

Subcommittee on Harmonization (SOH)

Update

Mark Barnes

David Forster

February 29, 2012

Membership

- **Albert Allen M.D.**
- **Susan Alpert, Ph.D, M.D.**
- **Mark Barnes, J.D., LL.M. - Co-Chair**
- **Gary Chadwick, Pharm.D., CIP**
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- **Karen N. Hale, RPh, MPH, CIP**
- **Justin P. McCarthy, J.D.**
- **Marjorie A. Speers, Ph.D.**
- **Susan Stayn, J.D.**

Meetings

- Convened meetings:
 - April 15-16, 2010
 - September 21-22, 2010
 - February 8-9, 2011
 - June 29-30, 2011
 - September 12-13 (joint meeting with SAS)
- Monthly teleconferences

Completed Activity – HHS Conflict of Interest Policies

- Recommendation regarding adoption of a single conflict of interest standard across DHHS entities.
- Adopted by SACHRP at July 21, 2010 meeting.

Completed Activity – Comparison of Common Rule and FDA Regulations

- Reviewed differences between Common Rule FDA at SOH meeting of September 21-22, 2010.
- Many of the differences are based in unique roles of the agencies and are not problematic:
 - Differences in waivers of documentation of consent
 - FDA emergency use regulation.
- This background is informing continuing SOH activities, but no recommendation on solely this comparison is planned.

Completed Activity – Commentary on NPRM on HITECH

- Recommendation adopted by SACHRP at October 19, 2010 meeting.
- Five topics:
 - Compound Authorizations
 - Future/Secondary Research
 - Minimum Necessary
 - Business Associates
 - Restriction on Sale of PHI

Completed Activity – Definition of Non-Scientist

- Recommendation adopted by SACHRP at October 19, 2010 meeting.

Completed Activity – Addition of FDA Considerations to SAS FAQs on Biospecimens

- Recommendation adopted by SACHRP at July 20, 2011 meeting.

Completed Activity – Definition of a Minor Change in Research

- Recommendation adopted by SACHRP at July 20, 2011 meeting.

Completed Activity – Early Processes in Research

- Application of 45 CFR 46 and 21 CFR 56 to early processes in research, such as identifying potential subjects, contacting subjects, and recruiting subjects.
- Recommendation adopted by SACHRP at July 20, 2011 meeting.

Four Items for SACHRP's Consideration

- Recommendation regarding applicability of FDA regulations.
- Recommendation regarding protocol deviations.
- Recommendation regarding individual patient treatment use protocols.
- Recommendation regarding OHRP, ORI, and FDA overlapping jurisdiction of research misconduct and non-compliance in HSR.

Applicability of FDA Regulations

- There is great uncertainty in the regulated community as to the jurisdiction of FDA regulations to records reviews, interviews, questionnaires, registries, and other such types of research.
- When FDA regulations apply, certain HHS regulations regarding exemptions, waiver of consent, and waiver of documentation of consent cannot be applied.
- There are 2,308 IRBs registered with both OHRP and FDA that face this issue on a regular basis.

Protocol Deviations

- Differences of opinion in the regulated community about the regulatory status of intentional protocol deviations.
- Goal of this recommendation is clearly stated FDA and OHRP policy.
- Confusing document because there are five “types” of protocol deviations that need to be differentiated.

Protocol Deviations

I and II. Intentional deviation



III. Unintentional deviation that can't be prevented



IV. Unintentional deviation discovered after the fact

V. Intentional deviation to prevent harm



V. Traditional change in research, with changes to written documents



Single Patient Treatment Use Protocols

- At October 4, 2011 SACHRP meeting, FDA asked for recommendations regarding single patient treatment use of investigational drugs and biologics.
- SOH developed this recommendation based on their request.

Misconduct and Non-Compliance: ORI and OHRP

- Addresses intersection of the jurisdictions, regulatory processes, and sanctions of the Office for Human Research Protections (OHRP), the Office of Research Integrity (ORI), and the Food and Drug Administration (FDA), especially as relating to FDA's 2010 proposal on sponsor obligations to report data falsification.

Future Topic –

Certificates of Confidentiality/ Confidentiality Protections

- Not all Common Rule agencies can issue certificates of confidentiality.
- Some have different regulatory protections, such as DOJ.

Future Topic - Standard practice vs. Innovative care vs. research vs. clinical investigation

- QA/QI activities, especially QA/QI activities involving FDA regulated products or products that may or may not be FDA regulated (example, skin cleaner on wash cloth versus a marketed product for cleaning skin.)
- CDC definition of research vs. QI vs. epidemiology.

Future Topic – Signatures by Illiterate subjects

- OHRP should agree with FDA allowance for X as signature for illiterate subjects.

Future Topic – Disclosure to subjects of IRB approval

- OHRP, ICH and FDA should agree on whether ok to disclose IRB approved a study.

Future Topic - Engagement of Community in Research

- How and when should community be engaged in research.
- No clear protocol or method, subjects are involved in design.
- HPTN, HVTN, NIADA CAB utilize community participation.
- Community consultations under 50.24.

Future Topic - Consent Issues

- Use of partially translated short form for non-English speakers. OHRP versus FDA. OCR silent.
- Documentation of consent/signature requirements. HHS signature vs. FDA signature and date vs. ICH signed copy and witness signature for illiterate subjects.

Future Topic - Application of Subparts B, C, D

- Unequal application of the subparts across agencies.

Future Topic - International

- Common Rule vs. FDA vs. ICH vs. OCR.
- Also European laws, other laws around the world.
- Preemption issues.

Future Topic - Incapacitated Adults

- SIIIDR report
- VA guidance
- new FDA information sheets
- ICH
- OHRP FAQ on LAR
- NIH Points to Consider
- Could and should all these be harmonized?

Future Topic - Safety Issues

- Unanticipated problems and overall protocol safety assessment by sponsors and others.
- FDA guidance on DSMBs and NIH requirements for DSPs.
- Continuing difference between FDA and OHRP UP guidances. Mostly issue of seriousness. Could it be a single guidance?

Future Topic - Local Attitudes

- FDA versus OHRP guidance

Future Topic - Procedural Issues

- Creation of a single new agency to oversee all human subjects research in the US.
- Procedural changes in the way that the common rule agencies establish guidance in order to promote harmonized guidance.
- Procedural changes to require or promote joint regulations and/or guidance from OHRP and FDA and other HHS agencies.



Feedback or Questions?