

Amendment Requests to CTEP

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Introduction

Any change to the protocol document or model consent form for ETCTN studies must be reviewed and approved by the NCI Cancer Therapy Evaluation Program (CTEP) and the NCI Central Institutional Review Board (CIRB) prior to implementation. The documents must comply with the CTEP electronic submission (eSubmission) guidelines. The purpose of this document is to provide guidance for ETCTN study amendments where the DF/HCC physician is the overall protocol chair.

An amendment is defined by CTEP as a change to the protocol or consent after full CTEP approval of the protocol whereas a revision is a change to the protocol or consent prior to full CTEP approval. Amendments include changes initiated by the overall protocol chair and those initiated by CTEP in the form of Requests for Amendments (RA) and Requests for Rapid Amendments (RRA). Questions about amendments should be directed to the NCI CTEP Protocol and Information Office (PIO) at pio@ctep.nci.nih.gov.

Procedure

- 1) Amendment Submission to CTEP
 - a) The protocol chair will prepare the amendment submission with assistance from the study team.
 - i) The documents must comply with the CTEP electronic submission (eSubmission) guidelines. Refer to the [DF/HCC ETCTN CTEP Submission Requirements](#) guidance document for detailed instructions.
 - ii) If the amendment is in response to an RA or RRA from CTEP, review the RA/RRA documents carefully as they will specify exactly what changes must be made to the protocol and consent documents. The documents will also indicate if any investigator-initiated edits can be made in addition to the CTEP requested changes.
 - b) The documents must be sent directly to the CTEP PIO via email at pio@ctep.nci.nih.gov.

- i) The PIO will acknowledge receipt of the submission and notify the submitter if the submission has been placed on hold because of missing information or if corrections are required.
 - c) CTEP will review the amendment and will either 1) approve without any comments, 2) approve with recommendations, or 3) disapprove the amendment (refer to [step 6](#)). If the amendment is approved or approved with recommendations, it will be sent to the NCI CIRB by the PIO for review. See [step 5](#) below for details about responding to CTEP recommendations.
- 2) Amendment Submission to NCI CIRB
 - a) If CTEP approves the amendment or approves with recommendations, the PIO will notify the protocol chair and the NCI CIRB that the approval is on hold pending NCI CIRB review and approval.
 - b) The protocol chair, with assistance from the study team, will submit the NCI CIRB Amendment Review Application.
 - c) The NCI CIRB may request modifications prior to issuing their approval
 - i) The protocol chair will add the NCI CIRB requested modifications to the existing summary of change by adding a new section and clearly labeling it as a response to NCI CIRB comments. The protocol chair must submit the updated documents directly to the NCI CIRB (not CTEP PIO).
 - ii) The NCI CIRB will ensure CTEP has an opportunity to review and approve the new edits.
 - d) The NCI CIRB will notify the study team and CTEP PIO once they have completed their review. Once any required changes to the Medidata Rave build are complete, the CTEP PIO will issue the amendment approval letter.
- 3) Verifying Medidata Rave Changes
 - a) If the amendment modifications impact the Medidata Rave database, a member of the Theradex Medidata Rave team will contact the protocol chair to review and approve the database changes.
 - b) CTEP PIO will not release the amendment approval letter until they have been notified by Theradex that the Rave build changes have been approved by the protocol chair.
- 4) Posting Amendments to Cancer Trials Support Unit (CTSU) Website
 - a) Upon CTEP/NCI CIRB approval, the protocol chair sends the amendment setup request to the CTSU Regulatory staff.
 - b) The protocol chair contacts the CTSU Operations staff to prepare for amendment release and site notification via web posting and CTSU Bi-monthly Broadcast.
 - c) The protocol chair notifies the NCI CIRB of amendment release/activation.
- 5) Responding to CTEP Recommendations

- a) CTEP may provide recommendations for future changes along with the amendment approval letter.
 - i) The protocol chair may elect to 1) incorporate the changes into the protocol and/or consent, 2) provide a written response to CTEP explaining why the recommended modifications will not be made, or 3) ignore the recommendations.
 - ii) If the protocol chair elects to incorporate the changes into the protocol and/or consent, they must be submitted to CTEP as a new amendment. The changes that were just approved by CTEP and the NCI CIRB need to be removed from the summary of change and the new amendment must have an updated version date and only include the newest modifications.

Note: In the event CTEP recommendations are provided at the time the PIO sends the amendment to the NCI CIRB for review and the NCI CIRB requests modifications, the protocol chair may address CTEP recommendations when responding to the NCI CIRB. The submission should still be sent to the NCI CIRB and the NCI CIRB will ensure the updated documents are reviewed by CTEP prior to final amendment approval.

- 6) Responding to CTEP Amendment Disapproval
 - a) CTEP amendment approval is all-or-nothing (i.e., if several different protocol edits are proposed with the amendment but CTEP cannot approve one of those modifications, the entire amendment will have to be disapproved). If an amendment is disapproved the protocol chair may elect to do one of the following:
 - i) Resubmit a new amendment correcting the issues described in the disapproval letter.
 - ii) Resubmit a new amendment with all previously submitted changes, less the item(s) that were specifically disapproved by CTEP.
 - iii) Provide additional justification to support the original request and petition CTEP to reconsider the disapproval.
 - b) The resubmission is considered a new amendment and must follow all eSubmission requirements including an updated version date for the protocol and model consent document.

Links

CTEP Investigator Handbook (section 8):

http://ctep.cancer.gov/investigatorResources/investigators_handbook.htm

Step by Step Guide for Submitting eSubmission Ready Documents to CTEP:

<http://ctep.cancer.gov/protocolDevelopment/amendments.htm>

Protocol Revision and Amendment Process Information Sheet:

http://ctep.cancer.gov/initiativesPrograms/etctn_information_checklists.htm