NCI Experimental Therapeutics Clinical Trials Network

A program of the National Cancer Institute of the National Institutes of Health

TRIAL DEVELOPMENT
Intended for those involved with the **development** of ETCTN trials

ETCTN Protocol Amendment Process Information Page

1. Introduction

All amendments (defined as any change to the protocol **after** full Cancer Therapy Evaluation Program (CTEP) approval of the protocol) made to protocols that are sponsored by the CTEP must be approved by CTEP and Central Institutional Review Board (CIRB) prior to implementation. Changes to a protocol shall be submitted to CTEP in the form of an amendment request.

For most ETCTN studies, the protocol will be authored by CTEP's Central Protocol Writing Support (CPWS). The study team must follow the directions given by the CPWS, until final CTEP approval of the study. Once CTEP approval is granted, authorship of the protocol transfers to the study team.

2. Requirements

Amendment requirements are like revision requirements. The initial amendment must be built on the final protocol documents provided by CPWS at the time of final CTEP approval of the protocol. Thereafter, the most recent CTEP-approved version of the protocol must be used.

- Protocol Document
  - Include summary of changes (SOC) as the first section of the document with hyperlinks to the relevant section of the protocol. The SOC must include every change made to the protocol since the last CTEP-approved version of the protocol.
  - Every submission must have a new version date for proper version control. If this is different from institutional policies regarding version dating, a CTEP Version Date should be added to the cover page of the protocol to comply with CTEP requirements for version dates.
- Informed Consent Document (ICD)
  - The ICD must be separate from the protocol document to comply with FDA electronic submission requirements.
  - Include an SOC as the first section of the ICD.
  - If there are no changes to the ICD from the previous CTEP approved version, it must still be submitted with a new CTEP version date that matches the protocol version date and a SOC that states that there are no changes to the ICD other than the version date.

3. Submission Process

Amendments must be submitted to the CTEP Protocol Information Office (PIO) via email at PIO@ctep.nci.nih.gov. All submissions must

- Comply with current electronic submission guidelines and be in Microsoft (MS) Word format; the CTEP Preparing Protocol Documents for eCTD Submissions to the FDA or the generic protocol template available on the Protocol Templates and Guidelines pages for MS Word format requirements contains more information.
- Be built on the most recent CTEP approved version of the protocol.
- Include track changes so that reviewers can easily see the changes from the last CTEP approved version of the protocol.
- SOC must clearly describe the changes made and include hyperlinks to the relevant section(s) of the document(s).

4. Approval Process

Approve as is or with recommendations

- Upon CTEP's decision to approve as is or with recommendations, PIO will submit the amendment to CIRB and Theradex for potential modifications to the study database in Medidata Rave on the study team's behalf.
- The study team must submit a CIRB application to CIRB so that CIRB can review the amendment.
- PIO will send an outcome letter once the CIRB approves the amendment (and notifies the study team and CTEP PIO of the decision), CTEP concurs with any CIRB stipulations, FDA confirms receipt of the amendment, and Theradex confirms that any Medidata Rave updates are complete.
    - CTEP approval - The protocol changes are sufficient and may be implemented as described in the protocol.
    - CTEP approval with recommendations - The protocol changes are sufficient and may be implemented as described in the protocol. CTEP provides recommendations with the option of incorporating into future versions of the protocol. If the recommendations are implemented, the changes must be included in the next amendment request to CTEP in the SOC.

Disapproval

If CTEP disapproves the amendment, the protocol changes may not be implemented. CTEP will provide explicit comments regarding the deficiencies in the requested changes. Another protocol amendment for approval must be submitted before implementing the changes. Other options include foregoing the

amendment with the changes (so that the last CTEP approved version of the amendment is the current version) or submitting a response to the disapproval in the form of another amendment addressing CTEP's comments. For the latter, a new version date and all changes since the last CTEP-approved version of the protocol must be included in the submission.

CTEP approval or disapproval of a revision or amendment is All or Nothing. For example, if an amendment has four changes and CTEP disapproves one of the changes, then the entire amendment is disapproved. The PI must re-amend the study, deleting and/or addressing the issue CTEP is concerned about, as well as re-sending the three changes CTEP did approve.

The CTEP Amendments page contains more information.

5. For Questions and Support

Contact CTEP PIO Help Desk via email at PIO@ctep.nci.nih.gov for questions about submitting protocol amendments.