MessageFrom: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Friday, December 16, 2005 9:33 AM
To: [purged]
Subject: RE: question concerning guidance for IRB and clinical investigators - 1998 update

Dear Mr. [purged]:

I will respond to each of your questions in turn.

Question 1. You asked if listing a non-local IRB on a 1572 would serve as adequate documentation of an agreement between the site and the IRB for the services provided.

Answer 1: No, the 1572 would not serve as adequate documentation of an agreement between the site and the IRB. Although the 1572 shows the name and address of the IRB that the clinical investigator plans to have review the study, it is not signed by the IRB, and thus does not, in fact, document what the non-local IRB is agreeing to do.

You described a scenario in which "...the CRO or sponsor has made an agreement with the non-local IRB and likewise has an agreement with the site for the conduct of the trial.." It's generally the responsibility of the clinical investigator to ensure that the study is reviewed by an IRB. Although sponsors may encourage the use of a non-local or "centralized" IRB review process, particularly for multi-center trials, it is very important to ensure that the IRB ordinarily responsible for reviewing the study, is aware of (and agrees to) such transfer of oversight. Note that the Information sheet to which you referred in your e-mail goes on to say, "A written agreement should be executed between the performance site where the research is to be conducted (e.g., private practitioner's office, clinic, etc.) and the IRB or its institution. The agreement should confirm the authority of the IRB to oversee the study." [emphasis added.]

If an institution, its IRB, and a central IRB agree to participate in a centralized IRB review process (under 21 CFR 56.114), we recommend that they document that agreement and ensure that all other parties involved receive copies of the agreement (e.g., the institution, the institution's IRB, the central IRB, investigators at the sites, the sponsor). If the agreement apportions IRB review responsibilities between a central IRB and the institution's IRB, the agreement should delineate the specific responsibilities of the central IRB and the institution's IRB for the initial and continuing

review of the study.

Question 2: Is there any requirement of the FDA on the content /form of such an agreement? Would a statement of the local IRB that for the purpose of the specific trial, they would allow non-local IRB review be sufficient for this purpose? In the specific case I assume that the spirit of the text indicates that in the given case there would need to be an agreement between the non-local IRB and the site as well (as listed above)?

Answer 2: If the review responsibility for the study has been totally delegated to the non-local IRB, then the agreement would be pretty simple. If the review responsibility is split between the two IRBs, then the agreement should spell out who is responsible for what. FDA does not have any specific requirements on the content/form of such agreements. See also the answer to Question 1.

Question 3: Although multi-center trials are not specifically done by cooperating sites, all sites will be conducting the same trial and as such one could argue that the phrase "reasonable methods of joint review" might be applicable. Following the reasoning, would it still be required for sites to obtain an approval of their local IRB to have a non-local IRB performing their review as well?

Answer 3: For multi-center trials, the sites need to ensure that the local-IRB is aware of and agrees to the transfer of responsibility for reviewing the study to the non-local IRB. See also the answers to 2 and 3 above.

I hope this is helpful.

Sincerely,
Carolyn Hommel
Consumer Safety Officer
Good Clinical Practice Program
Office of Science and Health Coordination
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This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or

otherwise obligate or commit the agency to the views expressed.

-----Original Message-----
From: [purged]
Sent: Tuesday, December 06, 2005 2:29 PM
To: Hommel, Carolyn - OC
Cc: [purged]
Subject: question concerning guidance for IRB and clinical investigators - 1998 update

Dear Mrs. Hommel

When reading through the guidance document for institutional Review Boards and Clinical Investigators (update 1998) available on the website of the FDA (http://www.fda.gov/oc/ohrt/irbs/nonlocalreview.html), some questions were raised by the colleagues.

1/ the document mentions that in case a non-local IRB is performing the review, there should be an agreement between the site and the IRB for the services provided. In case however the CRO or sponsor has made an agreement with the non-local IRB and likewise has an agreement with the site for the conduct of the trial, would it be considered adequately documented as the Principle Investigators would list the non-local IRB on the applicable 1572? Would the completed 1572 suffice the purpose of an agreement for this?

2/ the document mentions that a non-local IRB can not be involved in case the site has a local IRB available, unless the trial is beyond the scope of the IRB procedures, or if a written agreement is obtained from the local IRB.

"When an institution has a local IRB, the written procedures of that IRB or of the institution should define the scope of studies subject to review by that IRB. A non-local IRB may not become the IRB of record for studies within that defined scope unless the local IRB or the administration of the institution agree. Any agreement to allow review by a non-local IRB should be in writing.
"

Is there any requirement of the FDA on the content /form of such an agreement? Would a statement of the local IRB that for the purpose of the specific trial, they would allow non-local IRB review be sufficient for this purpose?

In the specific case I assume that the spirit of the text indicates that in the given case there would need to be an agreement between the non-local IRB and the site as well (as listed above)?

3/ how would the above listed relate to a multi-center trial coordinated by the sponsor or a CRO? As per paragraph "Cooperative Research" of the same guidance document the following is mentioned:
"Cooperative research studies involve more than one institution. The Food and Drug Administration (FDA) and Department of Health and Human Services (HHS) regulations permit institutions involved in multi-institutional studies to use reasonable methods of joint or cooperative review [21 CFR 56.114 and 45 CFR 46.114, respectively]. While the IRB assumes responsibility for oversight and continuing review, the clinical investigator and the research site retain the responsibility for the conduct of the study.
Although multi-center trials are not specifically done by cooperating sites, all sites will be conducting the same trial and as such one could argue that the phrase "reasonable methods of joint review" might be applicable. Following the reasoning, would it still be required for sites to obtain an approval of their local IRB to have a non-local IRB performing their review as well?

Thank you in advance for your feedback on the above-listed topics

Kind regards,

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