From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Wednesday, November 23, 2005 11:38 AM
To: [Redacted]
Subject: RE: Reporting Safety Information to local IRBs

Dear [Redacted]:

Your questions about reporting safety information to the IRB was forwarded to me for a response. I apologize for the delay in responding to you. I have pasted your questions into this e-mail and will answer each in turn.

(1) Does the participating US centre reserve the right to decide which safety reports (whether they be events on the trial in question or events from foreign trials using the agent under investigation) meet regulatory reportable definitions (i.e. the centre decides which are serious, related and unexpected even if we/sponsor thinks they are reportable). Is this acceptable under the FDA regulations or are they to follow the directions from the sponsor/coordinator?

Response: In general, we encourage sites to follow the directions of the sponsor with respect to reporting safety information. However, the descriptions of reporting requirements described in the study protocols should allow for triaging and batching of reports. We believe it is reasonable, given the expertise of other monitoring bodies (whether that be the sponsor, a designated monitor, or a DSMB), to have the external reports essentially batched and analyzed so that the IRB receives the analysis (or conclusion) rather than the individual reports.

In my opinion, the goal ought to be to minimize the burden on IRBs while at the same time ensuring that IRBs receive information that would influence their risk/benefit assessment of the study or information provided to subjects. Because reports of individual events occurring at a different location are hard to interpret by themselves and thus do not generally provide meaningful information, most IRBs develop some triage mechanism to limit their receipt of external reports. To the extent to which a third party (the sponsor, or its designated monitor) can analyze the individual reports and provide that analysis (rather than individual reports) to investigators and their IRBs, the more meaningful the review process can be. That is, the IRBs will get better information and fewer reports, and this process will increase the protections to subjects.

FDA has been aware for some time that the large number of individual AE reports submitted to IRBs are an ongoing problem for the research community. In March 2005, FDA held a public hearing to obtain the opinions of the IRB community and other interested parties on adverse event reporting to IRBs. Based on the input that we obtained, we hope to develop additional guidance on this issue.

(2) Our expectation is for safety reports that we deem to be regulatory reportable to be submitted to local IRBs within 30 days of receipt. Some centres are batching these reports and submitting them quarterly to their IRBs. Does the FDA allow 3 monthly reporting?

Response: Our regulations require that "...all changes in the research activity and all unanticipated problems involving risk to human subjects or others..." be reported ***"promptly"*** to the IRB. (See 21 CFR 312.66.) In addition, our regulations require that IRBs "[f]ollow written procedures for ensuring prompt reporting to the IRB...of [any] unanticipated problems involving risks to human subjects or others..." (See 21 CFR 56.108(b).]

Thus, IRBs have some discretion in establishing appropriate timeframes for when safety information should be submitted to them, and for identifying the reports that should be submitted sooner rather than later. Such timeframes, as well as any other expectations as to the format or other information that should be provided to them, are generally described in each IRB's SOPs or other policy guidelines.

(3) In addition to your feedback on the above questions, I would appreciate if you could provide me with some links to any relevant FDA regulations/guidelines regarding safety reporting.

Response: You might want to begin by visiting FDA's good clinical practice (GCP) website: http://www.fda.gov/oc/gcp. We have posted our regulations, draft and final guidance documents, FDA's Information Sheet Guidances, and other helpful information about human subject protection, informed consent, IRB review, and good clinical practice.

I hope this is helpful.

Sincerely,

Carolyn Hommel
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Good Clinical Practice Program
Office of Science and Health Coordination
Office of the Commissioner
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-----Original Message-----
From: [Redacted]
Sent: Wednesday, November 09, 2005 11:06 AM
To: gcpquestions@oc.fda.gov
Subject: Reporting Safety Information to local IRBs

Dear GCP office,

I have a couple of questions regarding the reporting of safety information to local IRBs. We are the lead protocol group for a few trials that are not only approved by our [Redacted] regulatory authority but are also under a US IND as there are participating US centres (for example, [Redacted]. As the sponsor for this trial in [Redacted] and coordinator of this study for the US centres we distribute events to all participating centres that our group deems to be serious, unexpected and related to the investigational agent in accordance with the IB/PM (and GCP). At the time of auditing some of these US participating centres we have become aware that some sites filter out the safety reports that we distribute to them for local IRB submission rather than submitting all that they are given.

(1) Does the participating US centre reserve the right to decide which safety reports (whether they be events on the trial in question or events from foreign trials using the agent under investigation) meet regulatory reportable definitions (i.e. the centre decides which are serious, related and unexpected even if we/sponsor thinks they are reportable). Is this acceptable under the FDA regulations or are they to follow the directions from the sponsor/coordinator?

(2) Our expectation is for safety reports that we deem to be regulatory reportable to be submitted to local IRBs within 30 days of receipt. Some centres are batching these reports and submitting them quarterly to their IRBs. Does the FDA allow 3 monthly reporting?

In addition to your feedback on the above questions, I would appreciate if you could provide me with some links to any relevant FDA regulations/guidelines regarding safety reporting.

Thanks in advance for your consideration. Your prompt reply will be greatly appreciated.

Regards,
[Redacted]