DEPARTMENT OF HEALTH & HUMAN SERVICES Office of the Secretary

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



**// Dated AUG 5 2011//**

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 in the form of FAQs relative to Department of Health and Human Services (HHS) human subjects protection regulations at 45 CFR part 46. These FAQs were passed by SACHRP at their March 2011 meeting.

On October 5, 2004**,** SACHRP approved a recommendation establishing a Subpart A Subcommittee (SAS). SACHRP's charge to this subcommittee was to review and assess all provisions of subpart A of 45 CFR part 46 (HHS' codification of the Federal Policy for the Protection of Human Subjects, also known as the Common Rule) 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 sets of FAQs on the topics of parental permission and assent, and documentation of informed consent, are provided for your consideration.

**FAQs on Parental Permission and Assent**

***1. Is assent of a child/adolescent required before participating in research?***

Assent is required unless an IRB determines and documents that one of the following conditions is met:

(1) the children are not capable of providing assent, or
(2) the research offers the prospect of direct benefit that is available only in the context of the research.

Note that condition (2) is not restricted to biomedical research, but may apply to behavioral interventions that hold the prospect for direct benefit.

If an IRB determines and documents that one of these conditions is met, assent is not required and therefore the issue of waiver of assent does not arise.

***2. If neither of the two criteria listed above is met, can the requirement for assent be waived?***

Yes, the IRB may waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.

***3. Does assent always need to be documented in writing?***

No. The regulations do not require that assent be obtained in writing. If an IRB determines that assent is to be obtained, IRBs have full discretion in determining whether and how assent will be documented. Separate written assent forms are not required. However, an IRB has the option to require a separate form if it determines it is appropriate for the research. IRBs must document their decision in IRB records as to how assent is to be obtained.

As there is no regulatory requirement for written assent, the issue of waiver of written assent does not arise.

***4. If an IRB determines that verbal assent is permissible, do you need to document that verbal assent was obtained?***

No. There is no regulatory requirement to document that verbal assent was obtained. IRBs have the flexibility to determine whether and how assent is documented. While not a regulatory requirement, institutions may have other policies or other reasons for documenting verbal assent.

***5. Does the assent process or form need to contain all the elements required in a consent document?***

No. There are no regulations that specify the elements of assent. Therefore, IRBs have the flexibility to determine what is appropriate to cover in an assent form or during the assent process.

***6. If the IRB determines assent is required, is there an age at which it becomes mandatory to obtain assent?***

No. There is no regulatory requirement for the age of assent within the HHS or FDA regulations. IRBs may set institutional policy that presumes that children of particular ages have or do not have the capacity to give assent, but should consider the maturity and psychological state of the children involved, as well as other factors, on a protocol-by-protocol basis.

Children should be offered the opportunity to participate in decisions about research participation to the extent they are able.

***7. Is parental/guardian permission always required before a child/adolescent participates in research?***

In most situations, permission of parents or guardian is required for children/adolescents to participate in research. However, there are three ways in which it is possible to involve children in research without parental/guardian permission. They are as follows:

(1) If a child or adolescent does not meet the definition of "child" for the purposes of research, their involvement in the research would not fall under the subpart D requirements. (As an example, in some states adolescents may obtain contraception without the permission of their parents. If a research protocol involves the comparison of different contraceptive methods, it is possible for the IRB to determine that, for purposes of the research, these adolescents do not meet the definition of a child). If the IRB determines that the subjects may be treated as adults for the purposes of the research, investigators should carefully consider each participant's capacity to consent to the research.

(2) The regulatory criteria found in §46.116 of Subpart A may be used to waive parental/guardian permission if the IRB determines that these criteria are met. This provision does not apply to FDA-regulated research.

(3) In accordance with Subpart D, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects, it may also waive the

parental/guardian permission requirements. Examples include research involving abused or neglected children, or research aimed to understand the psychological well being of adolescents who have not informed their families of their sexual orientation. This provision does not apply to FDA- regulated research. (see also Secretarial letter dated Nov 9, 2006)

***8. Is the permission of both parents required to enroll their children in research?***

Parental permission of both parents is required only for research that is approved under categories §46.406 or 46.407, if both parents are reasonably available. For research in categories §45.404 or 45.405, the IRB may determine that the permission of one parent is sufficient. The IRB is required to make this determination and advise the investigator as part of the IRB approval process.

***9. If a subject reaches the age of majority during the study do they need to provide consent in order to remain in the study?***

Minors who were initially enrolled with parental/guardian permission and then reach the age of majority must provide legally effective consent if the project continues to meet the definition of research involving human subjects. This includes interacting or intervening with the subject or having access to private identifiable information. However, the IRB has the ability to waive the requirements for consent if the criteria of §46.116 can be met. The IRB may consider whether consent will be required or waived when a subject reaches the age of majority, or as part of the initial review of a protocol that anticipates subjects reaching the age of majority during the course of the research.

## FAQs on Documentation of Informed Consent

***1. Who is required to sign the informed consent document?***

HHS and FDA regulations require that informed consent documents must be signed by the subject or their legally authorized representative, except in those cases where the IRB has waived the requirements for documentation of consent. There is no regulatory requirement that a member of the study team, the principal investigator, or a witness sign the consent form, except in the event that the short form is used. When the short form document is used, then a witness must sign both the short form and the written summary, and the person obtaining informed consent must sign the summary. It is noted that some non-regulatory guidelines (e.g., ICH GCP, JCAHO) may have additional documentation requirements.

***2. Do informed consent documents always have to be signed?***

No. IRBs may approve a waiver of documentation of consent in accordance with 45 CFR 46.117(c).

(Note: SACHRP has previously approved recommendations on waiver of documentation, which were included in the Secretarial letter dated September 2008.)

***3. Must the informed consent process and documentation of consent take place at the same time?***

No, the regulations do not indicate when documentation must occur in relation to the rest of the consent process. In fact, there may be instances where it is in the best interest of potential participants that the process includes time to contemplate their participation instead of immediately providing consent and documentation.

***4. Do individuals who sign consent forms need to write the date of their consent or initial each page of the form?***

HHS regulations do not require that participants or others include the date of their signature. Note, however, that FDA regulations do require the date of signature. There are no regulatory requirements that each individual page of the document be initialed and/or dated.

***5. May participants return signed consent forms to the researcher by mail, fax or e-mail?***

Yes, OHRP and FDA consider signed consent documents that are submitted to the investigator by mail or fax to be in compliance with the requirements for documentation. Scanned documents that are returned as attachments by email would also satisfy the requirements. A waiver of documentation is not necessary in this situation.

***6. Can waiver of documentation occur separately from waiver of informed consent?***

Yes. Informed consent and documentation of consent are separate concepts and separate regulatory requirements. IRBs can waive written documentation without waiving informed consent. In either case, the IRB must make separate determinations and document their decisions.

***7. Is it permissible to initiate a study (or selected study procedures) based on verbal consent prior to having obtained written documentation?***

This would be acceptable only if the IRB has made a prior determination that a waiver of documentation is appropriate in accordance with HHS regulations as specified in 45 CFR

46.117(c). Otherwise this is not permissible under the current OHRP interpretation of HHS regulations.

Note that FDA has not adopted the waiver of documentation found at 45 CFR 46.117(c)(1).

***8. Must the order of information provided on informed consent documents follow the order in which they appear in HHS or FDA regulations?***

No, there is no requirement in the HHS or FDA regulations that the elements of consent be presented in a particular order or format. The IRB shall determine what the appropriate format is for presenting the information on the consent document.

***9. May IRBs approve a waiver of documentation for studies that qualify for expedited review?***

Yes. A waiver of written documentation is allowed in expedited research. Many of the procedures that qualify for expedited review do not require written documentation outside of the research context. Therefore, consent documentation could be waived for much of the research approved using the expedited review process.

IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review utilized by the IRB, whether expedited or convened meeting review.

On behalf of SACHRP, I would like to thank you for your consideration of this report. The committee, the Subpart A Subcommittee and the Subcommittee on Harmonization 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