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May 26, 2005

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Via E-Mail [FDADockets@oc.fda.gov](mailto:FDADockets@oc.fda.gov)  
And hardcopy followup by U.S. Mail

Division of Dockets Management (HFA-305)  
Food and Drug Administration (FDA)  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852

Re: Comments on FDA's Draft Guidance for Industry on Using a Centralized Institutional Review Boards Process in Multicenter Clinical Trials (IRB Guidance), 70 Fed. Reg. 15635, March 28, 2005 - **Docket No. 2005D-0103**

To the Food and Drug Administration:

Thank you for this opportunity to comment on the FDA's IRB Guidance.<sup>1</sup> We are current or former volunteers, representatives of participants in clinical trial research, on authorized Community Advisory Board (CABs) which review government sponsored clinical trials testing vaccines to fight HIV/AIDS. We support FDA's effort to improve the ways IRBs participate in clinical trial monitoring and oversight, especially when those studies are necessarily conducted as global multicenter clinical trials as is the case with AIDS vaccine studies. IRBs face many challenges today, marked by increases in responsibility and evaluation of data.<sup>2</sup> When trials take place at coordinated domestic and international sites, those challenges may be increased by the variety of applicable regulatory requirements, cultural distinctions and the difficulties of responding to specific and sensitive public health conditions.

The IRB Guidance defines the roles of institutions, sponsors and investigators for centralized IRBs and suggests at least three mechanisms to ensure meaningful consideration of the ethical standards of the local community:

- Provision of relevant local information to the central IRB in writing by individuals or organizations familiar with the local community, institution, and clinical research
- Participation of consultants with relevant expertise, or IRB members from the institution's own IRB, in the deliberations of the central IRB
- Limited review of a central IRB-reviewed study by the institution's own IRB, with that

<sup>1</sup> <http://www.fda.gov/cber/gdlns/irbclintrial.pdf>. Page references in this letter will refer to this version.

<sup>2</sup> See for example, Roehr, B. (2005) Institutional Review Boards in Crisis. *The Scientist* (19)9; 42  
<http://www.the-scientist.com/2005/5/9/42/1>

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limited review focusing on issues that are of concern to the local community.<sup>3</sup>

The identified roles and mechanisms would not be sufficient to provide meaningful consideration of the relevant local factors affecting HIV/AIDS research if a centralized IRB were used. Domestic and international HIV/AIDS research must consider the fears, vulnerabilities, resources, stigmas and hardships of diverse populations. Everyone is affected by HIV/AIDS, but often the research addresses risks and concerns of specialized populations: women lacking effective protections from assault or coercion, injection drug users, at risk adolescents in high incidence areas, people experiencing discrimination on the basis of race, ethnicity or sexual behavior, preference or work. The experiences of these populations and the reactions of the communities in which they live are not uniform in every locality or country. They may vary considerably domestically. Hurdles exist to acceptance and understanding of basic materials such as informed consent or recruitment materials when cultural and linguistic differences are the norm.

It may be too much to expect that these groups would be alerted in a timely manner and sufficiently well supported to organize necessary write-in responses for a centralized IRB program. Many groups or affected communities lack computers or reliable internet connections, information sources, even telephones.

Infrastructure and medical systems IRBs refer to for preventative vaccine studies vary widely in domestic or international settings. Some provide access to medical treatment if HIV infection (a circumstance which is not related to the study product) occurs, some do not. Settings vary in the systems of privacy or confidentiality available or control over handling of biological samples. Jurisdictions differ in their adoption of ethical practice guidelines for protecting participants in research. Because HIV mutates within individuals or populations and is dispersed in different clades or recombinant forms, the decision to test specific products in any area also carries with it considerations affecting the local community.

This all too brief summary of factors which have been the subject of much published study<sup>4</sup> at least documents that participation of local communities and civil society could be more direct and substantial than contemplated by the IRB Guidance if a centralized IRB were used. A centralized IRB system applied to HIV/AIDS vaccine or other research may run into pitfalls and problems responding to local ethical standards.

We recognize the IRB Guidance does not presume that a centralized IRB will always be used for multicenter studies. Nevertheless, the decisions to form or permit a centralized system under the guidance or the regulations appears to lack sufficient input from affected, vulnerable, or at risk populations. The decisions to form a centralized IRB would benefit by obtaining

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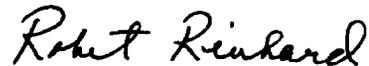
<sup>3</sup> IRB Guidance, pp. 4-5.

<sup>4</sup> This broad field of study could result in overly numerous cites, but see for example, Mills E., Cooper C., Guyatt G., Gilchrist A., Rachlis B., Sulway C., Wilson K. (2004) Barriers to participating in an HIV vaccine trial: a systematic review. *AIDS* Nov 19;18(17):2235-42.

consent of all affected communities and their agreement as to the proper scope of responsibility and the IRB's operational principles. The composition of any centralized IRB should include not only experts on local standards but also persons who directly represent and give voice to local concerns.

Thank you for consideration of these requests. The contact person for this letter is Robert Reinhard (Tel: 415/268-7469; email: [rreinhard@mofo.com](mailto:rreinhard@mofo.com) ) for questions or response you may have.

Very Truly Yours,

A handwritten signature in black ink that reads "Robert Reinhard". The signature is written in a cursive, slightly slanted style.

Robert Reinhard, Member of San Francisco  
Department of Public Health HIV Vaccine Trials  
Network (HVTN) CAB - and signing for,

Gail Broder, MHS, HIV Vaccine Community Educator  
Thomas Gibson, Member of HVTN CAB  
David Crawford, PhD, Member of HVTN Chicago Trial Unit CAB