From: OC GCP Questions
To: [redacted]
Subject: Qualifications for a Sub-Investigator
Date: Monday, June 26, 2017 9:02:00 AM
Attachments: [redacted]

Good morning –

As you state 312.53(a) states “A sponsor shall select only investigators qualified by training and experts appropriate experts to investigate the drug.”

That said the 1572 guidance -- https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf states -

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).

FDA regulations require sponsors of clinical investigations to select only investigators qualified by training and experience to investigate the test article (see 21 CFR §§ 312.53 and 812.43). FDA considers this to include the investigator meeting any licensing requirements of the jurisdiction where the trial takes place. The regulations further require investigators to supervise the testing (for investigations of drugs, including biological products, under 21 CFR Part 312, investigators commit themselves to personally conduct or supervise the investigation; for investigations of medical devices, under 21 CFR Part 812, investigators commit themselves to supervise all testing of the device involving human subjects). Investigators may delegate a task to individuals who are qualified to perform the task, including being appropriately licensed.

FDA's "Guidance for Industry: Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects" (available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf), includes the following information:

The investigator should ensure that any individual to whom a task is delegated is qualified by education, training, and experience (and state licensure where relevant) to perform the delegated task. Appropriate delegation is primarily an issue for tasks considered to be clinical or medical in nature, such as evaluating study subjects to assess clinical response to an investigational therapy (e.g., global assessment scales, vital signs) or providing medical care to subjects during the course of the study. Most clinical/medical tasks require formal medical training and may also have licensing or certification requirements. Licensing requirements may vary by jurisdiction (e.g., states, countries). Investigators should take such qualifications/licensing requirements into account when considering delegation of specific tasks. In all cases, a qualified physician (or dentist) should be responsible for all trial-related medical (or dental) decisions and care.

The document further states:

The investigator is responsible for conducting studies in accordance with the protocol (see 21 CFR 312.60, Form FDA-1572, 21 CFR 812.43 and 812.100). In some cases a protocol may specify the qualifications of the individuals who are to perform certain protocol-required tasks (e.g., physician, registered nurse), in which case the protocol must be followed even if state law permits individuals with different qualifications to perform the task (see 21 CFR 312.23(a)(6) and 312.40(a)(1)). For example, if the state in which the study site is located permits a nurse practitioner or physician's assistant to perform physical examinations under the supervision of a physician, but the protocol specifies that physical examinations must be done by a physician, a physician must perform such exams.

FDA would expect anyone who is involved with essential tasks in the conduct of a clinical study to be listed as a sub-investigator on the Form FDA 1572 (the 1572). The 1572, while an FDA form, is intended to supply the study sponsor with all pertinent information about the conduct of the study at the site in question. In addition, once signed, it serves as an agreement by the clinical investigator (CI) to comply with the investigational plan and pertinent regulations. It is important that the sponsor we aware of all study staff who perform essential tasks in the conduct of the study at the site.

If the CI or PI is away for an extended period of time, FDA recommends that whoever is taking over the responsibilities of overseeing the study should sign a new 1572 form.

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

This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.

From: [redacted]
Sent: Thursday, June 22, 2017 6:38 PM
To: OC GCP Questions
Subject: Qualifications for a Sub-Investigator

21 CFR 312.53(a) requires that “A sponsor shall select only investigators qualified by training and experience as appropriate experts to investigate the drug.”

Situation: In a drug study, a Principal Investigator (licensed and duly qualified MD) retains a foreign medical graduate who is not licensed in the US to function as a sub investigator, maintaining that the education, training and experience of the foreign graduate is adequate for these tasks in the professional opinion of the PI. The foreign medical graduate performs intake screening of subjects and consents subjects under the direct daily supervision of the PI. Site is located in the US.

PI goes off site for a family emergency for approximately two months, leaving the foreign medical graduate to operate independent of direct supervision. Foreign medical graduate continues with the same duties as when under direct supervision, however, now also decides whether to enroll subjects, directs that they be randomized into an IND-governed trial, and orders the dispensing of investigational medication, despite not being licensed to prescribe medication in the State in which the site is located.

Would the agency agree that a sponsor should not permit this situation on the grounds that the foreign medical graduate is not qualified within the meaning of 312.53(a) due to

the lack of prescribing rights? Would other factors need to be assessed, such as the adequacy of the medical training received outside the US? (Assume the foreign graduate has simply not attempted the US foreign graduate equivalency exam, not that she has attempted it and failed.)