From: OC GCP Questions
To: [redacted]
Subject: RE: Inspections of Contract Research Organizations
Date: Thursday, November 29, 2018 10:05:00 AM
Attachments: [redacted]

Dear [redacted] -

Thank you for your question. The regulations do not address your specific question. When the regulations are silent, sponsors, CROs, investigators, institutions and IRBs are free to develop their own procedures and practices as long as applicable regulatory requirements are met.

FDA has various guidance documents that address monitoring and electronic systems (noted in this response). In particular, FDA's guidance titled, "*Guidance for Industry – Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring*" that can be found at https://www.fda.gov/downloads/Drugs/.../Guidances/UCM269919.pdf advises sponsors to consider the objective, design, complexity, size and endpoints of a trial in determining the extent and nature of monitoring for a given trial. It also says that sponsors should consider risk-based approaches to monitoring using the format of study information (i.e., electronic, paper, or combination of electronic and paper), tools, and other resources available to them.

FDA's guidance titled, "*Use of Electronic Health Record Data in Clinical Investigations – Guidance for Industry*" found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM501068.pdf provides recommendations on ensuring the quality and integrity of Electronic Health Record (EHR) data collected and used as electronic source data in clinical investigations. The guidance says that sponsors and clinical investigators should ensure that policies and processes for the use of EHRs at the site are in place and that there are appropriate security measures employed to protect the confidentiality and integrity of the study data. "***How***" the sponsor or CRO goes about ensuring these important practices is not dictated by FDA.

As noted in the *ICH GCP E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry*, (which is recognized as official FDA guidance – see https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm464506.pdf), the sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials. The flexibility in the extent and nature of monitoring as described in this guidance is intended to permit varied approaches that improve the effectiveness and efficiency of monitoring. The sponsor should document the rationale for the chosen monitoring strategy (e.g., in the monitoring plan).

Here are some other FDA guidance/documents that may be of interest to you:

- FDA Draft guidance titled, "*Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 – Questions and Answers*" that can be found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM563785.pdf.
- FDA guidance titled, "*Guidance for Industry – Electronic Source Data in Clinical Investigations*" that can be found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM328691.pdf.
- FDA guidance titled, "*Guidance for Industry – Computerized Systems Used in Clinical Investigations*" that can be found at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070266.pdf.
- FDA has Compliance Program Guidance Manuals (CPGMs) for Bioresearch Monitoring inspections available at https://www.fda.gov/ICECI/ComplianceManuals/CompliancePrograMManual/ucm255614.htm. These CPGMs provide uniform guidance and specific instructions to FDA field personnel on the conduct of inspections of the various stakeholders (e.g., IRBs, sponsors, clinical investigators). The CPGM for inspections of sponsors, CROs and monitors can be found at https://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/ucm133770.pdf.

I hope this information is useful. If you need further information and/or have additional questions, please feel free to contact us at the official GCP mailbox, gcp.questions@fda.hhs.gov. You may also find it useful to access the set of redacted GCP e-mails found at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm since we find that many questions and concerns are repeated over time.

Best Regards,

Janet
Janet Donnelly, RAC
Policy Analyst

Office of the Commissioner
Office of Good Clinical Practice

U.S. Food and Drug Administration

From: [redacted]
Sent: Tuesday, November 27, 2018 1:29 PM
To: OC GCP Questions <gcpquestions@fda.hhs.gov>
Subject: Re: Inspections of Contract Research Organizations

Hello,

Does the FDA have expectation that sponsors or CROs are having monitors (CRAs) monitor and review audit trails of EMR systems at clinical trial sites? Not just confirming that they use and have audit trails turned on but that CRAs are routinely or periodically spot checking the audit trails.

Would this include if the site are making certified copies that print audit trails? etc?

Thank you,
[redacted]