

Subpart A Subcommittee (SAS)

Elizabeth Bankert and Daniel Nelson
SAS Co-Chairs

with David Borasky, SAS Member

Presentation to the
Secretary's Advisory Committee on Human Research Protections (SACHRP)
March 8, 2011

Outline of Today's Presentation

- **Subcommittee charge and membership**
- **Topics for consideration at this meeting**
 - **FAQs on informed consent**
 - **Parental permission and assent**
 - **Documentation of informed consent**
- **Update on ongoing work**

Charge to the Subcommittee

- **Review and assess**
 - **All provisions of Subpart A of 45 CFR 46**
 - **Relevant OHRP guidance documents**
- **Based on this review and assessment**
 - **Develop recommendations for consideration by SACHRP in three categories:**
 - **Interpretation of specific Subpart A provisions**
 - **Development of new or modification of existing OHRP guidance**
 - **Possible revisions to Subpart A**

*Based on memo to Subcommittee from E. Prentice, Chair of SACHRP, 1/14/05
and subsequent discussion by SACHRP*

Charge to the Subcommittee

- **Goals**
 - **Enhance protection of human subjects**
 - **Reduce regulatory burdens that do not contribute to the protection of human subjects**
 - **Promote scientifically and ethically valid research**

*Based on memo to Subcommittee from E. Prentice, Chair of SACHRP, 1/14/05
and subsequent discussion by SACHRP*

Subpart A Subcommittee

Present Members

- Elizabeth Bankert,* Dartmouth College
- Laura Beskow, Duke University
- David Borasky, RTI International
- Bruce Gordon, University of Nebraska Medical Center
- Susan Kornetsky, Children's Hospital Boston
- Gigi McMillan, We Can Pediatric Brain Tumor Network
- Daniel Nelson,* University of North Carolina - Chapel Hill
- Susan Rose, University of Southern California
- Michele Russell-Einhorn, Dana Farber Cancer Institute
- Ada Sue Selwitz, University of Kentucky

- With welcome input from
 - SACHRP members who choose to affiliate
 - Ex officio reps of Common Rule agencies

Subpart A Subcommittee

Past Members

- Ricky Bluthenthal, RAND Corporation
- Gary Chadwick, University of Rochester
- Felix Gyi, Chesapeake Research Review, Inc
- Isaac Hopkins, Community Research Advocate (UMDNJ) †
- Nancy Jones, Wake Forest University → NIH
- Moira Keane, University of Minnesota
- Ernest Prentice, University of Nebraska Medical Center
- Thomas Puglisi, PriceWaterhouse Coopers → VA
- Lorna Rhodes, University of Washington
- David Strauss, New York State Psychiatric Institute

- Not shown are multiple SACHRP members who chose to affiliate with SAS while members of parent committee

Subcommittee Meetings

- Jan 18, 2005 via teleconference
- Feb 14, 2005 in Alexandria, VA
- May 20, 2005 via teleconference
- July 20-21, 2005 in Alexandria, VA
- Oct 4, 2005 via teleconference
- Jan 9, 2006 via teleconference
- Jan 30-31, 2006 in Rockville, MD
- May 11-12, 2006 in Gaithersburg, MD
- Sept 11, 2006 via teleconference
- Oct 4, 2006 via teleconference
- Feb 15-16, 2007 in Arlington, VA (with retreat)
- Mar 9, 2007 via teleconference
- May 31-June 1, 2007 in Arlington, VA
- July 16, 2007 via teleconference
- Aug 16-17, 2007 in Arlington, VA
- Oct 3, 2007 via teleconference
- Feb 21, 2008 in Rockville, MD
- May 15-16, 2008 in Rockville, MD
- Sept 22-23, 2008 in Rockville, MD
- Jan 26-27, 2009 in Rockville, MD
- June 8 & 30, 2009 via teleconference
- July 8, 2009 via teleconference
- Sept 1 & 30, 2009 via teleconference
- Oct 21, 2009 via teleconference
- Feb 24 & 26, 2010 via teleconference
- Jun 1-2, 2010 in Rockville, MD
- Jun 30, 2010 via teleconference
- Sept 27, 2010 via teleconference
- Jan 26-27, 2011 in Rockville, MD
- Feb 18, 2011 via teleconference

Supplemented by Working Group calls and e-mails

Secretarial Letters Incorporating SAS Recommendations

- **5th SACHRP letter to Secretary Leavitt → 3/14/07**
 - Recommendations approved 2005-2006
 - Continuing Review → **Federal Register notice on 11/06/09**
 - Expedited Review → **Federal Register notice on 10/26/07**
- **6th SACHRP letter to Secretary Leavitt → 6/15/07**
 - Recommendations approved March 2007
 - Required Training → **Federal Register notice on 07/01/08**
- **7th SACHRP letter to Secretary Leavitt → 1/31/08**
 - Recommendations approved March & July 2007
 - Waiver of Informed Consent
 - Minimal Risk → Analytical framework and examples
- **8th SACHRP letter to Secretary Leavitt → 9/18/08**
 - Recommendations approved Oct 2007, March & July 2008
 - Exemptions
 - Alternative models of IRB review
 - IRB membership rosters
 - Waiver of documentation of informed consent
 - Institutional Officials
 - American Indians and Alaska Natives
 - (Letter also addressed disaster research, and systems-level commentary)
- **10th SACHRP letter to Secretary Sebelius → 7/15/09**
 - Recommendations approved March 2009
 - Designation of IRBs within FWA
- **11th SACHRP letter to Secretary Sebelius → 3/24/10**
 - Reaffirmation of previous rec on required education, after public RFI
- **12th SACHRP letter to Secretary Sebelius → 1/14/11**
 - Informed consent and research use of Biospecimens (FAQs)

**Subpart A Subcommittee (SAS) Report and
Recommendations to SACHRP**

**Improving the Form and
Process of Informed
Consent**

Informed Consent

- Previous work by SAS → approved by SACHRP
 - 2007 → Recommendations on waiver of IC
 - 2008 → Recommendations on waiver of documentation of IC
 - 2010 → FAQs addressing issues specific to informed consent for research use of biospecimens
- Current work focuses on broader sets of issues relating to IC
 - Areas where regulations may provide flexibility
 - Areas where interpretation or understanding may warrant clarification
 - Format → FAQs that embody recommendations

Parental Permission and Assent of Children

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

Assent is required unless an IRB determines 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 that one of these conditions is met, there is no requirement to waive assent.

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

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 the two criteria listed above do not apply, is there a way to waive the requirement for assent?

Yes, the IRB may waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A. However, the waiver is limited to minimal risk research.

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

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? REVISED

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:

continued...

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

(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 are adults for the purposes of the research, investigators should carefully consider the capacity of each subject to give consent.

(1) 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.

continued...

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

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.

10. Are electronic signatures considered valid documentation of informed consent?

OHRP recognizes electronic signatures as fulfillment of the requirement for documentation of informed consent as long as they are legally valid within the jurisdiction where the research is to be conducted. It is noted that some form of the consent document must be made available to the subjects in a format they can retain.

OHRP does not mandate a specific method of electronic signature. Rather, OHRP permits IRBs to adopt such technologies for use as long as the IRB has considered applicable issues such as how the electronic signature is being created, if the signature can be shown to be legitimate, and if the consent or permission document can be produced in hard copy for review by the potential subject.

Electronic signatures are defined as an electronic sound, symbol, or process, attached to or logically associated with a contract or other record and executed or adopted by a person with the intent to sign the record.

RECOMMENDATION ON HOLD PENDING INPUT FROM LEGAL COUNSEL

11. Does a participant's agreement to participate by internet (e.g. clicking an "I agree" link or a radio button on a web-based survey) constitute an electronic signature for the purposes of documenting informed consent?

As with other forms of electronic signature, OHRP accepts electronic signatures on informed consent documents, as long as they are legally valid within the jurisdiction where the research is to be conducted. (See FAQs on informed consent)

An electronic signature is any electronic means that indicates that a person adopts the contents of an electronic message. Electronic signatures are defined as an electronic sound, symbol, or process, attached to or logically associated with a contract or other record and executed or adopted by a person with the intent to sign the record.

When such documentation is not considered legally valid, the IRB must determine if the study qualifies for a waiver of documentation, if that approach is to be used.

RECOMMENDATION ON HOLD PENDING INPUT FROM LEGAL COUNSEL

12. Is the short form option for documentation of informed consent restricted to use with non-English speaking or illiterate subjects?

HHS [45 CFR 46.117(b)(2)] and FDA [21 CFR 50.27(b)(2)] regulations do not limit the use of the short form to these participant populations. IRBs should consider when the use of the short form is appropriate and what information should be included in the written summary.

PENDING....

FDA GUIDANCE ON NON-ENGLISH SPEAKING?

OHRP STANCE?

13. Is it permissible to use the short form option for documentation of informed consent in studies that are determined to be greater than minimal risk by the IRB?

HHS [45 CFR 46.117(b)(2)] and FDA [21 CFR 50.27(b)(2)] regulations do not limit the use of the short form to minimal risk research. IRBs should consider when the use of the short form is appropriate and what information should be included in the written summary.

SAS WORK IN PROGRESS

SAS Next Steps

- Complete additional Q&A on consent regulations at §46.116
- Review of the Short Form regulations at §46.117
- Examine the application of informed consent regulations in internet-based research
- Ongoing focus on shortening, clarifying, and/or repackaging consent documents to facilitate participant understanding

**Stay tuned... there is always
more to come from SAS!**

