From: Beers Block, Patricia on behalf of OC GCP Questions
Sent: Thursday, October 06, 2005 8:03 AM
To: [redacted]
Subject: RE: GCP Source Documentation Questions

Dear [redacted],

You raise interesting questions/issues about which we are often asked for advise. Perhaps it would be helpful to first address the issue of what constitutes source documents/documentation and then get into your specific questions thereafter.

As you may already know, the regulations found in 21 CFR 312 (Investigational New Drug regulations) and 21 CFR 812 (Investigational Device Exemption regulations) do not explicitly define "original documents", "source" documents/records"; nor do they require that these records be signed and dated (with the sole exceptions of the Form FDA 1572 and the informed consent used for a subject); nor do they stipulate where "original" records are to be retained.

Instead terms such as "source data", "source documentation", etc. appear in FDA's Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance (http://www.fda.gov/cder/guidance/959fnl.pdf). Quoting from this guidance:

"Documentation" means "all records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken." source documents

"Source Data" include "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)."

"Source Documents" include "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).

The term "certified copy" is described in the FDA Guidance for Industry Computerized Systems Used in Clinical Trials (see http://www.fda.gov/OHRMS/DOCKETS/98fr/2004d-0440-gdl0001.pdf for the draft version of this guidance). As you can see, 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.

(Please note, unlike regulations (which are legally binding requirements), guidances, like the E6 Good Clinical Practice Consolidated guidance, represent FDA's current thinking on a specific topic. The guidance does not create or confer any rights for or on any person and does not operation to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations.)

Concerning the issue of original/source vs. a record copy, the agency long ago adopted the policy that copies of original records can be substituted for original/source documents provided:

1) all records must be readily available for review and copying by FDA investigators at any reasonable time.
2) a reproduction must be a true and accurate copy of the original record. Thus, where the reproduction process results in a copy that does NOT reveal changes or additions to the original record, the original record must be retained. Also the reproduced copy and any image shown (on, for example, a view screen like a microfiche reader) must note, in a suitable manner, that an alteration has been made and that the original record is available.

So, as you can see, copies of original/source records can be utilized in lieu of the retention of original records when certain conditions are met.

Now, getting to your question about using an electronic system, we would expect any computerized system used for clinical trial (data recording and preservation) to be compliant with 21 CFR Part 11. Computer system requirements are described in the regulation; suggestions about how one might comply with this and other regulations governing good clinical practice can be found in the FDA's (final and newly released redraft) Guidance for Industry Computerized Systems Used in Clinical Trials (see link above).

To be Part 11 compliant, computerized systems must have controls in place that allow direct tracking to the person entering/approving data captured in the computerized system/software. Controls regarded as reasonable include ensuring that each system users enter and record information using his/her unique user account that is password controlled. All entries must be traceable and attributable to a specific person for the computerized system to be found acceptable for use. These systems must also track/document changes to data that fall into high-risk categories. FDA is using "enforcement discretion" with regard to certain Part 11 regulatory requirements. Although the draft guidance for Computerized Systems Used in Clinical Trials explains this, you might want to look at the root guidance document that further explains FDA's position on Part 11. This information is found in FDA's Part 11 Scope and Application guidance that was published in August 2003 (see http://www.fda.gov/ohrms/dockets/98fr/5667fnl.pdf)

I hope this information is helpful to you. If you would like to discuss this more, please feel free to contact me using my direct phone number (301-827-6473).

Sincerely,

Patricia M. Beers Block
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Good Clinical Practice Program (HF-34)
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-----Original Message-----
From: [redacted]
Sent: Wednesday, September 14, 2005 2:00 PM
To: gcpquestions@oc.fda.gov
Subject: GCP Source Documentation Questions

Good morning,

My name is [redacted]. I was hoping for guidance regarding authentication of source documentation. We [redacted] with a medical center electronic system that does not meet 21 CFR Part 11 nor is it a legacy system.

1. Can you confirm that source documentation produced by the investigator or reviewed by the investigator, e.g., dictation, Labs, EKGs, should be signed and dated by the investigator (delegated with that authority).

2. If we can authenticate the electronic source documentation (e.g., investigator re-enters password following review of document), is that sufficient to meet research requirements as long as we have an audit trail?

3. How does source documentation authentication work with in-patient studies when a large number of individuals are assessing the study subject, some of which may be standard of care? To clarify, all the individuals involved with the subject's care would not be considered key personnel for the study and some items, e.g., vitals, are directly entered into the electronic record, some of which may be used for study purposes.

4. On in-patient studies, would we meet the regulations by having the investigator review and sign-off on the in-patient source documentation that would be used for the study, e.g., [redacted], and maintain that copy in our research records? This question may not be applicable depending upon the answer to #3.

Feel free to contact me at [redacted] if you have any questions.

Thanks for your response.

[redacted]