be free from bias resulting from the investigator's financial conflicts of interest (including the investigator's spouse and/or dependent children).

These rules and instructions are in accordance with the U.S. federal regulations stipulated in "Title 42 CFR 50, Subpart F":

- a) Implement requirements of the federal regulations governing the University's and each investigator's responsibilities for promoting objectivity in Public Health Service (PHS) funded research.

- b) Publish and disseminate standards that provide a reasonable expectation that the design, conduct, and reporting of research under PHS-funded grants, sub grants or cooperative agreements will be free from bias resulting from Investigator financial conflicts of interest.

3. Scope

The rules and instructions stipulated in this document apply to all investigators and all research activities conducted at KI, where such activities are funded by PHS.

The stipulated rules and instructions are to be construed in accordance with the US federal regulations set forth herein and deemed to include all regulation requirements set forth by PHS directives.

4. Definitions

Disclosure of significant financial interests: An investigator's disclosure of significant financial interests to KI.

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: KI's report of a financial conflict of interest to an organization unit of the PHS that provides funding for the research.

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

Institutional responsibilities: An investigator's professional responsibilities on behalf of KI, and as defined in this document, which may include for example: activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Boards or Data and Safety Monitoring Boards.

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 PHS funded research, or proposed for such funding, which may include, for example, collaborators or consultants.

Key personnel: The investigator and any other person identified as senior or key personnel by KI in the grant application, progress report, or any other report submitted to the PHS by the Institution under Title 42 CFR 50, Subpart F (Promoting Objectivity in Research) of the Code of Federal Regulations.

PD/PI: A project director or principal investigator of a PHS-funded research project; the PD/PI is included in the definitions of senior/key personnel and investigator under this subpart.

Subrecipient: An organization or researcher that participates in research with the awardee Institution (e.g. subcontractors or consortium members).

Management: An action plan to address a FCOI, which can include strategies for reducing or eliminating the financial conflict of interest, to ensure that the design, conduct, and reporting of research will be free from bias.

PHS: Is the acronym for 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.

Grants Office (GO): KI's administrative unit charged with monitoring compliance with FCOI management plans.

Research: Scientific experiments, theoretical work, or scientific studies through observation, to which the work or studies are done to acquire new knowledge and developed on a scientific basis. The term encompasses basic and applied research (e.g. a published article, book or book chapter) and product development (e.g. a diagnostic test or drug). As used in this document, the term includes any such activity for which research funding is available from the PHS through a grant or cooperative agreement, including a research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or research resources award.

Significant financial interest (SFI): A financial interest consisting of **one or more** of the following interests of the investigator (including investigator's spouse, domestic partner, and dependent children) that reasonably appears to be related to the investigator's Institutional Responsibilities:

- a) 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.
- b) 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).
- c) Intellectual property rights and interests (e.g. patents, copyrights) upon receipt of income related to such rights and interests.
- d) 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.

Exceptions to significant financial interests: SFIs **do not** include the following type of financial interests:

- a) Salary, royalties, or other remuneration paid by the University to the Investigator if the investigator is currently employed or otherwise appointed by the University.
- b) Intellectual property rights assigned to the University and agreements to share in royalties related to such rights.
- c) 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.
- d) 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.
- e) 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.
- f) 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.

5. KI and Investigator Responsibilities

These instructions outline the rules and procedures that will be followed as per regulations (Title 42 CFR 50, Subpart F) for PHS funded research.

5.1. Investigator Responsibilities

Investigators are responsible for:

- Disclosing all significant financial interests.
- Providing updates to disclosed information as needed.
- If acting as the PI/PD, providing a list of individuals who meet the definition of “investigator” within the required disclosure timeline.
- Completing all required training and education.
- Completing the annual disclosure form even if they have no financial interests to report.
- Ensuring that an updated FCOI in Research Disclosure is on file at the time of Ethical Review Board or the Institutional Animal Care and Use Committee (IACUC) approval for any new research proposals.

5.2. Institutional Responsibilities

KI is responsible for:

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- Maintaining up-to-date, written, enforced instructions and rules on FCOI that complies with regulations stipulated in '42 CFR 50, Subpart F', and make them available via KI's publicly accessible Web site.
 - Informing each investigators of KI's rules and instructions on FCOI, the investigator's responsibilities regarding disclosure of SFIs, and of these regulations, and require each investigator to complete compulsory training prior to engaging in research related to any PHS-funded grant and at least every four years.
 - If KI carries out the PHS-funded research through a subrecipient (e.g. subcontractors or consortium members), the Institution (awardee Institution) will take reasonable steps to ensure that any subrecipient investigator complies with federal regulations stipulated in '42 CFR 50, Subpart F'.
 - Designating KI official(s) to solicit and review disclosures of SFIs from each investigator who is planning to participate in, or is participating in, the PHS-funded research.
 - Requiring each investigator who is planning to participate in the PHS-funded research to:
 - Disclose to KI's designated official(s) the investigator's significant financial interests (including investigator's spouse and dependent children) no later than the time of application for PHS-funded research.
 - Submit an updated disclosure of SFIs at least annually, in accordance with the specific time period prescribed by KI, during the period of the award.
 - Submit an updated disclosure of SFIs within thirty days of discovering or acquiring (e.g. through purchase, marriage, or inheritance) a new significant financial interest.
 - Providing guidelines for KI's designated official(s) to determine whether an investigator's SFI is related to PHS-funded research and, if so related, whether the SFI is a financial conflict of interest.
 - Implementing actions as deemed necessary to manage FCOI, including any financial conflicts of a subrecipient investigator, through the implementation of a management plan.
 - Providing initial and ongoing FCOI reports to the PHS as required.
 - Maintaining records relating to all investigator disclosures of financial interests and KI's review of, and response to, such disclosures (whether or not a disclosure resulted in KI's determination of a FCOI) and all actions under KI's policy or retrospective review, if applicable, for at least three years from the date the final expenditures report is submitted to the PHS or, where applicable.
 - Establishing adequate enforcement mechanisms and provide for employee sanctions or other administrative actions to ensure investigator compliance as appropriate.
 - Certifying, where applicable, that KI's policy and procedures are up-to-date and (i) enforce through an administrative process to identify and manage FCOIs in all PHS funded projects; (ii) enforce compliance with

the disclosure of SFIs; (iii) manage initial and ongoing FCOI reports; (iv) provide information promptly upon request to HHS in terms of disclosures of financial interests, KI's review of, and response to, such disclosures in the determination of FCOI; and (v) fully comply with the requirements stipulated in '42 CFR 50, Subpart F'.

6. Procedures

At KI, there is a FCOI committee for the identification, investigation, management and reporting of FCOI in PHS-funded research. The FCOI Committee consists of the University Director, Head of Legal Department, Vice President of Research and Head of the GO Department. The Head of Department affected by each case will also be co-opted to the committee.

6.1. Disclosure of Significant Financial Interests

Researchers conducting research at KI must disclose all significant financial interests (SFIs), which are relevant to the investigator's institutional research responsibilities, to GO before participating in PHS-funded projects. The application must have been received no later than the date of the research proposal submission. The investigator must also disclose all SFIs within 30 days after he/she becomes aware of a new SFI or after a financial conflict of interest has been eliminated for ongoing PHS funded research. Disclosure of SFIs must be reported annually. Investigators are responsible for completing the annual disclosure form even if they have no financial interest to report. New investigators participating in an ongoing PHS funded project are also required to disclose SFIs to GO within 30 days of joining the research project

6.2. Process of Reviewing Significant Financial Interests

GO performs an initial review of all SFI disclosures. If necessary, GO will contact the investigator for additional information. GO determines which SFI cases may qualify as being a potential FCOI and refers the case to the FCOI Committee for review. The determination of a FCOI will be based on the following criteria:

- I. Nature and extent of the financial interest in the relationship of the investigator/relative and the external organization.
- II. Terms and conditions of sponsored project agreements that can reduce or increase the risks
- III. Impact on integrity of research data.
- IV. Risks to rights and safety of animal and/or human research subjects.
- V. Potential risks of conflicts of interest.

An FCOI exists when the FCOI Committee at KI reasonably determines that the SFI could directly and significantly affect the design, conduct, or reporting of the PHS funded research.

6.2.1. Review of New Significant Financial Interests

If an investigator in an ongoing PHS-funded project reports a new SFI to KI, the FCOI Committee will review the information within 60 days to determine if the SFI is related to PHS-funded research and whether it constitutes an FCOI. In cases where a new FCOI is identified, KI will develop a management plan (section 6.3) and report the case to the funder.

6.2.2. Review of Existing Significant Financial Interests

In cases where KI identifies an existing SFI that was not disclosed timely by an investigator during an ongoing PHS funded project, the FCOI Committee will review the disclosure within 60 days to determine if the SFI is related to PHS funded research and whether it constitutes a FCOI. In cases where FCOI is identified, KI will develop a management plan (Section 6.3) and report the case to the PHS funder.

6.2.3. Retrospective Review of Significant Financial Interests

There are certain events that would constitute noncompliance of KI's FCOI instructions, rules, and procedures, thus, requiring a retrospective review. These include:

- The investigator fails to disclose an SFI that was determined to be a FCOI by KI.
- KI fails to review and manage a FCOI.
- The investigator fails to comply with a FCOI management plan.

If any one of these scenarios occurs, the FCOI Committee will determine noncompliance and 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. A retrospective review will be completed within 120 days of determining noncompliance.

6.3. Management of Financial Conflicts of Interest

In cases where FCOI is identified, a management plan will be developed by the FCOI Committee in collaboration with relevant researchers and institutions. The terms of the management plan will be determined in accordance with national law.

6.4. Reporting Requirements to NIH

Prior to the disbursement of research funding within the PHS-funded project, KI will, upon request, provide a FCOI report regarding all SFIs that prove to be a FCOI. KI must provide a FCOI report within 60 days from the date of a new SFI disclosure that is determined to be a FCOI, a new investigator with an identified FCOI begins participating in the project, or when KI identifies a FCOI not previously disclosed. The report must include the grant/contract number, PD/PI and name of investigator with FCOI.

6.4.1. FCOI report

In the FCOI report, KI must specify the nature of the FCOI (e.g. equity, consulting fees, travel reimbursement or honoraria). The report will also include the following information:

- Value of the financial interest or a statement that the interest is one whose value cannot be determined through reference to public prices or other reasonable measures of fair market value.
- Description of how FCOI relates to PHS-funded research and the basis for determining that the financial interest conflicts with such research.
- Summary of the management plan.

6.4.2. Annual FCOI report

KI will, upon request, provide annual updates of the report for the duration of the research project. The annual report will include the status of the FCOI, changes to the management plan and justification if FCOI no longer exists.

6.4.3. Updating the FCOI report

Based on the results of the retrospective review, KI will, if appropriate, update the previously submitted FCOI report, specifying the actions that will be taken to manage the financial conflict of interest going forward. Key elements that will be included in the updated report include the grant/project number, project title, PD/PI, name of investigator with FCOI, name of entity for FCOI, reasons for the retrospective review, methodology utilized for the retrospective review, findings and conclusions of the review.

If bias is identified in the retrospective review, in accordance with US federal regulations, KI must submit a mitigation report. The mitigation report will consist of key elements stipulated in the retrospective review above, and a description of the impact of the bias on the research project and KI's action plan to eliminate or mitigate the effect of the biased actions taken. Depending on the severity of the financial conflict of interest identified, KI may determine that additional interim measures are necessary with respect to the investigator's participation in the PHS-funded project between the date of determination of the FCOI or the investigator's noncompliance and the completion of KI's retrospective review.

Reports will be submitted to the NIH funder by uploading an initial (original) and annual FCOI report using eRA commons as required by US federal regulations.

6.5. Subrecipient Requirements

If a research project involves subrecipients, the subrecipient institution must provide written assurance that they have a (local) policy or equivalent for managing financial conflicts of interest that complies with all applicable US federal regulations in accordance with PHS. If the subrecipient does not have its own policy, a written agreement must be drawn up between KI and the subrecipient institution stating that KI's rules and instructions will also apply to the subrecipient.

6.6. Training Requirements

All KI investigators receiving PHS funding must complete mandatory FCOI training during the following intervals:

- Prior to engaging in PHS-funded research and at least once every four years thereafter.
- When these rules and instructions are revised in any manner that affects the requirements of investigators.
- When an investigator is new to KI and will take part in a PHS-funded project.
- When an investigator is noncompliant with KI's rules and instructions or management plan.

This training is primarily conducted via the CITI Program web-training course to which KI provides for all researchers.

6.7. Documentation

KI will preserve all documentation that is part of the implementation of these rules and instructions in accordance with Swedish applicable law.

6.8. Public Accessibility Requirements

This document will be published on KI's public website. In addition, information concerning identified FCOIs held by senior/key personnel will be made available upon request via an email response within five business days.

A written response will include:

- Name of Senior/Key personnel
- Senior/Key personnel's role in the research project
- Name of the entity in which the FCOI is held
- Nature of the FCOI
- Approximate dollar value of the FCOI or a statement that the value cannot be readily determined