From: OC GCP Questions
To: [redacted]
Subject: Questions Regarding Administration/Dispensing of Investigational Product in Clinical Trials
Date: Tuesday, January 20, 2015 10:42:45 AM

Good morning –

I can only respond to your FDA – regulated questions.

The FDA regulations regarding investigational product are as follows –

Sec. 312.61 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 subinvestigator responsible to the investigator. The investigator shall not supply the investigational drug to any person not authorized under this part to receive it.

Sec. 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.

(b) Case histories. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

(c) Record retention. An investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 61 FR 57280, Nov. 5, 1996; 67 FR 9586, Mar. 4, 2002]

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)). 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) states that, *"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."*

It also states --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). When tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study. 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.

The delegation of certain study-related tasks to employees would include clinical research coordinators.

The expectation is that investigators and sub-investigators and well as study staff (research coordinators) will be knowledgeable about good clinical practice, including human subject protection, data integrity, recordkeeping, etc. Note that sponsors have discretion in determining what qualifications will be needed to conduct a study and dispense study medication.

The dispensing of medication is not solely performed by clinical investigator. Clinical coordinators can dispense medication. However, any task outlined in the protocol would be subject to applicable state or local laws as required for licensed medical professional staff.

During BIMO inspections, FDA investigators may note any problems with accounting of investigational product. Problems with accountability of an investigational drug could be considered a failure to comply with the regulations. You may be interested in FDA's Compliance Program Guidance Manual (CPGM) for the conduct of BIMO inspections of sponsors, CROs, and monitors - http://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/UCM133770.pdf ; and, for inspections of clinical investigators - http://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/UCM133773.pdf). In this CPGM for inspections of investigators, see in particular Part III - Inspectional,

page 12 of 20, paragraph J. Below, is the information copied from this paragraph J:

J. TEST ARTICLE CONTROL

1. Accountability [312.62(a), 511.1(b)(7)(ii), and 812.140(a)(2)]

a. Determine who is authorized to administer or dispense the test article.

b. Determine whether the test article was supplied to a person not authorized to receive it.

c. Compare the amount of test article shipped, received, used, and returned or destroyed. Verify the following:

i. Receipt date(s), quantity received, and the condition upon receipt;

ii. Date(s), subject number, and quantity dispensed; and

iii. Date(s) and quantity returned to sponsor. If not returned to sponsor, describe the disposition of the test article.

d. Determine where the test article is stored, whether it was stored under appropriate conditions as specified in the study protocol, and who had access to it.

e. If the test article is a controlled substance:

i. Determine how it is secured; and

ii. Determine who had access.

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional questions. If I have not adequately answered your questions, you may contact the Center for Drugs (CDER) directly at druginfo@fda.hhs.gov.

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.

-----Original Message-----
From: [redacted]
Sent: Monday, January 19, 2015 12:43 PM
To: OC GCP Questions
Subject: Questions Regarding Administration/Dispensing of Investigational Product in Clinical Trials

Hello,

I have some questions regarding the above subject for which I would appreciate your input.

1) For a clinical trial of a non-FDA approved investigational product, being conducted at an investigational site under the supervision of a registered physician Principal Investigator, is it permissible for a Study Coordinator to administer and/or dispense the investigational product to study subjects? If yes, does the Study Coordinator need to be a RN or LPN?

2) Same situation as in #1 but the product under investigation is FDA approved but is being studied for a new indication?

3) Same situation as in #1 but the product under investigation is FDA approved and is being used within the boundaries of the approved labeling (not for a new indication)?

Are there any FDA Guidance Documents or Q & As that address these situations?

By "dispense" I primarily mean providing (handing over) the study medication to the study subject as labeled and provided by the study sponsor in accordance with the study protocol.

By "administer" I mean either providing an oral study medication to subjects to take in the clinic during a study visit, or injecting/infusing study medication in the clinic during a study visit.

Thank You in advance for addressing these questions.

Respectfully Yours,

[redacted]