A GUIDE TO AVOIDING FINANCIAL AND NON-FINANCIAL CONFLICTS OF INTEREST OR PERCEIVED CONFLICTS OF INTEREST IN CLINICAL RESEARCH AT THE NATIONAL INSTITUTES OF HEALTH (NIH)

Avoiding real or perceived financial and non-financial conflicts of interests is important for NIH. Maintaining the public's trust in the work of the NIH, ensuring the integrity of NIH research and protecting the rights, safety and welfare of research participants are vital to our mission to improve public health. The number and complexity of laws and regulations in this area sometimes make it difficult to know when there is a real conflict, or when a situation may be perceived as a conflict (referred to as an "apparent conflict"), and what to do in any given situation. This guide is intended to assist those engaged in the conduct of clinical research at NIH (including individuals involved in the statistical analysis of data), NIH IRB members, and IRB consultants, in understanding and identifying what might constitute a conflict, and avoiding real or apparent financial and non-financial conflicts of interest.

I. What gives rise to financial and non-financial conflicts of interest?

Actual and apparent conflicts of interest, financial and non-financial, arise when an individual's personal interests will or may be affected, or may be perceived to be affected by an agency matter in which the individual has an influential role. Clinical research involves developing knowledge that will advance human health by preventing, detecting, diagnosing, and treating disease and disability, as well as protecting the rights, safety and welfare of research participants. Sometimes, outside or personal interests, such as a spouse's job, stock holdings, retirement assets, and/or outside positions at universities or with professional organizations (referred to as "outside interests"), have the potential to compromise, or appear to compromise, the judgment of people involved in clinical research. When this occurs, efforts must be made to evaluate the circumstances to determine whether there is a real or apparent conflict of interest. Under government-wide ethical conduct rules, conflicts of interest and impartiality concerns ***must be resolved*** before a federal employee of the NIH, or any other agency, can proceed to work on an NIH clinical research project.

II. To whom does the guide apply?

The concepts and examples discussed in this guide are based on the government-wide ethical conduct rules that apply to all federal employees and the supplemental standards of ethical conduct that apply to NIH employees[1]. Thus, all NIH employees listed on covered research protocols[2] and/or Institutional Review Board (IRB)

[1] NIH employees include those NIH staff with an appointment to the federal government pursuant to, for example, Title 5, 38 or 42, or the Commissioned Corps, Special Government Employees, and may include some fellows and Intergovernmental Personnel Act (IPA) appointees.

[2] *Covered Research Protocol* (and covered substudies) include: (1) studies of investigational drugs and devices, (2) studies with a research question about a commercially available drug or device, and (3) studies involving collaborations with a substantially affected organization (SAO) or other for-profit entities when the entity is receiving data or specimens from the NIH for the purpose of developing a product. Most interventional protocols will be Covered Research

applications are required to adhere to the laws and regulations this Guide describes. Examples of individuals engaged in human subjects research include: Principal Investigators (PIs), Associate Investigators (AIs), or Medically Advisory Investigators (MAIs), individuals who obtain informed consent, and those who interact or intervene with research participants to collect or analyze identifiable information or identifiable biospecimens. This guide also applies to others who have key analytic roles that could bias the outcome of the research, including biostatisticians (see *Policy 102 Investigator Conflict of Interest and Government Royalties*) and to NIH employees who serve on the NIH IRB (see *Policy 202 Board Member Financial Conflicts of Interests*).

It is expected that the employees of other federal agencies who engage in clinical research at NIH will fully comply with all applicable federal laws and regulations governing their conduct and certify that they have no conflict of interest with the NIH protocol.

In addition, NIH expects that individuals who are not federal employees, including Adjunct Principal Investigators, Guest Researchers, Special Volunteers, contractors, Intramural Research and Cancer Research Training Awardees, Visiting Fellows and collaborators from academia and industry, who are engaged in human subjects research at the NIH (or whose activities otherwise meet the conditions specified in *Policy 102*), unaffiliated IRB members, and all IRB consultants, will review this guide and adhere to the rules set out. All such individuals must certify that they have received this guide and will comply with its tenets. If an individual cannot certify that he or she will comply with this guide, he or she may not be involved in the conduct of the research.

Please note that the NIH expects that all non-NIH investigators will comply with the ethics and conflict of interest policies and procedures set forth by their home institution or employer, if applicable. Questions or concerns about real or apparent conflicts of interest should be discussed with the NIH PI, ethics officials and employing institutions, as applicable and appropriate.

III. Examples of financial and non-financial conflicts of interest

As noted below, some of these examples of conflicts of interest are prohibited by regulation for NIH employees. We list them, however, as guidance for all other individuals who must comply with these requirements, such as non-NIH investigators, IRB consultants, and for unaffiliated IRB members who are reviewing this guide. It should be noted that in addition to his or her own financial interests and outside interests, the financial interests of others, such as an individual's spouse, dependent children, or household members should be taken into consideration. Examples of such interests are:

Protocols unless the intervention does not involve the criteria listed above.

- 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);

- 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 be competing with the product under study (prohibited activity for NIH employees); or

- Participating in an IRB decision that has the potential to affect your spouse's employer (prohibited activity for NIH employees);

- Participating in an IRB decision when the individual or his or her spouse, child, or household member is a member of the research team of the protocol under consideration; or

- 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 VI below).

When, for any reason, an individual investigator, IRB member or IRB consultant, feels that he or she cannot perform in an unbiased manner or provide an unbiased review or advice, the issue or concern should be discussed with the NIH PI, the Office of IRB Operations (IRBO), ethics officials and employing institutions, as applicable and appropriate.

IV. 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 addition, it is possible that the NIH investigator may receive government distributed royalty payments related to the patent or invention. (Note: Under federal law, neither royalty payments received nor the right to receive such payments from the Federal Government based on work done as a federal employee constitutes a disqualifying financial interest.) 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 or licensing payments from the NIH for the product(s) being tested, however, the following conditions apply:
When such an investigator conducts a trial, there will be full disclosure of the relationship to the IRB and to the research participants (i.e., information about royalties or licensing payments must appear in the consent form). The IRB will also consider whether additional measures are required to ensure the safety and welfare of human subjects and the quality and integrity of the study data. Such measures may include restrictions on the activities of the conflicted investigator, such as not being involved in the informed consent process or restrictions on performing data analysis.

V. Waivers to the conflict of interest requirements:

On rare occasion, the NIH Director may approve a waiver (18 U.S.C. § 208(b)) to the conflict of interest requirements for an NIH employee investigator involved in a clinical research protocol. In such instances, the investigator must inform the NIH IRB that such as waiver has been issued. The NIH IRB will determine whether disclosure in the informed consent and/or additional management strategies are necessary.

If the reviewing IRB is a non-NIH IRB, the investigator should not inform the reviewing IRB, but should inform OHSRP. OHSRP will determine whether any management strategies should be imposed on the conflicted investigator's activities.

VI. Investigator responsibilities when the NIH is relying on an external IRB.

The NIH may participate in research in which the reviewing IRB is not the NIH IRB. In such cases, the investigator must still follow all NIH policies related to conflicts of interest. The investigator may not submit to the external IRB, or commence research at the NIH site, until the COI review process is complete and the COI Outcome letter has been issued. The Office of IRB Operations will provide the COI Outcome letter to the reviewing IRB as part of its administrative review process.

Some external IRBs may ask the NIH Investigator to disclose their financial interests as part of the IRB application. With the exception of federal patent or royalty payments, NIH Investigators must not provide this information to the external

reviewing IRB. If there are questions as to what information is permissible to provide to the external IRB, consult with the Office of IRB Operations.