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 Revision and Amendment Process Information Page for Studies not Authored by the Centralized Protocol Writing Support

1. Introduction

All revisions or amendments made to protocols that are sponsored by the Cancer Therapy Evaluation Program (CTEP) must be approved by CTEP prior to implementation. Changes to a protocol shall be submitted to CTEP in the form of an Amendment or Revision request. **For most ETCTN studies, the protocol will be authored by CTEP's Central Protocol Writing Support (CPWS) and the study team should follow the directions given by the CPWS. The information contained in this page is only for the rare study that is not being authored by CPWS and the study team must interact directly with CTEP for development of the protocol.**

A revision is defined by CTEP as a change to the protocol prior to full CTEP approval of the protocol. An amendment is defined by CTEP as a change to the protocol after full CTEP approval of the protocol.

2. Submission Process

Revisions and 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 in Microsoft (MS) Word format. Refer to Preparing Protocol Documents for eCTD Submissions to the FDA or the generic protocol template available on the Protocol Templates and Guidelines page for MS Word format requirements.

CTEP requires submitting revisions and amendment documents with track changes so that reviewers can easily see the changes from the last version of the protocol. The summary of changes must also explicitly state what changes are made by listing the old text and supplying the new text.

Revisions require the submission of the following:

- The protocol document with a summary of changes as the first section of the document with hyperlinks to the relevant section of the protocol. Because revisions are usually changes requested by CTEP, a consensus review will have been sent in a format that should be cut and pasted as the summary of changes. The generic protocol template available on the Protocol Templates and Guidelines page provides an example of how this should look. Additional changes outside of those requested by CTEP in the protocol and summary of changes may be included. 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. Additional changes outside of CTEP comments must first be discussed with the lead reviewer, as additional changes may require extra revisions, which could result in delays to study activation.

- The informed consent document (ICD) must be separate from the protocol document to comply with Food And Drug Administration (FDA) electronic submission requirements. There must also be a summary of changes as the first section of the ICD. If there are no changes to the ICD from the previous version, it must still be submitted with a new CTEP Version Date that matches the protocol version date but will not require a summary of changes. Instead, note on the protocol's summary of changes that there are no changes to the ICD other than the change in version date.

Amendment requirements are similar to revision requirements:

- The protocol document with a summary of changes as the first section of the document with hyperlinks to the relevant section of the protocol. The summary of changes 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.
- The ICD must be separate from the protocol document to comply with FDA electronic submission requirements. There must also be a summary of changes 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 but will not require a summary of changes. Instead, note on the protocol's summary of changes that there are no changes to the ICD other than the change in version date.

3. Approval Process

Once CTEP reviewers have completed their review of the protocol amendment or revision, if the decision is to approve the amendment as is, or with recommendations, PIO will submit the amendment to the CIRB and to Theradex for building/potential modifications to the study database in Medidata Rave on the study team's behalf. At that time, the study team must submit a CIRB application to CIRB so that CIRB can review the amendment. Once the CIRB approves the amendment (and notifies the study team and CTEP PIO of the decision), CTEP concurs with any CIRB stipulations, and Theradex confirms that any Medidata Rave updates are complete, PIO will send an outcome letter:

- 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 is providing 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 summary of changes.

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 or

revision for approval must be submitted prior to 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.

Please note that 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.

For more information on revisions and amendments, refer to the CTEP Amendments page.

4. For Questions and Support

For questions about submitting protocol revisions and amendments, contact PIO:

- PIO Help Desk: PIO@ctep.nci.nih.gov