

Aventis Pasteur

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Dockets Management Branch (HFA-305)
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 [67 FR 10115, March 6, 2002]

04 June 2002

Dear Sir/Madam:

Aventis Pasteur Inc. would like to thank you for the opportunity to comment on the above-referenced advance notice of proposed rulemaking entitled "Institutional Review Boards: Requiring Sponsors and Investigators to Inform IRBs of Any Prior IRB Reviews." We offer the following comments/clarification for your consideration in determining whether to amend the institutional review board regulations to require sponsors and investigators to inform IRBs about any prior IRB review decisions.

We recommend that any obligation to report prior IRB involvement should be restricted to situations wherein:

- An IRB refuses to authorize a study, or imposes restrictions on a previously authorized study, based on patient safety issues, and the IRB has notified the investigator and sponsor in writing that such action was safety-related.
- The protocol being submitted, or study being conducted, under the supervision of a second IRB concerns the same investigational drug, biologic, or device or one sufficiently similar that there is a reasonable likelihood that the safety issue raised by the first IRB is applicable to the protocol or study in question.
- The study protocol at the second IRB is the same as, or sufficiently similar to the protocol at the first IRB that there is a reasonable likelihood that the same safety issue might be applicable. (Accordingly, if an IRB raised safety objections to a proposed protocol which were satisfactorily addressed through revisions to the protocol and subsequently approved by this IRB, there should be no obligation to inform other IRB's of the now-irrelevant objection raised by the first IRB.)

Reporting should be restricted to safety-related adverse actions because there are many causes for IRB initial rejections, or subsequent suspensions, most of which are not related to issues of patient safety, but rather to procedural issues. If a requirement is adopted to require reporting of such safety-related adverse actions to other IRBs, then there should be a parallel requirement that an IRB categorize such actions as being reportable safety-related actions. This would eliminate ambiguity, and subsequent disputes as to

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whether any particular IRB action was reportable. In addition, unless the IRB has categorized in writing as posing an "imminent and serious threat to patient safety," the IRB's written notice of safety-related issues should not trigger a reporting obligation until 2 weeks after issuance of the IRB's notice. This would allow time for the sponsor and/or investigator to evaluate the issue, determine an appropriate solution, and submit the solution for review by the IRB.

Reporting of prior or concurrent IRB reviews or actions not categorized in writing by the IRB as safety-related should not trigger an obligatory report, as this could unnecessarily slow down the IRB review process. The majority of the time multiple IRBs are involved is in instances where multiple institutions are participating in a multisite study. The risk would be high that, to ensure the careful performance of their reviews, each would require that the sponsor provide the assessment of all the others, and none would provide their assessments until the others had done so, creating gridlock.

Specific responses to the issues as numbered in the 06 March 2002 Federal Register notice are as follows:

1. *How significant is the problem of IRB shopping?*

We've never seen a new IRB sought because of an unfavorable evaluation from the initial IRB. It is apparently relatively uncommon, because most studies are done in, or in association with, institutions that require clearance by their own IRB. There are many justifiable reasons for seeking review at a new IRB (additional sites needed; studied submitted but not initiated in the past, now being activated at new site; etc).

2. *Who should make these disclosures?*

The party seeking initial IRB review (either sponsor or investigator) should be responsible for making subsequent disclosures to other relevant IRBs.

3. *Who should receive the disclosures?*

Any IRB reviewing or supervising a protocol or study concerning the same drug, biologic, or device, or any IRB reviewing a protocol for which the same safety concern(s) apply.

4. *What information should be disclosed? Should all prior IRB reviews, including approvals, be disclosed?*

and

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

Information required to be provided to notified IRBs would include a copy of the notifying IRB's letter and a statement explaining the issue; any subsequent actions taken by sponsor, investigator, or original IRB relative to the issue; and any actions being proposed to the notified IRB relative to the issue. Only IRB actions categorized in writing as taken to protect patient safety should trigger a notification requirement, as explained above.

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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?*

Not applicable, if the approach recommended herein is taken.

7. *How should FDA enforce the requirement?*

Presence of the written notice in the files of the IRB and the regulatory binder would alert the FDA to inquire or investigate further.

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

We do not believe the problem is significant enough to require regulatory action. If it is, then the approach suggested herein seems to be the least burdensome, least likely to trigger undesired consequences, and the most self-regulating.

On behalf of Aventis Pasteur Inc., we appreciate the opportunity to comment on the advance notice of proposed rulemaking regarding amending the IRB regulations to require sponsors and investigators to inform IRBs about any prior IRB review decisions, and thank you for your consideration.

Should you like to discuss any of our comments or concerns, please address them directly to Joseph H. Quinn, Director, Operations & Regulatory Information Management, by telephone at (570) 839-4359, or by facsimile at (570) 839-5529, or by email at joe.quinn@aventis.com.

Sincerely,

A handwritten signature in black ink, appearing to read "Luc Kuykens".

for Luc Kuykens, MD, MPH, DTM
Vice President, Regulatory Affairs, North America
and Authorized Official

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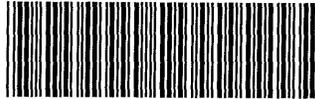
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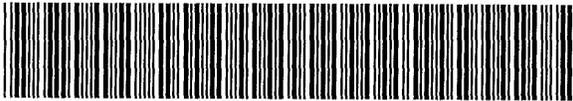
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