From: OC GCP Questions
To: [redacted]
Subject: Can nurses determine clinical significance of lab values for a clinical trial?
Date: Friday, July 31, 2015 7:12:30 AM

Good morning –

FDA regulations are very broad. The regulations require that sponsors choose investigators qualified by training and experience (see 21 CFR 312.53(a)). The regulations also require that investigators commit themselves to personally conduct or supervise the investigation (see 21 CFR 312.53(c)(1)(vi)(c)).

It might be helpful for you to review FDA's guidance on Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects (available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf) This guidance was developed to clarify for investigators and sponsors FDA's expectations concerning the investigator's responsibility (1) to supervise a clinical study in which some study tasks are delegated to employees or colleagues of the investigator or other third parties and (2) to protect the rights, safety, and welfare of study subjects.

The investigator should maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated. This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., can refer to an individual's CV on file), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator. The sponsor can also guide you as to what tasks can appropriately be reviewed by study team members other than the clinical investigator or the subinvestigator.

Please see the guidance document (link) here.
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf

4. Must the investigator be a physician?

The regulations do not require that the investigator be a physician. Sponsors are required to select only investigators qualified by training and experience as appropriate experts to investigate the drug (21 CFR 312.53(a)). In the event the clinical investigator is a non-physician, a qualified physician (or dentist, when appropriate) should be listed as a subinvestigator for the trial and should be responsible for all trial-related medical (or dental) decisions. (ICH E6 section 4.3.1; http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf).

Training, education, and experience required for sponsor personnel may necessarily, and appropriately, vary depending on the type of product, the indication, the study being conducted, and its associated risk. FDA's regulations are not explicit as to what constitutes adequate training, education and experience, nor do they outline specific qualifications, including whether such personnel must hold an active medical license. Moreover, sponsors have discretion in determining what qualifications are needed in certain positions based on the general recognition that this would include education, training and experience pertinent to the particular clinical study and its design and execution, as well as familiarity with human subject protection (HSP) regulations, recordkeeping, data integrity, and good clinical practice (GCP) standards and requirements. Whether or not certain sponsor personnel should hold an active medical license depends on the considerations outlined above.

An example of when a RN could possibly evaluate lab values – A cardiac RN (documented by the CV) could possibly evaluate lab values, specifically cardiac enzymes, to see if the subject had a myocardial infarction (heart attack) and advise the CI or subCI. However, this task should be approved by the CI and the sponsor.

That said FDA does expect an investigator to be in compliance with any state or local laws or requirements as part of being qualified. Therefore, an investigator (or a member of the investigator's staff) would need to maintain a medical license or other certification that is necessary to perform the study (for example, to diagnose or treat a patient or prescribing or ordering investigational product). If the license is subject to renewal, then a current license would be needed in order to be in compliance with the local requirements. So, although not specified in FDA's regulations, in order to be qualified, an investigator, subinvestigator, or study staff would need to maintain any required state or local licenses or certifications needed to perform the clinical tasks necessary to conduct the study.

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
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Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Thursday, July 30, 2015 5:09 PM
To: OC GCP Questions
Subject: Can nurses determine clinical significance of lab values for a clinical trial?

Hello my question-(Can nurses determine clinical significance of lab values for a clinical trial) has come up during many trials. I currently have a CRA [redacted] monitoring a site in Massachusetts where the P[redacted] is a nurse (RN). However, there is a medical doctor on the 1572 as a sub investigator. When I asked the CRA to assure the MD reviews the subjects lab values and assign clinical significance to abnormal values I received the following response from the site PI:

> Hi-
> Assessment of clinical significance has been documented by me (the PI) in all instances.
>
> As discussed with [redacted], unlike diagnosing disease or conducting a Physical Exam which are clearly defined by licensure, the nomenclature of CS and NCS are clinical research constructs wholly disassociated from license.
>
> The source documentation clearly indicates NCS and was reviewed by the responsible PI. No further action is required.
>
> Thanks-
> [redacted]

My understanding is as follows:

Clinically significant or not clinically significant refers directly to the impact the item being evaluated impacts the health and wellbeing of the subject and determines if further medical action is required. Therefore this would be a medical decision required for subject safety purposes. Per GCP a qualified physician (or dentist, when appropriate), who is an investigator

or a sub investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.

I hoping that you can clear this up for me so I can pass the official GCP decision along to my team. Thank you so much.

Kind Regards,

[redacted]