From: OC GCP Questions
To: [redacted]
Subject: Question Regarding Electronic Source Documents
Date: Monday, February 26, 2018 1:57:00 PM

Dear [redacted] –

Please see FDA's cleared response below.

Below is the cleared response from OMP and OSI.

Burning a CD at the end of the study is an acceptable method to archive study-related records. The integrity of the original data and the content and meaning of the record should be preserved. That said, during the clinical trial, when subject data is entered directly into an e-source system by study personnel at the site, FDA's expectation is that the sponsor should not have exclusive control of such data and the clinical investigator (or delegated study personnel) should be the only one authorized to make or approve any changes to the source data. The clinical investigator should review and electronically sign the eCRF for each subject that has concluded their participation in the study before the data are archived or submitted to FDA. The clinical investigator is responsible for ensuring that the records are maintained at the site, are retained throughout the record's retention period (see 21 CFR 56.115(b), 312.62, and 812.140) and are available to FDA during an inspection (21 CFR 56.115(b), 312.68, and 812.145). The source data maintained by the clinical investigator should include any important metadata and audit trail information to capture any changes made to the data.

If a CD is used to archive study data, the sponsor or a trusted third party (e.g., CRO, IT service provider) should send a certified copy of the final version of the source data to the clinical trial site. If the sponsor uses a trusted third party to manage the data for the trial, FDA prefers that the trusted third party create (e.g., burn) the CD and send a certified copy of the final version of the source data to the clinical trial site (directly or through the sponsor).

The certified copy of the data should include any important metadata in addition to audit trail information to capture any changes made to the source data. The relationship between records, source data, and all associated metadata and audit trails should be preserved in a secure and traceable manner. To make a certified copy, a process should be in place to certify that the electronic copy is an accurate representation of the original document. The copy should be generated through a validated process or verified (e.g., by a dated signature) as an exact copy having all of the same attributes and information as the original document, including any associated metadata (e.g., units of the data, date and time stamps, data originator, and other audit trail information associated with the data). In addition, a certified electronic copy may be retained in a different electronic file format to the original record but should retain the equivalent static or dynamic nature of the original record. You should have written procedures to ensure consistency in the certification process.

Alternatively, the study data can be archived on the server of a trusted third party provided the clinical investigator maintains control by having access to the data throughout the course of the clinical trial and until the end of the regulatory retention period. In cases where the study data resides with a trusted third party after the completion of a clinical trial, the study data should be "read only" for all users including sponsors, CROs, and clinical investigators. The study data should be available to FDA upon request and in a timely and reasonable manner (21 CFR 312.57, 312.58, 312.62, 312.68, 812.140, and 812.145).

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.

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-----Original Message-----
From: [redacted]
Sent: Wednesday, February 14, 2018 2:06 PM
To: OC GCP Questions <gcp.questions@fda.hhs.gov>
Subject: Re: Question Regarding Electronic Source Documents

Dear Ms Kezer:

Thank you.

Kind regards

[redacted]

Sent from my iPhone

> On Feb 14, 2018, at 1:52 PM, OC GCP Questions <gcp.questions@fda.hhs.gov> wrote:

>

> Hello --

>

> Just to be sure, I sent your second question to the Center for Drugs (CDER), Office of Medical Policy (OMP). There might be delay in responding.

>

> Kind regards,

>

> Doreen M. Kezer, MSN

> Senior Health Policy Analyst

> Office of Good Clinical Practice

> Office of the Commissioner, FDA

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> -----Original Message-----

> From: [redacted]

> Sent: Wednesday, February 14, 2018 12:58 PM

> To: OC GCP Questions <gcp.questions@fda.hhs.gov>

> Subject: Re: Question Regarding Electronic Source Documents

>

> Dear Ms. Kezer:

>

> Thank you for your response. I have a follow-up question.

>

> My concern relates to whether or not the investigator controls the

> data. Does the fact that the CD of source data is burned by a

> sponsor/vendor and not by the investigator (in the scenario described in

> my email below), meaning that the sponsor's vendor controls this process

> and the disposition of the original source, violate the requirement that

> the investigator retain control of the records?

>

> Thank you.

>

> Kind regards,

>

> [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

>

>> On 2/14/2018 12:41 PM, OC GCP Questions wrote:

>> Good afternoon --

>>

>> We have answered a similar question in the past. Please see below.

>>

>> Burning a CD at the end of the study is an acceptable method to archive study related documents. (FDA does not have any regulatory requirements as to the type of CD or DVD that might be used to preserve information (presumably to meet the regulatory requirements concerning clinical data/records). A company just needs to make certain that whatever media it uses does so in a manner that preserves the integrity of the original data/information. If a certified copy will serve as a substitute for the original, it would be desirable that they have a "standard operating procedure" (SOP) describing how such copies would be made, verified, and documented. For your information, both the general guidance on good clinical practice - ICH E6 (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf) - and the guidance on "Computerized Systems Used in Clinical Investigations" (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf) allow for the use of "certified copies," with the latter document defining a certified copy as:

>>

>> ..a copy of original information that has been verified, as indicated by dated signature, as an exact copy having all of the same attributes and information as the original.

>>

>> Please be aware that guidances represent the Agency's current thinking on good clinical practice and the conduct of clinical trials. They do not create or confer any rights for or on any person and do not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. However, in many places throughout these documents, specific regulations are cited and the requirements of the regulations are reiterated. The regulations are enforceable.

>>

>> FDA's regulations can be very general and while the regulations require that investigators to retain records of the clinical trial for a specified period of time, they do not specify how it is to be accomplished. When the regulations are not specific, sites are free to develop their own procedures and practices as long as the applicable requirements are met.

>>

>> From the limited information in your email, the scenario you describe appears to be acceptable.

>>

>> 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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>> Doreen M. Kezer, MSN

>> Senior Health Policy Analyst

>> Office of Good Clinical Practice

>> Office of the Commissioner, FDA

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>> -----Original Message-----

>> From: [redacted]

>> Sent: Wednesday, February 14, 2018 11:37 AM

>> To: OC GCP Questions <gcp.questions@fda.hhs.gov>

>> Subject: Question Regarding Electronic Source Documents

>>

>> Dear Sir or Madam:

>>

>> I am a Clinical QA Consultant working with a number of pharmaceutical

>> companies. I have been asked to advise on the use of electronic source

>> data (e-source).

>>

>> The "FDA Guidance for Industry: Electronic Source Data in Clinical

>> Investigations", states; "The clinical investigator(s) should retain

>> control of the records". 21 CFR 312.62 requires that investigators

>> prepare, maintain and retain records.

>>

>> There are vendors that offer e-source technology to sponsors. Sponsors

>> contract with these vendors to provide the system to the clinical trial

>> investigators. Subject data is entered directly into the e-source

>> system by site staff (appropriate audit trails are in place). Data is

>> extracted directly from the e-source, for the clinical trial database.

>>

>> At the end of the study, the system is locked, and investigators no

>> longer have access to it. They are provided with CDs containing copies

>> of the source data from their site. These copies are certified by the

>> vendor.

>>

>> Does the FDA consider e-source systems provided by vendors contracted by

>> sponsors, where the above scenario is followed, to be in compliance with

>> 21 CFR 312.62 and the above Guidance for Industry?

>>

>> Thank you for your attention to this question.

>>

>> Kind regards,

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