

by requiring that “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.” FDA regulations include identical language at 21 CFR 56.107(e).

Concerns have grown that financial conflicts of interest in research, derived from financial relationships and the financial interests they create, may affect the rights and welfare of human research subjects. Financial interests are not prohibited, and not all financial interests cause conflicts of interest or harm to human subjects. HHS recognizes the complexity of the relationships between government, academia, industry and others, and recognizes that these relationships often legitimately include financial relationships. However, to the extent financial interests may affect the rights and welfare of human subjects in research, IRBs, institutions, and investigators need to consider what actions regarding financial interests may be necessary to protect those subjects.

In May 2000, HHS announced five initiatives to strengthen human subject protection in clinical research. One of these was to develop guidance on financial conflict of interest that would serve to further protect research participants. As part of this initiative, HHS held a conference on the topic of human subject protection and financial conflict of interest on August 15–16, 2000. A draft interim guidance document, “Financial Relationships in Clinical Research: Issues for Institutions, Clinical Investigators, and IRBs to Consider when Dealing with Issues of Financial Interests and Human Subject Protection,” based on information obtained at and subsequent to that conference was made available to the public for comment on January 10, 2001.⁵ This document replaces that draft interim guidance. The Department notes that other organizations have also addressed financial interests in human research via reports, guidance and recommendations.⁶ Many of these

contain strong and sound ideas for actions to deal with potential financial conflicts of interest on the part of institutions, investigators and IRBs.

II. Guidance for Institutions, IRBs and Investigators

A. General Approaches to Address Financial Relationships and Interests in Research Involving Human Subjects

The Department recommends that in particular, IRBs, institutions engaged in research, and investigators consider

- The HHS Office of the Inspector General (OIG) has issued a series of reports examining regulation and activities of IRBs. A June 2000 OIG report addressed recruitment practices and found that about one-quarter of the surveyed IRBs consider financial arrangements with sponsors of research as part of their protocol review. (<http://oig.hhs.gov/oei/reports/oei-01-97-00195.pdf>).

- The National Human Research Protections Advisory Committee (NHRPC) offered advice to HHS regarding the content and finalization of the HHS Draft Interim Guidance in August, 2001 (<http://ohrp.osophs.dhhs.gov/nhrpac/documents/aug01a.pdf>).

- In December 2001, the General Accounting Office released report 02–89 “Biomedical Research: HHS Direction Needed to Address Financial Conflicts of Interest.” The report recommended that the Secretary of Health and Human Services develop specific guidance or regulations concerning institutional financial conflicts of interest (<http://www.gao.gov/>).

- A number of nongovernmental organizations recently have addressed financial interests in reports and issued new or updated policies or guidelines of varying scope and specificity, including the Association of American Universities, October 2001 (<http://www.aau.edu/research/COI.01.pdf>), the Association of American Medical Colleges, December 2001 and October 2002 (<http://www.aamc.org/members/coitf/firstreport.pdf> and <http://www.aamc.org/members/coitf/2002coireport.pdf>), the International Committee of Medical Journal Editors October 2001 (<http://www.icmje.org/sponsor.htm>), the American Medical Association, January 2002 (<http://jama.ama-assn.org/issues/v287n1/abs/jsc10070.html>), the American Society of Gene Therapy, April 2000 (<http://www.asgt.org/policy/index.html>), and the Institute of Medicine, October 2002, report “Responsible Research: A Systems Approach to Protecting Research Participants” (<http://www.nap.edu/books/0309084881/html/>).

Two accrediting bodies for human subject protection programs have included elements addressing individual and institutional conflicts of interest in their accreditation evaluations, the Association for the Accreditation of Human Research Protection Programs (http://www.aahrpp.org/images/Evaluation_Instrument_1.pdf), and the National Committee for Quality Assurance, (<http://www.ncqa.org/Programs/QSG/VAHRPAP/vahrpafindstds.pdf>).

Internationally, the World Medical Association’s revision in 2000 of the Declaration of Helsinki, (http://www.wma.net/e/policv/17-c_e.html) principle 22, includes “sources of funding” among the items of information to be provided to subjects. A number of individual institutions also have developed policies for their own situations, as noted in the NIH Guide Notice issued in June 2000 (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-040.html>). Some of these policies involve conflicts of interest management methods and address institutional financial interests as well as individual interests.

whether specific financial relationships create financial interests in research studies that may adversely affect the rights and welfare of subjects. These entities may elect to include the following questions in their deliberations:

- What financial relationships and resulting financial interests cause potential or actual conflicts?
- At what levels could those interests cause potential or actual conflicts?
- What procedures would be helpful, including those to
 - collect and evaluate information regarding financial relationships related to research,
 - determine whether those relationships potentially cause a conflict,
 - determine what actions are necessary to protect human subjects and ensure that those actions are taken?
- Who should be educated regarding financial conflict of interest issues and policies?
- What entity or entities would examine individual and/or institutional financial relationships and interests?

B. Points for Consideration

Financial interests may be managed by eliminating them or mitigating their potentially negative impact. A variety of methods or combinations of methods may be effective. Some methods may be implemented by institutions engaged in the conduct of research, and some methods may be implemented by IRBs. Some of those may apply before research begins, and some may apply during the conduct of the research.

In establishing and implementing methods to protect the rights and welfare of human subjects from conflicts of interest created by financial relationships of parties involved in research, the Department recommends that IRBs, institutions engaged in research, and investigators consider the questions below. Additional questions may be appropriate. The Department’s intent is not to be exhaustive, but to suggest ways to examine the issues so that appropriate actions can be taken for protection of the rights and welfare of human research subjects.

- Does the research involve financial relationships that could create conflicts of interest?

- How is the research supported or financed?
- Where and by whom was the study designed?
- Where and by whom will the resulting data be analyzed?

- What interests are created by the financial relationships involved in the situation?

⁵ <http://ohrp.osophs.dhhs.gov/humansubjects/fineitn/finguid.htm>.

⁶ Recent Federal and Private Sector Activities: In addition to the HHS initiative, several Federal organizations have examined the issues related to financial relationships in human subjects research:

- The National Bioethics Advisory Commission (NBAC), in a comprehensive examination of the “Ethical and Policy Issues in Research Involving Human Participants,” in Chapter 3 recommended development of federal, institutional, and sponsor policies and guidance to ensure that research subjects’ rights and welfare are protected from the effects of conflicts of interest (<http://www.georgetown.edu/research/nbac/nbac/human/overvoll.pdf>).