

Alternative Models of IRB Review

Workshop Summary Report

November 17-18, 2005

The National Institutes of Health

**The Office for Human Research Protections, Department of Health
and Human Services**

The Association of American Medical Colleges

The American Society of Clinical Oncology

Workshop Summary

Background

This report summarizes the findings of a workshop on “Alternative Models of IRB Review” held in Washington, D.C. on November 17-18, 2005. The workshop was suggested by the Secretary’s Advisory Committee on Human Research Protections (SACHRP) in the fall of 2004 as a means of understanding the issues associated with the use of alternatives to local Institutional Review Boards (IRBs) and informing future committee action, such as developing a consensus statement on alternative models for IRB review or suggesting guidance to be developed by the Office for Human Research Protections (OHRP). The workshop was viewed as a means of gathering opinions from various stakeholders regarding the factors that influence the selection of an IRB model in various research contexts. Participants, who represented a variety of perspectives, included IRB chairs, academic investigators, community-based researchers, attorneys, patients, ethicists, industry officials, and senior university and medical school research administrators.

The workshop was planned and supported by the Department of Health and Human Services/OHRP, which staffs and manages the SACHRP, as well as the Association of American Medical Colleges (AAMC), the American Society of Clinical Oncology (ASCO), the National Institutes of Health (NIH), and the Department of Veterans Affairs (VA).

Framing the Discussion

Participants divided into four concurrent breakout groups to explore topics in depth, presenting their conclusions to each other in plenary meetings that allowed for further discussion.

Models. A focal point of discussion was a matrix presenting seven models of IRB review that was developed in advance of the workshop as a tool to focus discussions. Three additional models were noted at the meeting and thus the following ten were identified:

- A local IRB reviews single site studies;
- Each local IRB participating in a multi-site study does its own review;
- Local IRBs share common materials and exchange information to facilitate work on multi-site studies (IRBNet);
- An institution relies on the review of another institution’s IRB for a particular study;
- A single independent IRB conducts a review on behalf of one or more sites, either for single or multi-site studies (examples include the Western IRB and Chesapeake Research Review, Inc.);
- A local IRB participates in a facilitated review for a multi-site study; following review by a central IRB, the local IRB accepts, modifies, or reviews its findings (an example is NCI’s Central IRB process);
- A national and regional IRB review the same protocol concurrently (an example is the model used by the Indian Health Service);
- Sites form a consortium and use the IRB of one of the sites to review a collaborative protocol (an example is the Multicenter Academic Clinical Research Organization [MACRO]);

- Sites form a consortium and a new entity is created for review purposes (an example is the Biomedical Research Alliance of New York [BRANY]); and
- Multiple IRBs review research at a single foreign site (an approach that has been used by the National Institute of Allergy and Infectious Diseases [NIAID]).

Many participants felt that the use of models such as these would improve the quality of scientific and ethical reviews because many institutional IRBs lack the expertise needed to review today's sophisticated projects. Most participants also agreed that institutional IRBs are overburdened; they saw relief for burgeoning work loads as a key advantage of various alternatives to local institutional review. Many believed that alternatives such as the use of a central IRB might allow the institution to focus on other responsibilities related to human subject protection, such as ensuring research quality and monitoring. However, some saw other means of addressing the problem of IRB stress, such as developing and disseminating work-saving tools and templates, revising existing guidance to reduce IRB workload, and shifting some duties away from IRBs.

Features. Participants reviewed an initial list of features and issues associated with alternative models. They confirmed that all were significant and added others. The final features and issues identified as part of the framework for discussion included the following:

Issues relating to individual institutions. Institutional control over research, institutional liability (regulatory compliance), institutional liability (legal), the institution's capacity to adapt to new ways of working (flexibility), institutional conflict of interest, the burden on the institution (including work load), cost, and promotion of a responsible culture of research within the institution.

Issues relating to quality of oversight. Scientific and ethical expertise on the IRB, knowledge of the local research context, knowledge of the community of participants, responsiveness to participants' concerns, transparency, accreditation, and individual or institutional conflicts of interest.

Issues related to efficiency in complex research. The starting list in this category included communication between/among IRBs, resolving disagreements between and among IRBs, consistency of oversight across sites, time to complete reviews, expeditiousness, elimination of redundancy, and separation of the initial review from ongoing monitoring. The funding source for the project also has implications for the optimum arrangement. One breakout group phrased these issues in the form of questions:

- How do you ensure communication among multiple local IRBs?
- How do you resolve disagreements among the sites?
- How do you ensure consistent review?
- How do you ensure consistent oversight?
- How do you ensure timeliness of multiple reviews?
- How do you manage the initial review versus ongoing monitoring?
- What is the best way to interact with Data and Safety Monitoring Boards (DSMBs)?

Factors Influencing the Choice of Model. Participants said that decisionmakers would need to consider the following as they determined the best review mechanism: access to expertise, the number of participating sites, the need for consistency among participating study sites, the level of risk, the sponsorship and type of study, the size of the institution's research program, how quickly approval is needed, the type of disease involved in a medical study, the potential for conflicts of interest, liability issues, and available resources. A variety of other factors will also influence the institution's willingness to consider alternatives, including the following:

- The philosophy of the local leadership, including the view of the local IRB chair;
- The culture and tradition of the institution;
- The posture and attitudes of institutional counsel;
- Media “spin” and coverage of IRBs (i.e., “bad press” concerning local research oversight or “good press” that comes with change and introspection);
- Previous experience with alternative models;
- The existence of a local system that is clearly “broken”;
- Budget cutbacks affecting local IRBs;
- The views and concerns of the local community and its cultures; and
- The history of communication among participating IRBs and Principal Investigators (PIs).

Identifying and Addressing Key Challenges

Participants identified five key interrelated areas of concern and considered how best to address them.

Key Challenges	Suggested Strategies
Assurance of review quality <ul style="list-style-type: none"> ▪ Loss of safety net of redundant review ▪ Insufficient attention to local concerns ▪ Inappropriate consent forms 	<ul style="list-style-type: none"> ▪ Identify independent indicators of quality. ▪ Provide performance data. ▪ Consider local IRB representation on the central IRB. ▪ Provide evidence of benefits. ▪ Ensure that all policies and procedures are transparent. ▪ Conduct reciprocal visits. ▪ Consult references. ▪ Consider a demonstration project. ▪ Create detailed agreements. ▪ Take steps to build public trust.
Sensitivity to local context <ul style="list-style-type: none"> ▪ Failure to understand culture, concerns, ethnic groups 	<ul style="list-style-type: none"> ▪ Develop means of accessing and using local information. ▪ Develop strong communication.
Liability (institutional and individual)	<ul style="list-style-type: none"> ▪ Show that the institution is fulfilling its responsibilities. ▪ Develop solid policies and procedures. ▪ Establish a crisp agreement between the local facility and the alternate model. ▪ Ensure “due diligence” in the selection of the alternative model. ▪ Provide education for those responsible for managing institutional risk. ▪ Develop guidance that clearly defines the responsibilities of the local IRB when using alternative review methods.
Control and accountability <ul style="list-style-type: none"> ▪ Possible damage to the institution’s reputation 	<ul style="list-style-type: none"> ▪ Clearly define and document roles.
Loss of resources <ul style="list-style-type: none"> ▪ Insufficient staff and funding remain for compliance audits and other local responsibilities 	<ul style="list-style-type: none"> ▪ Educate administrators on the IRB’s continuing importance and need for funding. ▪ Concentrate on other aspects of human research protection.

Attendees devoted attention to the issue of how responsibilities might be divided between a local institution and a central review body (see “control and accountability” in the table above). The text box on this page synthesizes suggestions for clearly delineating areas of responsibility. Well-defined responsibilities were seen as a means of reducing concerns about liability.

Suggestions for Dividing Responsibilities

Responsibilities of the local institution:

- Addressing issues to be assessed prior to IRB review, such as conflict of interest, radiation safety, and biosafety reviews
- Ensuring ICFs include local information and adaptations
- Receiving and managing reports of local adverse events (AEs)
- Handling subject complaints and allegations
- Monitoring the conduct of the approved trial, including assuring that applicable Federal rules are followed
- Conducting Quality Assurance/Quality Improvement (QA/QI) activities (self-audit)
- Assuring investigators and research staff are trained and competent
- Ensuring the trial is appropriate for the patient population in the institution

Responsibilities of the central review body:

- Review of the study design
- Review of the ethics of the study
- Ensure the quality of the consent template (e.g., readability, translations, level of language)
- Perform aggregate analysis of all AEs, including reports from the DSMB to the IRB
- Confirm the competency of the investigator

Institutional Officials, heads of research, and senior university officials;

- Entities with related missions, including professional associations and private or nonprofit organizations that have an interest in human research protection;
- Study sponsors;
- Government agencies (funding and regulatory);
- University attorneys; and
- Community physicians.

Participants were also concerned about the danger of “IRB shopping,” but many were convinced that this practice could be deterred by adding appropriate questions to the application form used when requesting review.

While participants were not universally positive about the use of alternatives to local institutional review, they agreed the topic was an extremely important one that deserved further exploration. Further research and information on experience with these mechanisms would be welcome. Most of those in attendance felt that many barriers to their use could be overcome by the use of strategies such as those cited above.

Stakeholders to be involved. Participants were asked to identify stakeholders who needed to be involved in educational or other outreach efforts regarding alternative models. In no particular order, these include the following:

- Members of the public, including research participants and advocacy groups;
- IRBs, including IRB chairs, members, and staff;
- Members of the research community, including Principal Investigators, Study Coordinators,

Proposed Next Steps

Participants identified specific actions that would assist in addressing the issues they documented.

Actions that could be taken by *Federal agencies* include:

- Regulatory agencies should clarify their views on the use of alternatives to local institutional review, especially on local responsibilities when such alternatives are used.
- Federal agencies can disseminate scenarios and information to illustrate how appropriate alternative models can be chosen.
- OHRP and FDA should develop guidance regarding the responsibilities appropriately exercised by an alternative review mechanism and those appropriately retained by the local IRB.
- NIH can publicize the results of the evaluation of the NCI central IRB.

Professional groups and associations with an interest in human subjects research are encouraged to:

- Disseminate information on best practices, guidance, and emerging models.

All entities with an interest in human subjects research could help by doing the following:

- Disseminate information on the costs of alternative models and when they are most likely to be a cost-effective option.
- Encourage the development of performance measures that can be used to compare the success of review strategies in protecting human subjects.
- Encourage accreditation of human research protection programs.
- Inform the public about alternative review mechanisms.
- Encourage or conduct research on the impact of the use of alternatives to local institutional review on institutional human research protection programs.

Participants stressed the importance of educating key stakeholders and had several specific suggestions. These included:

- Convene workshops targeted specifically to IRB Chairs, Principal Investigators, and Institutional Officials (IOs).
- Educate IRB staff on the potential usefulness of alternative models.
- Educate those responsible for the management of institutional risk.

Possible Topics for a National Conference on IRB Alternatives

Alternative Models

- Detailed descriptions and experience to date
- Lessons learned and emerging best practices
- Real-life case studies and experience
- How the emerging models apply to social and behavioral research and health services research

Roles and Boundaries

- Defining the respective responsibilities of the local institution and the alternative model
- Handling informed consent in alternative models
- The impact of alternative models on the institution

Liability Issues and Alternative Models

Economics of Alternative Models

Evaluating Alternative Models

- Strategies for evaluation
- Findings to date

Shaping a National Conference

Participants were asked to contribute suggestions for a possible national conference that would build on the work of this workshop. Proposed subjects to address are shown in the accompanying text box.

Participants generally agreed that, because of the complexity of the topic, the next conference should be national rather than international in scope. They suggested breakout groups for key audiences, such as IOs, other senior academic leaders, and lawyers. Attendees also wanted to see a diverse audience, plenty of opportunities for questions and discussion, and panelists presenting real-life experiences that speak to the issues identified in preceding tables.