Attachment C: approved by SACHRP July 20, 2011

SACHRP Recommendation regarding application of 45 CFR 46 and 21 CFR 56 to early processes in research, such as identifying potential subjects, contacting subjects, and recruiting subjects

The Health and Human Services (HHS) and Food and Drug Administration (FDA) regulations regarding research do not specifically address activities that are conducted prior to the subject's providing consent to participate in research. FDA and the Office for Human Research Protections (OHRP) have addressed this issue through guidance. The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and related guidance addresses activities conducted prior to the subject's providing authorization to participate in research. The Department of Education (ED) Family Educational Rights and Privacy Act (FERPA) regulations also specifically address access to and release of private information from education records for specific purposes, including research.

FDA addresses these issues predominately in two sections of the FDA Information Sheets:

Recruiting Study Subjects
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm (Attached as Appendix 1).

Screening Tests Prior to Study Enrollment
http://www.fda.gov/RegulatoryInformation/Guidances/ucm126430.htm (Attached as Appendix 2).

OHRP addressed this issue in 2004 with the issuance of joint guidance documents with FDA and the Office for Civil Rights (OCR) regarding implementation of the HIPAA Privacy Rule. In that guidance, OHRP recommended that IRBs approve a waiver of consent under 45 CFR 46.116(d) for all activities conducted prior to consent.

An example is the guidance entitled "Clinical Research and the HIPAA Privacy Rule," online at http://privacyruleandresearch.nih.gov/clin_research.asp. The relevant FAQ is attached as Appendix 3.

Based on this background, SACHRP makes two recommendations regarding application of 45 CFR 46 and 21 CFR 56 to early processes in research, such as identifying potential subjects, contacting subjects, and recruiting subjects.

First Recommendation:

SACHRP recommends that OHRP abandon the guidance that IRBs approve a waiver of consent under 45 CFR 46.116(d) for all activities conducted prior to consent, as exemplified in the guidance entitled "Clinical Research and the HIPAA Privacy Rule." There are several difficulties with this guidance.

- IRB approval of a waiver of informed consent does not serve any practical purpose in protecting the rights and welfare of human subjects. It is often necessary for investigators to identify potential subjects to recruit for research through either records' review or contact by e-mail, phone calls, or direct contact. There are many ethical issues involved in these activities. However, requiring a waiver of consent under 45 CFR 46.116(d) does not address these ethical issues. Rather, it is a pro forma determination that does not in itself provide any protection of subjects.

- Consideration of a waiver of consent under 45 CFR 46.116(d) involves analysis of whether the research is minimal risk. The criterion at 45 CFR 46.116(d)(1) is that "the research involves no more than minimal risk to the subjects." Much research is not minimal risk. Therefore, in order to apply this finding to all research that involves identification of human subjects using identifiable private information prior to consent, there must be an interpretation that the recruitment activity being considered for the waiver of consent is minimal risk, rather than the research as a whole. If this approach is not used, recruitment involving the use of identifiable private information would not be possible for research that involves more than minimal risk. Alternatively, if OHRP chooses to continue to recommend that IRBs waive consent under 45 CFR 46.116(d) for recruitment activities, then OHRP should issue guidance on the use of this waiver, and specifically address when the research as a whole has to be minimal risk, or when some "subsection" of the research can be determined to be minimal risk. Note: Consideration of subsections of research in other situations (e.g., exempt determinations) has generally been discouraged in OHRP guidance.

- Much research is regulated by both HHS and FDA, or HHS and ED. The FDA regulations do not include the 45 CFR 46.116(d) waiver of consent provisions. Thus, it is theoretically not compliant with FDA regulations, or at least awkward, to apply 45 CFR 46.116(d) to FDA regulated research. FERPA regulations (34 CFR 99.31) provide specific permission for access to education records without consent under certain conditions.

Because of these difficult interpretation issues, SACHRP recommends that OHRP abandon this approach to requirements for recruitment activities. When researchers intend to obtain informed consent to a study, then their activities incident to obtaining such consent (e.g., identifying and contacting the individuals for consent) should not be regarded as a separate research activity requiring a waiver of consent. Rather, OHRP should regard this extremely common situation as one overall research project and should not bifurcate it. It should be sufficient for an IRB to review these preparatory activities as an integral part of the overall project, ensure that access to identifiable information is appropriate as proposed and that any risks are minimized, and focus on the proposed consent process and its documentation. In other studies in which the researchers do *not* intend to obtain informed consent (e.g., medical record reviews), the researchers' preparatory activities to identify participants and their work to obtain and review records should similarly be regarded as one overall project and the IRB should consider whether a waiver of consent is permissible. This approach has several advantages: (1) it respects OHRP's

jurisdiction over preparatory activities to identify participants for studies; (2) it serves a harmonization goal (since both OCR, with respect to researchers that are part of a HIPAA covered entity, and FDA permit researchers to contact individuals for consent without requiring a prior consent or waiver thereof); and (3) it is a sound, workable policy that allows IRBs to review a study as a whole and focus on the proposed informed consent process and its documentation.

Alternatively, OHRP may wish to consider utilizing the 45 CFR 46.101(i) secretarial waiver. This section of the regulations states, "Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes or research activities otherwise covered by this policy." OHRP could waive the applicability of the consent requirements to recruitment activities, and instead of requiring consent or a waiver of consent, adopt the FDA guidance statements regarding the ethical standards for recruitment activities.

Second Recommendation:

SACHRP recommends that OHRP and FDA should take the necessary steps to issue a single joint guidance on recruitment of subjects so that IRBs have a single source of information regarding the agencies' viewpoint on this issue. This will reduce administrative burden on IRBs and ease compliance requirements. SACHRP recommends that OHRP should adopt the FDA approach to this issue as exemplified in FDA's guidance and take steps necessary to interpret the Common Rule so that this is possible. The joint guidance should clearly indicate that it applies equally to social, behavioral, and educational research, as well as medical research. The regulatory criterion for equitable selection of subjects should be addressed in the guidance. To the extent possible, OHRP, FDA, and OCR should also consider what activities must be performed due to the HIPAA Privacy Rule, and to what extent harmonization of interpretation can be implemented. Finally, OHRP and FDA should consider whether it would be useful to note in the guidance that other laws and regulations addressing recruitment activities might apply to the research, such as FERPA.