From: OC GCP Questions
To: [redacted]
Subject: GCP Questions
Date: Friday, November 20, 2015 10:26:58 AM

Good morning –

Please see my answers 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, November 19, 2015 12:27 PM
To: OC GCP Questions
Subject: GCP Questions

Hello-
I hope that you are doing well today! I have a few questions.

What constitutes a person to be a "legally authorized representative" for signing ICF for a research participant?
Can a research participant ask a friend to sign the ICF on their behalf while the research participant is present if the research participant is too sick or tired to sign the ICF?

The term "legally authorized representative" is used in the U.S., and is defined in FDA's regulations as "...an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research..." (See 21 CFR 50.3(l)). FDA's regulations provide only limited circumstances in which an investigational product can be given to a subject without first obtaining informed consent from the subject or the subject's legally authorized representative. In general, for studies conducted in the United States, who may serve as an individual's legally authorized representative is determined by State law. [Here is a link to all of FDA's human subject protection and good clinical practice regulations: www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm#Preambles.)

(The term "legally acceptable representative," is also defined in FDA's official guidance, ICH E6, Good Clinical Practice: Consolidated Guidance (Section 1.37) as "An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial." Although ICH E6 uses the term "legally acceptable representative" and FDA's regulations use "legally authorized representative," the definitions of these terms are essentially the same. "Legally acceptable representative," however, is often used in countries whose laws allow expedited appointment of a judge or independent physician to serve as an individual's "legally acceptable representative," and who can then provide consent for an individual and eliminate the need to waive

informed consent.) A link to the complete text of ICH E6 is posted on FDA's Good Clinical Practice webpage:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

Once a legally authorized representative has been designated for a subject, that individual is responsible for making decisions on behalf of the subject, and to assure that any such decisions are in the subject's best interest. As I said above, it is generally not customary for another individual to "step in" if a subject's legally authorized representative is temporarily unavailable.

That said you would have to follow state and local laws to decide if a friend could sign the ICD on behalf of the subject.

Is it a FDA requirement that all site study staff on the Delegation of Duties Log have CVs filed in the regulatory binder or is it just a requirement to have CVs for the PI and Sub-PIs listed on the 1572 filed in the regulatory binder?

FDA's regulations do not actually refer to "regulatory binders" but rather to the records that need to be maintained. Although binders provide a way to organize and maintain records, there is no requirement to use them. The regulations do not specify the method of storage (that is, a binder or a box). As long as your method of storage allows records to be maintained for the required retention period and records may be accessed with sufficient organization to allow documents to be retrieved as needed (for example, during an FDA inspection), I don't believe the specific method of storage is a concern.

The inclusion of specific information (e.g., clear affiliation with one of the study sites stated by name and address) in the curriculum vitae for the clinical investigator, subinvestigator, and associated study staff is usually a requirement of the sponsor, CRO, and/or the IRB as is whether sponsor is asking that the CVs of all study staff be placed in the regulatory binder. From an FDA standpoint, this is not a requirement according to the regulations.

If a site is using central lab only, is it ever a requirement to have local lab certifications filed in the regulatory binder?

Specifics as to what documentation clinical laboratories need to retain is covered under the Clinical Laboratory Improvement Amendments (CLIA), which is under the purview of the Centers for Medicare and Medicaid (CMS) not FDA. Information about CLIA can be found at www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html?redirect=/clia/

While a specific study protocol may require additional recordkeeping, if nothing is specified in the protocol the expectation is that the clinical laboratory that analyzes study samples/specimens will comply with the recordkeeping requirements of CLIA. In addition, the case report forms (CRFs) for the study subjects should contain information as to what specimens were sent for analysis, the date(s) they were both collected and sent, and any study-specific information regarding handling of the specimens and their transmittal to the laboratory and/or receipt of the results. If a bioresearch monitoring (BIMO) inspection was conducted at the site, FDA investigators would expect to see the original copies of protocol-specified laboratory results in each subject's study file and look to reconcile the dates on the results with the information in the CRFs. While FDA regulations do not address the chain of custody of study specimens, should there be any concerns about laboratory results for one or more study subjects, FDA would look for documentation of specimen collection, handling, shipment, etc. in search of potential causes of noted or suspected discrepancies.

There is no FDA requirement that the certifications be filed in the regulatory binder.

Thank you!!

[redacted]