



September 27, 2004

Division of Dockets Management
5630 Fishers Lane, Rm. 1061
Rockville, Maryland 20852

Re: Docket No. 2004N-0242, Federal Register: July 6, 2004 (Volume 69, Number 128, pp. 40556-40562)

Dear Sir/Madam:

The following comments are provided by the Biotechnology Industry Organization (BIO). BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states and 33 other nations. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products. BIO appreciates the opportunity to submit comments regarding the July 6, 2004 Proposed Rule issued by the Food and Drug Administration (FDA) concerning Institutional Review Board (IRB) Registration Requirements.

BIO believes strongly in protecting the rights and welfare of human subjects involved in biomedical research, and recognizes the critical function of Institutional Review Boards to this end. BIO also acknowledges the importance of complying with the regulations contained in 21 CFR Part 56—"the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations regulated by the Food and Drug Administration."

BIO therefore supports the proposal to create a single, comprehensive registry of both FDA and OHRP regulated IRBs to be maintained by the Department of Health and Human Services (HHS). Such a registry will facilitate HHS oversight and will make it easier for FDA and OHRP to convey important information to IRBs. We also support FDA's requirement that a senior officer of the IRB's institution be identified. Often, IRBs have been unable to meet their obligations because of the failure of their institutions to provide the necessary support. This will make the institutions that have IRBs more cognizant of and accountable for the IRBs' operations. We do, however, have some comments and recommendations regarding specific details of the Proposed Rule, as outlined below.

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1. Request for clarification regarding when an IRB must register.

The text in § 56.106(c) of the Proposed Rule regarding when an IRB must register is as follows:

Each IRB must submit an initial registration within 30 days before the date when the IRB intends to review clinical investigations regulated by FDA.

An ambiguity is present in the preamble, however, as it states:

The proposal would require initial IRB registration **within 30 days before the date when the IRB intends to review clinical investigations regulated by FDA.** To show how this would work, assume that a newly formed IRB has been asked to review a protocol for a clinical investigation regulated by FDA under section 505(i) of the act. The IRB would then be subject to FDA's IRB regulations (§ 56.101(a)), and **the IRB, under proposed § 56.106(c), would submit its initial registration 30 days before the date the IRB intends to review the protocol.** (emphasis added)

The text of the proposed regulation and the first bolded section of the preamble above require IRBs to register “*within 30 days before the date when the IRB intends to review clinical investigations regulated by FDA.*” Thus, an IRB could register anytime between one and 30 days before reviewing a protocol. However, the example given in the preamble in the second bolded section above indicates that the registration must be submitted “30 days *before* the date the IRB intends to review the protocol.” Thus, an IRB would have to register at least 30 days before reviewing the protocol. BIO recommends that the ambiguity in the preamble be corrected to deter inadvertent noncompliance. BIO prefers the language in the proposed regulation as it is now written.

2. Recommendation regarding the effective date of IRB registration.

Section 56.106(c) of the proposed regulation also states “IRB registration would become effective when HHS posts that information on its Web site.” Although the Proposed Rule contemplates an intention that the registration be accomplished at a specific Internet address to be provided by the FDA, the Rule will allow for written registration as an alternative in consideration of those IRBs that do not have Internet access. However, in such circumstances the IRB would have no control over the time it would take for DHHS to post the information on the Web site. Therefore, BIO suggests that this provision be changed to consider an IRB registered upon submission of a completed application, whether electronically or by written registration.

3. Request for clarification regarding IRB inspections.

The Introduction to the Proposed Rule asserts that one intended goal of the registry is to “help FDA identify IRBs for inspection.” BIO asks for confirmation that inspections will be governed by the guidelines currently described for IRB inspections as found in the Guidance for Institutional Review Boards and Clinical Investigators.

4. Response to the request for comment as to whether FDA regulations must be changed to consider administrative action against institutions using unregistered IRBs.

This proposed regulation is intended to make the IRBs register with the DHHS. Thus, FDA's first and foremost regulatory actions should be taken against IRBs that fail to register. Subpart E of Part 56 details the administrative action that FDA can take if an IRB is found to be in non-compliance with the registration requirements. BIO feels that there are adequate regulations in place to ensure compliance with the proposed amendment to Part 56. If FDA believes, as it appears, that it does not have sufficient regulatory authority to enforce the registration requirement against the IRBs directly, then the agency should seek whatever regulatory or statutory change would be necessary to give the agency the ability to enforce the registration requirement against the IRBs.

Using sponsors and investigators to enforce the registration requirement appears to put sponsors and investigators in an adversarial relationship with the IRBs, whereas sponsors/investigators and IRBs are most productive, and provide the best protection to research subjects, when their relationship is cooperative. Therefore, FDA should not use sanctions or administrative mechanisms against sponsors or investigators who use unregistered IRBs. Nor should the agency put a trial on clinical hold if an IRB is unregistered. FDA should focus its enforcement efforts on the IRBs that fail to register, not on the sponsors and investigators that might need to use the IRB in order to have their research done at a particular institution.

FDA also needs to consider what will happen if there is a failure of the Internet such that sponsors and investigators might not have access to the appropriate web-site for a period of time.

BIO agrees that an IRB's failure to register does not justify the disqualification of an IRB or institution pursuant to § 56.121, absent the extreme circumstances detailed in subsections (b)(1) and (2).

IF FDA persists with the requirement that sponsors and investigators use registered IRBs, then FDA should make clear that a sponsor or investigator meets that requirement if the sponsor or investigator uses an IRB listed on the appropriate DHHS website at the time the IRB reviews the clinical protocol. The sponsor or investigator should not be required to constantly monitor the registration status of the IRB. Rather, the burden should be placed on the IRB to notify the sponsor or investigator if the IRB loses its status as a registered IRB, and the sponsor or investigator should be given an opportunity to find a new IRB to continue the review of the ongoing trial without penalty.

5. Response to the request for comment regarding foreign IRBs.

Many clinical trials involving FDA regulated products are reviewed by foreign IRBs that are not subject to FDA's IND regulations and are subject to oversight by local authorities. While such foreign IRBs could be encouraged to register with HHS to benefit from educational materials and shared guidance on best practices, BIO feels that the registration of foreign IRBs should remain voluntary.

6. Response to the request for comment regarding information on accreditation status.

We recognize that FDA has limited resources to do handle its many public health responsibilities. Knowing whether an IRB is accredited, and if accredited by which organization, may give the FDA useful information when making decisions about which IRBs to inspect. It may also assist FDA in deciding whether there are areas that FDA should focus on in its educational activities, and whether there are other areas that are well covered by accrediting organizations.

7. Response to the request for comment regarding written registration.

We discourage the FDA from discontinuing written IRB registration. Since there are adverse consequences to both the IRB and any sponsor or investigator that might use the IRB if it is not registered, FDA should keep the simple, straightforward, and universally accessible option of written registration submissions.

We appreciate your consideration of these comments. Please do not hesitate to contact me should you have any questions.

Sincerely,

A handwritten signature in black ink that reads "Debra Aronson". The signature is written in a cursive style with a large initial "D".

Debra Aronson
Bioethics Director
Biotechnology Industry Organization