From: Toth-Allen, Jean
Sent: Monday, January 30, 2006 11:36 AM
To: [Redacted]
Subject: RE: Phase 3b and 4 Monitoring

Dear [Redacted],

Thank you for your inquiry regarding sponsor monitoring and data reliability responsibilities.

As you are aware, both parts 312 and 812 require sponsors to monitor studies and parts 314 and 814 require them to provide accurate and complete reports of supporting studies. However, FDA regulations do not specify the nature and extent of monitoring, as that is dependent upon the nature of the study. The only FDA-specific guidance presently available regarding monitoring - a 1988 document found at http://www.fda.gov/ora/compliance_ref/bimo/clinguid.html - is also not specific. However, the ICH GCP guidance (at 5.18.3) - found at http://www.fda.gov/cder/guidance/959fnl.pdf - does address some of your concerns more directly in that it states:

In general there is a need for on-site monitoring, before, during and after the trial; however, in ***exceptional circumstances*** (emphasis added) the sponsor may determine that central monitoring in conjunction with procedures such as investigators' training and meetings, and extensive written guidance can assure appropriate conduct of the trial in accordance with GCP. Statistically controlled sampling may be an acceptable method for selecting the data to be verified.

While FDA adopted this guidance document specifically with regard to pharmaceutical studies, we do believe that those sections of this guidance that are relevant to clinical studies in general are applicable across all clinical studies. In general, we encourage that monitoring be addressed upfront in the study protocol and discussed with FDA in the course of protocol development, particularly when variations such as central monitoring are being explored.

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, gcpquestions@oc.fda.gov, in lieu of responding to my personal e-mail address.

Sincerely yours,
Jean Toth-Allen, Ph.D.
Good Clinical Practices 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: [Redacted]
Sent: Saturday, January 28, 2006 11:54 PM
To: gcpquestions@oc.fda.gov
Subject: Phase 3b and 4 Monitoring
Importance: High

[Redacted] they had been informed, presumably by an FDA CSO, that monitoring of clinical trial sites remotely by phone is now acceptable.

Now I recognize that clinical trials in Phase 3b and 4 – in otherwords 'Post Market' is a strange animal and NOT specifically under the traditional scope of 312 and 812.

I also recognize that ICH allows, by loose interpretation, some of the same monitoring activities.

My real concern is that as companies allow a 'remote' process, data integrity with regards to data eventually submitted becomes problematical. We are not talking here of eDC or eDM. Nor am I addressing the use of technological 'shortcuts'.

I would like your views on the subject of Sponsor responsibility towards accuracy of Case Record Data which eventually will be submitted to FDA from a client site.

I am available by phone or email to discuss further.

Thank you.

[Redacted]