Monitoring vs. Auditing at Investigator Sites
ICH GCP (R2) Impact on Investigator Sites

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Agenda

- Monitoring vs. Auditing
- ICH GCP impact on Investigator Sites

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Auditing and Monitoring Defined

- Monitoring is defined as “the act of overseeing the progress of a clinical trial, and ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures(SOPs), GCP, and the applicable regulatory requirement(s)” [ICH 1.38]; and
- Audit is defined as “a systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor’s standard operating procedures (SOPs), GCP and the applicable regulatory requirement(s)” [ICH 1.6].

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Monitoring purpose in clinical research

- Monitoring is a quality control function where study conduct is routinely assessed on an ongoing basis at every step of the study.

- Monitoring of clinical research studies is mandatory per federal regulations (21 CFR812.3 (j), 812.25, 812.40 and 312.50). During the course of a U.S. regulatory audit, FDA has access to monitoring reports and their associated action items.

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Monitoring purpose in clinical research

- During a monitoring visit, all aspects of the study at a specific site will be checked in accordance with a monitoring plan, including:
  - **informed consent documents**
  - **eligibility criteria**
  - **protocol compliance**
  - **source document verification for data accuracy**
  - **query resolution (clarification or correction of inaccurate data)**
  - **occurrence and reporting of adverse events**
  - **investigational product accountability**
  - **maintenance of essential documents**
  - **oversight by the Clinical Investigator and IRB**
- Monitors must ascertain that the Clinical Investigator is adequately informed of his or her responsibilities to recruit eligible subjects and to collect high quality data.

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Auditing purpose in clinical research

- Auditing, a quality assurance function, is an independent, top-down, systematic evaluation of trial processes and quality control.
- Auditors can assess a wider study sample than monitors and can help evaluate trends at various levels by auditing a single or multiple sites, trial vendors and/or the sponsor.
- Auditors may look at study design, site/data management, and statistical analysis.
- In general, auditors evaluate compliance to recognized standards, i.e., FDA's Code of Federal Regulations, International Conference on Harmonization, International Standards Organization and Standard Operating Procedures.

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Auditing purpose in clinical research (cont'd)

- Audits are not done continuously the way that monitoring is performed during a study, but instead are compliance snapshots in time. In addition, audits are not required by the U.S. regulations, but are voluntarily performed.
- Other countries may require audits, like Japan and those conducting trials under ISO 14155 [section 6.11].
- Finally, during the course of a U.S. regulatory audit, FDA would not have access to an auditor's findings.

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Why do we audit?

- An audit is a tool to assess both the site and the sponsor process for conducting a clinical study.
- Monitoring is individual to a protocol and a site's performance of the protocol
- Auditing can assist in determining monitoring effectiveness
- Determine study team effectiveness
- Provide an independent assessment
- Manage non compliant sites
- Assess inspection readiness

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Monitoring + Auditing

While monitoring and auditing are distinct functions, together, they can complement each other to create an additive impact on the overall quality and integrity of a clinical trial.

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AFT Monitors and Auditors

- Monitors from Contract Research Organizations (CROs)/Third Party Organizations (TPOs) with oversight by AFT staff
- AFT staff or Pharmaceutical Partner representative (PP) may co-monitor
- Independent auditors from TPOs
- AFT staff auditor
- PP may co-audit

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Changes to ICH GCP (R2) that influence the investigator

Investigator

- 4.2.5 The investigator is **responsible for supervising any individual or party** to whom the investigator delegates study tasks conducted at the trial site.
- *4.2.6* If the investigator/institution retains the services of any party to perform study tasks they should ensure this **party is qualified** to perform those study tasks and should implement procedures to ensure the integrity of the study tasks performed and any data generated.
- 4.9.0 The investigator should maintain adequate and **accurate source documents** and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry and should be explained if necessary (e.g., *via* an audit trail).

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Q & A

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Thank you for your participation!

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