BC 10.180 - Audit/Monitor Visit: Preparation, Conduct and Follow-up

I. POLICY:

All clinical research conducted at Baystate Health are subject to quality assurance and quality control review, including those trials sponsored by pharmaceutical and/or device companies, NIH, other sponsors, and those that are investigator-initiated.

II. PURPOSE:

The primary purpose of this policy is to inform research personnel of their roles and responsibilities in ensuring that audit and monitoring visits at Baystate Health facilities are performed in a consistent, ethical and compliant manner, and that such visits are essential to protecting human subjects, verifying the validity and accuracy of data collection, identifying non-compliance, and taking corrective action when necessary. Implementing quality assurance and quality control of clinical trials promotes continuous improvement opportunities by providing an increased awareness of BH policies to researchers and staff as well as education in best practices to ensure BH is conducting consistent high-quality research.

III. SCOPE:

This policy applies to all employees, medical staff, associate professional staff, teachers, students, residents, fellows, volunteers, contractors, consultants, agents, and others associated with BH who are involved in clinical research at any BH affiliated entities including but not limited to: Baystate Medical Center ("BMC"), Baystate Wing Hospital ("BWH"), Baystate Franklin Medical Center ("BFMC"), Baystate Noble Hospital (BNH), and the University of Massachusetts Chan Medical School – Baystate.

IV. DEFINITIONS:

Audit: 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).

Contract research organization (**CRO**) is a company that provides research services on a contractual basis to the pharmaceutical, biotechnology or medical device industries. Relevant to this policy, sponsors commonly outsource clinical trials development, management, and monitoring services to a CRO that serves as the sponsor's liaison to Baystate Health.

Monitoring: 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).

Quality Assurance (QA): planned and systematic actions to ensure that the trial is performed, and the data are generated, documented (recorded), and reported in compliance with GCP and all applicable regulatory requirement(s).

Quality Control (QC): operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

V. PROCEDURE:

A. Investigator/Institution Responsibilities

The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority(ies), and which was approved by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.

The investigator/institution 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).

The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports

Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.

The investigator/institution should maintain trial documents as required by applicable Baystate policies and the applicable regulatory requirement(s). The investigator/institution should take measures to prevent accidental or premature destruction of these documents.

The investigator/institution should permit monitoring and auditing by the sponsor in accordance with contractual obligations, and inspection by the appropriate regulatory authority(ies).

Prior to the audit/monitoring visit, the investigator/institution are responsible for the following:

1. Gathering all inpatient and ambulatory records for the selected subjects related to the conduct of the trial
2. Gathering completed case report forms and research files for the selected subjects
3. Obtaining necessary approvals for the monitor/auditor to be cleared for an on-site visit (where necessary), and gain access to needed electronic systems (e.g. electronic health records, e-binders, clinical trials management system, etc.). These approvals will be obtained in accordance with BH policies and procedures.
4. Contacting the affiliate pharmacy for all records regarding the dispensing of investigational product, if applicable.
    a. Once an Investigational Drug Services (IDS) management system is operational, the monitor/auditor may be given access to review pharmacy records via that system, in accordance with Baystate's procedures for non-employee access.
5. Compiling original eligibility checklists, consents, and off-study forms for the selected subjects
6. Ensuring all source documentation is available to the monitor/auditor
7. Creating documentation to address discrepancies that require clarification for the research record
8. Ensuring the regulatory binder is complete and up to date
9. Uploading the following study-related and subject-related documentation in OnCore (as applicable):

a. All IRB records, such as all protocol and consent versions and their approval letters as well as records of all revisions
b. All subject records that are related to the study, such as all signed consents,

Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should provide direct access to all requested trial-related records.

The investigator/institution will notify the Human Research Protection Program (HRPP) and Sponsored Programs Administration (SPA) of the date(s) of the visit as soon as a visit is scheduled. In the case of an audit, Research Compliance must also be notified. The investigator/institution will schedule monitoring visits to the investigational drug service (IDS) pharmacy (if applicable) at least 2 weeks in advance, with an exception for first time monitoring visits which may occur within 2 weeks of enrolling the first participant.

The investigator/institution must provide adequate space for the monitor with access to the internet and a copy machine (if needed), and ensure the PI is available to meet the monitor, and the regulatory binder, informed consents, CRFs and medical records are available as appropriate. Study teams should consult with the Human Research Protection Program (HRPP) and/or Research Compliance regarding questions around monitor and auditor access.

The investigator/institution/IDS will provide the monitor with all necessary documentation and logs to evaluate proper handling of drug supply, storage, and temperature control since the last monitoring visit, and inform the monitor to be prepared to authorize return/destruction of used/expired investigational product.

B. Sponsor's Responsibilities

The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written standard operating procedures (SOP) to ensure that trials are conducted, and data are generated, documented (recorded), and reported in compliance with the protocol, Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

The sponsor is responsible for securing agreement from all involved parties to ensure direct access to all trial-related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities.

Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.

Agreements, made by the sponsor with the investigator/institution and any other parties involved with the clinical trial, should be in writing, as part of the protocol or in a separate agreement.

C. Contract Research Organization (CRO) responsibilities

A sponsor may transfer any or all of the sponsor's trial-related duties and functions to a CRO, but the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor. The CRO should implement quality assurance and quality control.

The sponsor should ensure oversight of any trial-related duties and functions carried out on its behalf, including trial-related duties and functions that are subcontracted to another party by the sponsor's contracted CRO(s).

Any trial-related duties and functions not specifically transferred to and assumed by a CRO are retained by the sponsor.

All references to a sponsor in this document also apply to a CRO to the extent that a CRO has assumed the trial-related duties and functions of a sponsor.

D. Auditing

Directed ("for cause") or scheduled ("not for cause") audits are conducted to assess investigator compliance with federal, state, and local law, and Institution policies, and to identify areas for improvement, and suggest recommendations based on existing policies and procedures. Directed audits of IRB-approved research studies are in response to identified concerns. Scheduled ("not for cause") audits are conducted using a systematic method to review IRB-approved research on a regular basis. (Refer to HRPP SOPs for further details.)

The purpose of a sponsor's audit, which is independent of and separate from routine monitoring or quality control functions, should be to evaluate trial conduct and compliance with the protocol, SOPs, GCP, and the applicable regulatory requirements.

- The sponsor should ensure that the auditing of clinical trials/systems is conducted in accordance with the sponsor's written procedures on what to audit, how to audit, the frequency of audits, and the form and content of audit reports.
- The sponsor's audit plan and procedures for a trial audit should be guided by the importance of the trial to submissions to regulatory authorities, the number of subjects in the trial, the type and complexity of the trial, the level of risks to the trial subjects, and any identified problem(s).
- For any requests for electronic access to Baystate systems, Baystate non-employee access policies and procedures must be followed.
- The observations and findings of the auditor(s) should be documented.
- To preserve the independence and value of the audit function, the regulatory authority(ies) should not routinely request the audit reports. Regulatory authority(ies) may seek access to an audit report on a case-by-case basis when evidence of serious GCP non-compliance exists, or during legal proceedings.
- When required by applicable law or regulation, the sponsor should provide an audit certificate.

E. Monitoring

Monitoring ensures participant safety and accurate reporting of results relies on appropriate planning, oversight, and continuous monitoring measures.
The purposes of internal monitoring are to verify that:

- The rights and safety of patients (i.e., human subjects) are protected
- The reported trial data are accurate, complete, and verifiable from source documents
- The conduct of trial follows the protocol, GCP and applicable regulatory requirements.

On-site monitoring is performed at the sites at which the clinical trial is being conducted. On-site monitoring involves having someone physically present at the trial site to oversee activities. Remote or centralized monitoring means that a sponsor or third party monitors all sites remotely.

Remote monitoring, in which the clinical or research monitor is not physically present at the study site, allows sponsors and CROs to conduct monitoring activities that were previously conducted on-site remotely.

Centralized monitoring involves the review of patient data from multiple research sites or across patient populations at a remote, central location. Centralized monitoring is performed by site monitors, data managers, and biostatisticians. Examples of centralized monitoring include the panel review of clinical data (e.g., structured interviews) by a third party for quality assurance purposes or regulatory submission, the review of patient laboratory results, and the auditing of clinical record documentation at a central office.

Review that may include statistical analyses of accumulating data from centralized monitoring can be used to:

- Identify missing data, inconsistent data, data outliers, unexpected lack of variability and protocol deviations
- Examine data trends such as the range, consistency, and variability of data within and across sites
- Evaluate for systematic or significant errors in data collection and reporting at a site or across sites, or potential data manipulation or data integrity problems
- Analyze site characteristics and performance metrics
- Select sites and/or processes for targeted on-site monitoring.

Reports of on-site, remote, centralized and/or internal monitoring should be used for education and feedback to the research staff and HRPP (including appropriate management and staff responsible for trial and site oversight) in a timely manner for review and follow up with appropriate corrective and preventive actions. should be provided to the sponsor (including appropriate management and staff responsible for trial and site oversight) in a timely manner for review and follow up with appropriate corrective and preventive actions. Results of monitoring activities should be documented in sufficient detail to allow verification of compliance with the monitoring plan and any necessary mitigation of discovered noncompliance.

F. Audit Response, Review and Submission

Upon receipt, the investigator/institution is responsible for providing a copy of the audit report to HRPP and Research Compliance.

The investigator/institution is responsible for developing plans to mitigate the audit findings, and providing the mitigation plan to the auditor, HRPP and Research Compliance in writing within 30 days of receipt of the audit report.

In cases of an HRPP audit, the investigator must respond to any audit findings, sign, and return audit report to HRPP within 30 days.

VI. POLICY REFERENCES:

Human Research Protection Program SOPs, effective October 2022
June 2023 E6 (R3) Good Clinical Practice: Integrated Addendum to ICH E6 (RI) Guidance for Industry
21 CFR Part II Electronic Records; Electronic Signatures
21 CFR 312.50 General responsibilities of sponsors
21 CFR 312.56 Review of ongoing investigations
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.62 Investigator recordkeeping and record retention
21 CFR 3 12.64 Investigator reports
21 CFR 312.68 Inspection of investigator's records and reports
21 CFR 812.40 General responsibilities of sponsors
December 8, 2008, Program 7348,81 1 Bioresearch Monitoring Clinical Investigators and Sponsor-Investigators Guidance for FDA Staff
October 2009 (Procedural) Guidance for Industry Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

APPROVALS:

		Date:
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