From: Toth-Allen, Jean
Sent: Thursday, June 22, 2006 12:41 PM
To: [Redacted]
Subject: RE: reporting protocol violations to the FDA

Dear [Redacted],

Thank you for your inquiry regarding reporting of protocol deviations.

Of all the FDA regulations regarding reports during the conduct of clinical trials (21 CFR Part 312 covering pharmaceutical studies, Part 812 covering device studies, and Part 56 regarding IRB review), only the device regulation specifically requires any reporting of protocol deviations. For device clinical investigators 812.150(a)(4) requires a report to the sponsor and reviewing IRB, but only if the deviation was necessary to protect the life or well-being of study subjects. The IRB regulations do require that an IRB have procedures to ensure prompt reporting of changes in research activity [56.108(a)] and for prompt reporting of any unanticipated problems involving risks to human subjects or others as well as any serious or continuing non-compliance with regulations [56.108(b)]. It is not clear that the majority of protocol deviations fit any of these categories, though there may be some exceptions.

Deviations from the investigational plan (protocol deviations) can affect the usefulness of the study data if they are sufficiently numerous and/or affect essential data. Should the study data as a result prove to be unusable or insufficient to support marketing, study subjects were put at risk through use of an unproven product without any ultimate benefit to anyone. Therefore, those responsible for the conduct of the study and the welfare of the study subjects - sponsors and IRBs as well as the FDA - should be aware of the types and frequency of deviations occurring in a study. Inclusion of this information in required progress reports to sponsors and IRBs by clinical investigators and the FDA by sponsors seems the appropriate venue for reporting, unless they are directly affecting the safety of subjects or the integrity of the study or were undertaken to protect the subjects well-being, for which regulation requires prompt reporting.

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: Wednesday, June 21, 2006 12:35 PM
To: OC GCP Questions
Subject: reporting protocol violations to the FDA

Hello,
I am wondering what the requirement is for reporting protocol violations to the FDA from the sponsor level. If a protocol violation occurs at one of our study sites, they immediately report it to their local IRB, but what is our (sponsor) requirement for reporting to the FDA? Can we report it with our annual report, or even final report, or is it required that it also be reported to FDA immediately?

Thanks in advance for your help.
[Redacted]