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Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852-1448

Re: Docket Number 01N-0322
Response to FDA Call for Comments
Advance Notice of Proposed Rule Making (ANPRM): "Institutional Review Boards:
Requiring Sponsors and Investigators to inform IRBs of Any Prior IRB Review"

Dear Sir or Madam:

Reference is made to the March 6, 2002 Federal Register ANPRM soliciting comments opposite the topic entitled "Institutional Review Boards: Requiring Sponsors and Investigators to inform IRBs of Any Prior IRB Review."

AstraZeneca has reviewed this notice and our comments are attached.

Please direct any questions or requests for additional information to me, or in my absence, to Mr. Leonid Freytor, Regulatory Affairs Associate Director, at (302) 886-2510.

Sincerely,

Mark Scott for M.Sc., Ph.D.

Dr. Mark Scott
Executive Director
Regulatory Affairs
(302) 886-8495

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Enclosure

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AstraZeneca Response to the FDA Advance Notice of Proposed Rulemaking:

“Institutional Review Boards: Requiring Sponsors and Investigators to Inform IRBs of Any Prior Reviews”

1. How significant is the problem of IRB shopping?

There are no definitive statistics on this question but from experience, so called IRB shopping does not happen very often and in a manner different than how the Office of the Inspector General report describes it. It is usually due to the initial IRB not understanding the protocol or FDA requirements. Or it is due to requests from the IRB that are unnecessary and sometimes legally perilous. In these few cases, the second IRB, a commercial IRB, is contacted to perform the review. If the study were disapproved by the first IRB, the disapproval would be communicated to the second IRB. In situations with a site being affiliated with an institution, use of a second IRB can only be done if the first IRB (which has jurisdiction for the institution) waives the review to the second IRB. To characterize these experiences as “shopping” generates a negative connotation that in most cases is not indicative of the problems being addressed. It is not the case that a careless use of IRBs is at work. Instead the concerns represent roadblocks to the development of pharmaceutical products that do not involve a diminution of human subject protection. There certainly maybe exceptions, but for the vast majority of instances the reasons are legitimate. Thus, the FDA should establish the existence of this phenomenon first, and that it has a substantive detrimental affect on human subject protection before any regulation is enacted.

2. Who should make these disclosures?

This suggestion, i.e., to have all disapprovals communicated to all IRBs, creates an enormous burden on the system without adding protection to human subjects. In actuality, an IRB should be able to make the correct decision concerning the study without any other information relative to decisions from other IRBs (with the exception of the case where a local IRB waives its review to a second IRB [21 CFR Part 56.114]). This is the premise upon which the IRB process works: independent evaluation of the study, the site and subject informed consent procedures. Moreover, many trials are conducted on an international scale with submissions to IRBs occurring according to a variety of schedules. The feasibility of exchanging the continual flow of information relative to these IRB reviews would be practically untenable.

If the regulation requires only disapprovals to be communicated to other participating IRBs, then this would not be a frequent occurrence although it still undermines the premise that the IRB should be qualified to approve or disapprove the research on its own, without the help of another IRB (unless specifically prearranged). The key problem with this requirement though, is that IRBs would then feel the need to wait

until all other IRB reviews were done in order to not "miss" something and thereby be perceived as deficient or even worse, as negligent.

3. Who should receive the disclosures?

This is addressed in the previous responses. An IRB should not need to hear the decisions of another IRB if the first IRB is fulfilling its obligations properly. The requirement to inform other IRBs will complicate the approval and continuing review processes significantly while making no improvement to human subject protection.

4. What information should be disclosed?

All prior IRB reviews should not be disclosed. This would be an enormous administrative burden. There would be literally thousands of decisions that would inundate an IRB. The burden to sponsors and investigators would also be incredibly great. There is no deficiency in the currently established procedure that should make disclosure necessary. The information could also be misinterpreted and could breach confidentiality regulations.

5. If a proposal would not require disclosure of all prior IRB decisions, what information should be disclosed?

This issue raises again the presupposition that the process does not provide for adequate review. This presupposition is incorrect. By regulation (21 CFR part 56.111), an IRB needs to be able to consider the proposed research. These regulations require the IRB to be able to evaluate the research on its own (provided it is given the requisite documentation and information from the investigator). Dependencies on other reviews without explanation or context could prove to be detrimental to the evaluation of the research and will certainly incur more cost and generate more bureaucracy than benefit.

If anything, the only requirement should be to have the investigator disclose to the IRB whether he or she has submitted the research study to any other IRB for their review or if the study was disapproved for that site by another IRB. At that point the IRB can decide whether it wants to collect more information on any previous IRB review for that site.

6. To permit a subsequent IRB to assess the value of a prior IRB decision, should information about the basis for the prior decision be disclosed?

The previous comments address this question. The increased administrative burden and subsequent potential for liability will make the research process perilously slow-moving without adding anything to human subject protection.

7. How should FDA enforce the requirement?

Enforcement of this regulation, if it is enacted, should follow the current approach for other areas of human subject protection, which would be to evaluate it when FDA inspections are conducted. During an inspection of a clinical investigator, for example, the FDA investigator could review whether the regulations were followed.

8. Are there other ways to deal with IRB shopping other than disclosure of prior IRB reviews?

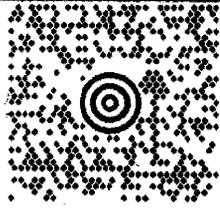
The problem is not significant enough to warrant a federal regulation. If anything, the only requirement should be to have the investigator disclose to the IRB whether he or she has submitted the research study to any other IRB for their review and if the study was disapproved for that site by another IRB. At that point the IRB can decide whether it wants to collect more information on any previous IRB review for that site.

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ASTRA ZENCA PHARMA
302 886-2806
1800 CONCORD PIKE
WILMINGTON DE 19803

SHIP

TO: FOOD AND DRUG ADMINISTRATION HFA 305
302 886 8495
DOCKETS MANAGEMENT BRANCH
ROOM 1061
5630 FISHERS LANE
ROCKVILLE MD 20852

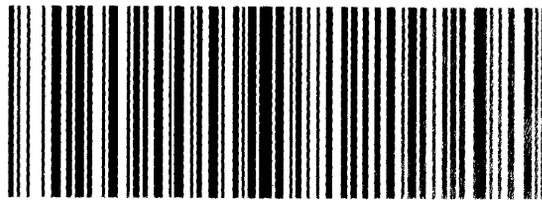


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