From: OC GCP Questions
To: [redacted]
Subject: PI's/SubI's entering causality data directly into EDC
Date: Wednesday, November 18, 2015 5:48:21 AM

Good morning –

FDA regulations are not specific as to how the causality information is entered into the EDC. If there is a specific SOP in place and it is being followed by all study personal, I don't think this would be cited as a violation if an FDA inspection would occur at your site. I can offer the following information on causality assessments.

The investigator is required to report serious adverse events to the sponsor and must include an assessment of whether there is a reasonable possibility that the drug caused the event (21 CFR 312.64). The sponsor is required to report serious and unexpected suspected adverse reactions to FDA and all participating investigators (21 CFR 312.32(c)(1).

The investigator should follow the protocol regarding the format for reporting the investigator's causality assessment to the sponsor. The IND safety reporting draft guidance includes the following:

"The sponsor should decide how to capture the investigator's causality assessment (e g., rating scale, yes/no response to a question such as, "Was there a reasonable possibility that the drug caused the adverse event?")."

Additionally "causality" is mentioned throughout the document below.
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM227351.pdf

As stated above, the investigator should report adverse events to the sponsor in accordance with the protocol, ensuring that at a minimum the investigator is complying with 21 CFR 312.64(b) (e.g., immediately report serious adverse events to the sponsor, report non-serious adverse events in accordance with the protocol): Code of Federal Regulations .

Please find the IND safety reporting final rule and draft guidance at:
www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrug NDApplication/ucm226358.htm

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: Tuesday, November 17, 2015 1:37 PM
To: OC GCP Questions
Subject: PI's/SubI's entering causality data directly into EDC

Within the last week, two different sponsor/CRO's have advised us that for data entry, the data managers/coordinators can enter, for example, the AE term "headache" and Grade (i.e. Grade 2); however they will be blocked from entering causality. It will be a PI or physician Sub-I who must go into the EDC and enter this data.

Source records, such as an AE log, will still be required to be completed, as this will serve to ensure that the physician has correctly entered the data into the EDC.

Both Sponsor/CRO's have stated that this is in response to the FDA's "increasing scrutiny" on investigator oversight, and apparently feel that this is an appropriate way to ensure oversight.

If a site has a process by which the physician already completes AE logs for causality by SOP and by delegation, it would seem the site is already meeting the intent of oversight.

[redacted]