From: OC GCP Questions
To: [redacted]
Subject: Question related to role of Non-Physician Practitioners in clinical trials for sites in US
Date: Friday, June 26, 2015 12:24:12 PM

Good afternoon –

The 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)).

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.

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) Please see section #1.

FDA would expect physicians and study staff to follow state and local laws regarding medical licensure and medical practice requirements in addition to sponsor requirements.

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

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: Friday, June 26, 2015 5:07 AM
To: OC GCP Questions
Subject: Question related to role of Non-Physician Practitioners in clinical trials for sites in US

Hi,

I have a question with respect to role of "Non-physician practitioners" in Clinical Trials.

For the purpose of the understanding I have provided one situation here for sites in US. A Non-physician practitioner (e.g; Nurse Practitioner, Clinical nurse specialist, Physician assistant) is listed as "Sub-Investigator" at site and delegated with important trial related activities including medical assessments.

As I interpret the FDA Guidance documents/regulations in general, there is no issue with appointing "Non-physician practitioner" (e.g; Nurse Practitioner, Clinical nurse specialist, Physician assistant) as Investigator because GCP and regulations in general do not define who can act as Investigator for the trial (Physician or Non Physician). However Sponsors are required to define and select only investigators qualified by training and experience. After referring to below mentioned FDA guidance documents, I have two questions to understand the correct interpretation.

Question 1) FAQ doc on statement of Investigator mentions that If Investigator is non-physician then all trial related medical decisions should be the responsibility of qualified physician. Does that mean that initial medical assessment/decisions could be done by non-physician practitioner as per state law applicable for non-physician practitioner but final assessment/final decision about the medical care and medical decision should be done by qualified physician.

Question 2) If trial protocol defines that a qualified physician, who is an investigator or a sub-investigator for the trial, must be responsible for all trial-related medical decisions then is my interpretation is correct that all medical decisions would include all important medical assessments related to trial (e.g; medical histroy/conditions assessments for subject eligibility, AE causality/severity assessment and withdrawing subject from trial as a result of AE/SAE) and protocol requirement must be followed for such tasks (medical assessments) even if the state law permits a Non-physician practitioners to perform the tasks (medical assessments). (ICH GCP 2.7)

References:

FAQ-Statement of Investigator (Form FDA 1572) :
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)

Guidance for industry: Investigator Responsibilities-Protecting the right, safety and welfare of study subjects
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.

The Principles of ICH GCP (#2.7):
The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist

Thank you for your help in advance

Kind regards,

[redacted]