ETCTN
Experimental Therapeutics Clinical Trials Network
Team Driven. Cancer Therapy Focused.
National Cancer Institute at the National Institutes of Health

TRIAL CONDUCT
Intended for those at clinical sites conducting ETCTN trials

ETCTN Monitoring and Auditing Information Sheet

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 in order 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 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 threefold:

- Centralized data receipt and management (via the Medidata Rave application)
- Study monitoring program
- Audit program

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

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

For more detailed information on the CTMS and the auditing program in particular, please refer to the Guidelines for Auditing of Clinical Trials for Experimental Therapeutics Clinical Trials Network (ETCTN).

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), GCP, and applicable regulatory requirements. It is a *continuous* process, can be conducted on-site or off-site, and involves oversight of all 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
- Timely reporting of adverse events and treatment-related morbidity information

- 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, and the date recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures, 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, to verify investigator compliance with protocol and regulatory requirements, adherence 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, good clinical practices (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:

- IRB/Informed consent content review
- Pharmacy and drug accountability; and
- Patient case review

3.1 Types and Frequency of Audits

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

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

- CTMS Routine: will be utilized for later phase studies. Audits will be conducted every 18-36 months (based on overall accrual at the site) as part of routine cancer center site visits.

Aside from regularly-scheduled audits, special audits or 'for cause' audits (off-cycle) 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 LAO or P2C to immediately notify CTMB 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.

Again, for details on site audit visits, please see the Guidelines for Auditing of Clinical Trials for Experimental Therapeutics Clinical Trials Network (ETCTN).

4. For Questions and Support

For any questions about CTMS data management or Medidata Rave, please contact the CTMS Help Desk at: CTMSSupport@theradex.com

For general questions relating to auditing, please contact the Clinical Trials Monitoring Branch at (240) 276-6545.