From: OC GCP Questions
To: [redacted]
Subject: RE: 2 questions
Date: Tuesday, July 14, 2015 10:32:00 AM

Dear [redacted],
As you know, the regulations do not specifically address the scenario you describe. When the regulations are silent, IRBs, institutions, sponsors, and investigators are free to develop their own procedures and practices as long as applicable regulatory requirements are met.

The responses to your questions 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.

(2) study record storage

FDA's regulations do not prohibit the off-site storage of study records. If an FDA Bioresearch Monitoring (BIMO) inspection of the research site were to occur, however, FDA investigators would expect to see the original records or certified copies of such. Therefore, the only requirement would be that stored records be made available for inspection when needed [See 21 CFR 312.68 www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.68 for studies involving investigational drugs and/or biologics and 21 CFR 812.140 and 812.145 http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812&showFR=1&subpartNode=21:8.0.1.1.9.7 for medical devices]. Specifics for storage of study records, and delivery when needed, would be the subject of written legal contracts between the research site and the storage facility. It may also be helpful to establish written SOPs for storage of the records and for tracking who is able to access them, so that the Agency can be assured that the records have not been tampered with or altered and that confidentiality of information has been maintained throughout the duration of the transfer and storage. Any change in location of the study records should be communicated to the study sponsor. Again, your IRB and/or 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 records and other materials related to the study.

Although the information above specifically addresses hard (paper) copies, I thought that it may be helpful to provide additional information regarding electronic study record storage. If study documents are copied to an electronic format - to microfilm or an electronic file - the site would need to certify that the resulting records are exact copies of the original documents. It would also be beneficial to have SOPs for the copying and certification process. These guidance documents may be helpful for additional information regarding electronic source documents and computerized systems:

Guidance for Industry: Computerized Systems Used in Clinical Investigations, which can be accessed at

http://www.fda.gov/OHRMS/DOCKETS/98fr/04d-0440-gdl0002.pdf

Guidance for Industry: Computerized Systems Used in Clinical Trials, which can be accessed at http://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/UCM133749.pdf ,

Guidance for Industry: Electronic Source Data in Clinical Investigations, which can be accessed at

http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm328691.pdf

Again, you may wish to consult ICH-E6 good clinical practice guidance, which can be accessed at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

(3) patient reimbursement

I'm not sure if you are referring to a patient stipend (i.e., payment for participation in the study), or reimbursement of their expenses for participating in the study (e.g., parking, meals, etc.). In either case, the payment should not be coercive, as determined by your IRB. The payment schedule should be included in the informed consent document, so the prospective subject knows what any payments will be, including how much, what form (e.g., cash, gift card, etc.) and how often they will receive the payment. Payments should be prorated throughout the study, and should not be contingent on completion of the study. Your IRB may have a policy as to when payments to subjects are to be made, or at least can guide you on this topic. FDA's *Payment to Research Subjects Information Sheet* may be helpful. It can be found at http://www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm . Information about subject payment may also be found in ICH E6, which can be found at http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073122.pdf

I hope this information is helpful to you. If you need further assistance, please feel free to contact the GCP mailbox at gcp.questions@fda.hhs.gov .

Best regards,

Sheila

Sheila Brown, RN, MS
Policy Analyst, Office of Good Clinical Practice
Office of Special Medical Programs, Food and Drug Administration

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From: [redacted]
Sent: Thursday, July 09, 2015 7:13 AM
To: OC GCP Questions
Subject: 2 questions

I have come up with 2 questions that I can't really find in the regs and wondered if you could help me.

Our CEO would like our department to continue to see patients and have our office in building A. He would like to move drug storage, source documents, regulatory items…to building B. These buildings are about 300 yards apart, but he is thinking of doing this at other campuses as well and the buildings may be a few miles apart. Is this allowed? As long as I have been in research (13 years) I never thought that this was "ethical" or permissible. Could you please refer me to any guidelines that would clarify this? I am specifically thinking about things like the charts/drugs/devices… being carried back and forth.

Basically I am trying to collect data to present to our CEO whether or not this is feasible for the research department, and per FDA, allowed or not allowed???

Also, is there anywhere in the guidelines that provide direction for patient reimbursements…specifically the length of time that it takes the patient to receive their stipend after their visit. Is there a time line for this?

Again, any guidance that you can give me is much appreciated. Thank you for your time.

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