Standard Operating Procedure – Guidelines for Monitoring MD Anderson IND Sponsored Protocols

SCOPE

These guidelines apply to all protocols of which The University of Texas MD Anderson (MDA) Cancer Center is the FDA sponsor of record.

PURPOSE

To define the roles and responsibilities of the MD Anderson IND Monitoring Services

REFERENCES

FDA Guidance for Industry-Oversight for Clinical Investigations-A Risk Based Approach to Monitoring

ICH Guideline for Good Clinical Practice E6 (R1) section 5.18 Monitoring

PROCEDURE

1. Introduction

The Food and Drug Administration (FDA) regulations assign multiple responsibilities for clinical studies to the sponsor, with the overall function being to ensure studies are properly designed and conducted. Monitoring oversight by the IND sponsor begins at the time of protocol initiation and continues through termination. This ongoing review allows for prompt identification of problems and solutions during the course of the study to protect the rights and safety of human subjects, and the integrity of the clinical research. Monitoring assists with ensuring that the data used to analyze study results is an accurate reflection of the primary source documentation. It assesses compliance with the informed consent process, eligibility determination, evaluation schedule, treatment administration and compliance/accountability, toxicity and response assessment/reporting, and adherence to institutional guidelines, good clinical practice, and federal regulations.

Unless otherwise specified, Monitoring Services, with the Investigational New Drug (IND) Office, will monitor all protocols under an MD Anderson Cancer Center sponsored IND. Guidelines for the monitoring roles and responsibilities will be based on the FDA’s Guidance for Industry-Oversight for Clinical Investigators-A Risk Based Approach to Monitoring, which describes strategies for monitoring activities that reflect a modern, risk-based approach that focuses on critical study parameters and relies on a combination of monitoring activities to oversee a study effectively.

The monitoring format is designed to ensure the following:

- Adequate protection of the rights and safety of human subjects
The integrity of the safety data collected and submitted to the FDA
The investigational plan/protocol is being followed as written
Protocol changes are submitted and approved by the IRB and FDA prior to implementation
Comprehensive research records are being maintained
Accurate and timely reports are being submitted to the IND Office, IRB and FDA
The investigator is carrying out the agreed-upon activities, and has delegated them appropriately

2. **The Initiation Meeting**

Once the protocol has received IRB and FDA approval, and all contracts with industry sponsors have been finalized, the IND Office will assign a Clinical Research Quality Specialist (CRQS) to assume the monitoring responsibilities for the trial. A site initiation visit (SIV) will be scheduled and conducted by the CRQS and representatives from the IND Medical Affairs and Safety group and Project Management teams. The initiation meeting will occur prior to the activation of the protocol, and participants must include the Principal Investigator (PI) and all research team members who will be significantly involved with the study (e.g. Research Nurse, Data Coordinator, Investigational Pharmacy, etc.).

3. **Monitoring Process and Timeline**

Monitoring visits will be completed according to the timelines identified in the protocol-specific Monitoring Plan, and may be modified as needed. Visits will routinely occur at 8-12 weeks intervals, and may be extended to every 6 months during periods of slow/halted enrollment (Monitoring Update status), or the trial meets the criteria outlined in the Limited Monitoring SOP. The investigational product and/or design, complexity of the study, and the rate of accrual will be considered when determining the frequency of monitoring visits.

The CRQS will send email notification of planned visits to the PI approximately 2 weeks prior to each review. The research team will be responsible for providing updated deviation logs, and access to all source documentation and the case report forms at the start of each monitoring visit. A review of the regulatory binder/files may also be requested, and should be facilitated by the research team.

4. **Review of Subject Records**

Subject review will be determined by the phase of the protocol, and as outlined in the study-specific Monitoring Plan. The following elements will be reviewed as part of the monitoring visit:

**Informed Consent Document:** The initial consent and required re-consenting will be reviewed, as outlined in the Monitoring Plan, and the following will be verified:
- Most current, approved ICD version was used for consenting
- Signatures and dates are present for the study subject, and the investigator obtaining the informed consent
- IRB policy is followed when consenting non-English speaking participants
- Informed consent process was documented in the medical record.

**Eligibility:** Protocol eligibility criteria will be verified through the review of medical record documentation. If documentation cannot be located, eligibility will be noted as unconfirmed due to insufficient data. The subject will be considered ineligible if one or
more eligibility requirements were not met and documentation of the appropriate override procedure was not obtained.

**Treatment Administration:** The CRQS will review the source documentation to verify the treatment/intervention was administered per protocol, and study drug/product accountability will also be reviewed.

**Protocol Compliance:** The timely completion of all protocol required evaluations will be verified.

**Toxicity:** All toxicities recorded in the case report form should be an accurate reflection of the toxicities recorded in the medical record and documented as outlined within the protocol. If a serious adverse experience (SAE) occurred, the CRQS will verify/confirm that the event was reported as required by the Code of Federal Regulations, MDA IRB policy, MDA IND policy, and the protocol.

**Response:** Documentation of baseline disease status, response, progression, or protocol defined outcome for each pre-selected subject will be verified by reviewing the source documentation.

**Source Documentation:** The overall quality of the source documentation in the medical record will be reviewed. Any inconsistent, incomplete, and/or illegible records will be noted.

5. Monitoring Reports
The CRQS will complete a written Monitoring Report following each monitoring visit. The report will include a summary of the subjects reviewed during the visit, any significant findings, and the actions requested and/or taken by the research team to secure compliance. The final report will be submitted to the IND Medical Monitor for review and signature. The original signed report will be maintained in the sponsor files in the IND Office. A follow-up letter summarizing the unresolved issues will be sent to the PI and a copy of this document will be filed in the regulatory binder.

6. Study Closeout
When monitoring has been completed for all pre-selected subjects, and all subjects have been removed from the study, the CRQS will conduct a closeout visit to ensure the essential regulatory documents are in order prior to termination.

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