From: OC GCP Questions
To: [redacted]
Subject: RE: Trial Master Files - what falls under 21 CFR 11
Date: Wednesday, September 28, 2016 4:06:05 PM

Hi [redacted]

I am not aware of any specific requirements for the scenario you have identified below. However it is recommended that sites develop a standard operating procedure (SOP) for consistency in reporting/recording study data for all staff to follow. FDA regulations do not specifically state that all copies of study documents need to be signed as certified copies. Again a (SOP) is recommended and documentation of training for study staff on newly developed SOPs is also recommended.

That said, I can offer you the following information below, which relates to study records and certified copies. Although it appears you are not referencing replacing the original document. It might be appropriate for someone to verify that the information contained in the scan matches the form at the site (if that for is not being audited/reviewed onsite).

Many institutions and sites are going to a fully electronic record system. If you do make certified copies of the medical records of study subjects, monitors and auditors will want to at least spot check the completeness of these records at the source - the electronic database. How they view them is at your discretion however. Either looking over the shoulder of a study staff member or having limited access to the medical records is common.
The reason at least a spot check is necessary is that the records can be selectively copied. So even though they are certified copies they may not be complete records. The monitor/auditor is checking to ensure that study inclusion/exclusion are met and that there are no concomitant issues that would preclude the individual's participation in the study or confound the results.

We are frequently asked if sites may archive records by converting paper documents into an electronic format-- in essence, creating certified copies of source documents. Neither FDA's regulations nor the ICH E-6 Good Clinical Practice: Consolidated Guidance
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf
defines certified copy", however, the term is mentioned in the E6 definitions for "source data" and "source document":

"1.51 Source Data: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies)."

"1.52 Source Documents: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medicotechnical departments involved in the clinical trial)."

Although the term "certified copy" is not defined in the ICH E6 guidance, we attempted to define this term in the CCT Guidance referenced below:

"Certified Copy means 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."

The use of certified copies as described above generally applies to situations where original records are copied to a different media for archiving purposes and the originals are destroyed. However, if it is decided to have a certified copy substitute for the original, it would be desirable to have a "standard operating procedure" (SOP) describing how such copies would be made, verified, and documented. The person who certifies the copy as an accurate and complete representation of the original, having all of the same attributes and information should be the same person who actually made the copy from the original. Certification should be accomplished by having the person who makes the copy, sign or initial and date the copy to indicate it meets the requirements of a certified copy as described above. This should be described in the SOP and can be accomplished by initialing and dating each copy or by initialing and dating a document certifying copies in bulk. Whichever method is used the SOP should describe the procedure. (There are many ways to accomplish this, and the procedures described above are only suggested examples.)

Burning a CD at the end of the study, converting e-mails into a PDF format or adopting a procedure to make certified copies are all acceptable methods to achieve 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.

The guidances listed below might be helpful to you.
Part 11 -Electronic Records -
www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126953.pdf
Computerized Systems Used in Clinical Investigations -
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf
Electronic Source Data in Clinical Investigations -
www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM328691.pdf

I hope this is useful.

Sincerely,
Bridget A. Foltz, MS, MT(ASCP)
Policy Analyst, Office of Good Clinical Practice
Office of the Commissioner, Food and 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: Monday, September 19, 2016 9:59 AM
To: OC GCP Questions
Subject: RE: Trial Master Files - what falls under 21 CFR 11

Hello Bridget,

What are the requirements for sites scanning in documents and sending them to us electronically? For example, we need to verify an ICF, so the site scans it in and sends it to us. Thank you!

Sincerely,

[redacted]

From: OC GCP Questions [mailto:gcp.questions@fda.hhs.gov]
Sent: Thursday, September 15, 2016 2:53 PM
To: [redacted]
Subject: RE: Trial Master Files - what falls under 21 CFR 11

Dear Ms. Perkins:

The following information was provided in response to your question below:

Audit trails apply to the record. The audit trail is a process that captures details such as additions, deletions, or alterations of information in an electronic record without obscuring the original record. Audit trails are important for the reconstruction of the course of such details relating to the electronic record.

If your TMF file is simply composed of scanned copies of paper documents and/or manual creation of electronic documents (using word processing software) and you intend to use the electronic copy in lieu of the paper source copy (i.e., you intend to destroy the paper source copy), we recommend the following:

- You should have a process in place to certify that (1) the scanned electronic copy is an accurate representation of the original paper document and (2) electronic copies of electronic originals have the same information, including data that describe the context, content, and structure of the data as the original. The electronic copy should be certified with a dated signature and you should have written procedures to ensure consistency in the certification process.

- The scanned electronic copy should retain the audit trail of the data that are recorded on the paper copy (any additions, deletions, or alterations of source information that had been made). For electronic copies that vary in terms of their ability to be modified, it would be important to have audit trails or other physical, logical, or procedural security measures in place to ensure the trustworthiness and reliability of the electronic copy.

For more information, please see Guidance for Industry: Electronic Source Data in Clinical Investigations. Available at:
http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm328691.pdf

I hope that this information is helpful.

Sincerely,
Bridget A. Foltz, MS, MT(ASCP)
Policy Analyst, Office of Good Clinical Practice
Office of the Commissioner, Food and Drug Administration

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From: [redacted]
Sent: Friday, September 09, 2016 9:59 AM
To: OC GCP Questions
Subject: Trial Master Files - what falls under 21 CFR 11

To Whom It May Concern:

If we are wanting to keep our Trial Master file in an electronic folder that is secure with limited access and backed-up, but not in a software system (manual creation of documents and scanned documents), how would we comply with the audit trail requirement, or does this only apply to software?

Sincerely,

[redacted]

This email and any attachments may contain confidential information to be used only by the intended recipient. Email communications are not considered secure. If you are NOT the intended recipient, please notify the original sender with a copy to hipaa.security (at) jaeb.org and destroy the message.