National Cancer Institute (NCI)
Experimental Therapeutics Clinical Trials Network (ETCTN) Guidance

CTEP-Initiated Amendments: Requests for Amendments (RAs) and Rapid Requests for Amendments (RRAs)

Contents

Introduction

The purpose of this document is to provide guidance for ETCTN study amendments where the DF/HCC physician is the protocol chair. 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 local submission and implementation. The documents must comply with the CTEP electronic submission (eSubmission) guidelines.

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 defined as: "a change to the protocol or consent prior to full CTEP approval". Amendments include changes initiated by the protocol chair and those initiated by CTEP in the form of Requests for Amendments (RA) and Requests for Rapid Amendments (RRA). For more information on Protocol Chair-Initiated Amendments to CTEP, please refer to the DF/HCC Chair-Initiated Amendments to CTEP Guidance Document. Questions about CTEP amendments should be directed to the NCI CTEP Protocol and Information Office (PIO) at pio@ctep.nci.nih.gov.

The purpose of CTEP Rapid Requests for Amendments (RRAs) are to alert investigators of changes to CAEPRs and Risk Lists based on updated IBs and or Package Inserts and updates to other new/modified risk-related information associated with study agents. As part of Good Clinical Practice, CTEP reviews each CAEPR list on an annual basis. The review includes literature search, CTEP-AERS submission review,

and comparison to the latest agent Investigator's Brochure. If the amendment is an RRA, an Action Letter will be posted to accompany the amendment. The purpose of an Action Letter is to alert investigators in studies conducted by NCI-CTEP of new and/or modified risk information associated with study drugs. In some serious cases, an Action Letter may be posted without a preceding amendment.

The purpose of CTEP Requests for Amendments (RAs) are to alert investigators of any blanket administrative changes which include but are not limited to: clarifications to CAEPRs and Risk Lists, corrections to shipping/contact info; changes in a biomarker plan; changes to dose modification and toxicity management information for a drug; and overall changes to the configuration of participating LAOs or sites.

If an RRA is not received and approved by CTEP by the deadline, there may be a hold placed on enrollment and a change in trial status.

Procedure

RA or RRA Notification and Submission to PIO

1) The Protocol Chair and study team will be notified of any CTEP-Initiated Amendments via an email notification from NCI CTEP Protocol and Information Office (PIO) (pio@ctep.nci.nih.gov).
    a) The Protocol Chair and study team will review the Request for Amendment (RA) or Rapid Request for Amendment (RRA) documents carefully as they will specify exactly what changes must be made to the protocol and consent documents and the deadline for the submission. The documents will also indicate if any Protocol Chair-initiated edits can be made in addition to the CTEP-requested changes. In general, additional changes are allowed for RAs. For RRAs, additional changes are not allowed if the study status is Active (since additional changes can extend the review time and subsequently result in accrual suspension if the amendment is not approved before the Action Letter release).
    b) The Protocol Chair with assistance from the study team will prepare the amendment submission, following instructions outlined in the Amendment Request notification email.
        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.
    c) The Study Chair or designee must send the updated protocol documents and informed consent forms directly to the CTEP PIO via email at pio@ctep.nci.nih.gov by the indicated deadline in the notification email.
        i) The PIO will acknowledge receipt of the submission and notify the submitter if there is any missing information or corrections required.
        ii) Failure to meet the RRA submission deadline can result in CTEP temporarily closing the study to accrual.

iii) Once PIO has completed their review, they will forward the documents to the CIRB to be pre-loaded into the CIRB Manager System for the next portion of the review.

RA or RRA Submission to NCI CIRB Manager System

1) The NCI CIRB will send an automated email message to the DF/HCC ETCTN Office indicating the study has received Approval on Hold status and study documents from the PIO. The email will also indicate the deadline in which the amendment must be submitted and include a link to the Amendment Application in the NCI CIRBManager System.
2) The amendment application form in the CIRBManager System will be pre-loaded with all documents approved by PIO/CTEP in Step 1.
3) The DF/HCC ETCTN Office, with assistance from the protocol chair and the study team, will submit the NCI CIRB Amendment Application to the CIRBManager System and include any additional requested documents. The application should be submitted ASAP because the CIRB will not complete their review until it is received, this can delay the amendment approval. The study team must provide the DF/HCC ETCTN Office with a clean copy of the ICF without the summary of changes at the top for inclusion in the submission if it has not been pre-loaded into the CIRB application.
4) The NCI CIRB will review the application and may request modifications prior to issuing their approval.
    a) The DFHCC ETCTN Office will work with the protocol chair and study team to add any NCI CIRB-requested modifications to Amendment Application in the CIRBManager.
5) The NCI CIRB will notify the DFHCC ETCTN Office, the protocol chair, study team and CTEP PIO once they have completed their review and issued CIRB approval. Please note that this is not indicative of final CTEP approval, which occurs after any CIRB-requested modifications have been reviewed and approved by CTEP, any pending administrative holds are resolved (e.g., investigator registration updates), and any required changes to the Medidata Rave build are completed. Once all of these items are complete, CTEP PIO will issue their notice of final approval for the amendment.
    a) Verifying Medidata Rave Changes.
        i) 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. Theradex will not begin their validation until the PI signs and returns the Theradex Configuration Document.
        ii) 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 and have been implemented.

Posting Amendments to Cancer Trials Support Unit (CTSU) Website

1) The CTSU Operations Protocol Coordinators will contact the study team protocol contact with an amendment set up request upon final CTEP Approval.
2) The study team with assistance from the protocol chair will respond to the amendment set up to prepare for amendment release to the CTSU Website and inclusion in the next CTSU Bi-monthly Broadcast. Please see the below for instructions on how to respond to the CTSU Amendment Set Up Request:
    a) Protocol Number: *CTEP Protocol Number from Protocol Document*
    b) LPO Amendment Number: *CTSU will populate Amendment number (NOT local OHRS Amendment Number)*
    c) Amendment Version Date: *From Protocol Document*
    d) Amendment Release Date: *Current date, CTSU Recommended date, or ASAP*
        i) Release Time (optional):
    e) Review Type: Full/Expedited/Full-Desired Expedited: *Match the review type of the amendment based on the CIRB review minutes*
    f) CTSU Collection Required: *Yes/No: The Protocol Chair determines this response given the content of the Amendment. Indicating 'yes' would implement an additional step that requires outside sites to submit IRB approval of the Amendment before the indicated "Required Date" to the CTSU Regulatory Submission Portal prior to that site being able to enroll patients.*
        i) Required By Date (date sites must submit IRB approval to the CTSU): *N/A or ASAP (There is no certain time, occasionally when the CTSU sends these notifications they may include an "earliest date" the amendment may be submitted by. Here you may record **"ASAP"** - We usually opt for the soonest available unless the protocol chair requests otherwise.)*
    g) Study Changes: In this version, has any of the following been modified: *Yes/No (Study Chair to Confirm)*
        i) Study Participants: *Study Chair to confirm*
        ii) Participating Countries: *Confirm against protocol coverpage*
        iii) IND/IDE: *Study Chair to confirm*
    h) Protocol-specific Requirements (if applicable): *Protocol Specific Requirements (PSRs) are any additional requirements that participating sites must complete prior to enrolling patients (ie. STS Training, eDTL, SIT). They can be study-specific as well as person training and/or institution requirements. You may respond to this question if there are any changes to existing PSRs, or additions of new requirements*
        i) Requirement Name:
        ii) Requirement Description on CTSU Website: *(if chosen to be different than the RSS)*
        iii) CTSU Processing Instructions:
        iv) LPO Contact for PSR, if applicable:

3) The CTSU Protocol Coordinators will notify the NCI CIRB, CTEP, and the Protocol Chair and study team of amendment release/activation. If the amendment is an RRA, an Action Letter will be posted to accompany the amendment. In some serious cases, an Action Letter may be posted without a preceding amendment.

Links

CTEP Step by Step Guide for Submitting eSubmission Ready Documents to CTEP:
https://ctep.cancer.gov/protocolDevelopment/amendments.htm