From: OC GCP Questions
To: [redacted]
Subject: RE: IRB Ongoing Review of studies closed except for data analysis
Date: Thursday, February 06, 2014 10:12:00 AM

Good morning,

I would refer you to FDA's guidance document "IRB Continuing Review after Clinical Investigation Approval" which is available at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf. Page 15of that document discusses continuing review of studies which are eligible for expedited review under category (8). This category applies to research:

"(a) Where
(i) the research is permanently closed to the enrollment of new subjects;
(ii) all subjects have completed all research-related interventions; and
(iii) the research remains active only for long-term follow-up of subjects; or
(b) Where no subjects have been enrolled and no additional risks have been identified; or
(c) Where the remaining research activities are limited to data analysis."

The guidance document goes on the discuss multi-site trials where some sites are continuing to collect follow-up data and/or conduct data analysis. The guidance states "The IRBs for site(s) performing an ongoing activity such as long-term follow-up or data analysis (e.g., the site operating the coordinating center or statistical center for the study) would need to ensure that continuing review of the study for those sites occurs at least annually. Other sites in a multi-site study may have completed the study and, having no further data analysis or other responsibility in the trial, may be closed out; continuing review for these sites would no longer be necessary."

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional questions.

Patrick J. McNeilly, Ph.D., C.I.P.
Office of Good Clinical Practice
Food and Drug Administration

From: [REDACTED]
Sent: Tuesday, February 04, 2014 5:18 PM
To: OC GCP Questions
Subject: IRB Ongoing Review of studies closed except for data analysis

Good Day,
I read with some concern today a warning letter (issued to [REDACTED]
on January 10, 2014;
http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm382730.htm) with the following citation:

> "…….Further, we note that your IRB's protocol states that "investigators should terminate a protocol when human subjects are no longer being followed or studied. As long as subjects (patients or otherwise) are still being followed at this site, even if the protocol is closed to subject accrual, or if data is still being analyzed, even if not being actively collected, a protocol is considered active and continuing review must be completed. If no subjects are being followed and data analysis is complete, the study may be officially terminated. When research has been terminated, the responsible investigator must inform the IRB. Investigators are encouraged to notify the IRB as soon as a study is terminated." Your IRB's status charts for the studies that you review and approve should be maintained and updated to identify whether a study is active, terminated, or another appropriate status."

Since the site is usually not responsible for the data analysis (unless it is a sponsor/investigator, or investigator initiated study), and because we know that this step can take a long time (years in some cases), I am confused about this citation.

Can we assume from this warning letter that the FDA feels the study is still ongoing? There seems to be a disconnect somewhere as the investigators obligations for responding to data queries, etc. are usually completed at data lock and their participation generally ends there.

In my experience each IRB may have a slightly different policy on when a study is 'completed' and may be closed. Some permit this once all subject follow-up visits and follow-up on any SAEs is completed, some do not allow it until the Close Out visit has been performed, if there is to be one. Still others require ongoing review until the database is locked, meaning the Site's data has been 'cleaned' and the data is ready for analysis.

It has not been my understanding that a study must be kept open and under ongoing IRB review until data analysis is complete. I would appreciate your feedback on this as I want to be sure we are properly following the regulations in this regard and that we are in compliance with the FDA's expectations.

Thank you for your insights.
Regards,

[REDACTED]