DZNE
Deutsches Zentrum für Neurodegenerative Erkrankungen in der Helmholtz-Gemeinschaft

DZNE Policy on US Public Health Service Regulation of Financial Conflicts of Interest

Internal Regulation/Policy on PHS FCOI
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Introduction and background

The United States of America (US) regulation on Promoting Objectivity in Research (42 Code of Federal Regulation (CFR) Part 50 Subpart F; in the following "FCOI-regulation") promotes objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct, and reporting of research funded under Public Health Service (PHS) grants or cooperative agreements will be free from bias resulting from Investigator financial conflicts of interest (FCOI).

The FCOI-regulation is applicable to the DZNE when the DZNE is applying for or receives PHS research funding by means of a grant or cooperative agreement, or funding from an organization that requires adherence to the FCOI regulation. Thus, the DZNE and each Investigator (as defined under A.) have to comply with the

regulation whenever they are planning to participate or are already participating in such research.

A. Definitions

(1) **"FCOI-regulation"** means 42 Code of Federal Regulation (CFR) Part 50 Subpart F.

(2) **"PHS"** means 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), Food and Drug Administration (FDA), Agency for Healthcare Research and Quality (AHRQ), Agency for Toxic Substances and Disease Registry (ATSDR) and the Centers for Disease Control (CDC).

(3) **"PHS Awarding Component"** means the organizational unit of the PHS that funds the research that is subject to this Internal Regulation/Policy. The term **"PHS-funded"** also includes activites supported by non-PHS organizations which require adherence to the PHS FCOI regulation.

(4) **"Investigator"** means 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 PHS-funded research, or research proposed for such funding, which may include, for example, collaborators or consultants**.

(5) **"PD/PI"** means 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 Internal Regulation/Policy.

(6) **"Senior/key personnel"** means the PD/PI and any other person identified as senior/key personnel by the DZNE in the grant application, progress report, or any other report submitted to the PHS by the DZNE under this Internal Regulation/Policy.

(7) **"Financial interest"** means anything of monetary value, whether or not the value is readily ascertainable.

(8) **"Significant financial interest"** (SFI):

a. means a financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse/registered domestic partner ("eingetragene(r) Lebensparter(in)") and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

(i) With regard to any publicly traded entity, a SFI 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 SFI 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/registered domestic partner ("eingetragene(r) Lebensparter(in)") 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.

b. means certain types of reimbursed or sponsored travel related to the Investigator's institutional responsibilities (*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).

c. The term SFI does not include the following types of financial interests:

- salary, royalties, or other remuneration paid by the DZNE to the Investigator if the Investigator is currently employed or otherwise appointed by the DZNE, including intellectual property rights assigned to the DZNE 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 US 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 and – for funding from other countries – domestic institutions equivalent to the US institutions listed above;
- or income from service on advisory committees or review panels for a US 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 and – for other countries – domestic institutions equivalent to the US institutions above.

(9) **"Dependent child"** means any child who is under the age of 19, under the age of 24 and a full-time student, or any age and totally and permanently disabled; and who has lived in the investigator's residence for at least six months prior to any disclosure of financial interests.

(10) **"Financial conflict of interest (FCOI)"** means a significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

(11) **"Disclosure of significant financial interests"** means an Investigator's disclosure of significant financial interests to the DZNE.

(12) **"Institutional responsibilities"** means an Investigator's professional responsibilities on behalf of the DZNE, which may include for example: activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards.

(13) **"Research"** means a systematic investigation, study or experiment designed to develop or contribute to generalizable knowledge relating broadly to public health, including behavioral and social-sciences research. 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). The term includes any such activity for which research funding is available from a PHS Awarding Component through a grant or cooperative agreement, whether authorized under the PHS Act or other statutory authority, such as a research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or research resources award.

(14) **"Manage"** means taking action to address a FCOI, which can include reducing or eliminating the FCOI, to ensure, to the extent possible, that the design, conduct, and reporting of research will be free from bias.

(15) **"FCOI report"** means the DZNE's report of a FCOI to a PHS Awarding Component.

(16) **"HHS"** means the US Department of Health and Human Services, and any components of the Department to which the authority involved may be delegated.

(17) **"Institution"** means any domestic or foreign, public or private, entity or organization (excluding a Federal agency) that is applying for, or that receives, PHS research funding.

B. General responsibilities of the DZNE

§ 1 Policy on FCOI

The DZNE maintains an up-to date, written enforced policy on FCOI by the Internal Regulation/Policy on PHS FCOI at hand, which is available via a publicly accessible Web site.

§ 2 Investigator's Training

The DZNE requires each Investigator to complete training regarding the Internal Regulation/Policy on PHS FCOI, the Investigator's responsibilities regarding disclosure of SFI, and the FCOI-regulations prior to engaging in research related to any PHS-funded grant and at least every four years, and immediately, if the following circumstances apply:

- The DZNE revises its financial conflict of interest policies or procedures in any manner that affects the requirements of Investigators;

- An Investigator is new to the DZNE; or
- The DZNE finds that an Investigator is not in compliance with the Internal Regulation/Policy on PHS FCOI or a management plan.

§ 3 Subrecipients

(1) If the DZNE carries out the PHS-funded research through a subrecipient (e.g., subcontractors or consortium members), the DZNE takes reasonable steps to ensure that any subrecipient Investigator complies with the FCOI-regulation by:
- incorporating as part of a written agreement with the subrecipient terms that establish whether the Internal Regulation/Policy on PHS FCOI of the DZNE or the financial conficts of interest policy of the subrecipient will apply to the subrecipient's Investigators.
- providing FCOI reports to the PHS Awarding Component regarding all FCOI of all subrecipient Investigators consistent with the FCOI-regulation, i.e., prior to the expenditure of funds and within 60 days of any subsequently identified FCOI.

(2) If the subrecipient's Investigators must comply with the DZNE's Internal Regulation/Policy on PHS FCOI, the agreement specifies time period(s) for the subrecipient to submit all Investigator disclosures of SFI to the DZNE. Such time period(s) will be sufficient to enable the DZNE to comply in a timely manner with its review, management and reporting obligations under this subpart.

(3) If the subrecipient's Investigators must comply with the subrecipient's financial conflicts of interest policy, the subrecipient certifies as part of the agreement that its policy complies with the FCOI-regulation. If the subrecipient cannot provide such certification, the agreement states that subrecipient Investigators are subject to the DZNE's Internal Regulation/Policy on PHS FCOI for disclosing SFI that are directly related to the subrecipient's work for the DZNE. Additionally, the agreement specifies time period(s) for the subrecipient to report all identified FCOIs to the DZNE. Such time period(s) will be sufficient to enable the DZNE to provide timely FCOI reports, as necessary, to the PHS as required by the FCOI-regulation.

§ 4 Institutional official(s)

(1) The DZNE designates an institutional 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. The institutional official(s) determines whether an Investigator's SFI is related to PHS-funded research and, if so related, whether the SFI is a FCOI.

(2) When determining the questions mentioned in para 1 sentence 2, the institutional official(s) follow the following guidelines, while involving the Investigator, if appropriate:

a. An Investigator's SFI is related to PHS-funded research when the SFI could be affected by the PHS-funded research or is in an entity whose financial interest could be affected by the research.

b. A FCOI exists when the SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded research.

§ 5 Records

The DZNE maintains records relating to all Investigator disclosures of financial interests and the Institution's review of, and response to, such disclosures and all actions under the Internal Regulation/Policy on PHS FCOI or retrospective review, if applicable, for at least three years from the date the final expenditures report is submitted to the PHS.

§ 6 Certification in each application

The DZNE certifies in each application for funding to which this the FCOI-regulation applies, that the DZNE

- has in effect an up-to-date, written, and enforced administrative process to identify and manage FCOIs with respect to all research projects for which funding is sought or received from the PHS;
- promotes and enforces Investigator compliance with the FCOI-regulation's requirements including those pertaining to disclosure of SFI;
- manages FCOIs and provides initial and ongoing FCOI reports to the PHS Awarding Component consistent with the FCOI-regulation;
- agrees to make information available, promptly upon request, to the HHS relating to any Investigator disclosure of financial interests and the DZNE's review of, and response to such disclosure; and
- fully complies with the requirements of the FCOI-regulation.

C. Responsibilities of the Investigator

§ 1 Disclosure of SFIs

(1) Each Investigator who is planning to participate in PHS-funded research has to disclose to the DZNE official(s) the Investigator's SFI (and those of the Investigator's spouse/registered domestic partner ("eingetragene(r) Lebensparter(in)") and dependent children) no later than the time of application for PHS-funded research.

(2) The Investigator must also 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. This disclosure includes the purpose of the trip, the identity of the sponsor/organizer, the destination and the duration. Additional information may be requested by the institutional official(s), including a determination or disclosure of monetary value. There is no obligation to disclose travel that is reimbursed or sponsored by a US 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 and – for other countries - domestic institutions equivalent to the US institutions listed above.

(3) Each Investigator who is participating in the PHS-funded research has to submit an updated disclosure of SFIs to the DZNE official(s)

- annually during the period of the award. Such disclosure includes any information that was not disclosed initially to the DZNE or in a subsequent disclosure of SFIs (e.g., any FCOIs identified on a PHS-funded project that was transferred from another Institution), and includes updated information regarding any previously disclosed SFI (e.g., the updated value of a previously disclosed equity interest).
- within thirty days of discovering or acquiring a new SFI (e.g., through purchase, marriage, or inheritance).

§ 2 Full Compliance

The Investigator has to fully comply with the Internal Regulation/Policy at hand and respective administrative procedures of the DZNE related to FCOI.

D. Enforcement mechanisms / Sanctions

(1) With announcement of this Internal Regulation/Policy compliance is compulsory.

(2) In case the Investigator does not comply with the Internal Regulation/Policy at hand, the DZNE can impose sanctions, including, but not limited to the following:

- the Institutional official(s) report the non-compliance to the Executive Board;
- the Investigator will be deemed ineligible to be principal investigator on PHS-projects;
- the Investigator will be deemed ineligible to be principal investigator on third party-funded projects;
- the Investigator will be deemed ineligible to enter into technology transfer agreements;
- disciplinary personnel measures;
- restitution of DZNE financial losses.

E. Management of FCOI

The DZNE takes the following actions as necessary to manage FCOIs, including any FCOIs of a subrecipient Investigator.

§ 1 Management of timely disclosed SFI

(1) Prior to the expenditure of any funds under a PHS-funded research project, the DZNE institutional official(s)

a. review all Investigator disclosures of SFIs;
b. determine whether any SFI is related to PHS-funded research;
c. determine whether a FCOI exists;
d. and, if so, develop and implement a management plan that specifies the actions that have been, and will be, taken to manage such FCOI.

(2) Following the FCOI-regulation examples of conditions or restrictions that might be imposed to manage a FCOI includes, but are not limited to:

a. public disclosure of FCOI,
b. disclosure of FCOI to probands,

c. 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;
d. modification of the research plan;
e. change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;
f. reduction or elimination of the financial interest (e.g. sale of an equity interest); or
g. severance of relationships that create FCOI.

For the DZNE conditions or restrictions that would be adapted include, but are not limited to:

a. public disclosure of FCOI by DZNE upon request (see § 4), and by the study investigators/personnel in publications and/or presentations of the research work;
b. disclosure of FCOI to potential study subjects during the consent process;
c. 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;
d. modification of the research plan;
e. change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;
f. reduction or elimination of the financial interest (e.g. sale of an equity interest); or
g. severance of relationships that create FCOI.

(3) Whenever, in the course of an ongoing PHS-funded research project, an Investigator who is new to participating in the research project discloses a SFI or an existing Investigator discloses a new SFI to the DZNE, the DZNE official(s) within 60 days take the measures named under para (1) with at least an interim management plan.

§ 2 Management of not timely disclosed/ not previously reviewed SFI

(1) Whenever the DZNE identifies a SFI that was not disclosed timely by an Investigator or, for whatever reason, was not previously reviewed by the DZNE during an ongoing PHS-funded research project, the DZNE official(s) take the measures named under § 1 para (1) with at least an interim management plan within 60 days.

(2) Additionally, whenever a FCOI is not identified or managed in time for whatever reason, the DZNE completes within 120 days of the DZNE's determination of noncompliance 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 noncompliance, was biased in the design, conduct, or reporting of such research. The documentation of this retrospective review includes:

- Project number;
- Project title;
- PD/PI or contact PD/PI if a multiple PD/PI model is used;
- Name of the Investigator with the FCOI;
- Name of the entity with which the Investigator has a FCOI;
- Reason(s) for the retrospective review;
- Detailed methodology used for the retrospective review (e.g., methodology of the review process, composition of the review panel, documents reviewed);
- Findings of the review; and
- Conclusions of the review.

Based on the results of the retrospective review the DZNE

- updates the previously submitted FCOI report, if appropriate;
- specifies the actions that will be taken to manage the FCOI; and
- if bias is found, promptly notifies the PHS Awarding Component and submits a mitigation report to the PHS Awarding Component including the key elements documented in the retrospective review mentioned above and a description of the impact of the bias on the research project and the action plan of the DZNE to eliminate or mitigate the effect of the bias (e.g. impact on the research project; extent of harm done, including any qualitative and quantitative date to support any actual or future harm; analysis of whether the research project is salvageable);
- thereafter the DZNE reports annually as specified under F para 4.

§ 3 Monitoring of Investigator's compliance with management plan

The DZNE monitors Investigator compliance with a management plan on an ongoing basis until the completion of the PHS-funded research project.

§ 4 Publication of SFI in case of senior/key personnel

Furthermore, prior to the expenditure as well as during and after expenditure of any funds under a PHS-funded research project, the DZNE makes information concerning any SFI disclosed to the DZNE available via written response to any requestor within five business days of a request under the following conditions:

- the SFI was disclosed and is still held by the senior/key personnel;
- the DZNE determines that the SFI is related to the PHS-funded research; and
- the DZNE determines that the SFI is a FCOI.

The Information made available by the DZNE includes:

- the Investigator's name;
- the Investigator's title and role with respect to the research project;
- the name of the entity in which the SFI is held;
- the nature of the SFI; and
- the approximate dollar value of the SFI (dollar ranges are permissible: $0–$4,999; $5,000–$9,999; $10,000–$19,999; amounts between $20,000–$100,000 by increments of $20,000; amounts above

$100,000 by increments of $50,000), or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value; and

- the note that the information provided is current as of the date of the correspondence and is subject to updates, on an annual basis and within 60 days of the identification by the DZNE of a new FCOI, which should be requested subsequently by the requestor.

Information concerning the FCOIs shall remain available for responses to written requests for at least three years from the date that the information was most recently updated.

F. Reporting of FCOI

(1) Prior to the expenditure of any funds under a PHS-funded research project, the DZNE provides to the PHS Awarding Component an FCOI report regarding any Investigator's SFI found by the DZNE to be conflicting and ensure that the DZNE has implemented a management plan in accordance with the FCOI-regulation. This does not apply if the DZNE identifies a FCOI and eliminates it prior to the expenditure of the PHS-awarded funds.

(2) In case of FCOIs identified subsequently to the initial FCOI report during an ongoing PHS-funded research project (e.g. upon the participation of an Investigator who is new to the research project), the DZNE provides to the PHS Awarding Component, within 60 days, an FCOI report and ensures that a management plan has been implemented in accordance with the FCOI-regulation.

(3) The reports mentioned under para (1) and (2) include:

- Project number;
- PD/PI or Contact PD/PI if a multiple PD/PI model is used;
- Name of the Investigator with the FCOI;
- Name of the entity with which the Investigator has a FCOI;
- Nature of the financial interest (e.g., equity, consulting fee, travel reimbursement, honorarium);
- Value of the financial interest (dollar ranges are permissible: $0–$4,999; $5,000–$9,999; $10,000–$19,999; amounts between $20,000–$100,000 by increments of $20,000; amounts above $100,000 by increments of $50,000), or a statement that the interest is one whose value cannot be readily determined through reference o public prices or other reasonable measures of fair market value;
- A description of how the financial interest relates to the PHS-funded research and the basis for DZNE´s determination that the financial interest conflicts with such research; and
- A description of the key elements of the management plan of DZNE, including:
    - Role and principal duties of the conflicted Investigator in the research project;
    - Conditions of the management plan;
    - How the management plan is designed to safeguard objectivity in the research project;

- Confirmation of the Investigator's agreement to the management plan;
- How the management plan will be monitored to ensure Investigator compliance; and
- Other information as needed to enable the PHS Awarding Component to understand the nature and extent of the financial conflict and to assess the appropriateness of the DZNE's management plan.

(4) Any FCOI reported to the PHS Awarded Component has to be updated for the duration of the project period (including extensions with or without funds) by means of an annual FCOI report that addresses the status of the FCOI and any changes to the management plan for the duration of the project period. This annual FCOI report specifies whether the FCOI is still being managed or explains why the FCOI no longer exists.

G. Remedies

(1) If the failure of an Investigator to comply with an Institution's management plan appears to have biased the design, conduct, or reporting of the PHS-funded research, the DZNE promptly notifies the PHS Awarding Component of the corrective action taken or to be taken.

(2) If the PHS Awarding Component refers the matter to the DZNE for further action, the DZNE will implement possible directions of the PHS Awarding Component.

(3) In any case in which the HHS determines that a 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 an Investigator with a FCOI that was not managed or reported by the DZNE as required by the FCOI-regulation, the DZNE requires the Investigator involved to disclose the FCOI in each public presentation of the results of the research and provide an addendum to previously published presentations.

H. Other HHS regulations that apply

Several other regulations and policies apply to the FCOI regulation. They include, but are not necessarily limited to:

- 2 CFR part 376 - Nonprocurement debarment and suspension (HHS)
- 42 CFR part 50, subpart D - Public Health Service grant appeals procedure
- 45 CFR part 16 - Procedures of the Departmental Grant Appeals Board
- 45 CFR part 74 - Uniform administrative requirements for awards and subawards to institutions of higher education, hospitals, other nonprofit organizations, and commercial organizations
- 45 CFR part 79 - Program fraud civil remedies
- 45 CFR part 92 - Uniform administrative requirements for grants and cooperative agreements to State, local, and tribal governments.