From: OC GCP Questions
To: [redacted]
Subject: Study Closure issue
Date: Friday, January 10, 2014 10:51:38 AM

Good morning –

FDA regulations state –

21 CFR 312.56 Review of ongoing investigations.
(a) The sponsor shall monitor the progress of all clinical investigations being conducted under its IND.

(b) A sponsor who discovers that an investigator is not complying with the signed agreement (Form FDA-1572), the general investigational plan, or the requirements of this part or other applicable parts shall promptly either secure compliance or discontinue shipments of the investigational new drug to the investigator and end the investigator's participation in the investigation. If the investigator's participation in the investigation is ended, the sponsor shall require that the investigator dispose of or return the investigational drug in accordance with the requirements of 312.59 and shall notify FDA.

If the CI site fails to comply with your requests as a sponsor for close-out documentation, you can report this non-compliance to the reviewing IRB or you can report the non-compliance to FDA's Office of Scientific Investigations (OSI) CDER-OSI@fda.hhs.gov. It is extremely important that the sponsor document in detail all efforts to receive the study files at study closure in case an FDA inspection should occur at either site (CI and sponsor)

That being said, FDA does not have a guidance document that provides details about how to close out a study. However, the following information is found in the "Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidance" (April 1996 ICH) http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf :

Trial master files should be established at the beginning of the trial, both at the investigator/institution's site and at the sponsor's office. A final close-out of a trial can only be done when the monitor has reviewed both investigator/institution and sponsor files and confirmed that all necessary documents are in the appropriate files.

Any or all of the documents addressed in this guidance may be subject to, and should be available for, audit by the sponsor's auditor and inspection by the regulatory authority(ies).

(See section 8.1, at http://www.fda.gov/downloads/Drugs/Guidances/ucm073122.pdf).

The activities a sponsor, CRO and investigator/site follow for a close out visit and any data query follow-up are usually addressed in Standard Operating Procedures (SOPs) of the sponsor, CRO, and site. The clinical investigator must ensure that any requirements to maintain IRB oversight per the regulations are met, and additionally, that any pertinent SOPs are followed.

Clinical investigators are responsible for the control of the investigational drug as per 21 CFR 312.61 and to maintain adequate records concerning the disposition of the drug under 21 CFR 312.62(a). The regulations state that if the investigation is terminated or discontinued, the investigator will return or provide the sponsor the disposition of the unused supplies of the drug as per 21 CFR 312.59. In addition to supplying the sponsor with routine progress reports during the investigational study (21 CFR 312.64(a)), the clinical investigator is required to provide the sponsor with adequate information in the form of a final report shortly after the completion of the investigator's participation in the study (21 CFR 312.64(c)).

As per 21 CFR 312.62(c), clinical investigators are required to retain records for a period of two 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 two years after the investigation is discontinued and FDA is notified. If investigational records are transferred off-site to a third party (e.g., CRO), the sponsor and FDA should be notified by the associated clinical investigator in the form of a final report.

When study enrollment and subject follow-up have been completed at a given site, the clinical investigator will often (usually for FDA-regulated studies) send the required final report to the IRB, thus closing out the study at the site.

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

Kind regards,

Doreen M. Kezer, MSN
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Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [Redacted]
Sent: Friday, January 10, 2014 8:43 AM
To: OC GCP Questions
Subject: Study Closure issue

To Whom It May Concern:

I have a site in New York City that I am assisting to conduct a study closure. The Sponsor has provided the site with their courier, United Parcel Service (UPS), account number for the site to use to send the remaining case report forms and other study documents to the Sponsor. However, the site is unwilling to call UPS or walk 1-2 blocks to obtain the applicable shipping supplies. In case we must resort to courier to the site a shipping invoice and envelope and the site is still unwilling to provide the documentation, what action(s) can the Sponsor take in this unfortunate pathetic situation?

Thank you.
[Redacted]