From: OC GCP Questions
To: [redacted]
Subject: Possible Assistance with certain topics for our SOPs
Date: Wednesday, March 29, 2017 9:52:00 AM
Attachments: [redacted]

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: Tuesday, March 28, 2017 10:33 AM
To: OC GCP Questions
Cc: [redacted]
Subject: Possible Assistance with certain topics for our SOPs

Hello, we are composing SOPs for our company and its research division (clinical trials, bench studies, etc.) and wonder if your organization has available or has suggestions for finding information on the following:

IP transportation and certification
Study drug return to vendor
Study drug destruction
Drug accountability

The general requirements for storage and distribution are below -

Under FDA regulations 21 CFR 312.61 states

Control of the investigational drug.

An investigator shall administer the drug only to subjects under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator. The investigator shall not supply the investigational drug to any person not authorized under this part to receive it.

312.62 Investigator recordkeeping and record retention.

(a) Disposition of drug. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If the investigation is terminated, suspended, discontinued, or completed, the investigator shall return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 312.59.

ICH E-6 - Good Clinical Practice-Consolidated Guidance
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122 .pdf
states

4.6 Investigational Product(s)

4.6.1 Responsibility for investigational product(s) accountability at the trial site(s) rests with the investigator/institution.

4.6.2 Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product(s) accountability at the trial site(s) to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.

4.6.3 The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) and trial subjects. Investigators should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product(s) received from the sponsor.

4.6.4 The investigational product(s) should be stored as specified by the sponsor (see sections 5.13.2 and 5.14.3) and in accordance with applicable regulatory requirement(s).

4.6.5 The investigator should ensure that the investigational product(s) are used only in accordance with the approved protocol.

4.6.6 The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product(s) to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly

As noted above, specific instructions for any investigational product storage would be the responsibility of the sponsor and the nature of the investigational product.

FDA's regulations regarding sponsor responsibilities for drug accountability include the following:

Sec. 312.57 Recordkeeping and record retention.

(a) A sponsor shall maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug. These records are required to include, as appropriate, the name of the investigator to whom the drug is shipped, and the date, quantity, and batch or code mark of each such shipment.

Sec. 312.59 Disposition of unused supply of investigational drug.

The sponsor shall assure the return of all unused supplies of the investigational drug from each individual investigator whose participation in the investigation is discontinued or terminated. The sponsor may authorize alternative disposition of unused supplies of the investigational drug provided this alternative disposition does not expose humans to risks from the drug. The sponsor shall maintain written records of any disposition of the drug in accordance with 312.57.

As you can see, the regulations do not specifically state that the sponsor must re-count, re-measure, re-weigh, but the sponsor does need to assure the return of all unused supplies of the drug.

Staff training on equipment prior to a study

GCP training is universally recognized necessity to protect human subjects in clinical trials. As our website states –

Adherence to the principles of good clinical practices (GCPs), including adequate human subject protection (HSP) is universally recognized as a critical requirement to the conduct of research involving human subjects. Many countries have adopted GCP principles as laws and/or regulations. The Food and Drug Administration's (FDA's) regulations for the conduct of clinical trials, which have been in effect since the 1970s, address both GCP and HSP.

Additionally below is what we have said in the past regarding GCP training –

FDA regulations regarding qualifications for those involved with the conduct of clinical studies are very broad. Both Title 21, Code of Federal Regulations (21 CFR) Part 312 (for drugs and biologics) and 812 (for medical devices) simply state that sponsors are required to choose clinical investigators and monitors that are qualified by training and experience. Logically, clinical investigators and monitors need to be knowledgeable about applicable regulations as well as specific areas essential to the conduct of the particular study.

The expectation is that investigators, sub-investigators and study staff will be knowledgeable about good clinical practice, including human subject protection, data integrity, recordkeeping, etc. As noted, the sponsors have discretion in determining what qualifications will be needed to conduct a study and may identify in the protocol a required frequency of GCP training, in which case the investigator and sub investigators would be expected to meet that frequency of training in order to comply with the sponsors requirements. Every effort should be made to train the investigational sites. This is the sponsor's responsibility.

Additionally what training is needed and how it is documented depends to some degree on the nature of the study. Some protocols need extensive training and others may need minimal, also dependent upon the background and experience of study staff.

Subject being given time to review and ask questions
regarding ICF, also
availability of doctor to answer medical questions per ICF

Please see FDA's guidance document on informed consent

Search for FDA Guidance Documents > A Guide to Informed Consent - Information Sheet

Collection of medical records and medical release

FDA's regulations relating to the confidentiality of clinical trial subjects includes the IRB regulations at 21 CFR 56.111, which outlines the criteria for IRB approval of research. One of those criteria [21 CFR 56.111(a)(7)] requires that, where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Note that neither the regulations or even guidance do not specifically address the methods used to maintain the confidentiality of records identifying the subject nor do they prohibit sponsors/CROs from receiving subject information, even with identifiers. Typically, study sponsors, CROs, and sites usually follow their own Standard Operating Procedures (SOPs) that direct document handling and maintaining confidentiality

In addition, the informed consent regulations at 21 CFR 50.25(a)(5) require that the informed consent include a statement describing the extent, if any, to which confidentiality of records identifying the

subject will be maintained and that notes the possibility that the FDA may inspect the records. The informed consent document signed by the subject usually includes a statement describing who will have access to the subjects' identifying records (e.g., the sponsor, CRO, and their representatives, the FDA, etc.).

ICH GCP E6 Good Clinical Practice: Consolidated Guidance, (which is recognized as official FDA guidance), section 2.11 states that the confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

Release of medical records is probably a HIPPA issue. FDA does not administer HIPAA; that law is implemented by the Department of Health and Human Services, Office for Civil Rights (www.dhhs.gov/ocr/office/about/index.html). For more information about the applicability of relevant HIPAA regulations, you would need to contact OCR directly.