
ETCTN Monitoring and Auditing Information Page

1. Introduction

The Cancer Therapy Evaluation Program's (CTEP) Clinical Trials Monitoring Branch (CTMB) is responsible for setting guidelines and standards for the conduct of clinical trials to ensure data quality and compliance with regulatory requirements for clinical research. To that end, the CTMB employs a program of monitoring and auditing for all CTEP trials that use CTEP held IND agents. Within the context of the ETCTN, that program is carried out by the Clinical Trials Monitoring Service (CTMS), which is currently managed by Theradex.

The CTMS/Theradex activities in this respect are:

- Centralized electronic data capture and management (via the Medidata Rave application);
- Study monitoring program;
- Audit program;
- Coordination of the ETCTN Data Safety Monitoring Board (for randomized studies).

All ETCTN trials that use CTEP agents will use the centralized data management services provided by CTMS to include:

- Study build in CTMS's instance of Medidata Rave for submission of data via electronic case report forms; and
- Centralized quality assurance review of submitted data by CTMS staff.

For additional information on the CTMS and the auditing program in particular, refer to [NCI Guidelines for Monitoring the ETCTN and Other Early Phase CTMS-Monitored Studies](#).

2. Monitoring Program

Monitoring is the act of overseeing the progress of a clinical trial and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), Good Clinical Practices (GCP), and applicable regulatory requirements. It is a *continuous* process that can be conducted on-site or off-site and involves oversight of selected patients on a trial. Study monitoring includes:

- Precise tracking of patient accrual;
- Ongoing assessment of patient eligibility and evaluability;
- Adequate measures to ensure timely submission of study data;
- Adequate measures to ensure timely medical review and assessment of individual patient data;

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- Timely reporting of adverse events and treatment-related morbidity information; and
 - Periodic evaluation of outcome measures and patient safety information.

By holding and managing the ETCTN study databases (i.e., the Theradex instance of Medidata Rave), Theradex is able to carry out continuous monitoring of the ETCTN studies.

3. Auditing Program

Auditing is a systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, recorded, analyzed, and accurately reported according to the protocol, sponsor's SOPs, GCP, and the applicable regulatory requirements. It is a *snapshot in time* (as opposed to the continuous nature of monitoring), commonly an on-site process, and consists of reviewing a subset of patients on a trial.

The specific purposes of the auditing program are to:

- Document the accuracy of data submitted to CTMS and NCI/CTEP;
- Verify investigator/site compliance with protocol and regulatory requirements;
- Adhere to the policies and procedures of the ETCTN; and
- If necessary, provide site staff with resources for a more thorough understanding of the regulatory requirements, GCP, data collection, and data management practices.

The major objective of the audit program is to verify study data that could affect the interpretation of primary study endpoints. The three components of a study audit are:

- Institutional Review Board (IRB)/informed consent content review/Delegation of Tasks Log (DTL) review;
- Pharmacy and drug accountability; and
- Patient case review.

3.1 Types and Frequency of Monitoring

All ETCTN sites (including Lead Academic Organizations [LAOs], integrated components, and affiliates) that accrue patients are subject to monitoring. The frequency of monitoring visits will be determined at the time of the CTEP Protocol Review Meeting and is generally based on the phase of the study (Phase 1 versus Phase 2) and experience with the agent(s).

- CTMS Comprehensive will be used for early phase studies (primarily phase I and phase I/II studies) where experience with the agent(s) is limited. Three monitoring visits will be conducted annually to include two *Data Review visits* and one *Annual Site Visit*. The two *Data Review visits* focus only on one monitoring component, the patient case review. The one *Annual Site Visit* will focus on all monitoring components, (i.e., the IRB/informed consent review/DTL, pharmacy and drug accountability, and patient case review). The annual on-site visit will also include a meeting with the Principal Investigator (PI) to review the PI's responsibilities and obtain an update on the progress of the trial.

- CTMS Routine Monitoring is conducted for studies where there is more experience with the agent(s) (primarily phase II studies). Reviews are conducted on an 18 to 36 month basis. More frequent visits are conducted if warranted by accrual, safety concerns, concerns related to data quality or timely submission and/or CTMB directives.

Aside from regularly scheduled monitoring visits, an off-cycle (for cause) review may be warranted when there are significant irregularities found through quality control procedures or when allegations of possible scientific misconduct are made. It is the responsibility of the ETCTN or Early Drug Development Opportunity Program LAO to immediately notify CTMB (Phone: (240) 276-6545 or email: CTMBResearchMisconductConcerns@mail.nih.gov) upon learning of any significant irregularities or allegations related to scientific misconduct by a staff member or site participating in their research program. CTMB may coordinate or request that the CTMS coordinate the special audits/for cause audits.

For details on site audit visits, refer to [NCI Guidelines for Monitoring the ETCTN and Other Early Phase CTMS-Monitored Studies](#).

4. Questions and Support

For any questions about CTMS monitoring, audits, data management or Medidata Rave, please contact CTMSVisitsWorkingGroup@theradex.com.

For general questions relating to monitoring and auditing, please contact CTMB at:

- Phone: (240) 276-6545
- Email: CTMBAuditGuidelines@mail.nih.gov