Subpart A Subcommittee (SAS)

David Borasky and Daniel Nelson

SAS Co-Chairs

Presentation to the
Secretary's Advisory Committee on Human Research Protections (SACHRP)
March 13, 2013

Outline of Today's Presentation

- Subcommittee charge and membership
- Overview of prior Subcommittee work
- Recommendations for consideration
  - Revisions and updates to the Expedited Review Categories
- Future work
  - Engagement of Institutions in Human Subjects Research

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

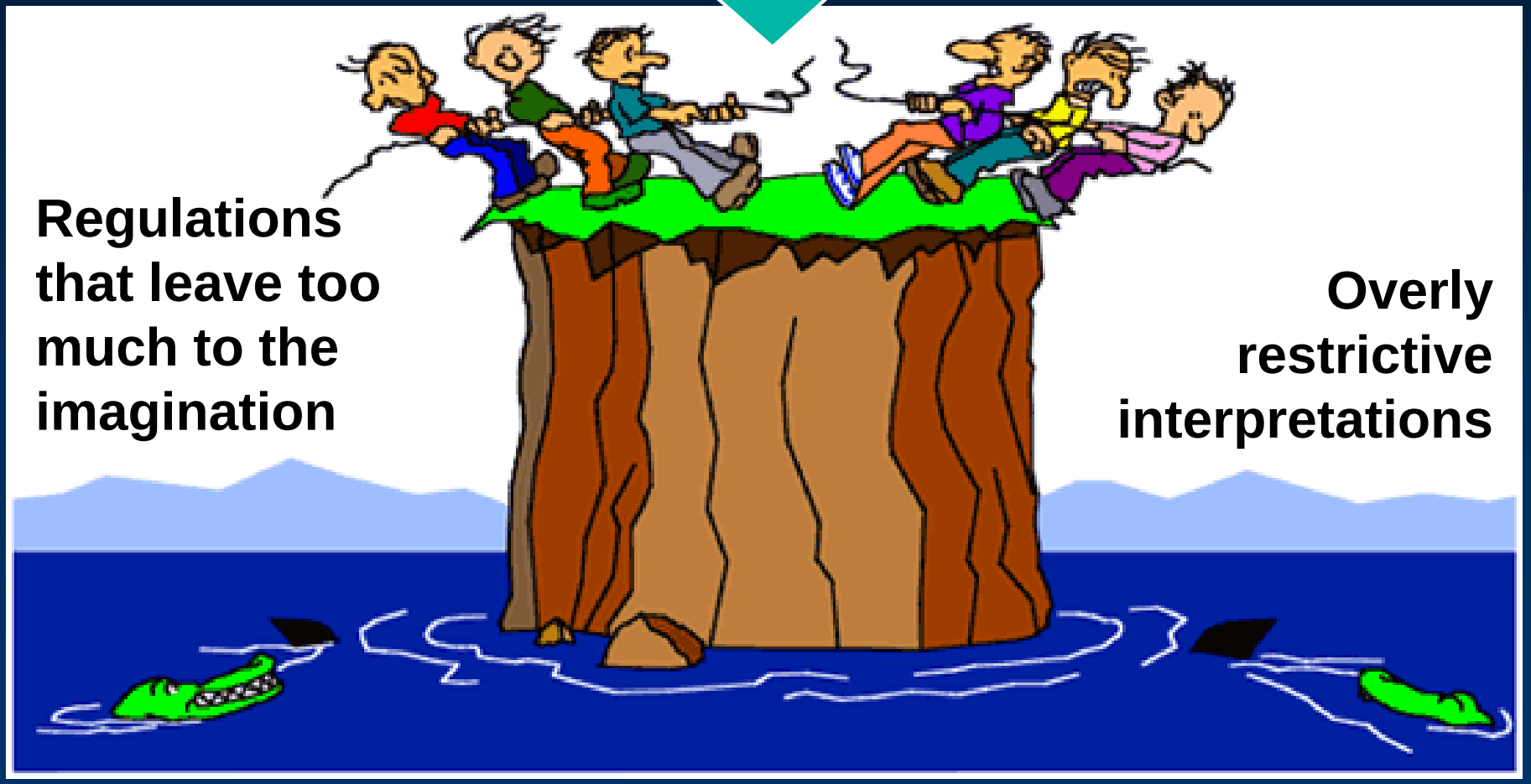
- Goals
  - Enhance protection of human subjects
  - Reduce regulatory burdens that do not contribute to the protection of human subjects
  - Promote scientifically and ethically valid research

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

What is the problem?

What are we trying to fix?

Investigators
Subjects
IRBs



Regulations that leave too much to the imagination

Overly restrictive interpretations

Subpart A Subcommittee
Present Members

- Elizabeth Bankert, Dartmouth College
- David Borasky,* University of North Carolina - Chapel Hill
- Gary Chadwick, University of Rochester
- 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

*co-chairs

Subpart A Subcommittee
Past Members

- Ricky Bluthenthal, RAND Corporation
- Laura Beskow, Duke University
- 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 9, 2012 via telecon
- Apr 12, 2012 via telecon
- May 3-4 in Rockville, MD
- Jun 7, 2012 via telecon
- August 6, 2012 via telecon
- Sept 5-6, 2012 in Rockville, MD
- February 20-21, 2013 in Rockville, MD

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
- **20th SACHRP letter to Secretary Sebelius → PENDING**
  - Recommendations approved Oct 2012
    - Investigator responsibilities
    - Informed consent and waivers of informed consent

Recommendations for 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

General Principles

- List of categories of research that may be reviewed through expedited procedure is helpful and should be maintained
- List should be evaluated and updated on regular basis (prior rec = 5 yrs)
- List contains *examples* that are neither all-inclusive nor exclusive
- Appearance on the list does not mean the procedure or approach MUST be expedited
  - Some still eligible for exemption
  - Some may require convened meeting review

Recommendations

- Clarification that the list does not apply to activities that do not meet the definition of human subjects research or are exempt
- Expedited reviewer need not be designated by the chairperson
- All current categories have been reviewed and revised; additional categories suggested

WRITTEN DRAFT FOR REVIEW:

Revisions to 45 CFR 46.110 and the List of Expedited Categories

FUTURE WORK:

Engagement of Institutions in Human Subjects Research

Background

- OHRP has issued guidance to help institutions determine when they are *engaged*
  - "Guidance on Engagement of Institutions in Human Subjects Research," Oct 16, 2008
  - Which replaced…
    - "Engagement of Institutions in Research," Jan 26, 1999
    - "Engagement of Pharmaceutical Companies in HHS-Supported Research," Dec 23, 1999

Background

- Format/goals of current guidance
  - III(A)(1-6): Scenarios that, in general, would result in an institution being considered engaged in a human subjects research project
  - III(B)(1-11): Scenarios that would result in an institution being considered NOT engaged in a human subjects research project
  - IV: IRB review considerations for cooperative research in which multiple institutions are engaged in the same non-exempt human subjects research project

Why does this matter?

"When an institution is *engaged* in non-exempt human subjects research that is conducted or supported by HHS, it must satisfy HHS regulatory requirements related to holding an assurance of compliance and certifying institutional review board (IRB) review and approval."

OHRP Guidance on Engagement of Institutions in Human Subjects Research, Oct 2008

Background

- Translation of previous slide: “Engagement determines whether, when and where the regs apply!”

- Guidance is amenable to clarification and change
- OHRP has asked SACHRP to consider

Background

- OHRP, institutions, IRBs and investigators all struggle with provisions
  - Institutions devote considerable resources to navigating complex scenarios, determining who is engaged, who is not, etc
- Examples in guidance are centered around the definition of HSR
  - Is the site obtaining information about subjects, obtaining consent, etc?
  - Creates potential for overlap and confusion

Who's on first?

"Regarding the relationship between the engagement of institutions in research and the terms of the FWA, we want to clarify that the Terms of Assurance apply to institutions that have already been determined to be engaged in the conduct of human subjects research. Through the FWA, the institution commits to HHS that it will comply with the requirements set forth in 45 CFR part 46, as well as the specific Terms of Assurance that identify certain requirements that the institution agrees to fulfill under the FWA. In contrast, OHRP's guidance document on engagement in research was developed to assist institutions in determining whether or not they are engaged in a particular human subjects research project. Therefore, the Terms of Assurance should not be used to determine whether an institution is engaged in a particular research project."

OHRP Correspondence on Engagement of Survey Firms, Jan 2009

Drawing the lines… is it HSR? Exempt? And where does "engagement" fit in?

NOTE: Some of the questions to determine engagement are similar to HSR, but it's not the same thing, and needs to be addressed in order

Adapted from OHRP

Issues to Consider

- Many exclusions or exceptions
  - Are direct awardees engaged, if all research activities are carried out elsewhere and prime is merely a conduit for funding?
    - Currently yes, but with case-specific exceptions
- Harmonization with FDA regulations
  - Example: onetime administration of experimental therapy → OHRP considers not engaged, but FDA requires 1572 for that site
  - FDA does not have equivalent assurance process

Issues to Consider

- All sites are not created equal
  - Example: Multisite clinical trial with activities at some sites limited to components that could be exempt
  - For research to be exempt, the entire study must fit under one or more categories of exemption
  - In this scenario, all components are bundled together, so all sites are reviewed at the same (highest) level
  - Could the exempt components be carved out from the bundle?

Issues to Consider

- Principles of engagement
  - There should be at least one IRB reviewing non-exempt human subjects research
  - Not a question of avoiding or eliminating IRB review… but how much *additional* IRB review is required, for multisite research?

- Can this be accomplished without current complexity and confusion?