

Subpart A Subcommittee (SAS)

David Borasky and Daniel Nelson
SAS Co-Chairs

**Presentation to the
Secretary's Advisory Committee on Human Research Protections (SACHRP)
February 28, 2012**

Outline of Today's Presentation

- Subcommittee charge and membership
- Topics for consideration at this meeting
 - Analysis of the Federalwide Assurance Mechanism
 - Work in progress
 - Expedited review categories
 - Criteria for waiver of consent

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
- Robert Frenck, Cincinnati Children's Hospital
- Susan Kornetsky, Children's Hospital Boston
- Daniel Nelson,* University of North Carolina - Chapel Hill
- Nancy Olson, University of Mississippi
- Susan Rose, University of Southern California
- Michele Russell-Einhorn, Dana Farber Cancer Institute
- Ada Sue Selwitz, University of Kentucky
- David Strauss, New York State Psychiatric Institute

- 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
- Bruce Gordon, University of Nebraska Medical Center
- Isaac Hopkins, Community Research Advocate (UMDNJ) †
- Nancy Jones, Wake Forest University → NIH
- Moira Keane, University of Minnesota
- Gigi McMillan, We Can Pediatric Brain Tumor Network
- Ernest Prentice, University of Nebraska Medical Center
- Thomas Puglisi, PriceWaterhouse Coopers → VA
- Lorna Rhodes, University of Washington

- 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 telecon
- July 20-21, 2005 in Alexandria, VA
- Oct 4, 2005 via telecon
- Jan 9, 2006 via telecon
- Jan 30-31, 2006 in Rockville, MD
- May 11-12, 2006 in Gaithersburg, MD
- Sept 11, 2006 via telecon
- Oct 4, 2006 via telecon
- Feb 15-16, 2007 in Arlington, VA (+ retreat)
- Mar 9, 2007 via telecon
- May 31-June 1, 2007 in Arlington, VA
- July 16, 2007 via telecon
- Aug 16-17, 2007 in Arlington, VA
- Oct 3, 2007 via telecon
- 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 telecon
- July 8, 2009 via telecon
- Sept 1 & 30, 2009 via telecon
- Oct 21, 2009 via telecon
- Feb 24 & 26, 2010 via telecon
- Jun 1-2, 2010 in Rockville, MD
- Jun 30, 2010 via telecon
- Sept 27, 2010 via telecon
- Jan 26-27, 2011 in Rockville, MD
- Feb 18, 2011 via telecon
- April 18, 2011 via telecon
- May 9, 2011 via telecon
- June 13-14, 2011 in Rockville, MD
- Sept 12-13, 2011 in Rockville, MD
- Jan 13 & 25, Feb, 2012 9 via telecon

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)

Secretarial Letters Incorporating SAS Recommendations (continued)

- **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
- **13th SACHRP letter to Secretary Sebelius → 1/24/11**
 - FAQs on informed consent and research use of biospecimens (see below)
- **14th SACHRP letter to Secretary Sebelius → 8/5/11**
 - Parental permission, child assent, and documentation of informed consent
- **17th SACHRP letter to Secretary Sebelius → 10/13/11**
 - FAQs on biospecimen consent, revised and expanded to address HIPAA and FDA
 - Applying the Regulatory Requirements for Research Consent Forms: What Should and Should Not be Included?
- **18th SACHRP letter to Secretary Sebelius → 10/13/11**
 - SACHRP comments on federal ANPRM

Analysis of the Federalwide Assurance (FWA) Mechanism

Regulatory Background

- **45 CFR 46.103(a)** - "Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy."

Request from OHRP

- Consider alternatives to the current assurance mechanism (FWAs)
 - Could the assurance process be more effectively implemented/managed by being incorporated directly into the grant-making process?

Input from *ex officio* representatives

- Dept. of Education
- Dept. of Energy
- Dept. of Justice
- NIST
- NIH
- CDC
- Indian Health Service
- EPA
- FBI
- NSF
- VA
- AHRQ

Questions and Concerns

- Shifting to the grant process would create greater administrative burden for grantees and funding agencies
- Potential to diminish the perceived importance of the assurance
- Responsibility for compliance?
 - Institution vs. IRB vs. Investigator
- Does (or could) the enhanced IRB registration process serve some of the needs covered by the FWA?

Questions and Concerns

- Real problems may be more related to the “rules of engagement,” which define the need for assurance, rather than FWA per se
- Would loss of the single FWA force Common Rule agencies/departments to establish their own separate assurance mechanisms?
- Works against the goals of harmonization
 - SACHRP, PCSBI, ANPRM

Conclusions

- There was serious consideration given to this topic, and recognition that the current FWA process is not perfect.
- There was not, however, support for moving the assurance mechanism to the grant-making process.
- SAS consensus was to maintain the status quo, with attention to “engagement.”

WORK IN PROGRESS:

**Potential Revisions to the
Expedited Review
Categories**

Regulatory Background

- **45 CFR 46.110(a)** "The Secretary, HHS, has established, and published as a Notice in the Federal Register, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the Federal Register."

Request from OHRP

- **Current expedited review list was last revised in 1998**
- **SACHRP has previously approved a limited recommendation to revise Category 7 → Fed Reg Notice 2007**
- **SAS was asked to review list and propose additional revisions**

Revisions Under Consideration

- Allow some forms of radiation exposure (e.g., dexta scans, single x-ray)
 - Would need experts to help set thresholds?
- Clarify if taking *extra* bone marrow or CSF during a clinically-indicated procedure is considered noninvasive
 - Some may already expedite this, but there is inconsistency across institutions?

Revisions Under Consideration

- Skin punch biopsies that do not require sutures
 - Nuances to this procedure may make it difficult to set parameters?
- Blood sample restrictions
 - Remove the frequency parameter and base on volume only?
 - Reconsider the weight and volume restrictions, and address inadvertent effect of prior edits to list?

Revisions Under Consideration

- Clarify that research with NSR device can be approved through expedited review
 - Currently in FDA guidance for minimal risk and no IDE, but not explicitly on the list?
- Confirm that Humanitarian Use Device (HUD) protocols can be renewed via expedited review

Revisions Under Consideration

- Expand/clarify Category 5 to allow data collected for research purposes
 - Consider data coordinating centers?
- Allergy skin testing
- Extend to anesthesia / analgesia when procedures are otherwise on the list

Revisions Under Consideration

- Long-term follow-up (e.g., oncology patients, device recipients) where data have both research value and clinical relevance
 - Remove from Category 8?
- Oral history
 - Expedited review vs. exempt vs. NHSR?

Revisions Under Consideration

- Protocols using subject pools (e.g. Psych 101) for recruitment
 - Some expediting now, but not consistently?
- Include more examples of social and behavioral research
 - Ethnographic research, social networking, virtual reality, online research, on-line gaming research, deception, behavioral tasks and minimal risk experimentation?

Revisions Under Consideration

- Clarify that “Minor changes to previously approved research” (i.e., amendments) are changes that do not alter the risk:benefit analysis

WORK IN PROGRESS:

**Review of Criteria for Waiver
of Informed Consent**

Regulatory Background

- *An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:*
 - *Research involves no more than minimal risk to the subjects;*
 - *Waiver or alteration will not adversely affect the rights and welfare of the subjects;*
 - *Research could not practicably be carried out without the waiver or alteration; and*
 - *Whenever appropriate, the subjects will be provided with additional pertinent information after participation.*

Request from OHRP

- Examine criteria for waiver of consent given the permissibility/likelihood of substantive regulatory change (see ANPRM)
- See also previous recommendations on waiver of consent → Secretarial Letter dated 1/31/08

Points to Consider

- “Minimal risk” remains variably understood and applied → see prior recommendations
- “Rights and welfare”
 - Most subjective of four criteria
 - Legal vs. inherent rights?
 - Redundant with §116(e)?

Points to Consider

- “Practicability” remains variably understood and applied
 - Practicability of research (in the absence of waiver) vs. practicability of obtaining consent?
- How is post-participation debriefing to be applied in biomedical research under waiver (e.g., retrospective chart reviews)?

Points to Consider

- Are all four criteria relevant?
- Are additional criteria needed?
- Threshold too high for some partial waivers of consent
 - Difficulty of waiving selected elements works against desire to simplify and shorten consent documents

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

