From: Brown, Sheila (OGCP)
To: [redacted]
Cc: [redacted]
Subject: RE: Informed consent & collecting AEs?
Date: Wednesday, August 12, 2015 12:54:00 PM
Attachments:

Dear [redacted],
My responses are below your questions. I hope this information is helpful to you. If you need further assistance, please feel free to contact the GCP mailbox at gcp.questions@fda.hhs.gov .

Best regards,

Sheila

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This communication does not constitute a written advisory opinion under Title 21 CFR 10.85, but rather is an informal communication under Title 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: Monday, August 10, 2015 11:37 AM
To: OC GCP Questions
Cc: [redacted]
Subject: Informed consent & collecting AEs?

Hello,

My questions are as follows:

1) At what point are you supposed to start collecting Adverse events, once the subject signs Informed Consent but has not yet received the investigational product or not until the subject is administered the investigational device or drug? There seems to be different schools of thought on this based on the ICH definition.

FDA's definition of an adverse event found in 21 CFR 312.32(a) is:

Any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. The definition of Unanticipated Adverse Device Effect can be found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.3 .

Because a subject has not yet received study drug in the scenario you describe, the event could not be considered associated with the use of the study drug. In general, if a subject experiences an event, such as an illness or condition (e.g., infection, headache, rise in blood pressure) after the subject agreed to participate in the study, signed the IRB-approved informed consent form, and passed the screening tests but before administration of any study drug, this event should not be reported as an adverse event/serious adverse event (AE/SAE).

However, because an event such as an illness or condition could affect the subject's eligibility/continued eligibility for the study, the event should still be recorded by the study site in the study records, tracked, and be reported to the sponsor. The investigator should also ensure that the subject receives appropriate medical care, for example, by providing it directly or by referring the subject back to the subject's primary

care physician (see FDA's guidance "Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects" at www fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm187772.pdf for additional discussion of medical care).

It is best for investigators to follow the IRB-approved protocol and to consult the sponsor regarding expectations and any questions related to events that occur after a subject has signed the consent form, but before they receive any dose of study medication. Also, in accordance with 21 CFR 312.66 and 812.150, investigators must promptly report to the IRB all unanticipated problems involving risk to human subjects or others so you may want to consult your IRB to find out if such an event requires reporting to the IRB.

2) What if a subject signs IC, but has not been administered the investigational product and something really bad happens, would this be captured as an SAE?
See response to Q1

3) Does this pertain to both device and drug?
In general, yes, but please discuss expectations for reporting AEs, SAEs, and unexpected adverse device effects (UADEs) (21 CFR 812.150(a)(1)) with the study sponsor and your IRB. You may also find the following guidances helpful: *Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting Improving Human Subject Protection*, http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126572.pdf and *Guidance for Industry and Investigators Safety Reporting Requirements for INDs and BA/BE Studies*

http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm227351.pdf

Thank you for your time,

[redacted]