Safety Assessment AE/SAE reporting Script # 5

Inspector: What is your background and experience?

Responder: I am Medical Doctor (MD) by background. I graduated from Medical school in 2001. I participated in six HIV clinical trials. I am study physician for ASPIRE study.

Inspector: What training did the Sponsor/CRO provide on safety reporting? Did you follow any particular guideline/manual?

Responder: The site was trained on study protocol and all manuals during the site activation call. The safety reporting requirements are described in the protocol, in the MTN-020 SSP Manual and in in the Manual for Expedited Reporting of Adverse Events (AE) for DAIDS. We also have site procedure (SOP) in place for safety reporting.

Inspector: What is the definition of AE?

Responder: Any untoward medical occurrence in a clinical research participant administered an investigational product and that does not necessarily have a causal relationship with the investigational product.

Inspector: Will this definition apply to all study groups (IP/placebo)?

Responder: Yes.

Inspector: Will the definition include laboratory abnormalities?

Responder: Yes.

Inspector: Will you document all AE in the source documents and in the CRF?

Responder: Yes (response not in line with protocol requirements)

All in the source documents and a subset of AEs which must be reported in CRF is defined in the protocol.

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Inspector: Who was responsible for safety monitoring at your site?

Responder: The study nurses were responsible for interviewing the participants during the study visits.(study nurses could not be the only one responsible for safety assessments, physicians involvement is a must)

All team members who had interactions with participants were to some extent responsible for safety monitoring but the ultimate responsibility was with IoR and study physicians.

Inspector: Who assessed abnormal lab results? How was the review documented?

Responder: The lab results were reviewed by the nurses and signed by the study physicians (unclear answer put the inspector that physician only signed and di not review.)

The lab results were initially reviewed by the nurses. They highlighted all abnormal values. Then the results were reviewed and signed by the study physicians.

Inspector: Is there a process in place for notifying the site about alert (significantly out of range) lab values?

Responder: I am not aware of such process. All laboratory results were sent to us the same way. What process you have in mind? What would be your expectation? (asking inspector for advice, putting in the question the need for such process)

We have never had any alert values for ASPIRE study but the lab Staff will be able to explain what process they have in place.

Inspector: What arrangements were in place to allow patients to make contact with the study team in an emergency?

Responder: Study participants were provided instructions for contacting the study site to report any untoward medical occurrences they may experience. The contact details/ phone number were provided in the Informed Consent Form (ICF).

Inspector: Who reported SAEs and what process was used?

Responder: The reporting was within three business days via electronic reporting system DAERS and I must say that this system was not user friendly. Few cases were not reported by us in a timely manner since we did not have complete information and it took more than 3 days to obtain all details. (making inappropriate comments on the system quality, volunteering Information)

The reporting was by delegated staff within three business days via electronic reporting system DAERS.

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Inspector: Did you have back-up reporting system in case of problems with DAERS

Responder: I do not know

Inspector: Would congenital anomaly /birth defect require expedited reporting?

Responder: I am not sure. (GCP definition, each individual involved in Clinical trials must be able to demonstrate the basics knowledge of GCP)

Yes as per ICH GCP definition.

Inspector: Was the information in DAERS report always reviewed by IoR or sub-investigator?

Responder: I guess yes.(guessing, should be reviewed by IoR or study physician)

Yes.

Inspector: One of the SAE report which I reviewed was signed by Dr XXX and I do not see her on the study Delegation of Authority Log.

Responder: It must be an omission or maybe she was a back-up to somebody on this one occasion.(never say never, check documentation and come back with an answer)

I will check the records and will come back with an explanation.

Inspector: For AEs/SAEs, who made the assessment of causality? Were these assessments documented in the source data?

Responder: Study physician. It was documented in the source documentation (SD) or directly in the system/CRF.(incorrect answer, SD must be always available)

Study physician. It was documented in the source documentation.

Inspector: How is expectedness assessed and by whom?

Responder: By study physician. He/she assesses if AE might be anticipated from the pharmacological properties of the product.(incorrect answer, see protocol definition)

By study physician. He/she assesses AE using information in the Investigator Brochure.

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Inspector: Have you ever discussed the SAEs with IoR?

Responder: No. Should I? (IoR must be informed, inspector should not be asked for advice)

Yes. IoR was informed about all SAEs.

Inspector: Have you ever reported social harms? What is the process?

Responder: We did not report any. We have an SOP on that. I will provide you with the copy after the interview.(volunteering information, SOP was not requested)

We did not report any. We have an SOP on that.

Inspector: Are AE/SAE routinely reported to EC/IRB? What is the process? Who is responsible?

Responder: Study coordinator is responsible for reporting to EC.