# A GUIDE TO AVOIDING FINANCIAL AND NON-FINANCIAL CONFLICTS OR PERCEIVED CONFLICTS OF INTEREST IN CLINICAL RESEARCH AT NIH
## December, 2012 (Approved 12/09/12)

Avoiding financial and other conflicts of interests is important for NIH, where the trust and protection of research participants is vital to our mission to improve the public health. The number and complexity of laws and regulations in this area makes it difficult to know when there is a conflict or perceived conflict and what to do. This guide is intended to assist those engaged in clinical research and NIH IRB members in avoiding real or perceived financial and non-financial conflicts of interest.

## I. What are potential conflicts of interest for those engaged in clinical research?

All clinical researchers have primary obligations. These include obtaining knowledge that will promote health and health care and helping ensure the safety and health of research participants. Clinical researchers may also have other, personal or secondary interests, which could include teaching trainees, supporting a family, and earning income. These secondary interests are not, themselves, unethical, but in some circumstances they have the potential to compromise, or appear to compromise, the judgment of clinical researchers regarding their primary obligations. When these secondary interests have the potential to compromise judgment, or appear to do so, there is a conflict between the secondary and primary interests.

This guide provides information to identify and prevent or mitigate financial and other conflicts, thereby helping to ensure both the integrity of our research and the safety of participants.

## II. To whom does the guide apply?

The restrictions discussed in this guide are based on the laws that apply to NIH employees.[1] All NIH employees should be listed as investigators[2] or key research personnel[3] in the protocol when they substantively participate in the development, conduct, or analysis of clinical research protocols (both diagnostic and therapeutic) and must adhere to the rules described below. These rules also apply to NIH employees who serve on NIH Institutional Review Boards (IRBs) and Data Safety and Monitoring Boards (DSMBs). It is expected that non-employees[4] who serve as investigators in key research personnel roles or as IRB or DSMB members will review this guide and adhere to the rules set out. All investigators and key research personnel (employees and non-employees) listed on a protocol shall, by initialing the NIH Intramural Clinical Protocol Submission Form, acknowledge receipt of this guide. Non-NIH Investigators should be mindful of real and potential conflicts, discuss such conflicts with the protocol's PI and sign a Certification that this has occurred. Please note that the National Institutes of Health expects that all non-NIH investigators will comply with the ethics and conflict of interest policies and procedures set forth by their institution or employer.

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[1] NIH employees are those NIH staff with an appointment to the federal government pursuant to, for example, Title 5, 38 or 42, or the Commissioned Corps, and may include some fellows. Personnel appointed through an Intergovernmental Personnel Act (IPA) agreement may have federal government appointments as well.

[2] Investigators are those NIH employees who occupy the following positions: Principal Investigator, Associate Investigator; Accountable Investigator; Medical Advisory Investigator; Research Contacts and Lead AI's.

[3] Key research personnel include those NIH employees who: 1) obtain consent from human subjects; 2) recruit human subjects; 3) evaluate the response of human subjects, including adverse or unanticipated events and 4) analyze or interpret data collected, and may include research coordinators.

[4] Non-NIH employees include Adjunct Principal Investigators, Guest Researchers, Special Volunteers, contractors, Intramural Research and Cancer Research Training Awardees, and collaborators from academia and industry. Note: clinical investigators who are not NIH employees, but are Special Government Employees or IPA appointees, may serve as PIs on NIH clinical protocols.

## III. Examples of investigator, key research personnel, and IRB and DSMB member financial conflicts of interest

As noted when applicable, some of these examples of financial conflicts of interest are prohibited by regulation for NIH employees. We list them, however, as guidance for non-employee investigators, key research personnel, and IRB and DSMB members who are reviewing this guide. It should be noted that in addition to his or her own financial interests and outside interests, *an NIH employee's financial interests also include the financial interests of others, such as his or her spouse, dependent children, or household members.* Examples of such interests are:

- Serving as a director, officer or other decision-maker for a commercial sponsor of clinical research (prohibited activity for NIH employees);
- Holding stock or stock options in a commercial sponsor of clinical research (unless below the applicable de minimis amount or held within a diversified, independently managed mutual fund);
- Receiving compensation for service as consultant or advisor to a commercial sponsor of clinical research (excluding expenses) (prohibited activity for NIH employees);
- Receiving honoraria from a commercial sponsor of clinical research (prohibited activity for NIH employees);
- Personally accepting payment from the clinical research sponsor for non-research travel or other gifts (for NIH employees, government receipt of in-kind, research-related travel is not included and other exceptions may apply);
- Obtaining royalties or being personally named as an inventor on patents (or invention reports) for the product(s) being evaluated in the clinical research or products that could benefit from the clinical research (special rules apply in this case when NIH holds the patent – see Section VII below);
- Receiving payments based on the research recruitment or outcomes (prohibited activity for NIH employees);
- Having other personal or outside relationships with the commercial sponsor of the clinical research (prohibited activity for NIH employees);
- Having financial interest above the applicable de minimis in companies with similar products known to the investigator to be competing with the product under study (prohibited activity for NIH employees); or
- Participating in an IRB or DSMB decision that has the potential to affect your spouse's employer (prohibited activity for NIH employees).

## IV. Examples of non-financial real or apparent conflicts of interest for IRB and DSMB members

- Voting on a protocol when the member of the IRB is the protocol's Principal Investigator, Associate Investigator or study coordinator;

- Voting on a protocol when the member of the IRB or DSMB is or has a spouse, child, household member or any other individual with whom the protocol's Principal Investigator, Associate Investigator or study coordinator has the appearance of a conflict of interest[5]; or

- Voting on a protocol when the protocol's Principal Investigator is the IRB member's supervisor (up the chain of command to the Clinical Director).

**As noted in Section II - The National Institutes of Health expects that all non-NIH investigators are in compliance with their institutional/employer's conflict of interest policies.**

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CLEARANCE OF NIH EMPLOYEES ONLY – PERSONAL FINANCIAL HOLDINGS

## V. NIH's system to assist in identifying and preventing personal financial conflicts for investigators in clinical research

The Principal Investigator is responsible for assuring that each investigator and all key research personnel listed on the protocol receive a copy of this guide. The guide should be distributed to any new investigator/ key research personnel added to a protocol while the protocol is active.

### a. New Protocols

At the earliest point possible, the PI is responsible for providing his or her IC Deputy Ethics Counselor (DEC) with a completed copy of t**he "Clearance of NIH Investigator Personal Financial Holdings" *(PFH Clearance)*** (see Appendix 1) which lists all investigators. Alternatively, an electronic equivalent could be used to provide this information.

Upon receipt of the Protocol PFH Clearance, the IC DEC will read the précis to determine if: 1) any commercial drugs/devices are being studied or 2) if any standard of care treatments will be used in the protocol. If there are no commercial interests associated with this protocol, the DEC may approve the research via an expedited process. This eliminates the need for review of the investigator's holdings in any organization that are significantly affected by NIH research (SAOs). The DEC always has the discretion to complete a full conflict of interest analysis if s/he feels it necessary.

For each protocol:

1) If the protocol involves the use of a commercial drug/device, or has the potential to affect the value of other commercial products, the DEC will verify that all investigators who are employees

[5] The IRB or DSMB member determines, in his/her own opinion, whether a personal relationship with the protocol's Principal Investigator or another member of the research team exists. If such a determination is made, the IRB or DSMB member shall disqualify him or herself from the protocol to avoid any appearance of a conflict of interest.

have a form 716/717 on file and that the personal investment information on the form 716/717 is current (within 6 months) as of the date on the PFH Clearance. The IC DEC will then review file copies of the PI's and each AI's 716 or 717 forms that enumerate stock holdings in SAOs.

2) If SAO holdings are above the de minimus values, the DEC will provide the PI with an anonymous list of AI's holdings in SAOs as reported on these forms so the PI can determine if any pose a conflict of interest for the protocol in question. Any investigator who has a potential conflict will be contacted by his or her DEC to determine how to resolve any actual or apparent conflict. The employee's supervisor and/or the Clinical Director will be consulted as necessary if a conflict exists. The conflicts review will occur in parallel to the IRB submission process.

At the completion of the personal financial holdings review, the IC DEC will return a signed copy of the Protocol PFH Clearance to the PI. The PI will then note the date of DEC clearance on the *Protocol Application* and ensure that the Protocol PFH Clearance is included in the protocol packet.

The DEC clearance form will become part of the protocol packet forwarded to the IRB Chair for final approval. The IRB chair may not provide final approval by signing a protocol until the completed Protocol PFH Clearance is included in the protocol packet.

### b. Continuing Review

A COI analysis will take place at the time of continuing review using the same process as described above. The Protocol PFH Clearance will be used for this process. For the conflicts analysis, the addition of new investigators, any changes related to the use of commercial products or any change to an IND/IDE will be evaluated by the IC DEC.

### c. Amendment

A COI analysis will take place for amendments involving the addition of NIH employee investigators to a protocol, any changes related to the use of commercial products, or any change to an IND/IDE. The Protocol PFH Clearance will be used for this process following the procedure above. If just adding a new investigator, only that investigator needs to be cleared.

Although government-wide regulations allow NIH employees to hold de minimis amounts of publicly-traded stock without triggering conflict of interest restrictions, there may be other factors to consider with respect to stock ownership. If a publication should result from the protocol, most journals require the authors to disclose individual financial holdings within the text of the published paper. Such disclosures could raise at least the appearance of the conflict of interest. Thus, all investigators should consider these outside factors when making personal financial investments.

## VI. IRB and DSMB Clearance for COI

- Before beginning protocol review activities, the Chair asks whether any member is aware of any real or apparent conflict of interest. The minutes will reflect which individual(s)has a real or apparent conflict of interest. No IRB or DSMB may have a member participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB or DSMB.

- When the Principal Investigator or Associate Investigator is the Institute Director, or Scientific Director, the protocol will be reviewed by an IRB not affiliated with that institute.

- When the Principal Investigator is the Clinical Director (CD) it shall be the prerogative of an IRB either to review such protocols or refer them to another Institute's IRB. IRBs reviewing protocols in which their CD is the PI must have a majority of voting members present at the meeting who are not employed by the CD's Institute, otherwise any alternative plan must have prior approval by the Clinical Center Director and the Deputy Director for Intramural Research.

## VII. NIH Intellectual Property and Royalties

In some instances, NIH clinical research protocols will evaluate or potentially advance product(s) in which NIH (i.e., the government) owns patents or has received invention reports. In such cases:

- An NIH investigator may participate in the clinical trial, even if the investigator is listed on the patent or invention report and/or may receive royalty payments from the NIH for the product(s) being tested.

- When such an investigator participates in a trial, there will be full disclosure of the relationship to the IRB and to the research subjects (i.e., information should appear in the consent form) with review and approval by the IRB. This is to ensure the quality and integrity of the data collected.

- In the case of continuing review of current protocols where NIH has a new or amended intellectual property interest in the invention, investigators should provide a new human subjects consent form or correspondence outlining the relationship, for review and approval by the IRB.

- An independent entity or individual must review the integrity/accuracy of the results/quality of data to assure the safety of human subjects and to assess whether there is a change in the risk benefit ratio or introduction of possible bias.

## CLEARANCE OF NIH INVESTIGATOR PERSONAL FINANCIAL HOLDINGS BY IC ETHICS OFFICE (PFH)

**Instructions:** Email the completed document to the IC DEC for your Institute and include the protocol précis for ALL protocols. To facilitate this process, ensure that the list of investigators is current and complete by comparing this with the protocol face sheet and PQS (**http://pqs.cc.nih.gov/**).

[1]**Date Received by Ethics Office:**_____
[2] **Date of Memo** _____
[3]**Date of IRB Meeting:** _____
[4]**Date Protocol Expires:** _____

☐ [5]New Protocol
☐ [6]Continuing Review
☐ [7]Amendment: check all that apply
- ☐ Investigator Added
- ☐ Product Added or Changed

[8]**To:** _____
I.C. Deputy Ethics Counselor

[9]**From:** _____
Principal Investigator
cc:

[10]**Protocol #:**
[11]**Research Type:**
- ☐ Screening
- ☐ Training
- ☐ Nat. History – Dx Progression/Physiology
- ☐ Nat. History–Sample/Data Collection/Analysis: ☐ Recruiting ☐ Not Recruiting
- ☐ Pharmacokinetics/Dynamics
- ☐ Clinical Trial: Phase: ☐ 0 ☐ 1 ☐ 1-2 ☐ 2 ☐ 3 ☐ 4

[12]**Title:**
[13]**Principal Investigator's I.C.:**
[14]**Responsible IRB:**

[15]**: Does this study include any commercial interests?: ☐ Yes ☐ No**
**Does this study involve any technology transfer? ☐ Yes ☐ No**
**Does this study involve any products made by a commercial interest? ☐ Yes ☐ No**
[16]**Manufacturer of study product(s) (drug, biologic or device):**
[17]**IND/IDE# (if applicable):**
[18]**IND/IDE Sponsor (if applicable):**
[19]**Do you know of competitors for study drug, biologic or device manufacturer(s) for purposes related to this protocol? If yes, please list :**
[20]**: Objective of the study *(one sentence summary)***:

[21] **List individuals serving on the protocol as an:** Adjunct PI, Accountable Investigator, Medical Advisory Investigator, Lead Associate Investigator, Associate Investigator, key research personnel and/or Research Contact, identifying for each their affiliation (i.e., outside entity) and if an NIH Employee or Non-NIH Employee.
Name, Affiliation, Employment Status (NIH Employee/Non-NIH Employee)

**The information below is for IRB information only and shall not be included on the protocol consent form.**

[22] ☐ No conflicts identified for NIH employees, or conflicts have been resolved through divestiture or waiver.
[23] ☐ No conflicts exist however one or more NIH employees have a de minimis holding in the manufacturer of the product(s) used in the study. Name of manufacturer(s):
[24] ☐ No conflicts exist however one or more NIH employees have an over the de minimus holding in the manufacturer of the product(s) used in the study and has been cleared to participate by waiver. Name of manufacturer(s):

_____ _____ _____
Deputy Ethics Counselor for IC of P.I. Date Signed Date Returned to P.I.

Ethics Office Use Only: DER ☐ 7/8/10