Developing a New Experimental Therapeutics Clinical Trials Network (ETCTN) Clinical Trial

This document will be used by the protocol chair and study team to understand the steps required to submit and activate a new ETCTN trial with the National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP) and NCI Central Institutional Review Board (CIRB).

Key
- 🟩 CTEP, CTSU, Theradex
- 🟦 Protocol Chair
- 🟧 NCI CIRB
- 🟪 FDA
- 📄 Guidance Document

CTEP selects a specific agent(s) to investigate. CTEP sends Project Team Announcement (PTA) to all ETCTN Lead Academic Organizations (LAOs)

Confirm investigator at LAO is registered and rostered with the NCI and ETCTN?

No: Refer to the DF/HCC ETCTN Registration and Rostering Guidance documents

Yes

Investigator sends completed Project Team Member Application (PTMA) to CTEP

Refer to the DF/HCC ETCTN PTMA Guidance document

Review Time: ~ 30 Days

CTEP accepts PTMA?

No: Investigator may submit unsolicited LOI. Refer to the DF/HCC ETCTN LOI Guidance document.

Investigator could also participate in another CTEP ETCTN study. Refer to the Joining an ETCTN Guidance documents.

Yes

PIO sends PTMA approval letter

Investigator participates in drug development project team. *(Entails frequent teleconferences and webinars over a 8-12 week period resulting in one or more clinical trial proposals)*

Investigator presents the project team's drug development plan including clinical trial proposal(s) to the Investigational Drug Steering Committee (IDSC) (*Done in conjunction with other project team members and investigators typically present their proposal(s) remotely)*

IDSC accepts drug development plan?

No: Investigator discusses possible plans with project team leaders

Yes

Investigator incorporates recommendations into drug development plan

CTEP presents the drug development plan to the NCI Senior Advisory Committee (SAC)

SAC accepts drug development plan?

No: Drug development team reconvenes to revise drug development plan

Yes

CTEP requests a Letter of Intent (LOI) from the Protocol Chair

LOI Preparation 30 Days

Protocol Chair sends the completed LOI form to CTEP PIO.

Refer to the DF/HCC ETCTN LOI Guidance document

OEWG Timeline: 210 Days (Phase I/II Studies)

CTEP reviews the LOI

OEWG Clock Starts when the initial LOI review takes place

CTEP approves the LOI document?

No: CTEP sends the Protocol Chair review comments.

If this is the first set of LOI review comments, CTEP schedules a OEWG teleconference with the Protocol Chair.

Protocol Chair submits revised LOI to CTEP PIO

Yes

CTEP sends pharmaceutical collaborator the LOI for review and drug commitment.

CTEP sends the Protocol Chair a notice of approval on hold pending drug commitment* along with the CTEP consensus review. If this is the first set of review comments, CTEP schedules a OEWG teleconference with the Protocol Chair to discuss the consensus review.

* NCI Biomarker Review Committee (BRC) approval may also be required prior to final LOI approval. See BRC Guidance document.

Pharmaceutical collaborator requests LOI changes?

Yes: CTEP relays pharmaceutical collaborator comments to Protocol Chair.

No

CTEP PIO sends LOI approval letter

Protocol Preparation 60 Days

Protocol chair submits protocol and model consent form to CTEP PIO. *<u>Must</u> use the CTEP Protocol template and CIRB ICF template.*

Refer to the DF/HCC ETCTN Protocol and Consent Development Guidance document

CTEP reviews the protocol and consent. CTEP sends the consensus review comments to the Protocol Chair and schedules an OEWG teleconference.

Protocol Chair submits a protocol revision to CTEP PIO

Refer to the DF/HCC ETCTN CTEP Revisions Guidance document

CTEP approves the revision?

No: CTEP sends a follow-up review to the Protocol Chair.

Yes

IND filing protocol?

Yes: CTEP submits the protocol to the FDA. (Review and approval of studies being filed under a new IND will take approximately 4–5 weeks)

CTEP sends the Protocol Chair a notice of approval on hold pending IND activation.

FDA requests protocol changes?

Yes: CTEP relays FDA comments to Protocol Chair.

No

CTEP sends the Protocol Chair notice of approval on hold pending CIRB approval and Medidata Rave and OPEN build completion.

CTEP sends the protocol and consent to the NCI CIRB and alerts Theradex to start the Medidata Rave and OPEN builds.

Medidata Rave and OPEN build and review time: ~4 to 6 weeks

NCI CIRB provides the Protocol Chair an application to allow the CIRB to review protocol and consent

Protocol Chair sends completed NCI CIRB application and requested study documents to the NCI CIRB

NCI CIRB reviews the study

NCI CIRB approves the study?

No: Protocol Chair submits protocol revision to NCI CIRB.

NCI CIRB reviews the revised documents

The NCI CIRB will provide the revised documents to CTEP for their review and approval

NCI CIRB approves the study?

No

Yes

NCI CIRB sends the Protocol Chair notice of approval

NCI CIRB notifies CTEP and Theradex of the CIRB approval

Theradex completes Medidata Rave and OPEN builds

Protocol Chair reviews Medidata Rave and OPEN builds.

Protocol Chair approves builds?

No: Protocol Chair works with Theradex to update Medidata Rave and OPEN builds.

Yes

PIO will issue final approval letter.

CTSU regulatory staff and Protocol Chair will prepare trial on Regulatory Support System (RSS) to allow for proper collection of regulatory documents.

Protocol Chair will email NCI CIRB (earlyphasecirb@emmes.com) with following (or similar) language "NCI protocol #123 is CTEP approved and ready for distribution for IRB review at the participating organizations on the protocol cover page." Include CTSU (ctsuprotocol@westat.com and ctsuregsetup@ecogchair.org)

CTSU operations and regulatory staff to finalize activation memo and RSS.

Protocol Chair accepts RSS and activation memo?

No: CTSU updates the RSS/ Activation memo

Yes

LAO's Site Administrator will work closely with CTSU to change status in RSS to active.

OEWG clock stops

CTSU operational staff posts protocol and other study documents to CTSU website.

File the Study Specific Worksheet with the CIRB and complete all local activation steps prior to enrolling subjects.

Refer to DF/HCC ETCTN Local Activation Guidance documents