From: OC GCP Questions
To: [redacted]
Subject: Reporting of Expected Adverse Events
Date: Monday, March 31, 2014 2:17:55 PM

Good afternoon –

As stated previously, all AEs need to be recorded (on CRFs) but not all need to be reported. t is difficult to specifically answer your question. For example, if the study (investigational product) involved a new blood thinner and the subject had surgery, bruising and hematoma severity would be an important surgical side effect to note as an AE and may be related to the study drug and therefore would need to be reported. Another example -- in some cardiac investigations involving devices, death was not considered an AE that needed to be reported. The protocol should dictate what should be reported as an AE.

If you are still unsure what should be reported as an AE, you can always ask the FDA review division for direction and clarification. FDA is always happy to provide more clarity in situations like this.

I hope this information is helpful.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [Redacted]
Sent: Monday, March 31, 2014 10:18 AM
To: OC GCP Questions
Cc: [redacted]
Subject: Reporting of Expected Adverse Events

Thank you for your previous response in regards to reporting expected AEs (i.e., post-surgery bleeding, pain, bruising, etc). You stated sponsors commonly miss the fact that expected AEs for example post-surgery bleeding or pain need to be captured on a CRF as the severity and/or duration of such could signal a problem caused by the investigational product. I further read in your FDA guidance "Safety Reporting Requirements for NDs and BA/BE Studies", page 19, **"The sponsor can arrange that only specific types of adverse events be reported to the sponsor (e.g., those that resulted in withdrawal from the study or cessation of therapy, modification of dose, or addition of another drug) provided the director of the FDA review division that has responsibility for review of the IND has agreed to that arrangement in advance (21 CFR 312.32(c)(3))."**

Without the above mentioned FDA approval/arrangement that only specific types of AEs need reporting, is it appropriate for sponsors to ask investigators to consider whether a normal consequence of creating a wound (i.e., post-surgery mild pain, bleeding) and the clinical findings associated with the normal reparative process (bruise, hematoma, itching, etc.) are truly Adverse Events (according to standard definitions)? And if they are not, then they should not reported as such to the sponsor? My interpretation from your previous email is that this is not acceptable. Is it more accurate to say that investigators should report the expected findings (i.e., post-surgery mild pain, bleeding, bruise, hematoma, itching, etc.) so that we can track severity and duration? Or is it appropriate for investigators to only report them if they observe increased severity/duration?

In other words, should the investigator report all expected AEs, or are investigators only required to report the AEs if the severity/duration changes from what is expected?

Please let me know if you need clarifications regarding my questions. I am just trying to make sure I fully understand the reporting requirements of expected adverse events since sponsors are commonly confused, which leads to investigator sites becoming confused as well.

Thank you for your time and discussion,