From: OC GCP Questions
To: [redacted]
Subject: Response is in-progress: Clinical Database AE Cut-off Dates
Date: Monday, February 24, 2014 12:58:54 PM

Dear [redacted] –

As promised with much delay, please see CDER OMP's responses below. I also sent this email back to CDRH to see if they have anything else to add. They might not. If I hear from CDRH, I will forward their response as well.

I hope you find the answers adequate. Again I apologize for the delay in responding.

Kind regards,

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

From: CDER OMP
Sent: Monday, February 24, 2014 10:33 AM
To: OC GCP Questions
Subject: RE: Response is in-progress: Clinical Database AE Cut-off Dates

Scenario: The subject's last study visit per protocol is at 24 months. At the 24-month visit, the subject is exited and documented as having completed the study. The protocol and informed consent form have no provision for anything beyond the 24-month visit.

1. A subject experiences an AE or SAE that is ongoing at the 24-month visit. The PI plans to ensure the individual receives medical care, as appropriate, after the subject has exited the study. For an individual whose continued medical care is provided by the doctor who happened to be the study PI, that data will be captured in the individual's medical record.
    a. Can or should a "sponsor" *collect* data on an individual, who is no longer considered a study subject, after their 24-month visit?

Response- A sponsor should continue to collect data on a subject experiencing an ongoing adverse event beyond the 24 month visit (and record the data in the CRF) if the information that would be obtained is pertinent to the investigation (e.g., could contribute useful information about the safety profile of a drug). Factors to consider include whether the event is serious and the extent to which the event is already characterized. If the event is serious, the investigator should generally continue

to follow the patient, and should always follow if the event is also unexpected. For nonserious events there may be less reason to continue to follow, particularly for events already listed in the Investigator Brochure.

b. Should the PI record in the CRF and the sponsor report in the clinical database that the event is ongoing at the 24-month visit (meaning the sponsor would *collect* no further data)?

Response- No. See 1.a.

c. If FDA expects the sponsor to collect data beyond the 24-month visit, how long after does this expectation extend (3 months, 6 months, indefinitely)?

Response- Generally, the protocol should provide for follow-up of some types of adverse events until they are resolved (or clinically stable if not expected to resolve). The investigator should seek clarification from the sponsor if necessary. If the sponsor has specific concerns, they should discuss them with the review division.

2. Similarly regarding data collection after a subject has exited from the study, an individual returns two weeks later to their primary care physician (who happens to be the PI in the study the individual just participated in) with a new AE , SAE, or request to remove the implant. Although the *study* is ongoing, this individual has already completed the study and ended their participation. Can or should a "sponsor" collect the additional data learned about this individual since the individual is no longer in the study?

Response- It is not usually necessary to collect information on an adverse event that occurs after study completion. The follow-up period provided for in the protocol is generally considered adequate to capture adverse events that may be related to the test article. However, if an investigator believes an event occurring after the patient has completed the trial may be related to the test article, the investigator should inform the sponsor. The sponsor should evaluate as it would any other event reported by the investigator.

The information provided in response to this inquiry does not address any product or trial specific considerations. Follow up questions regarding specific products or trials should be directed to the appropriate FDA review division by the sponsor.

From: OC GCP Questions
Sent: Wednesday, January 22, 2014 2:32 PM
To: CDER OMP
Subject: Response is in-progress: Clinical Database AE Cut-off Dates

CDER/OMP
I sent this question to you on 12/19 and Pat followed up with a phone call while I was on AL as the response below did not answer the question. The writer [redacted] is asking again today for a response from CDER. Can you assist?

Thanks, Doreen

Doreen M. Kezer, MSN

Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: OC GCP Questions
Sent: Thursday, December 19, 2013 9:51 AM
To: CDER OMP
Subject: FW: Clinical Database AE Cut-off Dates

CDER-OMP, can you assist with this question? Thanks Doreen

From: [Redacted]
Sent: Wednesday, December 18, 2013 3:26 PM
To: OC GCP Questions
Subject: Clinical Database AE Cut-off Dates

Dear FDA Representative,

A question regarding the cut-off date for capturing AE data in the CRF and clinical database has come across my desk that I would appreciate FDA's feedback on due to varying thoughts on the matter from industry. This specific question is regarding a medical device study (implant); however, I would request a response that would answer the questions regardless of whether the investigational product was a drug or device.

Scenario: The subject's last study visit per protocol is at 24 months. At the 24-month visit, the subject is exited and documented as having completed the study. The protocol and informed

consent form have no provision for anything beyond the 24-month visit.

1. A subject experiences an AE or SAE that is ongoing at the 24-month visit. The PI plans to ensure the individual receives medical care, as appropriate, after the subject has exited the study. For an individual whose continued medical care is provided by the doctor who happened to be the study PI, that data will be captured in the individual's medical record.
    a. Can or should a "sponsor" *collect* data on an individual, who is no longer considered a study subject, after their 24-month visit?
    b. Should the PI record in the CRF and the sponsor report in the clinical database that the event is ongoing at the 24-month visit (meaning the sponsor would *collect* no further data)?
    c. If FDA expects the sponsor to collect data beyond the 24-month visit, how long after does this expectation extend (3 months, 6 months, indefinitely)?
2. Similarly regarding data collection after a subject has exited from the study, an individual returns two weeks later to their primary care physician (who happens to be the PI in the study the individual just participated in) with a new AE , SAE, or request to remove the implant. Although the *study* is ongoing, this individual has already completed the study and ended their participation. Can or should a "sponsor" collect the additional data learned about this individual since the individual is no longer in the study?

Your response is greatly appreciated.

Kind Regards,

[Redacted]