Second Annual
Medical Research Summit

March 25, 2002
Washington, D.C.

Irene Stith-Coleman, Ph.D.
Director, Division of Policy, Planning and Special Projects

Office for Human Research Protections
Department of Health and Human Services

HHS Conference on Human Subject Protection and Financial Conflict of Interest

August 15-16, 2000

U.S. Department of Health and Human Services

Office of the Secretary

National Institutes of Health

Centers for Disease Control and Prevention

Food and Drug Administration

Purpose of Conference

- HHS initiative to strengthen human subject protection in clinical research
- Current PHS/FDA regulations, guidelines and guidance
- Examples of how financial COI is dealth with: Institutions, IRBs, and Clinical Investigators

Purpose of the Conference

- Questions in the Federal Register Announcement of Conference
- Guidance on Financial Conflicts of Interest
- Information to Develop More Useful Guidance

Themes from the Conference

- Financial COI is a Major and Growing Concern
- Some Professional Organizations Had Taken Positions; Mostly re-Clinical Investigators
- Wide Spectrum of Views: Management of Financial COI versus Prohibition of Certain Financial "Arrangements"

Themes from the Conference

- Potential Research Subjects Should be Told About Relevant Financial COI/Financial Interests.
- IRBs Should Not be the Sole Focus or Arbiter of Financial COI Issues
- Research Community: Guidance, not New Federal Regulations

Draft HHS Interim Guidance January 2001

- Draft Interim Guidance: 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

COI Recommendations, Guidelines, Policies

- National Bioethics Advisory Commission (Aug ’01)
- National Human Research Protections Advisory Committee (Aug ’01)
- International Committee of Medical Journal Editors (Sept ’01)

COI Recommendations, Guidelines, Policies

- AMA (‘01)
- AAU (Oct ’01)
- GAO (Nov ’01)
- AAMC (Dec ’01)

Common Rule §46.116 General requirements for informed consent

"..... no investigator may involve a human being as a subject in research..... unless the investigator has obtained the legally effective informed consent of the subject....."

Common Rule §46.116 General requirements for informed consent (cond)

- "An investigator shall seek such consent only under circumstances that provide the prospective subject....sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence...."

Declaration of Helsinki, October 2000

- Financial COI Excerpt

"22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, **any possible conflicts of interest,** institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail."

AMA's Council on Ethical and Judicial Affairs

- "The nature and source of funding and financial incentives offered to investigators **must be disclosed** to a potential participant as part of the informed consent process."

International Committee of Medical Journal Editors

- "Investigators should disclose potential conflicts to study participants, and should state in the manuscript whether they have done so."

Common Rule §46.109 IRB review of research

- "(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116."

Common Rule §46.109 IRB review of research

- "(b)The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would **meaningfully add to the protection of the rights and welfare of subjects.**"

NHRPAC's Recommendations on HHS' Draft Interim Guidance

- "In a research protocol in which an actual conflict of interest has been identified, subjects could be advised in the IC process of the possible conflict and the nature of that conflict, with terms, conditions and extent of disclosure calibrated by the COI committee and IRB to correspond to the level of risk that the possible conflict poses."

NBAC Report, *Ethical and Policy Issues in Research Involving Human Participants*

Recommendation 3.8

- "Sponsors and Institutions should develop policies and mechanisms to identify and manage all types of Institutional, IRB, and investigator conflict of interest.
- In particular, all relevant conflicts of interest should be disclosed to participants."

AAMC Task Force Report, *Protecting Subjects, Preserving Trust, Promoting Progress*

- "Research consent forms should ....disclose the existence of any significant financial interest held by a covered individual conducting the human subjects research."

Common Rule §46.109 IRB review of research.

- "(e) An IRB ....shall have authority to observe or have a third party observe the consent process and the research."

AMA's Council on Ethical and Judicial Affairs' Report

- "The IC process must differentiate between physician's role as clinician and investigator;
- Differentiation is best achieved when someone other than treating physician obtains the participant's informed consent to participate in the trial."

Common Rule §46.111 Criteria for IRB Approval of Research

- "(a) ... to approve research...the IRB shall determine...the following are satisfied: ....

  (1) Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, ..."

AAU Task Force *Report on Individual Institutional and Financial Conflict of Interest*

- "Since research involving humans creates risks that non-human research does not, any related financial interest in research should generally not be allowable."

AAU Task *Force Report on Individual Institutional and Financial Conflict of Interest*

- "However, if compelling circumstances justify exception, research should be subject to more stringent management measures, including disclosure to participants and students."

AAMC Task Force Report, *Protecting Subjects, Preserving Trust, Promoting Progress*

- "Institutional policies should establish the rebuttable presumption that an individual who holds a significant financial interest in research involving human subjects may not conduct such research."