

Report from 2006 PRIMR Conference

From December 16 to 18th, 2006, the PRIMR conference (Public Responsibility in Medicine and Research) was held in Washington, D.C. PRIMR, an organization of physicians, bio-ethicists, philosophers, institutional review board (IRB) members and compliance officers from government and academia met to discuss the state of human research protection.¹ The PRIMR conference each year provides a snapshot of the state of IRB and bio-ethicist oversight over clinical trials both in the U.S. and abroad.

Why is IRB review important to HIV prevention research? IRB review is mandated for all US government funded research or research that would lead to an FDA approved drug or vaccine. Local IRB review is also a component of the clinical trial process in most countries. IRBs review all HIV prevention trials. IRBs include groups of scientists, bio-ethicists and advocates who meet to review proposed research at institutions. IRBs, both in the US and abroad, have broad authority to modify and even reject proposed study protocols. IRB oversight is increasingly important for HIV vaccine and prevention research. As the HIV prevention field moves toward decisions on issues surrounding trials, such as interventions for control arms, adolescent trials and access to antiretroviral (ARV) drugs for trial participants, IRBs have an increasingly important part to play in ensuring that research moves forward in an ethical and expeditious manner.

The three day PRIMR conference covered a variety of topics related to the ethics of clinical trials and the interpretation of regulations, and laws concerning human research protections.

Evidence Based Review. IRBs often review proposals quickly, and in areas where they may not have a strong knowledge base. Several speakers identified the need to support evidence based review by IRBs. Social science and other disciplines can provide IRBs with valuable tools for reviewing a study's impact on trial participants. For example, one panel moderated by Jeremy Sugarman discussed rethinking our notions of vulnerability. Vulnerable groups, such as children, the elderly and resource poor groups, are granted special consideration under IRB rules. Should these groups be expanded to include new groups? Should there be subsets within vulnerable groups that may not need heightened consideration? The view expressed by many at the Conference was that IRBs need to use social science and other evidence to look beyond the conventional wisdom or the categorization of vulnerability found in the IRB rules.

Statistical Power for Trials. Several panels discussed the potential benefits to trial participants from clinical trials. A number of panelists touched upon the need to insure that clinical trials were sufficiently powered. One panelist, Jeff Rodamar, stated that it was unethical to do a study with insufficient statistical power to provide answers to the questions posed by the study.

Comparative Arms. One panel addressed interventions for control arms in international clinical trials. Robert Levine, moderating a panel, addressed the question of when a trial is

¹ Kevin Fisher Senior Policy Associate at AVAC attended the meeting and presented a poster entitled *The Role of IRBs in Review of Testing of Adolescents in HIV Vaccine Trials under Subpart D of the Common Rule*.

permitted to use a placebo as a control, or how interventions are selected for the control group. For HIV vaccine trials, this question bears upon the interventions (condoms, counseling or potentially new interventions such as circumcision) that must be provided to trial participants. Levine noted that Council for International Organizations of Medical Sciences (CIOMS) amended its recommendation to require any “established effective intervention.” The COIMS standard replaced the standard of “best proven therapeutic (preventive or diagnostic) method” as set forth in the Helsinki accords. Levine pointed out that this standard permitted the control intervention to be an intervention approved by a significant minority of clinicians.

Reconciling international and local regulations. In a panel on international trials, Robert Levine discussed the current division of responsibility with IRBs over research in trial sites outside the sponsoring country. Local IRBs and regulators are becoming increasingly involved in reviewing and approving clinical trials. Local IRBS often set standards for informed consent, privacy and indemnification for injury. Researchers from Harvard University working with the WHO are creating a web-based Global Research Ethics Map to act as a resource for local ethical standards.

Benefits to trial participants. A panel on international trials found no clear consensus of the question of whether sponsors have an ethical obligation to provide ARV therapy to trial participants that become HIV infected in HIV prevention trials. One panelist, Reidor Lie, noted that there was no clear ethical guidance imposing an obligation to provide post-trial long term care.

WHAT ARE THE ADVOCACY MESSAGES?

The PRIMR Conference highlights the importance of engaging in dialogue with IRBs involved in HIV prevention trial reviews inside and outside the US. Advocacy messages coming out of the conference include the need for:

- **Supporting capacity building directed at providing IRBs with tools to permit evidence based review of HIV prevention trials.**
- **Engaging IRBs and bio-ethicists on the issues of ARV treatment for clinical trial participants infected in HIV prevention trials.**
- **Integrating of US and European IRB review with IRB review in communities where HIV prevention trials are taking place.**