From: OC GCP Questions
To: [redacted]
Subject: Investigational product retention requirement for phase II, III and IV clinical trial
Date: Monday, June 19, 2017 11:31:00 AM
Attachments: [redacted]

Good morning --

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.

Further insight into FDA's expectations may be gained from FDA's Compliance Program for sponsor inspections, which may be accessed at
https://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/UCM133770.pdf

This document identifies what an FDA investigator is supposed to look at during an FDA inspection of a sponsor. Concerning test article accountability, it includes the following

1.Determine whether the sponsor maintains accounting records for use of the test article including:

a. Names and addresses of clinical investigators receiving test articles (report names and addresses). See 312.57, 511.1(b)(3), and 812.140(b)(2).

b. Shipment date(s), quantity, batch or code mark, or other identification number for test article shipped. See regulations above.

c. Final disposition of the test article. See 312.59, 511.1(b)(7)(ii), and 812.140(b)(2).

d. Final disposition of food-producing animals treated with the test article (511.1(b)(5).

A detailed audit should be performed when serious violations are suspected.

2.Determine whether the sponsor's records are sufficient to reconcile test article usage (compare the amount shipped to the investigators to the amount used and returned or disposed of).

3.Determine whether all unused or reusable supplies of the test article were returned to the sponsor when either the investigator(s) discontinued or completed participation in the clinical investigation, or the investigation was terminated.

4.If the test article was not returned to the sponsor, describe the method of disposition and determine if adequate records were maintained.

Please note that the regulations do allow for the sponsor to authorize alternative disposition of unused supplies of the investigational drug provided the alternative disposition does not expose humans to risks from the drug, see citation above for section 312.59.

Under ICH E6: Good Clinical Practice: Consolidated Guidance (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf), which is official guidance recognized by FDA, does address storage temperatures in the following sections:

5.13.2 The sponsor should determine, for the investigational product(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.

5.14.3 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)).

The manufacturer/sponsor of the investigational product generally determines (via controlled studies) the appropriate storage conditions for the investigational product. The study protocol usually states the conditions/controls under which the investigational product should be stored in an effort to preserve the quality, strength, purity and identity of the product.

You may wish to consult with the study sponsor if you have specific questions that are not addressed in the protocol.

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

Kind regards,

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Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Thursday, June 15, 2017 11:17 PM
To: OC GCP Questions
Subject: Investigational product retention requirement for phase II, III and IV clinical trial

Dear team,

Please provide USFDA requirements for retention of investigational product (quantity, duration and responsibility of retention) for phase II, III and IV Clinical trial.

Thank you

With regards

[redacted]