From: OC GCP Questions
To: [redacted]
Subject: Does eTMF need to comply with 21CFR Part 11?
Date: Monday, September 15, 2014 11:33:23 AM

Good morning:

Our IT specialists in CDER (Center for Drugs) have said the following regarding Part 11 compliance--

There are no restrictions on which documents are maintained electronically or signed with e-signatures, including eTMFs. If the record or signature is required by FDA regulations, and not subject to the enforcement discretion exceptions in the Scope and Application guidance, **Part 11 controls are necessary**.

Please see:
Part 11, Electronic Records; Electronic Signatures — Scope and Application
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072322.pdf

For general information on the use of computer systems in clinical trials in FDA regulated clinical trials, please reference the following guidance:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf

Or draft e-Source Guidance:
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM239052.pdf

Additionally, 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
http://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 medico-technical 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 above:

"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.

If you are not the sponsor and are a clinical site, you should check with the sponsors of your studies to see how they would like you to store the study documents.

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

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Friday, September 12, 2014 6:20 PM
To: OC GCP Questions
Subject: Does eTMF need to comply with 21CFR Part 11?

Good afternoon,
I am currently working with a device sponsor to improve their "trial master file" for a device study. While US FDA regulations do not currently define a TMF, the industry standard definition is

A collection of documentation that allows the conduct of the clinical trial, the integrity of the trial data and the compliance of the trial with GCP to be evaluated.

Therefore the TMF would include the Sponsor master file and copies of the Site essential documents that should be on file per ICH E6. The TMF includes
Documents across a variety of different departments and systems including Data Management, Clinical Trial Supplies, Legal, Regulatory etc.

As the system used to store and maintain these records is a computerized system Internal & External Security Safeguards would be implemented.

The question is whether FDA would expect an eTMF system used in conjunction with SOPs to comply with all aspects of 21 CFR Part 11? Please provide details on any and all applicable sections of the Part 11 regulation that an eTMF must comply with.
Thank you