

**A GUIDE TO PREVENTING FINANCIAL AND NON-FINANCIAL CONFLICTS OF INTEREST  
IN HUMAN SUBJECTS RESEARCH AT NIH**

October 11, 2006

Avoiding financial and other conflicts of interests is important for NIH, where the trust and protection of research subjects 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 problem and what to do. This guide is intended to assist clinical investigators and NIH IRB members in avoiding real or perceived financial and non-financial conflicts of interest.

**I. What are a clinical investigator's potential conflicts of interest?**

All clinical investigators 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 investigators 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 compromise judgment, or appear to do so, there is a conflict between the secondary and primary interests.

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

**II. To whom does the guide apply?**

This specific guide applies to all investigators who are NIH employees and who substantively participate in the development, conduct, or analysis of clinical research protocols, both diagnostic and therapeutic, and are listed as investigators on the front sheet of protocols. The description and examples of conflict of interest(s) also apply to individuals who serve on NIH Institutional Review Boards (IRBs). In particular the guide applies to:

- Principal Investigators
- Investigators (Associate, MAI, Research Contacts) -- i.e. all persons whose names appear on the front sheet of a protocol. NIH regards an "Investigator" to be the principal investigator and any other person who is responsible for the design, conduct, analysis, or reporting of research funded by the DHHS. In addition to his or her own financial interests and outside interests (see Section III, below) an investigator's financial interests also include the financial interests of others such as: his or her spouse, dependent children, or household members, and
- NIH IRB members

**III. Examples of investigator and IRB financial conflicts of interest:**

- Serving as a director, officer or other decision-maker for a commercial sponsor of the human subjects research;
- Holding any stock or stock options in a commercial sponsor of the human subjects research (unless held in a diversified, independently managed mutual fund);
- Receiving compensation for service as consultant or advisor to a commercial sponsor of the human subjects research (excluding expenses);
- Receiving honoraria from a commercial sponsor of the human subjects research;
- Personally accepting payment from the human subjects research sponsor for non-research travel or gifts (government receipt of in-kind, research-related travel is not included);
- Obtaining royalties or being personally named as an inventor on patents (or invention reports) for the product(s) being evaluated in the human subjects research or products that could benefit from the human subjects research (special rules apply in this case when NIH holds the patent--see below);
- Receiving payments based on the research outcomes;
- Having other personal or outside relationships with commercial sponsors of the human subjects research;\* or
- Having financial interest in companies with similar products known to the investigator to be competing with the product under study.

**IV. Examples of non-financial conflicts of interest for IRB's and their members**

- Voting on a protocol when the IRB member is a Principal Investigator, Associate Investigator or a study coordinator
- Voting on a protocol when the IRB member is a family member or has a close personal relationship with the Principal Investigator, Associate Investigator or study coordinator

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\* Employees are reminded that applicable authorities prohibit them from having, for instance, outside activities, gifts, or other forms of compensation from outside entities that are related to the performance of official duties from/with commercial sponsors of clinical research in which they participate.

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- Voting on a protocol when the Principal Investigator is the IRB member's supervisor
- 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 on which their CD is the PI must have a majority of members who are not employed by the CD's Institute otherwise any alternative plan must have prior approval by the Director, CC, and the Deputy Director for Intramural Research.

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

The Principal Investigator is responsible for assuring that each investigator listed on the protocol front sheet receives a copy of this Guide. The guide should be distributed to any new investigators 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 list of all investigators using the Protocol COI Statement (see Appendix I). This submission date will be noted on the form 1195.

Upon receipt of the Protocol COI Statement the IC DEC will verify that all investigators who are employees have a form 716/717 on file and that the personal investment information on the form 716/717 is current as of the date on the Protocol COI Statement. The IC DEC will then review file copies of each PI's and AI's 716 or 717 forms that enumerate stock holdings in all organizations that are significantly affected by the NIH (referred to as "SAOs").

For each protocol, the DEC will provide the PI with an anonymous list of AIs' holdings in SAOs 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 conflicts review, the IC DEC will return a signed copy of the Protocol COI Statement to the PI. The PI will then note the date of DEC clearance on the Form 1195 and

ensure that the Protocol COI Statement 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 COI Statement 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 COI Statement will be used for this process. For the COI 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. Amendments**

A COI analysis will take place for amendments involving the addition of investigators to a protocol, any changes related to the use of commercial products or any change to an IND/IDE. The Protocol COI Statement will be used for this process following the procedure above.

Although government-wide regulations allow employees to hold de minimis amounts of publicly-traded stock without triggering conflict of interest restriction, the NIH believes that it is prudent for clinical investigators to hold no stock whatsoever when the results of their clinical research could have a direct and predictable effect on the value of that stock. In cases where investigators do not wish to divest, and are not required by law to do so, the PI in consultation with the DEC will determine a course of action appropriate to that protocol.

**VI. IRB Clearance for COI**

o **IRB Members**

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

**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 filed invention reports. In such cases:

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- 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 product(s) being tested.
- When such an investigator participates in a trial, there should 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.
- In the case of continuing review of current protocols where NIH has an 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, such as a DSMB, must review the results of all such human subjects research.
- These relationships must be reported to the DDIR as part of the quarterly report, without reference to specific individuals, but should not impede the pursuit of the trial.

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## PROTOCOL CONFLICT OF INTEREST STATEMENT

(Appendix 1)

**Date:** \_\_\_\_\_  
I.C. Deputy Ethics Counselor

**To:** \_\_\_\_\_  
I.C. Deputy Ethics Counselor

**From :** \_\_\_\_\_  
Principal Investigator  
CC:

**Re: Documentation of Discussion of Conflict of Interests with P.I.**

New Protocol (attach **précis**)  
 Continuing Review  
 Amendment

**Protocol #:**  
**Type of Protocol:**  
**Title:**  
**Principal Investigator's IC:**  
**Responsible IRB :**

**Study Drug or Device:**  
**IND/IDE #:**  
**IND/IDE Holder:**  
**Manufacturer of study drug or device :**  
**Do you know of competitors for study drug or device manufacturer for purposes related to this protocol ?**  
**Key words as per 1195:**

**Accountable Investigator :**  
**Medical Advisory Investigator:**  
**Research Contact:**

**List of Associate Investigators:**

**Name of Investigator**

**NIH Employee's Institute or Non-NIH Affiliation**

<input type="checkbox"/> No conflicts identified	<input type="checkbox"/> Conflicts if identified are resolved. Explain:
_____ Deputy Ethics Counselor for IC of P.I.	_____ Date Signed
	_____ Date Returned to P.I.