

National Organization for Rare Disorders, Inc. @



... out of the darkness.
into the light ...

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March 14, 2002

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Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No. 01 N-0322, **OC2001148**
Institutional Review Boards: Requiring Sponsors and
Investigators to Inform IRBs of any Prior IRB Reviews

Dear Sir or Madam:

The National Organization for Rare Disorders (NORD) represents an estimated 25 million Americans with more than 6,000 rare "orphan diseases." Each rare disease, as defined by the Orphan Drug Act of 1983, affects fewer than 200,000 Americans. Clinical research is critically important to people with rare disorders because few of these health conditions are treatable with current therapies. Therefore, human subject protection rules are of critical importance to the rare disease community because in many cases the only available treatment options are investigational.

NORD strongly supports FDA's proposed rule requiring sponsors and investigators to inform IRBs of any prior IRB reviews. The recent HHS Office of Inspector General reports have documented instances of "IRB shopping" that undermines the spirit and intent of human subject protections. Our goal is to make the system more responsive to the needs of human research volunteers, and less of a secretive institutional protection system. We envision a day when scientific investigators will observe human subject protection rules not because they have to, but because they want to.

Even more important than "IRB shopping" is the current tendency toward multi-site clinical trials, and the fact that under our current system each site can have completely different informed consent documents even though all human subjects at each site will be participating in the exact same experiment. There ought to be a way to coordinate IRBs at each participating site so that all research volunteers will sign closely related informed consent documents for the same protocol. By requiring investigators to disclose previous IRB reviews, each IRB will surely benefit from shared information, and begin to rebuild public trust in a system that has been shaken by highly publicized scandals.

OIN-0322

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Associations are joining continuously for newest listing, please contact the NORD office

Rev 4/01

Dedicated to Helping People with Orphan Diseases

In answer to your questions:

1. **We cannot document or quantify the problem of “IRB shopping”.** However, we can tell you that informed consent documents at multi-site clinical trials tend to vary widely, and most often the differences appear in legal areas that tend to address the liability of the institution. It seems that informed consent documents are increasingly evolving into liability protection documents for institutions rather than human subject education documents that clearly outline possible risks and benefits. Human volunteers can hardly make an “informed” decision about participation when a multi-site trial stresses unproven benefits and minimizes risks in some informed consent documents, while at other sites patients may be told the complete opposite. The only way to stop this problem is by requiring disclosure and encouraging each site to share IRB minutes and consent documents.
2. **Who should make the disclosures?** If the study is conducted by an academic investigator, as a member of the institution’s faculty, the investigator must seek IRB approval (not the sponsor). However commercial clinical trials that are not housed at academic institutions sometimes use commercial “National IRBs”. In these cases, the sponsor usually seeks IRB approval. The sponsor, however, is usually the only party that is aware of all IRB decisions and recommendations, so the sponsor should be responsible for submitting subsequent information about previous IRB reviews to an IRB.
3. **Who should receive the disclosures?** IRBs should be told that a protocol has been reviewed by another IRB, and what that IRB’s recommendations were. Similarly, an IRB should be told that a protocol has been submitted to another IRB even if that IRB’s decision is still pending.
4. **What information should be disclosed?** We believe that both positive and negative relevant information should be shared by IRBs. We particularly urge that IRBs disclose their approved informed consent documents. We suggest that institutions post informed consent documents on the Internet so that human subjects considering participation in a multi-site clinical trial would be able to read informed consent documents from other participating sites. The very fact that such documents will be disclosed may encourage IRBs to be more candid and less deceptive, and to share information and ideas with each other so that informed consent documents will be more uniform and truthful. Additionally, IRBs should be required to post the minutes of their meetings on the Internet so that prospective human subjects can understand the points of IRB debate. It is essential to rebuild public trust in the IRB system, and transparency of the human subject protection process will assure that no negative aspects remain hidden from the public.
5. **We strongly believe that disclosure should be required, including requirements for additional reviews, as well as disapprovals, requests for changes, etc.** Such disclosure should encourage IRBs to communicate with each other, and discourage secrecy that undermines public trust. We also believe that informed consent documents should be made public so that potential human subjects will have access to them. This may result in more uniformity for multi-site trials, and indicate that volunteers at site #1 are told about the same risks as volunteer subjects at site #2.
6. **Should information about the basis for a prior decision be disclosed?** Detailed information should be shared among IRBs and the FDA, but not necessarily the public because of the technical aspects of major discussions. Instead, the minutes of IRB meetings should be made public so a summary of major decisions will be available to the public.

7. **Researchers and sponsors who do not comply with the rules** could be sanctioned through:

- a) A clinical hold on the experiment so no further subjects will be enrolled until the problem is resolved.
- b) Refer the sponsor/investigator to OHRP.
- c) Impose other sanctions for violations such as monetary penalties for the sponsor or institution.

8. **Other ways to deal with this problem:** We believe that making information public (e.g., putting informed consent documents on the Internet, posting IRB minutes on the Internet, requiring sharing of IRB data, etc.) should encourage **IRBs** to learn from each other, while keeping the public and the patient community informed. There seems to be basic flaws in the current system when one IRB makes decisions that conflict drastically with decisions of other **IRBs** reviewing the same protocol. Mandating disclosure will benefit human subjects, but it will also enhance the analytical tools of all **IRBs** and help them to make better decisions. Additionally it will share important information with other scientists and the general public, thereby rebuilding public trust in a system that has been shaken by human protection violations.

Very truly yours,



Abbey S. Meyers
President

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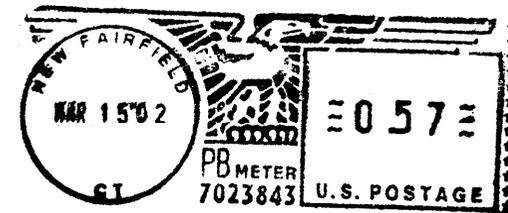
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