From: OC GCP Questions
To: [redacted]
Subject: Question Regarding the Prompt Reporting of Serious Adverse Events
Date: Monday, November 16, 2015 1:14:40 PM

Good afternoon again –

I found some additional information that might assist you with your question although the answer is the same.

Regarding reporting of serious adverse events, 21 CFR 312 64(b) requires an investigator to "immediately report to the sponsor any serious adverse event" to the sponsor, except for study endpoints. Study endpoints that are also serious adverse events are reported to the sponsor in accordance with the protocol, unless there is evidence suggesting a causal relationship between a drug and an event (e.g. death from anaphylaxis).

Study protocols and other aspects of the investigational plan may also provide additional instructions to clinical investigators regarding serious adverse event reporting, such as the timeline for submitting a report to the sponsor after a clinical investigator becomes aware of the event's occurrence and what the sponsor considers appropriate documentation of awareness. Investigators have an obligation under 21 CFR 312.60 to ensure that the trial is conducted according to the investigational plan. FDA's Guidance for Industry: Investigator Responsibilities -- Protecting the Rights, Safety, and Welfare of Study Subjects recommends that investigators develop a plan for supervision and oversight of the clinical trial, including procedures for ensuring that study staff comply with the protocol and adverse event assessment and reporting requirements. (See http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf). Such procedures might reasonably include processes for ensuring that information about hospitalizations and other serious adverse events is obtained by the site in a timely manner, and in turn reported to the sponsor in accordance with the protocol and 21 CFR 312.64(b) ."

Although "timely" is not specifically defined, we would expect the report to be submitted in a way (time) that would protect the safety and welfare of the research subjects.

A discussion related to this issue occurs in FDA's draft guidance "Safety Reporting Requirements for NDs and BA/BE Studies" (available at http://www.fda.gov/downloads/Drugs/.../Guidances/UCM227351.pdf).

The revised requirements for IND safety reporting became effective March 28, 2011. Please see link below

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm226358.htm

Kind regards,

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

From: OC GCP Questions
Sent: Monday, November 16, 2015 1:07 PM
To: [redacted]
Subject: Question Regarding the Prompt Reporting of Serious Adverse Events

Good afternoon –

The 24 hour clock starts when a physician on the FDA 1572 or on the study team (research nurse, study coordinator) becomes aware of the event. Please see the guidance document below; specifically section D on page 17.

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM227351.pdf

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional questions.

Kind regards,

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

From: [redacted]
Sent: Monday, November 16, 2015 11:07 AM
To: OC GCP Questions
Subject: Question Regarding the Prompt Reporting of Serious Adverse Events

Good Morning,

This question is in regard to the prompt reporting of Serious Adverse Events.

Per 21 CFR 312.64 (b) "An investigator shall promptly report to the sponsor any adverse event that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately."

Proposed scenario: The protocol specifies that serious adverse events must be reported to the sponsor within 24 hours of the investigator becoming

aware of the event. A patient is admitted to an emergency room at a facility where the clinical trial is being held and a physician not on the FDA 1572 becomes aware of the event. Would the 24 hour clock start when this physician first became aware or would the 24 hour clock start when a physician on the FDA 1572 or on the study team (research nurse, study coordinator) becomes aware of the event?

Thank you,