From: Lee, Bonnie on behalf of OC GCP Questions
Sent: Thursday, March 03, 2005 10:31 AM
To: [Redacted]
Subject: RE: IRB/Ethics annual review

Dear [Redacted],

While progress reports may contain the information necessary for the IRB to conduct its formal continuing review of the study, that is unlikely. It is more likely that the progress reports provide an abbreviated summary of the study's status rather than a complete review of the study.

Continuing review of research should be substantive and meaningful. FDA regulations at 21 CFR 56.111 set forth the criteria that must be satisfied in order for the IRB to approve research. These criteria include, among other things, determinations by the IRB regarding risks, potential benefits, informed consent, and safeguards for human subjects. The IRB must ensure that these criteria are satisfied at the time of both initial and continuing review.

In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including:
-The number of subjects accrued;
-A summary of adverse events and any unanticipated problems involving risks to subjects or others and any withdrawal of subjects from the research or complaints about the research since the last IRB review;
-A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review;
-Any relevant multi-center trial reports;
-Any other relevant information, especially information about risks associated with the research; and
-A copy of the current informed consent document and any newly proposed consent document.

At least one member of the IRB (i.e., a primary reviewer, if you use a primary review system) also should receive a copy of the complete protocol including any modifications previously approved by the IRB. Furthermore, upon request, any IRB member also should have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting.

When reviewing the current informed consent document(s), the IRB should ensure the following:
-The currently approved or proposed consent document is still accurate and complete;
-Any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(b)(5).
-Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB, but informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the informed consent document.

When reviewing research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above-referenced documentation, including the complete protocol.

I hope this information is helpful to you.

Sincerely,

Bonnie

Bonnie M. Lee
Associate Director for Human Subject Protection Policy
Good Clinical Practice Program, FDA

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: [Redacted]
Sent: Wednesday, March 02, 2005 9:54 PM
To: OC GCP Questions
Subject: RE: IRB/Ethics annual review

Thank you so much regaring continuing review. The next question asked by staff is what about progress reports? Are they the same as continuing review? I would not think so. Most [Redacted] sites think that if they give a progress report annually this is the same as Ethics reviewing the protocol and all related documents. This is not happening in [Redacted] for US funded trials.

Help.
[Redacted]

-----Original Message-----
From: Lee, Bonnie [mailto:BLee@OC.FDA.GOV] On Behalf Of OC GCP Questions
Sent: Thursday, 3 March 2005 1:27 AM
To: [Redacted]
Subject: RE: IRB/Ethics annual review

Dear [Redacted],

FDA's IRB regulations state, in part, that "An IRB shall conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but not less than once per year..." See 21 CFR 56.109(f).

Several scenarios for determining the date of continuing review apply for protocols reviewed by the IRB at a convened meeting. To determine the date by which continuing review must occur, focus on the date of the convened meeting at which IRB approval occurs. (These examples presume the IRB has determined that it will conduct continuing review no sooner than within 1 year).

Scenario 1: The IRB reviews and approves a protocol without any

conditions at a convened meeting on October 1, 2002. Continuing review must occur within 1 year of the date of the meeting, that is, by October 1, 2003.

Scenario 2: The IRB reviews a protocol at a convened meeting on October 1, 2002, and approves the protocol contingent on specific minor conditions the IRB chair or his/her designee can verify. On October 31, 2002, the IRB chair or designee confirms that the required minor changes were made. Continuing review must occur within 1 year of the date of the convened IRB meeting at which the IRB reviewed and approved the protocol, that is, by October 1, 2003.

Scenario 3: The IRB reviews a study at a convened meeting on October 1, 2002, and has serious concerns or lacks significant information that requires IRB review of the study at subsequent convened meetings on October 15 and October 29, 2002. At their October 29, 2002 meeting, the IRB completes its review and approves the study. Continuing review must occur within 1 year of the date of the convened meeting at which the IRB reviewed and approved the protocol, that is, by October 29, 2003.

For a study approved under expedited review, continuing review must occur within 1 year of the date the IRB Chair or IRB member(s) designated by the Chair gives final approval to the protocol.

Review of a change in a protocol ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply a change to it.

When continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur. This would be, for example, October 1, 2003, in the above Scenarios 1 and 2, and October 29, 2003, in Scenario 3, even if the continuing reviews took place up to 30 days prior to these dates.

The key to picking the date for continuing review is to ensure that no more than one year will elapse between reviews (assuming the interval for review has been set for yearly). Therefore, in response to your question, it would be the most recent review date (assuming that's review of the whole study--continuing review--and not just a change to it).

I hope this information is helpful to you.

On a separate note: FDA will be holding a public hearing in Rockville, Maryland, on March 21 to solicit views on the process by which IRBs obtain and review information on adverse events that occur during the conduct of clinical investigations. Registration to attend and/or speak at the hearing is required and can be done online at http://www.accessdata.fda.gov/scripts/oc/dockets/meetings/meetingdocket.cfm.
We encourage registrants to participate as speakers. Information about the hearing is available at http://www.fda.gov/OHRMS/DOCKETS/98fr/oc04297.pdf.
If you have questions or difficulty registering, we encourage you to contact Nancy L. Stanisic at 301-827-1660 or at stanisicn@cder.fda.gov.
The Federal Register document also describes how interested individuals

can submit written comments in lieu of attending the hearing.

Sincerely,

Bonnie

Bonnie M. Lee
Associate Director for Human Subject Protection Policy
Good Clinical Practice Program, FDA

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-----Original Message-----
From: [Redacted]
Sent: Wednesday, March 02, 2005 1:53 AM
To: gcpquestions@oc.fda.gov
Subject: IRB/Ethics annual review

Dear GCP help desk,

We are sending out reminders to our sites regarding obtaining IRB/Ethics annual reviews.

We have read the [Redacted] GCP's and we can not find reference to annual review timelines for Ethics. Is there any US FDA title 21 regulations to review?

Question?
Does the date of review go back to the original approval date, if it is different from the last annual review date given by Ethics or is it the from the most resent date from the last annual review?

For example, A site might have been late in submitting progress reports to Ethics in the past, therefore the approval date now is inconsistent with the original date of approval. Do we use this new date or go back to the orginal date for tracking future progress reports?

Your response would be most appreciated,

[Redacted]
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