DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

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

MAR 14 2007

The Honorable Michael O. Leavitt
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Leavitt:

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 list of recommendations relative to Department of Health and Human Services (HHS) regulations at 45 CFR part 46, subpart A (the Basic HHS Policy for the Protection of Human Research Subjects). These recommendations represent the fifth in a series of recommendations from SACHRP.

Background

On October 5, 2004, SACHRP approved a resolution establishing a Subcommittee on Subpart A. SACHRP's charge to the subcommittee was to review and assess all provisions of subpart A of 45 CFR part 46 and relevant Office for Human Research Protections (OHRP) guidance documents, and based on this review and ongoing assessment, to develop recommendations for consideration by SACHRP in three categories: (1) recommendations on interpretation of subpart A provisions; (2) recommendations for development of new, or modification of existing, OHRP guidance; and (3) recommendations for possible revision of subpart A.

The goals of this review and assessment of subpart A of 45 CFR part 46 are threefold: (1) to enhance the protection of human subjects; (2) to reduce, where possible, regulatory burdens that do not contribute to the protection of subjects in a meaningful way; and (3) to promote scientifically and ethically valid research. To that end, the following recommendations were discussed and approved by SACHRP over a period of four meetings (November 1, 2005; March 13, 2006; July 31, 2006; and November 2, 2006).

Recommendations Related to the Continuing Review of Research by Institutional Review Boards (IRBs)

(1) OHRP should clarify its guidance on the required duration of continuing review. Continuing review may end when all research interventions and interactions with subjects are over and data collection for research purposes is complete, as described in the approved study plan/protocol, at the research site for which the IRB has oversight. The IRB must have reviewed and approved the investigator's plan for data analysis and the safeguards in place for confidentiality protections. The investigator still retains the responsibility to notify former subjects and the IRB if subsequent analyses and/or new information raise concerns about rights, safety, and welfare of human subjects.

(2) OHRP should issue an Advance Notice of Proposed Rule Making to seek comments regarding changing section 46.109(e) to allow IRBs latitude in setting review dates beyond one year (but not more than two years) for minimal risk studies, but potentially for other studies as well.

(3) OHRP should revise its interpretation and develop new guidance to (a) define simplified criteria and the expectations for the content of continuing review based upon current risk level; and (b) to permit IRBs to develop, within their written procedures, policies and procedures for the selective application of section 46.111 to continuing review. The Food and Drug Administration's (FDA's) guidance should likewise be updated in regard to (b).

(4) OHRP should modify its interpretation of expedited review category (8)(b) so that expedited review is permitted if no additional risks have been identified at any research sites and no interventions or other study activities have occurred at the IRB's research site since the preceding review. Guidance should be revised to reflect this interpretation.

(5) OHRP should revise its current guidance to give more examples of when continuing review is not necessary and when expedited review category 9 may be used.

(6) OHRP should revise its guidance to clarify an expectation that the investigator is responsible for the review and interpretation of "recent and relevant" literature for IRB evaluation. Guidance should clarify that it is not an IRB responsibility to perform a review of the scientific literature.

(7) OHRP should revise its guidance to emphasize that once a research protocol is determined to be exempt, and all subsequent research activities continue to meet exemption criteria, there is no regulatory requirement for ongoing review.

(8) OHRP should prepare simplified, unified, and practical guidance for continuing review that focuses on the substance of review.

(9) OHRP should revise its guidance to reflect that the final IRB approval of a study "sets the clock" for continuing review. For multi-site reviews, this may differ by site.

(10) OHRP should revise its "30-day rule" to remove unnecessary restrictions on IRBs in scheduling continuing reviews. If a defined time window is deemed necessary, 60 days would be more appropriate.

(11) OHRP should modify its guidance on continuing review so that, when the study has been reviewed by the IRB (at a convened meeting or through an expedited process, as appropriate) and the IRB finds that there are no substantive concerns in terms of the risk-benefit relationship, informed consent, or other key protections, suspension of all research activity is not required when the expiration date passes, provided that IRB review is completed within 30 days past the expiration date.

(12) Regarding the issue of continued participation of already enrolled subjects in research during temporary lapses in IRB approval, wording in current OHRP guidance that refers to "individual requests" should be revised to clarify that approval of a general request for all research subjects to continue in the research during the review process is acceptable.

(13) OHRP guidance on continuing review should be revised to state that a "protocol summary" may or may not be a separate document; and that combination of information sources, such as consent forms and the continuing review application, may appropriately constitute a "summary" for the IRB members.

(14) OHRP should clarify its guidance to state that qualified IRB staff may act as a consultant to the IRB and accomplish the review of the full study protocol.

Recommendations Related to the Expedited Review of Research by IRBs

(1) Implementation of changes to approved research that are solely clerical or administrative should not require convened or expedited IRB review. OHRP and FDA should issue guidance permitting IRBs to define in their written policies and procedures changes to approved research that can be processed by qualified IRB staff.

Such changes should be limited to those that are entirely clerical or administrative in nature and have no effect on the conduct of the research, its underlying science or methodology, associated risks and benefits, or the potential willingness of subjects to continue participation (e.g., correction of clerical or typographical errors; changes to telephone numbers, addresses, and other contact information; renumbering of pages or sections without changes in content; other changes, as defined in written IRB policies and

procedures, that clearly have no effect on the conduct of the research, its underlying science or methodology, associated risks and benefits, or the potential willingness of subjects to continue participation).

(2) IRBs may give appropriately qualified staff authority for clerical and administrative functions.

(3) OHRP and FDA should initiate the process of modifying HHS and FDA regulations to replace the term "expedited review" with the term "delegated review," which more accurately describes the process and regulatory intent. SACHRP encourages all agencies under the Common Rule to harmonize with the new terminology (i.e., delegated rather than expedited review).

(4) OHRP and FDA should issue expanded guidance (a) clarifying that final approval of stipulations from convened meeting review (i.e., "contingent approval") is not a form of expedited review; and (b) permitting IRBs to describe in their written policies and procedures "stipulation mechanisms" for verifying changes required for approval of proposed research under which (i) the IRB Chairperson, or designated member-reviewer, may exercise reasonable judgment in verifying that the stipulations of the convened IRB have been satisfied; and (ii) a qualified IRB administrator may verify that the investigator has implemented specific language (e.g., in the protocol, informed consent document, or advertisements) dictated by the convened IRB (and requiring no subjective judgment on the part of the administrator).

(5) Expedited review category (7) should be revised as follows:

> Research (a) on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, affective states, interpersonal relationships, identity, language, communication, cultural beliefs or practices, and social behavior); or (b) employing methods commonly used in social, behavioral, epidemiologic, health services and educational research (including, but not limited to, survey, interview, oral history, participant observation, ethnographic, focus group, program evaluation, human factors evaluation, or quality assurance methods). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

(6) OHRP will review the expedited review categories at least every five years, harmonizing the list with FDA guidance.

Mr. Secretary, I trust you will find this report acceptable. Your committee members and SACHRP subcommittee members have worked hard in their pursuit of the charges contained in the charter. SACHRP has also worked closely with Dr. Bernard Schwetz and the rest of the OHRP staff and has benefited greatly from their expertise and leadership. We look forward to

continuing our work and providing you with recommendations which will enhance human subject protections and advance science for the benefit of all Americans.

Sincerely,

Ernest D. Prentice, Ph.D.
Chair, Secretary's Advisory Committee
on Human Research Protections

cc: Bernard A. Schwetz, D.V.M., Ph.D., Executive Secretary, SACHRP
Catherine Slatinshek, M.A., Executive Director, SACHRP