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June 1, 2002

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Writer's Direct Dial Number
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Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Re: **Docket No. 01N-0322** -- Institutional Review Boards: Requiring Sponsors and Investigators to Inform IRBs of Any Prior IRB Reviews -- Advanced Notice of Proposed Rulemaking (IRB ANPRM) -- 67 Fed. Reg. 10115, March 6, 2002

To the Food and Drug Administration:

I. Introduction and Summary.

These comments on the Food and Drug Administration's (FDA) IRB ANRPM are submitted on behalf of the Protocol Working Group (PWG) of the Global Community Advisory Board of the HIV Vaccine Trials Network (HVTN). Formed in 1999, by the Division of AIDS (DAIDS) of the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), the HVTN mission is to develop and test preventive HIV vaccines. This research is done through multi-center clinical trials in a global network of domestic and international sites. The PWG is comprised of volunteer community representatives, including participants in these clinical trials, who serve as members of HVTN protocol teams and/or its science committees. The PWG advocates for ethical treatment of human research subjects and progress in clinical research. We appreciate the opportunity to comment on this proposal. Please note, as citizen advisory volunteers, we do not speak on behalf of the HVTN or NIH.

The PWG requests an exemption for HVTN's multicenter trials if the FDA regulates sponsors and investigators to inform IRBs about any prior IRB review decisions. As discussed in more detail below, the proposed requirement could slow the progress of vaccine clinical trial research significantly without any benefit to human research subjects in terms of added protection or ethical treatment. We believe there is no adequate basis for the FDA's proposal to address a perceived problem with "IRB shopping" in clinical trials conducted at multiple research sites by the HVTN.

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II. Evaluation of IRB ANPRM

A. The perception of IRB shopping as a basis for regulation does not apply to HVTN.

Selection of HVTN trial sites is based on a set of complex criteria which include HIV infection characteristics, HIV genetic and antigenic variability, site preparedness and infrastructure capability, proximity to and matching of a particular at-risk population for vaccine products and past success in recruitment of a particular population. The HVTN currently has 25 domestic and international sites. Four new sites are to be added in 2002-2003. These locations are established to support clinical trials of numerous candidate HIV vaccines over a long period of time by experienced investigators and clinic staff. Selection of trial sites for a test HIV vaccine is determined without regard to IRB characteristics or expected IRB reaction to protocol design. In addition to HVTN committee review by principal investigators, when individual protocols enter the development pipeline, community members are included on the Protocol Teams in the early stages to be advocates for the safety and ethical treatment of the human volunteers.¹ As trials move forward to the point of submission to an IRB for approval, any concerns raised by one IRB are shared by the Protocol Team with the other participating sites so as to hasten the time to implementation.²

The FDA's reported basis for its IRB ANPRM does not apply to HVTN trials. In our experience, HVTN recognizes that IRB "shopping" would significantly impair the ability of the HVTN to carry out its mission and raises serious ethical concerns that are at odds with its commitment to conduct trials in a fair and equitable manner to protect human research subjects.

¹ The PWG has received support from the HVTN to implement community participation and review guidance principles advocated by international organizations, including those principles found in the Joint United Nations Programme on HIV/AIDS guidance document, "Ethical Considerations in HIV Preventive Vaccine Preventive Research," May 2000, pp. 19-20.

² For a description of the HVTN structure demonstrating further why "IRB shopping" is avoided in HIV vaccine trials, please see the HVTN website generally and in particular <http://www.hvtn.org/structure/> for an organizational overview.

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B. The FDA proposal (if adopted) would cause significant disruption and confusion, and would slow vaccine clinical trials without any benefit.

The HVTN system already employs a communications and review model to apprise those involved of comments raised by any IRB. In fact, the PWG itself is one of the ways in which the HVTN has provided for protection of human subjects in research. Through monthly conference calls, we are able to evaluate any specific trial to determine if there are cross-trial concerns and to report them to the HVTN or other trial unit sites.

The FDA proposal has the potential for slowing down the implementation of vaccine clinical trials. Because the proposal is vague as to the types of IRB objections that would be reportable, IRB “traffic jams” could occur simply because of insignificant or last minute site specific language changes in protocols that may be time sensitive due to test product expiration dates or the ability of trial participants to reschedule participation commitments.

As examples, we can recall when an IRB took issue with particular language, “will provide”, and wanted it revised to “may provide.” Another IRB preferred to change language that volunteers would be “paid for participation” to clarify that they would be “reimbursed for time and expenses.” The substantive payments were the same; the explanation slightly more precise in consent forms. Reporting this information to every IRB places an undue burden on the researchers and the community which stands to benefit from the outcome(s) of the research. These and other changes may in fact be untranslatable or irrelevant to the variety of international participating sites.

For these reasons we request an exemption for HVTN’s multicenter trials if FDA regulates sponsors and investigators as proposed.

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Thank you for considering our comments on the IRB ANPRM. Robert Reinhard has agreed to act as a contact person for any questions or response you may have in connection with this submittal. **contact info:** Robert Reinhard, 425 Market Street, 32nd floor, San Francisco, CA 94105; telephone: 415/268-7469; fax: 415/268-7522; email: rreinhar@mofo.com

Yours truly,

A handwritten signature in black ink that reads "Robert Reinhard". The signature is written in a cursive style with a large, looping initial "R".

Robert Reinhard



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