From: OC GCP Questions
To: [redacted]
Subject: Audit trail
Date: Monday, April 09, 2018 9:09:00 AM
Attachments: [redacted]

Good morning –

See below.

FDA regulations do not specifically speak to audit trails. However, both regulations regarding the conduct of clinical trials (21 CFR Part 312 for drugs and biologics and Part 812 for devices) require that adequate and accurate records be maintained by clinical investigators (21 CFR 312.62 and 812.140(a)). For records to be accurate, any changes to the original data that was entered need to be visible, attributed to the person making the change, and explained. Therefore, some type of audit trail needs to be maintained for clinical study documents. This is discussed in the guidance document on the use of computerized systems in clinical investigations (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf - see IV.D.2. in particular).

This means that hard copies of records can be printed when an alteration is found necessary, and changes made - with initials, date, and reason for the change - and maintained with the study file in lieu of an electronic audit trail for that document.

21 CFR 11 refers to electronic records and signatures, but does not address specific elements to be included. Section 11.10(e) indicates that "Use of secure, computer-generated, time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying." www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11&showFR=1.

Below is information found in FDA's guidances that refer to electronic data capture systems and audit trails:

Guidance for Industry Electronic Source Data in Clinical Investigations https://www.fda.gov/downloads/drugs/guidances/ucm328691.pdf gives the following recommendation for data edits:

Each data elements should have data element identifiers that reflect the following:

-Originators of the data element

-Date and time the data element was entered into the eCRF (the audit trail begins at the time the data are transmitted to the eCRF)

-Clinical investigation subjects to which the data element belongs

Only a clinical investigator(s) or delegated clinical study staff should perform modifications or corrections to eCRF data. Modified and/or corrected data elements must have data element identifiers, such as date, time, originator and must not obscure previous entries (see 21 CFR 11.10(e)). A field should be provided allowing originators to describe the reason for the change (e.g., transcription error). Automatic transmissions should have traceability and controls via the audit trail to reflect the reason for the change.

If I have not adequately answered your questions, you may contact FDA's Office of Medical Policy at CDEROMP@fda.hhs.gov . They are the experts on part 11 compliance.

Kind regards,

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

From: [redacted]
Sent: Monday, April 09, 2018 3:52 AM
To: OC GCP Questions <gcpquestions@fda.hhs.gov>
Subject: Audit trail

Dear Sir/Madam,

We are a clinical research organization, currently trying to develop a software LMS - Learning Management System.

Request your kind guidance on the following:

1. Audit trail requirements such as capturing 'who, what, when and why' will be applicable to such a software?
2. Secondly, can we use paper forms to document the changes made in the software. (Reason for change along with the data changed)? Will this be an acceptable practice to maintain audit trail ? In such circumstances will the software then be deemed part 11 compliant? Yes

The guidance on part 11, electronic records; electronic signatures - scope and application dated August 2003, mentions in section 5 that paper and electronic records can co-exist (hybrid situation). Will point 2 mentioned above fall into the hybrid situation? Yes

Requesting you to kindly guide.

Your guidance is highly appreciated.

Kind regards,

[redacted]