From: OC GCP Questions
To: [redacted]
Subject: PI"s/SubI"s entering causality data directly into EDC
Date: Friday, December 11, 2015 6:10:59 AM

Good morning –

Sorry for the delay. I contacted our Office of Medical Policy (OMP) for a response. Please see their answer below.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Thursday, December 10, 2015 8:04 AM
To: OC GCP Questions
Subject: RE: PI's/SubI's entering causality data directly into EDC

Doreen,

OMP's response below –

Under 21 CFR 312.53(c)(1)(vi)(c), investigators commit (through a signed Form FDA-1572) to personally conduct or supervise a clinical investigation. The investigator is also responsible for conducting studies in accordance with the protocol (21 CFR 312 53(c)(1)(vi)(a); see also 21 CFR 312 60 and Form FDA-1572). The IND regulations do not prohibit investigators from delegating transcription of source data into case report forms. FDA's *Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects* guidance states that "[i]n 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…" (section III.A.1, page 3).

The *Investigator Responsibilities* guidance clarifies FDA's expectations concerning the investigator's responsibility (1) to supervise a clinical investigation in which some study-related tasks are delegated to employees or colleagues of the investigator or other third parties and (2) to protect the rights, safety, and welfare of subjects. As described in the guidance, it is common practice for investigators to delegate certain study-related tasks to employees, colleagues, or other third parties (individuals or entities not under the direct supervision of the investigator) (section III A, page 2). When tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator should ensure that any individual to whom a task is delegated is qualified by education, training, and experience to perform the delegated task (section III A.1, page 3).

For additional information, please see FDA's *Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects* guidance, available at http://www.fda.gov/downloads/Drugs/.. /Guidances/UCM187772.pdf, and FDA's *E6 Good Clinical Practice Consolidated Guidance*, available at http://www.fda.gov/downloads/Drugs/.../Guidances/ucm073122.pdf.

Please note that the information provided in this response does not address any product or trial specific considerations. Follow-up questions regarding specific products or trials should be directed to the appropriate FDA review division by the sponsor.

From: [redacted]
Sent: Wednesday, November 18, 2015 1:20 PM
To: OC GCP Questions
Subject: RE: PI's/SubI's entering causality data directly into EDC

Thank you for your response.

My question does not relate to who or how causality for AE's is reported. My question relates to whether it is appropriate for the sponsor to circumscribe the ability of the PI to delegate tasks based on education, credentialing and training. At our site, our PI and sub-I's perform all causality and severity assessments and document their assessments in source, following the sponsor's prescribed taxonomies. Our PI also chooses to delegate the task of "eCRF entry" to other personnel who are qualified to perform this role.

By requiring, through the use of user rights, that only the PI can enter the causality and severity data into eCRF, isn't the sponsor effectively circumscribing the PI's right to delegate tasks to others? How can the sponsor permit the PI to delegate some data entry tasks to non-physicians (eg, the AE start and end dates itself), but restrict other data entry tasks to physicians (in this case, causality and severity)? Since we are recording the PI's assessment in source, the sponsor cannot take the position that this eCRF access restriction is necessary to ensure that only investigators perform causality and severity assessment; that procedure is done prior to eCRF entry. If anything, the sponsor's stated rationale shows they may be interpreting eCRF entry as the source entry, when that is clearly in violation of basic GCP principles that source entry be the *original* recordation of a data point, not the transcription. Without this rationale, there does not appear to be any justification for the sponsor dictating who can enter what data points in eCRF, unless they are taking the position that the entry of words such as "related" or "not related" (the type of words transcribed into the causality section) somehow require an MD whereas words such as "hyperlipidemia" (entered into the medical history section of eCRF) do not.

Your clarification would be greatly appreciated.