From: OC GCP Questions
To: [redacted]
Subject: Question for reimbursement of study drugs
Date: Wednesday, January 03, 2018 10:50:00 AM
Attachments: [redacted]

Good morning

The responses are separated into 3 categories: (1) investigational drug storage, (2) study record storage, and (3) patient reimbursement

(1) Investigational drug storage:

The pertinent FDA regulations relating to drug accountability 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 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.

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...

Sec. 312.69 Handling of controlled substances.

If the investigational drug is subject to the Controlled Substances Act, the investigator shall take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

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.

The regulations for investigational drugs are available here:
www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=312

There is a wide variety and type of investigational products that may be used in a clinical investigation, requiring varying storage conditions. I suggest you take a look at the ICH GCP E-6 guidance (which is recognized as official FDA guidance). The following sections may be helpful:

Section 4.6.4 (Investigator - Investigational Products) says 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). The sponsor is responsible for establishing the appropriate storage conditions for the investigational product, and the investigator is responsible for ensuring that the investigational product is stored as specified by the sponsor.

Section 5.13 (Sponsor - Manufacturing, Packaging, Labeling, and Coding Investigational Products) which says that the sponsor should determine, for the investigational products(s), acceptable storage temperatures, storage conditions (e.g., protection from light), storage times, reconstitution fluids and procedures, and devices for product infusion, if any. The sponsor should inform all involved parties (e.g., monitors, investigators, pharmacists, storage managers) of these determinations.

Section 5.14 (Sponsor - Supplying and Handling Investigational Products) further says that in supplying the investigational product to investigators, the sponsor should ensure that written procedures include instructions that the investigator/institution should follow for the handling and storage of investigational product(s) for the trial and documentation thereof. The procedures should address adequate and safe receipt, handling, storage, dispensing, retrieval of unused product from subjects, and return of unused investigational product(s) to the sponsor (or alternative disposition if authorized by the sponsor and in compliance with the applicable regulatory requirement(s).

I recommend that you consult your sponsor(s) and discuss their expectations about how your site should handle access and storage of their investigational drugs. Your IRB and/or facility legal counsel may be helpful in determining if there are state or local laws, or facility policies, that may affect off-site storage and transport of investigational drugs and other materials related to the study. It is also recommended that your site consider implementing written standard operating procedures (SOPs) to cover adequate and safe receipt of investigational product, handling and access, storage, dispensing, retrieval of unused product from subjects, and return of unused investigational product(s) to the sponsor (or alternative disposition if authorized by the sponsor and in compliance with the applicable regulatory requirement(s). You may also wish to include a procedure to be followed for monitoring storage conditions (e.g., temperature, light, etc.). You may also want to consider an SOP for on-site storage of drugs for distribution to subjects, and collection of drugs that are returned, and how/when drugs will be transported from one location to the other, and by whom. Secure storage and access of investigational products is required at all times.

As mentioned previously I cannot comment on CSA agreements. You might want to consult your institutional officials or your institutional legal department. Please also consider consulting the FDA RPM of the IND.

Kind regards,

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

U.S. FOOD & DRUG ADMINISTRATION

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.

From: [redacted]
Sent: Tuesday, January 02, 2018 6:51 PM
To: OC GCP Questions <gcp.questions@fda.hhs.gov>
Subject: RE: Question for reimbursement of study drugs

Dear Doreen M. Kezer,

Thank you for your kind feedback.
However, it seems my previous email was not clear to deliver my message. Please accept my apology.

The subject of reimbursement is not patients. It is investigators/institutions(hospital).

If CSA between sponsor & investigators does not define reimbursement of study drugs, Sponsor can resupply study drugs to investigators as much as investigators used for patient treatments?
Or the contract between sponsor & investigators should be amended for that sponsor has to pay investigator fee (money) in order to reimburse as much as investigators used?

I would appreciate if you kindly provide feedbacks.

Thank you.

-----Original Message-----
From: "OC GCP Questions"<gcp.questions@fda.hhs.gov>
To: [redacted]
Cc:
Sent: [redacted]
Subject: Question for reimbursement of study drugs

Good afternoon –

I can't specifically answer your question from a GCP standpoint. It is best to ask the FDA regulatory project manager of the IND for guidance. I can offer you information below regarding subject reimbursement and compensation.

Generally in the guidance below, it states in part -"…payment of a small proportion as an incentive for completion of the study is acceptable to FDA, providing that such incentive is not coercive.

Guidances>Payment to Research Subjects - Information Sheet

www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm

It is best to have IRB approval first, however, if the subject needs to be seen sooner than IRB approval is given a note to file as well as notifying the reviewing IRB and sponsor as soon as possible would be appropriate.

Please note that routine reimbursement to subjects should have IRB oversight and approval and also

should be explained in the informed consent document.

Subject compensation is not a regulatory requirement. In fact, both FDA and reviewing IRBs take a careful look at such provisions when reviewing study protocols, as they can be a source of "undue influence" if inappropriate. Reimbursement for expenses incurred are usually allowed, which you are likely referencing here given your terminology. If a subject waives any reimbursement, that should be documented for the site's protection should the individual have different thoughts about study participation in the future and attempt to falsely accuse the site of refusing just compensation.

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional GCP questions.

Kind regards,

Doreen M. Kezer, MSN

Senior Health Policy Analyst

Office of Good Clinical Practice

Office of the Commissioner, FDA

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From: [redacted]
Sent: Tuesday, January 02, 2018 3:45 AM
To: OC GCP Questions <gcp.questions@fda.hhs.gov>
Subject: Question for reimbursement of study drugs

Dear Sir,

I would like to inquire a reimbursement of chemotherapy drugs for clinical trials.
Basically, it should be supplied by sponsor however due to technical reasons, site's own drugs were used for patient treatment.
According to the CSA, the reimbursement was not agreed since it was already defined as one of essential materials.
It was only identified that sponsor has the obligation of chemotherapy drugs supply.
So now, the investigator asked sponsor to additionally supply drugs as much as used. But it cannot be investigator's fee since it was not initially contracted.
Thus, my question is... is there any concerns about sponsor provides real drugs (instead of investigator's fee)?
It would be a GCP violation?

Please let me have your advice for above matter.

Thank you.