DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary

Secretary's Advisory Committee on
Human Research Protections
Washington, DC 20201

//March 24, 2010//

The Honorable Kathleen Sebelius
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Ms. Sebelius:

In accordance with the provisions of the charter for the Secretary's Advisory Committee on Human Research Protections (SACHRP), I respectfully submit for your consideration a set of recommendations relative to Department of Health and Human Services (HHS) human subjects protection regulations at 45 CFR part 46. These recommendations were passed by SACHRP at their July and October 2009 meetings. This letter represents the eleventh in a series of recommendations from SACHRP.

I. Recommendation Regarding IRB Accountability

A. Background

SACHRP passed the following recommendation after a panel presentation in which Office for Human Research Protections (OHRP) staff reported on an analysis of responses to its Advanced Notice of Proposed Rulemaking (ANPRM) on Holding External Institutional Review Boards (IRBs) Directly Accountable. The ANPRM was published on March 5, 2009 and may be found at: http://edocket.access.gpo.gov/2009/E9-4628.htm.

The ANPRM was initiated in part to address the concerns of some institutions that appear to be reluctant to designate external IRBs and rely on cooperative review arrangements. That reluctance stems from the fact that, currently, should there be any issue of noncompliance on the part of an external IRB listed on the institution's FWA, OHRP currently holds the institution that is actually "engaged in human subjects research" accountable for noncompliance. This ANPRM sought to address that issue.

While the number of responses to the ANPRM was limited, the overall response was overwhelmingly positive, endorsing OHRP to pursue such a regulatory change. Further, most thought that the concern about regulatory liability would be attenuated by such a change. Respondents differed, however, in the extent to which they felt OHRP should specify which of the institution's responsibilities should and should not be delegated; many felt this should be left to the discretion of the institution based on the nature of the study and other variables.

SACHRP members noted that the responsibility for protocol review would be delegated, while the responsibility for oversight and compliance would remain with the institution 'engaged' in human subjects research. A number of individuals supported the suggestion that OHRP develop model template agreements, defining the allocation of responsibility to either the reviewing IRB or the institution. That said, SACHRP members endorsed the concept that any regulatory change should give the institutions sufficient flexibility to establish models and agreements, in that no single template will address the specific nuances of all types of research. SACHRP wished to emphasize its strong support for OHRP pursuing potential regulations or guidance to increase use of external IRBs where appropriate by holding them directly accountable. SACHRP therefore voted unanimously to endorse the following recommendation.

B. Recommendation

SACHRP endorses the concept that external IRBs and IRB organizations be held directly accountable for meeting certain regulatory requirements of the Department of HHS regulations for the protection of human subjects, as presented by the ANPRM, whether that be through regulations or guidance.

II. Recommendation Regarding New SACHRP Subcommittee on Harmonization

A. Background

SACHRP members discussed future committee directions and priorities, and ex officios were invited to provide input. Two dominant themes emerged from the discussion: (1) harmonization and simplification of the regulations (with a correlative effort to reduce regulatory burden) and (2) exploration of collaborative partnerships between participants and investigators, between communities and investigators, Following extensive discussion, the Chair asked members to consider empanelling a new SACHRP subcommittee that would undertake a broad-based review focusing on harmonization of regulations and guidance from different offices, including OHRP, the Food and Drug Administration (FDA), the Office for Civil Rights (OCR), and potentially the U.S. Department of Veterans Affairs (VA) and the National Institutes of Health (NIH). SACHRP subsequently approved a recommendation at its July meeting. However, at the following meeting in October the Chair stated that many SACHRP members wished to amend the recommendation that had previously been made. Members felt the objectives had not been crisply stated and the rationale for the recommendation should be more explicit; therefore an amended recommendation was passed.

B. Original July 2009 Recommendation

SACHRP recommends establishment of a subcommittee to identify areas in which harmonization and simplification in the guidance and regulations of HHS agencies and signatories under the Common Rule would be of benefit to the research community and contribute to the protection of research subjects.

C. Revised October 2009 Recommendation

Harmonization of human subject protection issues will result in better allocation of resources that will serve to enhance human subject protection, facilitate research, and improve public health. SACHRP recommends establishment of a subcommittee to identify, prioritize, and propose directions for resolving areas in which harmonization and simplification in the guidance and regulation of HHS agencies and signatories under the Common Rule would be of benefit to the research community and contribute to the protection of research subjects. We appreciate the importance of this project to the research community, anticipate that it will help advance research of benefit to the patient community, and appreciate the support of the Secretary and her designees for this critical endeavor.

III. Recommendation Regarding Ex-officio Representation

SACHRP respectfully suggests that a representative from the Office for Civil Rights be invited to participate on SACHRP as an ex officio member.

IV. Recommendation Regarding Standards for the Reporting, Disclosure, and Review of Financial Conflicts of Interest

A. Background

The SACHRP charter makes specific reference to investigator conflicts of interest, although 45 CFR Part 46 is essentially silent on this issue . A panel presentation included Dr. Bernard Lo's summary of the recent findings of the April 2009 Institute of Medicine report on this issue (www.nap.edu/catalog.php?record_id=12598) as well as perspectives and commentary from leaders in academia and the pharmaceutical industry. SACHRP members were impressed with the fact that all speakers called for uniform guidelines or standards in conflict of interest disclosures, both in the interest of making multi-site reviews easier and in facilitating public disclosures. Indeed, differences and discrepancies in reporting could lead to confusion and misunderstanding. Uniformity in approach, for the entire research community, would decrease administrative burden. While uniformity and clarity is paramount, all affected stakeholders (e.g investigators; academia; industry; human research participants; representatives of OHRP, FDA, VA, and other diverse government regulatory agencies) should participate in the development of appropriate regulations or guidance. SACHRP passed the following recommendation.

B. Recommendation

SACHRP recommends that the Secretary of HHS work with affected stakeholders to consider the need for regulations or guidance that define consistent standards for the reporting, disclosure, and review of financial conflicts of interest for those responsible for the design, conduct, or reporting of human subject research. These regulations or guidance should be uniform within the components of HHS (OHRP, NIH, FDA, etc.) and should include (1) uniform standards of reporting to any applicable entity, (2) uniform standards of public disclosure, (3) uniform expectations for appropriate information to permit human subject consent to be informed, (4) thresholds for evaluating and potentially limiting participation in human subject research based on financial COI s and (5) potential management approaches to limit undue influence and bias. Taken together, these approaches should promote industry-academic-public partnerships, allow transparency, ensure fair reporting, promote human subjects protections, and enhance public trust.

V. Reaffirmation of Previous SACHRP Recommendations on Education

A. Background

OHRP staff reported on input received from a July, 2008 Request for Information (RFI) that asked whether HHS should develop a regulation requiring that institutions engaged in human subjects research conducted or supported by HHS implement training and education programs for certain individuals involved in the conduct, review, or oversight of human subjects research; and, in addition, whether OHRP should issue additional guidance recommending the implementation of such training and education programs.

In a previous letter to the Secretary dated June 15, 2007, SACHRP made a recommendation that OHRP require institutions to provide training for a variety of specified audiences. Following the July presentation, the Chair asked if SACHRP members were prepared to reaffirm the recommendations made on March 29, 2007.

B. Recommendation

SACHRP reaffirms its recommendation of March 29, 2007, recommending that OHRP require institutions to ensure that initial and continuing training is provided for IRB members, IRB staff, the Institutional Signatory Official and the Human Protection Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person), investigators, and other members of the research team with responsibility for conducting human subjects research.

In addition to the above recommendations, SACHRP approved recommendations from the Subpart A Subcommittee which relate to informed consent and the future use of biospecimens; these recommendations, which consumed a great deal of the committee's time and deliberations, are part of a larger set of Frequently Asked Questions (FAQs) which will be communicated to your office at a later date, following SACHRP review and approval.

On behalf of SACHRP, I would like to thank you for your consideration of this report. The committee and the Subpart A Subcommittee have been actively working in pursuit of their charges, and we look forward to continuing this work to enhance human subjects protections for the benefit of all Americans.

Sincerely,

//Signed//

Barbara E. Bierer, M.D.
Chair, Secretary's Advisory Committee
on Human Research Protections
(SACHRP)

cc: Jerry Menikoff, M.D., J.D., Executive Secretary, SACHRP
Julia Gorey, J.D., Executive Director, SACHRP