

Human Subjects Protection 101 – Core Issues to Consider

David G. Forster, J.D., M.A., C.I.P.

Vice President, Compliance
Western Institutional Review Board (WIRB)

Auxiliary Faculty
University of Washington
Department of Medical History and Ethics

HCCA's Research Compliance Conference
Las Vegas, NV – September 17, 2006

Goal of Presentation

Provide an overview of human subjects protection from two viewpoints.

1. Overview of issues to consider/implement in a human subject protection program.
2. Common non-compliance issues often encountered.

**Issues to Consider for a
Human Subject Protection
Program**

Research Ethics

Dual Role of IRBs – Ethics Committee and Regulated Committee

- IRBs are ethics committees that use and interpret ethical principal rules.
- IRBs are regulated entities that must comply with regulations.

Dual Role of IRBs – Ethics Committee and Regulated Committee

- Sometimes ethical research does not meet regulatory requirements.
- Sometime research satisfies the regulatory requirements, but is not ethical.

Dual Role of IRBs – Ethics Committee and Regulated Committee

You may have to defend an action that does not have clear regulatory support. For instance, IRBs often decide that given research data cannot be used or published because the investigator did not follow the IRBs requirements. No regulations support this action.

Dual Role of IRBs – Ethics Committee and Regulated Committee

- HHS FederalWide Assurance (FWA) requires that institutions adopt guiding ethical principles.

Dual Role of IRBs – Ethics Committee and Regulated Committee

- There are ethical dilemmas involved in research. Realize that the IRB will inevitably make decisions that can be ethically questioned.
- Example: Justice versus Beneficence.
- Is it ethical for a protocol to be limited to English speaking subjects only?

Dual Role of IRBs – Ethics Committee and Regulated Committee

Be aware that there are hotly contested debates regarding research ethics, separate from regulatory issues.

Example:

- Is clinical equipoise a necessary condition for IRB approval?
- If you as counsel can't answer this question, who can?
- How do you get ethical expertise to your IRB meetings?
- How do you train your IRB members on ethical issues?

Regulatory Jurisdiction

Regulatory Jurisdiction

You need to have a process in place to determine what regulations (and other laws) apply to the research conducted at your institution.

Regulatory Jurisdiction

Examples:

- National Institutes of Health (NIH)
- Food and Drug Administration (FDA)
- Department of Defense (DOD) components
- Environmental Protection Agency (EPA)
- Department of Justice (DOJ)
- Veteran's Affairs (VA)
- State Law
- Other Federal Laws

Regulatory Jurisdiction

- All of these agencies have unique regulatory requirements, sometimes as unique changes to the common rule or more often as additional regulations.
- Who provides this analysis? IRB staff? IRB chair? Counsel?

Bureaucratic Harmony

Bureaucratic Harmony

How do you organize the IRB review with the other committees that review research and medical practice?

Examples:

- Institutional Biosafety Committee (IBC)
- Radiation Committee
- Embryonic Stem Cell Research Oversight Committee (ESCRO)
- Pharmacy and Therapeutics Committee (P&T)
- Conflict of Interest Committee (COIC)

Is review sequential or concurrent? Who goes first?

Bureaucratic Harmony

- Harmony between CTA and subsequent committee decisions.
- You need a system to check the Clinical Trials Agreement (CTA) against the IRB approved consent form as to compensation for injury (45 CFR 46.116(a)(6)) and costs to subjects (45 CFR 46.116(b)(3)).

Bureaucratic Harmony

The billing system must be organized so that research procedures can be identified and properly billed (or not billed).

IT System

IT System

- Will you use an IT system for parts or all of the human subject protection system?
- Purchased or Created?
- Compliant with FDA 21 CFR Part 11, “Electronic Records; Electronic Signatures?” Debatable whether compliance with Part 11 is necessary.
- Part 11 compliance requires validation. Very costly.
- Compliant with HIPAA Security Rule?

Culture of Compliance

Culture of Compliance

Create a culture of compliance

- Institutional officials, investigators and IRBs can get into the trap of trying to sidestep bureaucracy and regulations, and it is very difficult to recover once that happens.
- This is a resource and a leadership issue.

Components of the Human Subject Protection System

Institutional Official (IO)

- The signatory official on the FederalWide Assurance (FWA).
- Must have legal authority to commit the institution to the terms of the FWA.
- The higher the official, the better.
- However, some IO's are too busy to know or care about the human subject protection system.

Investigators and other Research Staff

- The most important part of the human protection program.
- They interact with the subjects, perform the research.
- Need adequate resources and training.

Problem Investigators

- Have a process in place to take appropriate action against problem investigators.
- In this process, the subjects comes first, not the investigator or institution.

IRB

Create respect for the IRB in the institution

- Have it report high in the institutional hierarchy.
- Provide a prestigious meeting room.
- Provide perks (parking, meals, % time on workload).
- Avoid having IRB appointment based on lack of seniority, i.e, the newest member of the department gets appointed.

IRB

However, watch for problem IRBs

- The IRB must be careful not to become a secret committee that takes unreasonable action without accountability.
- Be as open as possible, establish a dialogue with research participants, investigators, and sponsors.
- Particularly an issue of debate in the non-medical fields.

IRB Staff Issues

Appropriate Staffing and Resources

- Essential to have adequate resources dedicated to the IRB office, including materials, staffing, and training.
- How do you convince administration of this?
- How do you measure the effectiveness of a subject protection system?
- How do you measure the value of a subject protection system?
- How do you calculate costs of a regulatory action, or negative publicity?

IRB Member Issues

Decision making of IRB members should follow this hierarchy:

- Subject safety and welfare
- Regulatory compliance
- Institutional/Business concerns

Training of IRB Members

IRB members need initial and continuing training on ethics, regulations, other applicable laws, institutional requirements and SOPs.

IRB Issues

Written Procedures

- Even the smallest IRB needs written procedures by regulation.
- The bigger the IRB, the more complex.
- The SOPs must be in sufficient detail that practices can be consistently followed by various staff and over time.

Consistency across IRBs

- If you have more than one IRB, there must be efforts to establish consistency.
- Worst case scenario: Different panels in different components (medical school, public health school) using different procedures and different computer systems.

Research Participant Complaints

- Have a process in place to review, receive and address complaints from research participants.
- In this process, the participant comes first, not the investigator or institution.

Procedures for Determining Necessary Level of Review

Triage Process:

- Is it research? 45 CFR 46.102(d)
- Does it involve human subjects? 45 CFR 46.102(f)
- Is it exempt research? 45 CFR 46.101(b)
- Can it be approved through expedited review? 45 CFR 46.110.

Full Board for everything that goes past those steps.

Procedures for Determining Necessary Level of Review

A quality control process to ensure proper triage is strongly advised.

Continuing Review System

- IRBs must approve research “at intervals appropriate to the degree of risk, but not less than once per year.”
- However, new information is submitted to the IRB much more regularly, and there must be processes in place to consider this new information.

Continuing Review System

Examples:

- adverse events,
- protocol variances,
- changes in research,
- new risk information,
- subject complaints,
- disgruntled employee complaints,
- FDA inspection reports,
- news stories,
- updated investigator brochures, etc.

Continuing Review System

What goes to full board, what goes to expedited, who decides, who does the work?

Site Visits or other Monitoring

Ideally, the IRB will have sufficient resources to do site visits and training for investigators.

FDA Device Protocols

- IRBs have an extra role on behalf of FDA when reviewing research involving FDA-regulated devices.
- The IRB must decide whether a device study is non-significant risk (NSR), significant risk (SR), or exempt from such a determination.
- See 21 CFR 812, Subpart D, and the FDA Information Sheet “Significant Risk and Nonsignificant Risk Medical Device Studies,” on-line at <http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf>.

Accreditation

Accreditation

- Receiving accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP) will ensure all the above recommendations are met.
- Expensive and resource intense.