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

Letter of Intent (LOI) Development

Contents

Introduction

Investigators wishing to conduct an ETCTN clinical trial must submit an LOI outlining a plan for the new clinical trial. Prior to submitting his or her first LOI, the investigator should review the CTEP Investigator's Handbook to become familiar with CTEP policies, the review process, and the responsibilities of a CTEP investigator.

LOIs emanating from the Drug Development Plan created by the Drug Development Project Team and approved by the Investigational Drug Steering Committee (IDSC) are considered solicited LOIs. After the IDSC meeting, there is typically one additional level of NCI-CTEP approval, after which LOIs are requested from clinical project team members. Clinical project team members who prepared a Career Development Project Team Member Application (PTMA) go on to prepare a Career Development LOI (CrDL).

Unsolicited LOIs are submitted by investigators to examine a novel hypothesis that is supported by pre-clinical data for any agent in the CTEP portfolio. Before preparing an LOI, it is highly advisable to schedule a conference call with the appropriate CTEP Investigational Drug Branch (IDB) monitor for the specific agent to be studied. This is a requirement for unsolicited Career Development LOIs. For drugs around which there are Project Teams, unsolicited LOIs may only be submitted after the Project Team has completed deliberations and the Drug Development Plan has been approved. In general, unsolicited LOIs cannot propose studies that compete with any of the studies that are part of the Drug Development Plan put forward by the Project Team.

Procedure

1) Solicited LOI
   a) A clinical investigator who is part of a Drug Development Project Team will typically be asked to submit an LOI following approval of the project team's Drug Development Plan.
      i) The investigator must download and complete the LOI Submission Form from the CTEP website.

(1) Refer to CTEP Guidance: Components of a Competitive Letter of Intent
(2) Carefully follow the DF/HCC ETCTN CTEP Submission Requirements Guide
(3) Drs. Shapiro, Kufe and Flaherty should be informed of an LOI to be submitted, so that appropriate funding from the UM1 grant can be planned. LOIs from DFCI and BIDMC may list Dr. Shapiro or Dr. Kufe as the UM1 grant PI. LOIs from MGH should list Dr. Flaherty as the UM1 grant PI.
(4) A Career Development LOI (CrDL) requires the CV of the applicant, as well as mentor and institutional support letters. For LOIs from DFCI or BIDMC, Dr. Shapiro or Dr. Kufe will provide the institutional letter; for LOIs from MGH, Dr. Flaherty will provide the institutional letter.

b) The investigator emails the completed LOI submission to CTEP PIO at PIO@ctep.nci.nih.gov.
c) The CTEP Protocol Review Committee (PRC) reviews the LOI and the CTEP PIO provides a consensus review with the LOI Review Decision.
   i) LOI Review Decisions include but are not limited to:
      (1) Approval on hold pending drug commitment from the pharmaceutical collaborator and/or pending Biomarker Review Committee approval
      (2) Request to submit a revised LOI
      (3) Disapproved (unlikely for solicited LOIs)
d) An Operational Efficiency Working Group (OEWG) conference call between the CTEP reviewers and Investigator to discuss the comments in the consensus review is scheduled by the PIO when the LOI has approval on hold and when a revised LOI is requested. The Investigator can request a conference call if the LOI was disapproved and they wish to discuss the disapproval with the CTEP reviewers.
e) The CTEP PIO provides a conference call summary. The conference call summary must be used when responding to CTEP comments in situations where a revised LOI is requested. Refer to the DF/HCC ETCTN CTEP Submission Guide for details.
f) CTEP sends the LOI to the pharmaceutical collaborator, who will be asked to review the study and provide a formal drug commitment letter. The company may request that the LOI be further revised.
g) CTEP approves the LOI and requests that the protocol and consent be submitted within 60 days.

2) Unsolicited LOI
   a) For agents for which there are Project Teams, investigators not involved in the Drug Development Project Team may submit an LOI after the Project Team has finished with the development process and the Drug Development Plan has been approved. For agents with no associated Project Team, an unsolicited LOI may be submitted at any time. It is highly advisable for investigators to schedule a conference call with the appropriate CTEP Investigational Drug Branch (IDB) monitor before submitting an unsolicited LOI. This is a requirement for an unsolicited Career Development LOI (CrDL). Drs. Shapiro, Kufe and Flaherty should be informed of all planned LOIs.

i) Investigator downloads and completes the LOI Submission Form from the CTEP website. For LOIs from DFCI or BIDMC, Dr. Shapiro or Kufe may be listed as the grant PI. For LOIs from MGH, Dr. Flaherty is listed as the grant PI.
   (1) Refer to CTEP Guidance: Components of a Competitive Letter of Intent
   (2) Carefully follow the DF/HCC ETCTN CTEP Submission Requirements Guide
   (3) Prepare all supplemental documentation. Career Development LOIs require mentor and institutional letters. For DFCI and BIDMC, Dr. Shapiro or Dr. Kufe will supply the institutional letter. For MGH, Dr. Flaherty will provide the institutional letter. It is also advisable for LOIs from investigators that are not Career Development LOIs to also be submitted with an institutional letter. This letter will indicate to CTEP that there are plans to support the protocol via the UM1 grant.

b) The Investigator emails the completed LOI submission to CTEP PIO at PIO@ctep.nci.nih.gov.

c) The CTEP Protocol Review Committee (PRC) reviews the LOI and the CTEP PIO provides a consensus review with the LOI Review Decision. About one-third of unsolicited LOI are approved by CTEP.
   i) LOI Review Decisions include but are not limited to:
      (1) Approval on hold pending drug commitment from the pharmaceutical collaborator and/or pending Biomarker Review Committee approval
      (2) Request to submit a revised LOI Disapproved

d) An Operational Efficiency Working Group (OEWG) conference call between the CTEP reviewers and Investigator to discuss the comments in the consensus review is scheduled by the PIO when the LOI has approval on hold and when a revised LOI is requested. The Investigator can request a conference call if the LOI was disapproved and they wish to discuss the disapproval with the CTEP reviewers.

e) The CTEP PIO provides a conference call summary. The conference call summary must be used when responding to CTEP comments in situations where a revised LOI is requested. Refer to the DF/HCC ETCTN CTEP Submission Guide for details.

f) CTEP sends the LOI to the pharmaceutical collaborator who will be asked to review the study and provide a formal drug commitment letter. The company may request that the LOI be further revised.

g) CTEP approves the LOI and request that the protocol and consent be submitted within 60 days.

Note: In all cases, the OEWG timeline begins at the time of LOI submission. A protocol must be activated by CTEP within 450 days once the timeline begins or it cannot move forward. It is the responsibility of investigators to be aware of this timeline and to contact Drs. Shapiro, Kufe and Flaherty if there are delays that may jeopardize the protocol.

Links

CTEP LOI Website: http://ctep.cancer.gov/protocolDevelopment/letter_of_intent.htm

CTEP Investigator Handbook:
https://ctep.cancer.gov/investigatorResources/investigators_handbook.htm

LOI Submission Form: https://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm

CrDL Instructions: http://ctep.cancer.gov/protocolDevelopment/letter_of_intent.htm#instructions

Components of a Competitive Letter of Intent:
https://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm

CTEP Agents and Active Agreements: http://ctep.cancer.gov/protocolDevelopment/agents_drugs.htm