A Guide to Preventing Conflicts of Interest
In Human Subjects Research at NIH
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Avoiding financial conflicts of interests and other conflicts of interest 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 in avoiding real or perceived conflicts of financial and other 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 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.

In particular the guide applies to:

- Principal Investigators
- Associate Investigators -- 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 any outside entity or foundation in which any of these persons have a

financial or other interest that could be directly affected by the conduct of the research.

III. Conflict examples:

- 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.

[*] 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.

IV. How It Works

The NIH has established a 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 receive a copy of the Guide. Any investigator who has a potential conflict must inform the Principal Investigator of the conflict and how they plan to eliminate this conflict, consult with his or her IC Deputy Ethics Counselor to determine how to resolve any actual or apparent conflict, and then report back to the PI on the plan to eliminate the conflict.

- In ProtoType, or in a short memo accompanying the protocol, the Principal Investigator will answer the question as to whether the Guide was provided to each investigator on the protocol and whether any conflict of interest was identified for the protocol as a whole. If no, then nothing need be done. If yes, the Principal Investigator will describe what the conflict was and how it was eliminated. This will take place at the time of initial and continuing review.

- The Clinical Director (CD) who signs the protocol document will thus be aware of the Principal Investigator's answer(s) and the IRB will also receive a copy of the disclosure for the protocol as a whole at the time of the initial and continuing reviews.

- The DDIR will receive a quarterly report (generated from ProtoType) of any conflicts of interests and how they were eliminated without reference to specific individuals.

- The Principal Investigator is required to distribute the Guide to all investigators and update each protocol at the next continuing review based on comments received from the investigators.

V. How will NIH Intellectual Property and Royalties Be Handled?

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:

- 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. This will be done via ProtoType.