MEDICAL RESEARCH SUMMIT CONFERENCE

A REPORT ON THE ACTIVITIES AND PROGRESS OF SACHRP

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April 23, 2004

Disclaimer

This presentation will address the activities and recommendations of SACHRP to date without the benefit of cross-checking the transcripts of the March 29-30 meeting, which is necessary before a final report is provided

“We must make sure we allow science and medical research to advance for the good of all Americans but not at the expense of the people who participate in clinical trials.”

HHS Secretary Tommy Thompson
HHS Press Release, January 3, 2003

SACHRP Charter

SACHRP will advise the Secretary on matters concerning the protection of human subjects with particular emphasis on special populations such as neonates, children, prisoners, the decisionally impaired; pregnant women, embryos, and fetuses; international studies; identifiable samples; investigator COI; OHRP activities.

October 1, 2002

Members of SACHRP

Thomas Adams, C.A.E.
Celia Fisher, Ph.D.
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Nancy Jones, Ph.D.
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Mark Barnes, J.D.
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Susan Weiner, Ph.D.

Ernest D. Prentice, Ph.D. (Chair)
Bernard A. Schwetz, D.V.M., Ph.D. (Executive Secretary)
Catherine Slatinshek, M.A. (Executive Director)

SACHRP Activities

	Topic	Work Plan
1.	Research With Children	Subcommittee
2.	Research With Prisoners	Subcommittee
3.	HRPP Accreditation	Subcommittee
4.	Adverse Event Reporting	Presentations
5.	International Research	Presentations
6.	Litigation/Liability	Presentation
7.	HIPAA Privacy Rule	Presentations

Subcommittee on Research Involving Children

Provide recommendations for consideration by SACHRP on a Subpart D 407 Panel review process that will best achieve the goals of transparency, public input, expert input, timeliness, clarity, harmonization (OHRP/FDA) and “consensus”. Provide recommendations on interpretation of Subpart D.

Co-Chairs: Celia Fisher, Ph.D. and
Susan Kornetsky, M.P.H.

Overview of HHS Regulations at 45CFR46, Subpart D

Additional protections for children involved as subjects in research

FR 48(No 46), March 8, 1983
effective June 6, 1983

The Risk-Benefit Protections Escalation Principle

As the risk of the research increases beyond the *"minimal risk threshold"* in relation to the absence of direct benefit to the subject, the criteria for IRB approval under Subpart D categories become more stringent.

Categories of Pediatric Research

46.404 **50.51**

46.405 **50.52**

46.406 **50.53**

46.407 **50.54**

Category

46.407	50.54

Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

Requirements

46.407	50.54

- The research does not meet the other Subpart D categories.
- The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

Requirements Cont'd

46.407	50.54

- An *HHS-OHRP/FDA* panel of experts must review a *407/54 Application* which includes the IRB's review, determination, rationale, and documentation
- Provide recommendations to *HHS-OHRP/FDA on approvability of the research*
- Opportunity for public review and comment
- Final decision made by HHS/FDA

Question

How does an IRB decide if an HHS funded study should be submitted for a 407 review?

IRB Determination

The IRB must:

1)Determine and document why the research does not meet the requirements for approval under 46.404, 46.405, or 46.406

AND

2)Decide the research should be submitted for 407 review

AND

3)Prepare and submit a 407 application

SACHRP Recommendations Concerning the Subpart D 407 Review Process

SACHRP Recommendations: OHRP 407 Screening Process

- OHRP should screen 407 applications in a timely manner and determine if a 407 designation is appropriate
- OHRP should inform the funding agency, IRB, and PI of the determination
- If a 407 designation is appropriate and the application is complete, OHRP will appoint a panel

SACHRP Recommendations: The 407 Panel Review Model

- The *non-FACA open panel model* should be used for the 407 review

SACHRP Recommendations: 407 Review Panel Composition

Panel Composition

- Experts in science, ethics, pediatrics, and the disorder/condition under study
- At least one public member who can adequately represent and voice the interests of the subjects
  - A public member from a family that has experience with this disorder or condition
  - A child advocate when the subjects do not have a disorder or condition

SACHRP Recommendations: OHRP Screening Actions(s)

- OHRP may decide, for safety reasons, to suspend enrollment at all active sites
- OHRP may decide, for safety reasons, to terminate the study at all active sites
- Site IRBs should ensure that parents (and subjects) are promptly informed and consented for continued participation (if required by OHRP and/or the IRB)

SACHRP Recommendations: OHRP/FDA Harmonization

- Harmonization of the process utilized by OHRP and FDA for Subpart D (407; 50.54) reviews should be a priority
- OHRP and FDA Subpart D (407; 50.54) joint reviews should maintain goals of transparency, public input, expert input, clarity, and consistency

SACHRP Recommendations: Monitoring 407 Review Process

- OHRP should provide a yearly report to SACHRP on 407 activity including OHRP/FDA harmonization
- During the year, OHRP should keep SACHRP informed about the number of 407 Applications under review
- A subcommittee of SACHRP should work with OHRP to achieve quality improvement

Workplan of the Subcommittee on Research Involving Children

Reminder

Children involved in research should not be under-protected, overprotected, or inconsistently protected across study sites. The key is to define and clarify the meaning and application of the terms in Subpart D (HHS/FDA) which address IRB approval criteria.

Workplan

The subcommittee will provide a report for consideration by SACHRP, which defines and clarifies the meaning and application of the following inter-related terms in Subpart D: *minimal risk; direct benefit to individual subjects; minor increase over minimal risk; commensurate; disorder or condition; vital importance and assent*.

Accreditation Subcommittee

Provide recommendations for consideration by SACHRP on the following aspects of HRPP accreditation:

- Perceived value;
- Incentives;
- Assessment of impact;
- Role (if any) of the government

Co-Chairs: Tom Adams, C.A.E. and Felix Gyi, Pharm.D.

AAHRPP®
Association for the Accreditation of Human Research Protection Programs, Inc.®

Partnership for Human Research Protection, Inc.
A JCAHO/NCQA COLLABORATION

SACHRP Recommendations Concerning HRPP Accreditation

SACHRP Recommendations: Perceived Value of HRPP Accreditation Process

- SACHRP supports the concept of HRPP Accreditation
- Accreditation *promises* to be a useful mechanism which can lead to self improvement of systems and outcomes

SACHRP Recommendations: Incentives for Accreditation

It is premature for government agencies to offer incentives to research institutions to seek accreditation.

SACHRP Recommendations: Eval. of Accreditation Impact

- There should be a systematic evaluation of accreditation as an assurance of quality research and subject safety.
- HHS/OHRP should organize a conference to evaluate voluntary accreditation and self-regulatory initiatives undertaken over the past few years.

SACHRP Recommendations: Federal Role in Accreditation

The government should have no role in endorsing one accrediting organization over another.

Subpart C Subcommittee

Provide recommendations for consideration by SACHRP on interpretation, reinterpretation, and ultimately revision of Subpart C to ensure that regulations do not obstruct ethically and scientifically appropriate research.

Co-Chairs: Mark Barnes, J.D. and
Nancy Dubler, LL.B.

Interim Report
(Short Term Solutions)

- Clarify the definition of a prisoner
- Clarify applicability of Subpart C when incarceration occurs post-enrollment
- Clarify the necessary qualifications of the prisoner representative on the IRB
- Clarify the meaning of *"control groups which may not benefit"* that triggers an HHS expert panel review [46.306 (a)(2)(D)]

Interim Report
(Long Term Solutions)

Subpart C should be totally revised to ensure that regulations do not obstruct ethically and scientifically appropriate research involving prisoners for the benefit of prisoners and others.

SACHRP Recommendations: Adverse Event Reporting (AER)

SACHRP recognizes the overwhelming workload problem which is associated with IRB review of an extremely large number of IND safety reports (external AERs) which are generated during a multi-center IND trial. SACHRP recommends that OHRP and FDA promptly issue clear and consistent guidance on IRB review of both internal and external AERs which will best serve to protect human subjects and effectively reduce regulatory burden. A model was discussed and distributed to OHRP/FDA, but was not directly endorsed.

SACHRP Recommendations: Litigation/Liability in Research

The Morreim Report to SACHRP on litigation and liability should be transmitted to the IOM. No further action will be taken at this time.

SACHRP Actions: HIPAA Privacy Rule

A SACHRP drafting committee will develop recommendations concerning revision of the HIPAA Privacy Rule to achieve greater harmonization with the Common Rule, ensure protection of privacy rights, and reduce regulatory burden.

SACHRP Actions: International Research

The topic of international research is deferred for future discussion.

SACHRP Workplan for the July 26-27, 2004 Meeting

SACHRP Workplan

- Research Involving Children (Continued)
- Research Involving Prisoners (Continued)
- Distinction Between Research and Non-Research (Panel)
- Social and Behavioral Science Research (Panel)
- 45CFR46, Subpart B (Panel)

Acknowledgement and Thanks

SACHRP members, subcommittee members, ad-hoc members, the OHRP leadership, OHRP staff and UNMC staff have enthusiastically worked together as a team in pursuing the charge given to SACHRP by Secretary Tommy Thompson.

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