

Title: **CP-CTNet Cross-Network Trials Guidelines**

Version: 4.0

Version Date: October 31, 2025

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
4.0	OCT-31-2025	Updated the document to reflect the DMACC to DMASC name and structure change. Removed the references to the rapid response to restricted funds mechanism.
3.0	FEB-07-2025	Updated the <i>Algorithm to Assess a Potential Unanticipated Problem</i> and <i>Algorithm to Assess Potential Noncompliance</i> links to reflect the new URLs.
2.0	JAN-19-2024	Addition of several new sections: Definitions, Organizational Structure of CP-CTNet cross-network trials, Roles and Responsibilities, Communication Plan, Rapid Response Restricted Funds, References, and Appendices.
1.0	AUG-10-2020	Original version of document

1. INTRODUCTION AND PURPOSE

This document provides the guideline for cross-network clinical trials for the Cancer Prevention Clinical Trials Network (CP-CTNet).

2. DEFINITIONS

Term	Definition
AO	Affiliated Organization
CCSA	CCS Associates, Inc.
CIRB	Central Institutional Review Board
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DSMB	Data and Safety Monitoring Board
IRB	Institutional Review Board
LAO	Lead Academic Organization
M-SOP	Manual of Standard Operating Procedures
MTA	Material Transfer Agreement
NCI	National Cancer Institute
PI	Principal Investigator
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SVAR	System Variable Attribute Report

3. DEFINITION OF CROSS-NETWORK TRIALS

A CP-CTNet cross-network trial is a trial involving a collaboration between two or more LAOs whereby each LAO agrees to provide accrual and funding for the trial. Each LAO receives credit for the participants accrued by its participating AOs.

- 3.1. Each LAO (or its AOs) must plan to make a substantive contribution to accrual.
- 3.2. The accrual and biomarker analysis do not need to be divided equally between the LAOs.
- 3.3. Accrual targets and plans for biomarker analysis are determined by the collaborating institutions.
- 3.4. Statistical support for all new cross-network trials is provided by the DMASC Statistical Support Unit (see exceptions in section 4).
- 3.5. The following constructs do not meet the definition of a cross-network trial:
 - An AO affiliated with one LAO chooses to participate in a second LAO's trial and all accrual costs are provided from the second LAO's budget (the LAO with which the AO is affiliated does not provide funding for the trial).
 - An investigator from one LAO's own organization chooses to participate in a second LAO's trial and all accrual costs are provided by the second LAO (the LAO at the investigator's organization does not provide funding for the trial).

4. DEVELOPMENT OF CROSS-NETWORK TRIALS

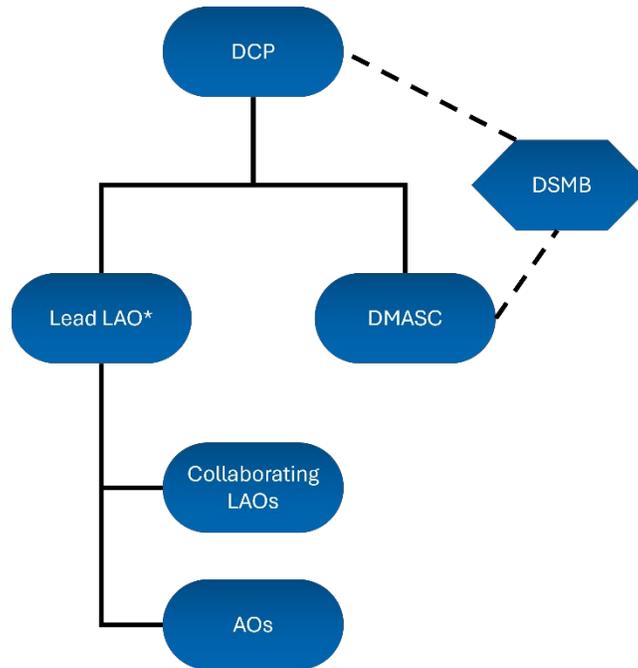
Three proposed routes for cross-network trials are possible, as outlined below. **It should be emphasized that if at all possible, a cross-network trial should be developed with a DMASC statistician from the start (section 4.1).**

- 4.1. If two or more LAOs collaborate on concept development (solicited or unsolicited concepts), the concept is submitted to DCP for scientific review.
 - Scientific Review of all trials is provided by the DCP Concept Review Committee as per usual procedures.
 - DCP-approved concepts are reviewed by the Steering Committee for approval.
 - The proposed trial is presented by the appropriate LAO Investigator(s) to the Steering Committee for approval. The concept submitted to DCP is shared with the Steering Committee.
 - In order to have a record of the vote to approve the proposal as a cross-network trial, the vote is done via a confidential electronic or paper process. A letter confirming the approval of the project is issued by DCP.

- 4.2. If a trial is already ongoing in CP-CTNet (and thereby has already undergone DCP scientific review) and there is a desire to convert it to a cross-network trial, the trial summary is presented to the Steering Committee for approval as above. The LAO investigator provides a short background document providing an overview of the trial, status update, and justification for converting to a cross-network trial.
 - Since the trial is ongoing, the original statistician remains the statistician of record, while DMASC Statistical Support Unit may provide consultation as necessary.

- 4.3. If a study is already ongoing in a non-CP-CTNet context, or funding for aspects of the trial has been applied for or received (e.g., from NCI R01s, a foundation, etc.), the PI should first discuss with DCP the appropriateness of the trial for CP-CTNet cross-network trial designation.
 - The study then needs to undergo DCP scientific review as well as receive Steering Committee approval, as above. While DCP scientific review should precede Steering Committee presentation, tight timelines (e.g., for grant submission or acceptance) may allow Steering Committee presentation to precede DCP scientific review.
 - Discussion is needed regarding the statistician of record, depending on the level of effort expended by the original study statistician.

5. ORGANIZATIONAL STRUCTURE OF CROSS-NETWORK TRIALS



*For cross-network trials that are developed as described in Section 4.2 and 4.3, the LAO statistician reports to the DSMB during the open session and a designated DMASC statistician reports to the DSMB during the closed session.

6. ROLES AND RESPONSIBILITIES

Roles and responsibilities of CP-CTNet entities in supporting CP-CTNet cross-network trials are summarized below.

Definitions:

Lead LAO: One LAO takes primary responsibility for the administrative aspects of the trial. These include, but are not limited to, communications with DCP and CIRB (e.g., concept and protocol submission, etc.), SVAR development with DMASC, ClinicalTrials.gov reporting, etc. The Lead LAO organizes study calls, develops study materials (with help from collaborating LAOs) and communicates with the entire study team (see QKREFGD18 *Roles and Responsibilities for CP-CTNet Cross-Network Trials*). The Lead LAO also has oversight responsibilities for its own AOs. The Lead LAO submits the initial budgets from all Collaborating LAOs.

Collaborating LAO: LAO involved in the trial that is not the Lead. The Collaborating LAO has oversight responsibilities for its own AOs but not for cross-network administrative aspects of the trial. The Collaborating LAO prepares its own budget but the per subject payment for clinical activities must be consistent with that set by the Lead LAO. The Collaborating LAO submits its budget to DCP starting with the second budget submission.

Entity	Function
NCI/DCP	Sponsor
DMASC	Statistical support and data management
DSMB	Data and safety monitoring
CCSA	Regulatory oversight

Entity	Function
CIRB	IRB of Record
MRI Global	Study agent management and distribution
Protocol PI/Study Chair	Oversight of protocol conduct (Scientific/clinical)
Lead LAO	Overall study management and oversight
Collaborating LAO	Oversight of participating AOs
AOs/Site PIs	Enrollment of participants

Additional details can be found in QKREFGD18 *Roles and Responsibilities for CP-CTNet Cross-Network Trials*.

7. COMMUNICATION PLAN

The communication plan serves as a guide for the study team to reference in addressing various issues and questions arising in the cross-network trials.

Note: The Lead LAO should be copied on all communication to assist in determining patterns, trends, and commonly asked questions.

Condition	Procedure
Clinical protocol-related questions	<ul style="list-style-type: none"> The AOs send the question to their Collaborating LAO. The Collaborating LAO sends the question to the overall study PI and copies the Lead LAO, the DCP Nurse Consultant, and the Medical Monitor/Scientific Lead(s). Once a response is received, the Collaborating LAO responds to the AO. The Lead LAO determines the distribution plan to stakeholders (e.g., Collaborating LAOs, all participating AOs, DMASC, etc.) and distributes the information accordingly. If questions are sent directly to the Lead LAO, then the Lead LAO should determine the response using the same channels as the Collaborating LAO would have used, respond to the AO asking the question, determine the distribution plan to stakeholders, and distribute the information accordingly.
Non-clinical protocol-related questions	<ul style="list-style-type: none"> The AOs send the question to their Collaborating LAO. The Collaborating LAO responds to the question if possible and copies the Lead LAO on the email response. If guidance is needed, the Collaborating LAO sends the question to the Lead LAO and other applicable stakeholders (DMASC, DCP, etc.). Once a response is determined, the Collaborating LAO communicates this to their AO. The Lead LAO determines the distribution plan to stakeholders (e.g., Collaborating LAOs, all participating AOs, DMASC, etc.) and distribute the information accordingly. If questions are sent directly to the Lead LAO, the Lead LAO should refer the questions to the Collaborating LAO(s) unless the answer has already been determined, in which case the Lead LAO should respond to the AO and determine the distribution plan to stakeholders as above.

Condition	Procedure
Regulatory questions	<ul style="list-style-type: none"> • The AOs send the question to their Collaborating LAO. • The Collaborating LAO responds to the question if possible and copies the Lead LAO on email response. • If guidance is needed, the Collaborating LAO sends the question to the Lead LAO and other applicable stakeholders (CCSA, DCP, etc.). • Once a response is determined, the Collaborating LAO communicates this to their AO. • The Lead LAO determines the distribution plan to stakeholders (e.g., Collaborating LAOs, all participating AOs, DMASC, etc.) and distributes information accordingly. • If questions are sent directly to the Lead LAO, the Lead LAO should refer the questions to the Collaborating LAO(s) unless the answer has already been determined, in which case the Lead LAO should respond to the AO and determine the distribution plan to stakeholders as above.
SAEs	<p>The AO sends the SAE to the:</p> <ul style="list-style-type: none"> • Lead LAO • Collaborating LAO • Study PI • DCP Medical Monitor/Scientific Lead/Nurse Consultant • DCP Regulatory Contractor <p>If an SAE meets the definition of an Unanticipated Problem then it needs to be reported to the CIRB. The Study PI, DCP and the Lead LAO should be involved in the discussion regarding any CIRB submissions for Unanticipated Events.</p>
Protocol deviations	<p>Per SOP 02-02 <i>Reporting Protocol Deviations</i>, if a site-specific protocol deviation needs to be reported (an Unanticipated Problem/Potential Non-Compliance) to the CIRB, the AO should notify DCP, the Lead LAO, Collaborating LAO, and Study PI and is responsible for reporting to the CIRB and the local IRB per institutional guidelines. The AO sends the protocol deviation to the:</p> <ul style="list-style-type: none"> • Lead LAO/Collaborating LAO • Per SOP 02-02 <i>Reporting Protocol Deviations</i>, the Administrative LAO review is completed by the Collaborating LAO only. <p>For trial-wide Unanticipated Problem/Potential Serious Non-Compliance, the Lead LAO submits the appropriate CIRB worksheet. After CIRB determination, the Lead LAO shares the trial-wide information with all sites, for local IRB reporting as necessary.</p>
Request for review of new and/or revised study related documents	<ul style="list-style-type: none"> • The AOs send the request to their Collaborating LAO. • The Collaborating LAO sends the request to the Lead LAO for review. • The Lead LAO reviews the request and responds to the Collaborating LAO; the Lead LAO is responsible for revising all study related documents as applicable. • The Lead LAO obtains necessary DCP/CIRB approvals. • The Lead LAO communicates the response across the network.

Condition	Procedure
	<ul style="list-style-type: none"> Site-specific participant facing materials should be submitted to the Collaborating LAO for review and submission to DCP, with a copy to the Lead LAO.

8. DATA AND SAFETY MONITORING

Data and safety monitoring for cross-network trials is provided by the CP-CTNet Cross-Network Trials DSMB established by the NCI/DCP. The DSMB operates under its Charter approved by the NCI/DCP. Reporting for CP-CTNet cross-network trials (that are developed as described in Section 4.1) to the DSMB is prepared by the members of the DMASC Statistical Support Unit. Regardless of whether a cross-network trial is blinded or not, the statistician of record remains blinded to avoid introducing any bias in the trial conduct. For cross-network trials that are developed as described in Section 4.2 and 4.3, the LAO statistician reports to the DSMB during the open session and a designated DMASC statistician reports to the DSMB during the closed session.

9. MATERIAL TRANSFER AGREEMENT (MTA)

In cases where multiple sites are sharing participant specimens, there are multiple testing/analysis sites, and no subcontracts exist between a third-party LAO and the AO, MTA's *may* not be needed if the flow of samples is described in the subcontracts between the LAO and their accruing LAOs and AOs. Protocol and IRB consent forms should also cover specimen management. However, some institutions may still require an MTA, no matter what. The protocol must be attached to the statement of work. Potentially, all specimens are sent to the Lead LAO but, alternatively, in some cases it may be more advantageous to send some or all of the specimens another LAO or AO.

10. REFERENCES

Note: All CP-CTNet SOPs are included in the [CP-CTNet Manual of Standard Operating Procedures \(M-SOP\)](#), which is available on the [CP-CTNet DMASC public website](#).

Document	ID	Location
Algorithm to Assess a Potential Unanticipated Problem	Reference	ncicirb.org
Algorithm to Assess Potential Noncompliance	Reference	ncicirb.org
Reporting Protocol Deviations	SOP 02-02	Program Resources
Roles and Responsibilities for CP-CTNet Cross-Network Trials	QKREFGD18	Program Resources

11. APPENDICES

None