From: Toth-Allen, Jean
Sent: Friday, December 15, 2006 9:05 AM
To: [purged]Subject: RE: Does discarding noncompliant data constitute "compliance"?

Dear Mr. [purged]:

Thank you for your inquiry regarding reporting of investigator noncompliance.

Last questions first - there is presently no regulation or guidance available in this regard but a proposed rule regarding reporting of instances of actual or suspected fraud is in clearance within the agency. (The document will be posted to the GCP website, on issuance, for easy availability.) It makes no difference to FDA as to when, relative to the timing of the conduct of a study, that noncompliance and/or questionable data has been uncovered.

Back to the main issue, FDA wants to know when issues of noncompliance and/or questionable data integrity arise for clinical studies, even if a sponsor is successful in obtaining compliance or discontinues use of a troublesome site. There are commonly both human subject safety concerns and data concerns that result. If a site or investigator is removed from a study, arrangements may need to be made to insure the safety of the subjects who have already been enrolled and treated at the site in question, particularly if they will not be continued as part of the official study. In addition, any and all data that is collected on an investigational product need to be shared with FDA, even if the data will not be usable to support marketing of the product. Such data need to be discussed in the next study progress report and a summary, that includes a justification for rejecting the data if that is the case, included in any marketing application/submission that uses the study's results. It would be beneficial to both the sponsor and FDA reviewers if there is a discussion, as soon as practical, of any such findings and their repercussions so both the sponsor and FDA can determine what needs to be done regarding human subject protection and the extent of information regarding the questionable data that might be needed.

Hope this information is useful. If you need further information and/or have additional questions, please submit them once again to the official GCP mailbox, gcp.questions@fda.hhs.gov, in lieu of responding to my personal e-mail address.
Sincerely yours,
Jean Toth-Allen, Ph.D.
Good Clinical Practice Program
OSHC, Office of the Commissioner, US 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.

From: [purged]
Sent: Saturday, December 09, 2006 10:50 AM
To: OC GCP Questions
Subject: Does discarding noncompliant data constitute "compliance"?

FDA's "Compliance Program Guidance Manual" states that during a site inspection, "if serious deviations occurred, obtain evidence that the sponsor obtained compliance or terminated the clinical investigator's participation in the investigation and reported it to FDA." (§ III.B.a.C.7)

There appear to be cases where a sponsor audit of a site identifies some subjects whose data cannot be used because of the investigator's fraud or unbelievable ignorance. If the data from those subjects is discarded and the apparently compliant data is used, is the investigator now in compliance or must the sponsor report the deviations to the FDA?

Does it matter whether the audit occurs during or after the site completes the study?

Are there any regulations or other guidances that touch on this question?

Thanks!

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