NCI Cancer Prevention Clinical Trials Network

A program of the National Cancer Institute of the National Institutes of Health

CP-CTNetDMASC
Cancer Prevention Clinical Trials Network
Data Management, Auditing, and Statistical Center

CP-CTNET MANUAL OF STANDARD OPERATING PROCEDURES (M-SOP)

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Cancer Prevention Clinical Trials Network (CP-CTNet)
Data Management, Auditing, and Statistical Center (DMASC)
www.cp-ctnet-dmasc.org

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes

7.0	FEB-24-2026	Updated the title page and all included SOPs.
		• SOP 01-01 *Essential Records Submission for Sponsor's Trial Master File*
		  ○ Updates made to align with ICH E6(R3). The requirement for investigators on the cover page of the protocol to maintain an RCR account, the requirement for an LAO Oversight report, and the eDTL option are added. Includes new Site Information Form and Updated DTL information. Updated DMACC to DMASC throughout the document.
		• SOP 01-02 *Study Initiation Meeting*
		  ○ Updated section 6 *Documentation Requirements* to clarify that documented evidence of training should be present for all accruing LAO and AO staff listed on the DTL, regardless of whether they attended or did not attend the original SIM. Updated DMACC to DMASC throughout the document.
		• SOP 01-03 *Accruing LAO and AO Activation*
		  ○ Added section 4 *Required Steps for Study Activation*. Updated section 6 *Confirmation of Accruing LAO or AO Activation* and section 7 *Accruing LAO or AO Activation to a Protocol Amendment* to highlight that LAOs should maintain confirmation of site activation tracking lists for each accruing LAO and AO. Updated section 7 *Accruing LAO or AO Activation to a Protocol Amendment* to clarify LAO responsibilities when a protocol amendment is approved after a study is closed to accrual. Updated section 8 *Protocol Training Requirements* to include additional information regarding the use of an email-based documentation method and the appropriate procedure for accruing LAOs and AOs to follow to document an institutional policy on protocol and/or protocol amendment training that differs from the CP-CTNet policy. Updated DMACC to DMASC and the name of SOP 01-01 throughout the document. Made minor editorial updates throughout the document.
		• SOP 02-01 *Reporting Serious Adverse Events*
		  ○ Updated the *DCP Serious Adverse Event Report Form* and the *Serious Adverse Event Report Form: Instructions for Completion and Submission* links to reflect the new URLs. Updated DMACC to DMASC throughout the document.

		• SOP 02-02 Reporting Protocol Deviations Updated Section 4 *Responsibilities for Prompt Reporting of Protocol Deviation*s to include a timeframe for reporting protocol deviations in Medidata Rave and to clarify that LAO Administrative Teams should query the *Minor or Moderate/Major* protocol deviation grade question if the grade provided by the accruing LAO or AO does not align with the protocol deviation grade definitions included in the question's help text. Made updates throughout the document to reflect the updated *CP-CTNet Protocol Deviation Notification* eCRF. Updated DMACC to DMASC throughout the document. • SOP 02-03 *System Variable Attribute Report (SVAR) and Electronic Case Report Form (eCRF) Development* o Updated section 4 *Responsibilities* to remove the DCP Regulatory Contractor from the eCRF Review Team and to add an updated link to more information on CDE standards. Updated DMACC to DMASC throughout the document. • SOP 02-04 *Participant Recruitment, Retention, Adherence, and Reporting Requirements* o Updated DMACC to DMASC throughout the document. • SOP 02-05 *Policy on Standard Operating Procedures* o Updated section 5 *M-SOP*, subsection 3 *M-SOP Training/Sign-off* to clarify that M-SOP training may also be documented using an electronic or paper institutional sign-off log or an email-based documentation method. Additional information regarding the use of an email-based documentation method was added for consistency across LAOs, accruing LAOs, and AOs. Minor editorial updates and clarifications were made throughout the document. Updated DMACC to DMASC throughout the document. • SOP 02-06 *Biospecimen Submission Requirements* o Added clarifying information about submitting biospecimens to DMASC for inclusion in the VSR. Updated DMACC to DMASC and made minor editorial updates throughout the document. • SOP 02-07 *Unblinding Participants* o Updated DMACC to DMASC throughout the document. Updated the name of SOP 04-02 to *Study Closeout* throughout the document. Added a link to v20 of the *DCP CP-CTNet Chemoprevention Protocol Template* in section 7 *References*. • SOP 03-02 *Site Preparations for Quality Assurance Audits* o Updated DMACC to DMASC, essential documents to essential records, and source documents to source records throughout

		the document. Updated the name of SOP 01-01 to *Essential Records Submission for Sponsor's Trial Master File*. • SOP 03-03 *LAO Oversight Activities* o Updated section 4 *LAO Roles and Responsibilities*, subsection 2 *Study Initiation Meetings and Targeted Training of Accruing LAO and AO Staff* to clarify that accruing LAOs and AOs are responsible for tracking the training of the staff at their site. Updated section 4 *LAO Roles and Responsibilities,* subsection 5 *Documentation Requirements* to reference maintaining confirmation of site activation tracking lists for each accruing LAO and AO. Updated section 4 *LAO Roles and Responsibilities,* subsection 6 *Informed Consent Document Review and Confirmation of Eligibility* to clarify that accompanying source documents should be kept with the signed eligibility checklist at the enrolling site. In addition, this subsection was updated to add that the protocol audit risk level is now included in the protocol and that if a protocol deviation is reported for an eligibility violation on a study deemed to be low or intermediate risk, then the LAO must review and confirm eligibility for three additional participants to ensure participant safety. Finally, this subsection was updated to add that the LAO should maintain a tracking sheet documenting their informed consent document reviews and confirmations of eligibility. Updated section 4 *LAO Roles and Responsibilities*, subsection 8 *Study Agent* to include pharmacy oversight activities as per the protocol audit risk level and to provide details on the frequency of review. Updated DMACC to DMASC throughout the document. • SOP 04-01 *Instructions for Accruing LAO and AO Closeout* o Updated DMACC to DMASC, essential documents to essential records, and source documents to source records throughout the document. Updated the name of SOP 01-01 to *Essential Records Submission for Sponsor's Trial Master File*. • SOP 04-02 *Study Closeout* o Updated DMACC to DMASC and source documents to source records throughout the document.
6.0	FEB-21-2025	Updated the title page and SOP 02-04.
5.0	FEB-07-2025	Updated the title page, SOP 01-03, SOP 02-01, SOP 02-02, SOP 02-05, SOP 02-06, SOP 02-07, and SOP 04-01. Added SOP 04-02.
4.0	AUG-13-2024	Updated the title page, SOP 01-01, SOP 01-02, SOP 01-03, SOP 02-03, SOP 02-04, SOP 02-07, SOP 03-02, and SOP 03-03.

3.0	JAN-26-2024	Updated the file format, title page, SOP 01-01, SOP 01-02, SOP 01-03, SOP 02-01, SOP 02-02, SOP 02-04, SOP 02-05, SOP 02-06, SOP 02-07, SOP 03-03, and SOP 04-01.
2.0	JUL-13-2023	Updated the title page, SOP 01-01, SOP 02-03, SOP 02-04, SOP 02-05, and SOP 03-03.
1.0	FEB-21-2023	Original version of document.

TABLE OF CONTENTS

Title: Essential Records Submission for Sponsor’s Trial Master File

Document ID: CP-CTNet SOP 01-01

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REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
10.0	FEB-24-2026	Updates made to align with ICH E6(R3). The requirement for investigators on the cover page of the protocol to maintain an RCR account, the requirement for an LAO Oversight report, and the eDTL option are added. Includes new Site Information Form and updated DTL information. Updated DMACC to DMASC throughout the document.
9.0	AUG-13-2024	The requirement for pharmacists to be added to the DCP DTL has been removed from section 6 *Required Essential Records Guidelines*, subsection 6 *Delegation of Tasks Log*. Review of site essential records is performed by the DCP regulatory contractor annually instead of prior to audit timeline. Minor updates were made throughout the document.
8.0	JAN-26-2024	Added Health Canada requirements. Added requirements for DTL records.
7.0	JUL-13-2023	Clarification on the collection of laboratory records and laboratory certifications for those institutions not certified by CLIA, and clarification on the submission of laboratory normal values.
6.0	FEB-21-2023	Renamed document. Major rewrite of the entire document.
5.0	APR-27-2022	Additional clarification was added regarding RCR and the records collected from RCR. Minor edits were made throughout the document to provide clarification on records collected from LAOs and AOs.
4.0	JAN-25-2022	The required essential site records in section 3 were reordered and updated. Additional clarification was added to the sections on Form FDA 1572 and the DTL.
3.0	SEP-02-2021	Additional information about CTEP-IAM and clarification of DTL requirements.
2.0	JUN-01-2021	DTL changes.
1.0	AUG-17-2020	Original version of the document.

1. INTRODUCTION AND PURPOSE

"The essential records permit and contribute to the evaluation of the conduct of a trial in relation to the compliance of the investigator and sponsor with Good Clinical Practice (GCP) and applicable regulatory requirements and the reliability of the results produced. The essential records are used as part of the investigator oversight and sponsor oversight (including monitoring) of the trial." as per ICH Guideline for Good Clinical Practice E6 (R3). This document provides the essential records requirements for the sponsor's TMF. The records provided by the sites to the DCP Regulatory Contractor should be maintained at each accruing Lead Academic Organization (LAO) and Affiliated Organization (AO) and be available for sponsor audits and inspection by regulatory authorities. Refer to ICH Guideline for Good Clinical Practice E6 (R3) Appendix C, for additional guidance on records that must be maintained by the Investigator Site.

The Cancer Prevention Clinical Trials Network (CP-CTNet) is developed and sponsored by the National Cancer Institute's (NCI's) Division of Cancer Prevention (DCP). CP-CTNet LAOs and AOs are required to prepare, submit, and maintain essential records throughout the duration of each study in accordance with GCP guidelines. Each accruing site must submit the full complement of essential records required for Drug Shipment Authorization (DSA) before it is allowed to open to accrual. Once these records have been received and reviewed, the DCP Regulatory Contractor issues the DSA (accruing sites) or email confirming receipt of required essential records (admin/non-accruing sites).

A number of essential records require updates throughout the course of the study. Refer to the section describing each record to determine if and when submission of updates is required.

The final closeout of the study at each accruing site requires confirmation from the DCP Regulatory Contractor that all essential records are current and complete. All essential records and communication should be maintained at each site during the study and for at least three years after its completion.

2. SCOPE

This document details the submission of essential records required from LAOs and AOs for the sponsor's TMF. The DCP Regulatory Contractor maintains the sponsor's TMF.

3. DEFINITIONS

Term	Definition
A	Associate
AO	Affiliated Organization
AP	Associate Plus
APIW	Annual Principal Investigator Worksheet
ASIW	Annual Signatory Institution Worksheet
CAP	College of American Pathologists
CIRB	Central Institutional Review Board
CITI	Collaborative Institutional Training Initiative
CLIA	Clinical Laboratory Improvement Amendments
CLP	Clinical Laboratory Permit
COR	Contracting Officer Representative
CP-CTNet	Cancer Prevention Clinical Trials Network

Term	Definition
CPC	Cancer Prevention and Control
CRA	Clinical Research Associate
CTEP	Cancer Therapy Evaluation Program
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DO	Doctor of Osteopathic Medicine
DSA	Drug Shipment Authorization
DTL	Delegation of Tasks Log
DTLA	Delegation of Tasks Log Administrator
eDTL	Electronic Delegation of Tasks Log
FDA	Food and Drug Administration
FDF	Financial Disclosure Form
FWA	Federal Wide Assurance
GCP	Good Clinical Practice
H&P	History and Physical
HC	Health Canada
IAM	Identity and Access Management
IB	Investigator's Brochure
ICD	Informed Consent Document
ICH	International Council for Harmonization
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
IVR	Investigator
LAO	Lead Academic Organization
LNV	Laboratory Normal Value
M-SOP	Manual of Standard Operating Procedures
MD	Doctor of Medicine
ML	Medical License
MM	Medical Monitor
NC	Nurse Consultant
NCI	National Cancer Institute
NIH	National Institutes of Health
NP	Nurse Practitioner
NPIVR	Non-Physician Investigator
NTF	Note-to-File
OHRP	Office for Human Research Protections
PA	Physician's Assistant
PhD	Doctor of Philosophy

Term	Definition
PI	Principal Investigator
PIO	Protocol Information Office
QI	Qualified Investigator
RCR	Registration and Credential Repository
RN	Registered Nurse
SIF	Site Information Form
SL	Scientific Lead
SSW	Site Specific Worksheet
TMF	Trial Master File
US	United States

4. REQUIRED ESSENTIAL RECORDS FOR SPONSOR'S TMF

DCP's list of required essential records for the sponsor's Trial Master File (TMF), is provided below, followed by guidelines for completion and submission of each record type.

1. NCI Biosketch*
2. Professional Licensure*
3. GCP Training Certification*
4. Statement of Investigator (Form FDA 1572)*
5. Financial Disclosure Form (FDF)*
6. Site Information Form
7. Delegation of Tasks Log (DTL)
8. Principal Investigator (PI) Acknowledgement of Investigator's Brochure (IB) or Package Insert
9. Office of Human Subject Protections (OHRP) Assurance
10. Current Laboratory Certification
11. Laboratory Normal Values (LNVs)
12. Central Institutional Review Board (CIRB) or Independent Ethics Committee (IEC) Approval
13. Informed Consent Document (ICD)
14. CIRB- or IEC-approved Patient/Recruitment Materials
15. CIRB Annual Signatory Institution Worksheet (ASIW) Approval Letter
16. CIRB Annual Principal Investigator Worksheet (APIW) Approval Letter
17. CIRB Approval of the Site Specific Worksheet (SSW)
18. Local Site IRB Acknowledgements or Approvals (US Sites)
19. Certificates of Translation (if applicable)
20. Conclusion Signature Page

*Records collected from RCR

5. NCI REGISTRATION AND CREDENTIAL REPOSITORY (RCR)

NCI policy requires all persons participating in the conduct of an NCI-sponsored clinical trial to be registered in the NCI Registration and Credential Repository (RCR). Investigators and all study staff listed on the Delegation of Tasks Log (DTL) are required to register. The RCR provides a self-service online person registration application with electronic signature and submission capability. Individuals must use their ID.me credentials to log into the RCR.

1. Individuals registering in the RCR should choose one of the following four registration types depending on their credentials and the task(s) they have been assigned on the DTL:
    1.1 Investigators holding a medical license (MD or DO) register as an Investigator (IVR).
    1.2 Investigators who are advanced practice providers, such as Nurse Practitioners or-Physician Assistants, or graduate level researchers (PhD) without a medical degree register as a Non-Physician Investigator (NPIVR).
    1.3 Clinical site staff (study coordinators, regulatory coordinators, study nurses, data managers, etc.) register as an Associate Plus (AP).
    1.4 Other clinical site staff who are not generating study data or accessing data entry applications may be registered as an Associate (A).
2. All study staff designated must provide the following in the RCR:
    2.1 NCI Biosketch
    2.2 Professional Licensure (e.g., medical and/or nursing), as applicable
    2.3 GCP Training Certification
    2.4 FDF
    2.5 Study staff registered in RCR as **IVR** or **NPIVR** must, in addition, complete a Form FDA 1572

The RCR serves as the official repository for the above records for the DCP Regulatory Contractor and auditors. Study staff must maintain an ACTIVE RCR account status. The RCR is an annual registration, therefore, the ACTIVE or NOT ACTIVE status of the registration determines whether the credentials of the individual are acceptable. To issue the DSA, all staff listed on the DTL must have an ACTIVE status in the RCR and maintain active status throughout the duration of their participation in the study (i.e., until the end date for the staff added to DTL). Failure to maintain an ACTIVE status in the RCR may result in staff suspension in trial participation until RCR status is brought into compliance.

Study staff registered in RCR as 'A' are not required to be added to the DTL. However, if they are added to the DTL, DCP requires them to have proof of GCP training. The GCP training certificate must be provided to the DCP Regulatory Contractor for each 'A' added to the DTL.

Study-level statisticians and investigators listed on the study protocol cover page may not be added to the DTL, however, they must be registered in RCR and should maintain an active account until the study is FDAAA completed or removed from the study protocol cover sheet. The DCP Regulatory Contractor checks for RCR status and downloads the records for the sponsor's record at the time of study initiation and/or at the time of DSA if affiliated to a site, and annually from the date of DSA.

All records downloaded from RCR by the DCP Regulatory Contractor are maintained in the sponsor's TMF. Sites are not required to maintain "shadow" copies of the records uploaded in the RCR in their regulatory binder or submit copies of these records to the DCP Regulatory Contractor or LAO.

6. REQUIRED ESSENTIAL RECORDS GUIDELINES

1. **NCI Biosketch**

   1.1. An NCI Biosketch is required for study staff who participate in the clinical investigation and hold an RCR registration type of IVR, NPIVR, or AP, including international site staff. The purpose of the NCI Biosketch is to document that the individual who is assigned a task on the DTL is qualified by training, experience, and/or education to perform their assigned task(s).

   1.2 The NCI Biosketch should display the study staff's current affiliation and dates of involvement with the institution.

2. **Professional Licensure**

   2.1. Each study staff member listed on the DTL who holds a professional license (e.g., MD, DO, RN, NP, PA, etc.) and holds an RCR registration type as IVR, NPIVR, or AP should update their license information in RCR. A controlled substance license is not an accepted form of professional licensure.

   2.2. The DCP Regulatory Contractor downloads the professional licensure from the RCR when staff is added to the DTL and the renewed license for the duration of staff participation in the study (i.e., until the end date specified on the DTL).

3. **GCP Training Certification**

   3.1. GCP training certification is required for all personnel listed on the DTL.

   3.2. A GCP training certificate must be uploaded into the RCR for those who hold an RCR registration type of IVR, NPIVR, or AP. For 'A' registration type, a GCP training certificate must be provided to the DCP Regulatory Contractor separately via email, if not uploaded in RCR.

   3.3. Collaborative Institutional Training Initiative (CITI) GCP training comes in two versions, FDA and ICH. The FDA version is preferred, though the ICH version is also acceptable.

   3.4. GCP training certification from NIH, TransCelerate GCP Mutual Recognition Program, or the staff member's own institution is acceptable.

   3.5. Expiration of GCP training certification is based on the training provider/institution.

   3.6. The DCP Regulatory Contractor downloads the GCP training certificate from the RCR when a staff member is added to the DTL and the renewed certificates for the duration of staff participation in the study (i.e., until the end date specified on the DTL).

4. **Statement of Investigator (Form FDA 1572)**

   4.1. DCP requires all investigators (IVR and NPIVR) conducting clinical investigations to complete Form FDA 1572 within the RCR and to provide accurate and current information. Form FDA 1572 provides documentation of Principal Investigator (PI) oversight; therefore, a Protocol Signature Page or PI Statement of Responsibility is not needed.

   4.2. Instructions for the completion of Form FDA 1572 are provided in the RCR. Of note for Cancer Prevention Clinical Trials Network (CP-CTNet) studies:

- **Section 5:** NCI's Cancer Prevention and Control (CPC) Central IRB (CIRB) is the IRB of record for LAO and AO sites in the US and its territories (e.g., Puerto Rico) and should be included in this section. For international sites, the name and address of their Independent Ethics Committee (IEC) or equivalent should be included instead.

4.3. The DCP Regulatory Contractor downloads Form FDA 1572 from the RCR for all IVR and NPIVR staff listed on the DTL and as necessary for Food and Drug Administration (FDA) submissions.

4.4. If an investigator at an international site cannot submit the Form FDA 1572, an agreement equivalent to the Form FDA 1572 is required to be submitted. For studies conducted under a DCP-held Investigational New Drug (IND), an approved waiver from the FDA, submitted to the FDA by the DCP Regulatory Contractor, is also required.

5. **Financial Disclosure Form (FDF)**

5.1. The FDF must be signed and dated electronically by staff who hold an RCR registration type of IVR, NPIVR, or AP and are listed on the DTL.

5.2. If any financial interests are indicated, they should be disclosed on the FDF in the RCR.

5.3. The DCP Regulatory Contractor downloads the FDF from the RCR. The FDF is reviewed in the RCR by the DCP Regulatory Contractor annually from the date of DSA. The FDF is downloaded if any changes are made.

5.4. The downloaded FDF is reviewed by DCP for conflict of interest. If any potential conflict is identified, DCP discusses it with the LAO.

6. **Site Information Form**

6.1. The Site Information Form (SIF) captures the study-specific information, such as protocol details, the site location(s) where the study will be conducted, labs used for the study, IRB of record, and DSA information. The form must be completed and submitted to the DCP Regulatory Contractor for sponsor records to obtain DSA.

6.2. When a protocol has received DCP 'Approval on Hold,' the DCP Regulatory Contractor will complete the 'Protocol information,' 'Site Principal Investigator Information' as provided in the protocol, and 'IRB of Record (for US sites)' and provide the form to the LAO for distribution to the respective sites.

6.3. The Site PI signs the form at the time of study initiation and when there is an update.

6.4. The site must maintain the form current until the study is closed at the site. Updated forms must be submitted to the DCP Regulatory Contractor. They will review and maintain the form for sponsor records.

6.5. For IND studies, at least one of the research sites listed under Site Information, IRB of Record, and Laboratory Information should match the LAO PI and site PI's Form FDA 1572.

6.6. The Laboratory Information on SIF should be verifiable. It is highly recommended to match the laboratory name and the address on the SIF as it is provided on the CLIA (US laboratories using CLIA) or laboratory certificate.

6.7. When a laboratory is no longer in use for the study, the SIF must be updated with the laboratory's end date and submitted to the DCP Regulatory Contractor. No further updated records are required for the laboratory after the end date is added.

6.8. When there is an update to the DSA address, MRIGlobal (if necessary) will be notified by the DCP Regulatory Contractor.

7. **Delegation of Tasks Log (DTL)**

7.1. The DTL is the primary source for tracking staff who perform study-related duties. All study staff members, including the PI, who are registered as IVR, NPIVR, AP, and A, are to be listed on the DTL. The site can choose to add all staff to the same page of DTL or add one staff per page of the DTL.

- Sites can choose to use the Electronic Delegation of Tasks Log (eDTL) of their choice, provided they can provide all the necessary information and utilize the task codes on the DCP DTL. The DTL must be maintained and current. Sites using an eDTL must ensure that the signature platform is 21 CFR Part 11 compliant at all times. When providing an eDTL to the DCP Regulatory Contractor, sites should provide an audit trail, if applicable.

7.2. Once a protocol has received DCP "Approval on Hold" status, the LAO can provide the accruing LAO or AO's DTL to the DCP Regulatory Contractor for review. A copy of the finalized DTL will be saved in the sponsor's record.

7.3. The study staff's first and last name, CTEP Person ID, and tasks on the DTL must align with the individual's RCR registration. Tasks assigned to study staff must be appropriate for their level of training and qualifications.

7.4. Tasks assigned to study staff listed on the DTL should be indicated as described below:

Agent/Intervention Prescribing	Primary Study/Site Contact
Site Principal Investigator	Rave CRA
Consenting Person	Rave Investigator
DTL Administrator (DTLA)	Regulatory Contact
Eligibility Assessments	RT/Imaging Support
End Point Assessments	Source Documentation Completion
Enrolling Person/Treating Investigator	Study-related Interventions
History and Physical (H&P) Assessments	Toxicity Assessment
Investigational Product Accountability	Unblinded Study Personnel
Pathology Laboratory Support	Other (Specify)
Patient Screening/Recruiting	

7.5. Unblinded Study Personnel are required to be assigned only for blinded studies. When this task is assigned, a plan or SOP should be in place at the site that articulates the steps to be followed to prevent possible unblinding to others. This must be included in the site's TMF and need not be provided to the DCP Regulatory Contractor.

7.6. Only one site PI can be assigned at each site.

Note: For sites in Canada, if the QI is not the same person as the PI, both the QI and PI are required to sign the DTL and conclusion page.

7.7. Assignment Minimum as specified on the *Delegation of Task Log (DTL) Master Task List* must be met for the site to receive DSA.

7.8. Study staff performing non-protocol-specific research (e.g., biomarker analysis, gene expression, etc.) are not required to be added to the DTL. Examples include nurses, residents, pharmacists, fellows, and office staff who provide only ancillary or intermittent care. No essential records are collected for these staff.

Note: DCP does not require pharmacists to be added to the DCP DTL. A site can add pharmacists to the DTL based on their preference or policy. When added to the DCP DTL, pharmacists must register in the RCR, and based on the type of registration, records are collected from the RCR and saved for the sponsor's TMF.

7.9. The DTL must be signed by each study staff member next to their designated task codes, and the site PI. The site PI's signature or initials acknowledging the staff member's role may not precede the staff member's signature date. The end date for the performance of the tasks should be entered when the staff member leaves the study.

7.10. The DTL can be signed electronically (preferred) or with wet ink and then scanned. The signed DTL provided to the DCP Regulatory Contractor need not be original. The signature must be 21 CFR Part 11 compliant.

7.11. LAOs provide the DTLs to the DCP Regulatory Contractor, who reviews and maintains the records for the sponsor's record. The DCP Regulatory Contractor sends the signed DTL to the Data Management, Auditing, and Statistical Center (DMASC) when DSA is issued for a site.

8. **PI Acknowledgement of IB or Package Insert**

8.1. The DCP Regulatory contractor provides the IB or Package Insert acknowledgement form to the LAO.

8.2. The LAO, accruing LAO, and AO PIs must sign the acknowledgement form provided by the DCP Regulatory Contractor, stating that he/she has reviewed each version of the IB or package insert provided for each agent under investigation in the study.

8.3. LAOs provide the signed acknowledgement form to the DCP Regulatory Contractor, who reviews and maintains the record for the sponsor's TMF.

9. **OHRP Assurance**

9.1. All sites participating in federally funded studies are required to have Federal-wide Assurance (FWA).

9.2. LAOs provide the OHRP assurance for the site to the DCP Regulatory Contractor, who reviews and maintains the record for the sponsor's TMF.

10. **Laboratory Certification**

10.1. CLIA and CAP certification for laboratories in the US is highly recommended. When CLIA and or CAP are not available, state licenses or other recognized certificates (e.g., Joint Accreditation, COLA) are acceptable. At least one certificate is required to be provided for a laboratory. If there are no certificates available (e.g., research laboratories), an NTF confirming the same is required on the institutional letterhead signed and dated by site staff.

10.2. For international laboratories, when CLIA/CAP is not available, provide certification pertinent to the country or state.

10.3. LAOs provide a copy of the certification(s) to the DCP Regulatory Contractor, who reviews and maintains the record for the sponsor's TMF.

- Current CLIA Certification
- Current CAP Certification
    - The laboratory name on the CAP certificate does not always match that on the CLIA certificate; however, the CLIA number should match.
    - If a renewed CAP certificate is not available, a CAP extension letter provided by the laboratory is acceptable.

11. **Laboratory Normal Values (LNVs)**

11.1. A set of LNVs is required for each laboratory listed on SIF. The LNVs should be current.

11.2. The laboratory for which LNVs are provided should be uniquely identifiable with the information provided on the document such as laboratory name, address, CLIA number, or any other unique identifiable local laboratory certification number.

11.3. An NTF specifying the location of the LNVs where the ranges can be found is acceptable instead of a full list of LNVs. The laboratory in reference should be uniquely identifiable with the information provided on the document such as laboratory name, address, CLIA number, etc. The NTF must be signed and dated.

11.4. LAOs provide the LNVs and/or NTF to the DCP Regulatory Contractor, who reviews and maintains the record for the sponsor's TMF.

12. **CIRB or IEC Approval**

12.1. CIRB approval of the protocol is required; this is obtained from the DCP Protocol Information Office (PIO).

12.2. For international sites, protocol approval, and annual review approval, if applicable, are required from the IEC or equivalent only. The exception is for sites in US territories (e.g., Puerto Rico), which are overseen by the CIRB.

13. **Informed Consent Document (ICD)**

13.1. CIRB (or IEC or equivalent for international sites) approval must be provided for each ICD. The ICD version on the form must match the approval memo.

13.2. The CIRB approved version of the ICD template is provided to sites. The sites (within US and US territories) incorporate the boilerplate language and formatting (including any local IRB approval stamps, if required) from their institution's own CIRB ASIW approval letter, CIRB SSW, and/or CIRB APIW approval letter into the CIRB approved template to create their own "localized version" of the ICD. This localized version is the one that must be used for participant enrollment. A copy of the localized version of the ICD (including any versions translated into another language) must be provided to the DCP Regulatory Contractor for review and approval for site to obtain DSA. The subsequent versions of ICD provided to the DCP Regulatory contractor post-DSA are not reviewed. The LAO is responsible for reviewing the local ICD to ensure that it is consistent with the approved CIRB template and any approved boilerplate language.

13.3. The localized version of the ICD may require local IRB approval. Each institution has individual guidelines for versioning IRB submissions for local review. If required by the local IRB, the localized ICD version and date may be included in addition to the ICD template version and date.

13.4. If the institution has an approval stamp, the ICD with the incorporated template language should be stamped and provided to the DCP Regulatory Contractor.

13.5. CIRB template of short form consents need not be provided to the DCP Regulatory Contractor.

13.6. International sites make necessary changes to the CIRB approved ICD template as per local requirements and must provide the IEC or equivalent approved localized ICD to the DCP Regulatory Contractor.

13.7. During the course of the study, localized versions of ICD amendments (including all applicable translations) must be provided to the DCP Regulatory Contractor who maintains the document for the sponsor's record.

Note: A stand-alone HIPAA document need not be provided to the DCP Regulatory Contractor.

14. **CIRB- or IEC-approved Site-Specific Patient/Recruitment Materials**

14.1. DCP obtains approval for all study-level Participant/Recruitment Materials, and they are provided to the DCP Regulatory Contractor, LAO, and AO by the DCP PIO.

14.2. CIRB (or IEC or equivalent for international sites) approval must be provided for any site (LAO/AO) specific patient/recruitment materials (drug diaries, quality of life questionnaires, local advertising, etc.) for sites in the US and its territories.

14.3. The patient/recruitment materials version should match the approval memo.

14.4. Some sites utilize a local version of the patient/recruitment materials. The modified document (and any translated versions of the document) should be sent to the LAO for submission to the DCP. Once DCP approval is obtained, the document (and any translations) is submitted to the CIRB for review/approval via the SSW. Submit any modified records to the DCP Regulatory Contractor who maintains the records for the sponsor's TMF.

Note: Information sheets provided to participants, which are not specific to the study, do not require DCP or CIRB review and approval.

14.5. The patient/recruitment material version and date may be included if approved as part of the institution's boilerplate language. The date may be a different date than the version date on the CIRB-approved document, as each institution has individual guidelines for versioning IRB submissions.

15. **Other CIRB Approvals**

15.1. The CIRB ASIW and APIW approval letters must be provided to the DCP Regulatory Contractor to issue the DSA. During the course of the study, all ASIW amendments approved by the CIRB must be provided to the DCP Regulatory Contractor for the sponsor's record.

15.2. When a site PI changes, CIRB approval letter of the PI must be provided to the DCP Regulatory Contractor

15.3. The CIRB approval of the SSW for the study must be provided to the DCP Regulatory Contractor when the LAO obtains it for the sponsor's record. This approval letter is not required for DSA. Any document approved with the SSW must be provided to the DCP Regulatory Contractor for the sponsor's TMF.

16. **Local Site IRB Acknowledgement or Approvals (US Sites)**

16.1. According to CIRB policies and procedures, the local IRBs in the US give authority to the CIRB for review and approval of protocols. The collection of any local IRB acknowledgement letters for those sites that produce them is managed by the LAOs.

16.2. All approvals and/or acknowledgments issued by the local IRB must be provided to the DCP Regulatory Contractor.

16.3. IRB acknowledgment or approval of protocol and ICD must include the version number in the letter. If information is not provided in the letter, the site must confirm the version date.

17. **Certificates of Translation**

17.1. Certificates of translation should be provided for ICDs, IRB or IEC approvals, patient/ recruitment materials, or any other documents that are translated from one language to another.

17.2. An NTF attesting to the accuracy and completeness of the translated document, with information about the person who translated the document, can be submitted in lieu of certificates of translation. This document must be signed by either the translator or the site PI.

7. LAO, AO, AND THE DCP REGULATORY CONTRACTOR RESPONSIBILITIES

1. **Records Submission for DSA**

1.1. Check Appendix I *DSA Records Checklist* on the list of records that must be submitted to the DCP Regulatory Contractor to obtain DSA for a site.

1.2. Prior to forwarding essential records to the LAO, an inspection of materials by the AO is recommended to reduce the submission of expired, illegible, and invalid records.

1.3. Upon receipt from the AO, the LAO should forward the essential records to the DCP Regulatory Contractor, who conducts a full quality review based on the criteria for each record type described in section 6 of this document. As detailed above, except for records downloaded from the RCR by the DCP Regulatory Contractor, all other essential records should be submitted to the DCP Regulatory Contractor in electronic format at regulatory@ccsainc.com.

1.4. Upon receipt of essential records, the DCP Regulatory Contractor confirms that each investigator providing a Form FDA 1572 is not listed on the FDA Disqualification Proceedings and Warning Letters websites.

- FDA Disqualification Proceedings
- Warning Letters

1.5. If an investigator is listed on either website, he/she may not participate in the study.

1.6. The DCP Regulatory Contractor requests the LAO to communicate any quality review comments and/or requests for revised records to the submitting AO.

1.7. When all essential records for the sponsor's TMF have been received, reviewed, and approved, the DCP Regulatory Contractor emails a DSA to the DCP PIO Office, LAO, AO, Medical Monitor (MM), Scientific Monitor (SM), Nurse Consultant (NC), Scientific Lead (SL), DMASC, and drug distributor (e.g., NCI repository contractor).

2. Records Submission for Non-Accruing and Administrative Sites

2.1. The following essential records are required for non-accruing and administrative site activation, if applicable:

- PI's Form FDA 1572, NCI Biosketch, professional licensure, GCP training certification, and FDF.
- PI's acknowledgement of IB or package insert.
- OHRP assurance.
- CIRB or IEC approval of the protocol (no ICD).

2.2. As detailed above, except for records downloaded from the RCR by the DCP Regulatory Contractor, all other essential records should be submitted to the DCP Regulatory Contractor in electronic format at regulatory@ccsainc.com.

2.3. The DCP Regulatory Contractor will send a confirmation email to the DCP PIO confirming receipt of all essential records for the non-accruing or administrative site.

3. Records Submission During Course of Study

3.1. Each LAO and AO is responsible for submitting updated essential records throughout the duration of the study, except for records that are downloaded from the RCR. Records must be maintained current until the study at the site is closed with the CIRB or ethics committee that has oversight. All updated records should be forwarded to the DCP Regulatory Contractor.

3.2. **Canadian sites**: Post-DSA, prior to activation of all protocol amendments, the LAO must confirm with the DCP Regulatory Contractor if the protocol amendment can be activated at the site(s).

3.3. After the DSA is issued for a site, the DCP Regulatory Contractor performs the review of staff RCR status and essential records within 30 days of the DSA anniversary date (one year from the DSA issuance date or when the notification was sent, all Essential records were received by the DCP Regulatory Contractor for the administrative site or site participating in studies without agents). LAO is notified of the list of outstanding records and staff who have inactive RCR status.

3.4. The LAO should respond to the outstanding records within 30 days of receipt. A comprehensive report on the LAO/AO response rate to the annual essential record review will be provided by the DCP Regulatory Contractor prior to the DMASC LAO oversight audit. The report will be provided to the LAO PI, the LAO lead coordinator/contact and the DMASC audit team.

3.5. The following essential records require submission of updated versions to the DCP Regulatory Contractor:

- Site Information Form.
- DTL.

- OHRP assurance.
- Laboratory Certification.*
- LNVs, when updated.*
- CIRB or IEC approval of the protocol (including any amendments), ICD, and participant/recruitment materials.
- Local IRB approval or acknowledgement, if applicable.

*Laboratory certifications and LNVs need to be provided while the laboratory is in use for the study.

3.6 DTL Updates

- A DTL must be updated when there are updates to site information, laboratory information, drug shipment address, study staff, task assignment, or the role of study staff. The DCP Regulatory Contractor must be informed of any updates made to the DTL, and a copy of the DTL must be provided to the DCP Regulatory Contractor, who reviews and maintains the document for the sponsor's record.
- If an individual site study staff member no longer performs study-related tasks, the end date can be added to the DTL for that staff. The updated DTL is submitted to the DCP Regulatory Contractor. No further updated records are required for the staff after the end date is added to the DTL. RCR registration must be maintained ACTIVE by staff until the end date specified on the DTL.

4. Records Submission at the End of Study

4.1. Conclusion Signature Page must be signed by the site PI when all study activities at the site are complete.

8. REPOSITORY

1. DCP uses SharePoint to store all Essential records. Records collected from sites are stored in the CP-CTNet library. All records finalized by the DCP Regulatory Contractor up to two weeks prior to the audit must be available at the time of the audit.

9. ADDITIONAL INFORMATION

Please send questions and comments to regulatory@ccsainc.com.

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.

Resource	ID	Location
CTEP Identity and Access Management	Application	CTEPcore.nci.nih.gov
DCP CP-CTNet Conclusion Signature Page	Form	Program Resources
DCP CP-CTNet Site Information Form	Form	Program Resources
DCP Delegation of Tasks Log	Form	Program Resources
DCP Delegation Task Log Master Task List	Reference	Program Resources

Resource	ID	Location
FDA Disqualification Proceedings	Reference	Accessdata.fda.gov
Guideline for Good Clinical Practice E6 (R3)	E6(R3)	ICH.org
NCI Registration and Credential Repository	Application	CTEPcore.nci.nih.gov
OHRP Website	Reference	OHRP.cit.nih.gov
Warning Letters	Reference	FDA.gov

11. APPENDICES

1. Appendix I: DSA Records Checklist

Appendix I

DSA Records checklist

Records to be provided to the DCP Regulatory Contractor to obtain DSA for a site.

☐ Signed DTL.

☐ Site Information Form

☐ Staff listed on DTL must have active RCR registration.

☐ LAO PI signed IB/PI Acknowledgement Form (if not already provided for study).

☐ PI signed IB/PI Acknowledgment Form.

☐ Current Laboratory Certifications for all laboratories added to the DTL.

☐ Current LNV for all laboratories added to the DTL.

☐ Federal Wide Assurance (OHRP).

☐ Local ICD (including other languages).

☐ Local IRB letters (if applicable).

☐ Site Specific or stamped by local IRB Patient/Recruitment Materials (if applicable).

☐ CIRB ASIW.

☐ CIRB APIW.

☐ Certificate of Translation (if appliable).

Title: Study Initiation Meeting

Document ID: CP-CTNet SOP 01-02

Version: 7.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
7.0	FEB-24-2026	Updated section 6 *Documentation Requirements* to clarify that documented evidence of training should be present for all accruing LAO and AO staff listed on the DTL, regardless of whether they attended or did not attend the original SIM. Updated DMACC to DMASC throughout the document.
6.0	AUG-13-2024	Added a reference and link to section 6 *Documentation Requirements* in section 7 *SIMs for New Accruing LAOs or AOs Added to Existing Studies*. This clarifies that the documentation requirements for the original SIM apply to any SIM(s) for new accruing LAO(s) or AO(s) added to an existing study, which must be available for review during DMACC quality assurance audits. Made minor updates throughout document.
5.0	JAN-26-2024	Replaced references to sites with accruing LAOs and AOs and added references to the *CP-CTNet Study Initiation Meeting Agenda Template*. Made minor updates throughout document.
4.0	FEB-21-2023	Added a section about study initiation meetings for new sites that are added to existing studies.
3.0	JUL-18-2022	Updated the DMACC role and contact information for scheduling and conducting study initiation meetings, added references to accruing LAOs, and made minor updates throughout document.
2.0	SEP-13-2021	Updated the action item documentation procedure and added a section about storing and sharing the study initiation meeting recording.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

It is the Lead Academic Organization's (LAO's) responsibility to conduct the study initiation meeting (SIM). The purpose of the SIM is to meet with key staff from each accruing LAO and Affiliated Organization (AO) who will conduct the study, Division of Cancer Prevention (DCP) staff, and Data Management, Auditing, and Statistical Center (DMASC) staff. This meeting provides an opportunity to:

1. Provide an orientation to the study and review study-specific details (e.g., the procedures for investigational agent management, reporting requirements, and data and specimen management).
2. Confirm all roles, responsibilities, and performance expectations.
3. Highlight that the following items need to occur before each accruing LAO and AO may begin enrolling participants:
    3.1. Staff at each accruing LAO and AO have received the required access and training for DMASC systems (e.g., Medidata Rave, Stars, etc.).
    3.2. All regulatory requirements have been completed for each accruing LAO and AO.
    3.3. Each accruing LAO and AO has met all other accruing LAO or AO activation requirements as per SOP 01-03 *Accruing LAO and AO Activation*.

2. SCOPE

This document details the responsibilities of the LAO Investigators, LAO Coordinators, and their designees regarding the SIM.

3. DEFINITIONS

Term	Definition
AO	Affiliated Organization
CIRB	Central Institutional Review Board
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DTL	Delegation of Tasks Log
LAO	Lead Academic Organization
M-SOP	Manual of Standard Operating Procedures
MM	Medical Monitor
NC	Nurse Consultant
NCI	National Cancer Institute
SIM	Study Initiation Meeting
SL	Scientific Lead

4. ROLES AND RESPONSIBILITIES

1. The LAO Investigator, LAO Coordinator, and/or their designee(s) are responsible for conducting the SIM for each study.
2. Key staff members from each accruing LAO and AO are responsible for attending the SIM before consenting or enrolling participants.

5. PROCEDURES

The LAO Investigator, LAO Coordinator, and/or their designee(s):

1. Schedule the SIM:
    1.1. The meeting is typically scheduled after:
        - DCP issues a "Notice of Study Approved on Hold" letter to the LAO; and
        - The NCI CIRB has approved the protocol.
    1.2. The meeting is scheduled as close to the anticipated study activation date as possible.
    1.3. The meeting may be held at the LAO institution, accruing LAO or AO institution, other location, or remotely. If held onsite, remote conferencing for participants unable to attend in person is scheduled.
    1.4. The meeting is typically scheduled for a two- to three-hour time period.
    1.5. Schedule a meeting date that is mutually convenient for LAO staff, key staff from each accruing LAO and AO, DCP staff, and DMASC staff. Consider the following list of staff from the LAO, each accruing LAO and AO (as applicable to the study), DCP, and DMASC:
        - Investigator(s)
        - LAO Coordinator(s)
        - Accruing LAO and AO Coordinator(s)
        - Study Pathologist(s)
        - Study Statistician(s)
        - Study Pharmacist(s)
        - Data Management team
        - Other staff with study responsibilities, such as key laboratory staff
        - DCP MM, SL, NC, and other representatives
        - DMASC staff (via DMASC_SIM_CP-CTNet@frontierscience.org)

          Note: If there are many accruing LAOs and AOs participating in a study, separate SIMs may need to be conducted to accommodate all accruing LAO and AO staff. If separate SIMs are not feasible, access to a recording of the original SIM is provided to staff from accruing LAOs and AOs who are unable to attend or whose accruing LAO or AO is added as a new enrolling institution at a later date.
    1.6. Send an email confirmation of the meeting date to all participants.

2. Prepare for the SIM:

    2.1. Prepare an agenda prior to the meeting that outlines all relevant discussion topics and designates a facilitator for each topic. Refer to the *CP-CTNet Study Initiation Meeting Agenda Template* and the CP-CTNet TMPL02 *Study Initiation Meeting Report* to review the list of topics that may be applicable.

    - DMASC participates in the preparation process for each SIM by working with the LAO Coordinator to develop a study-specific training topic list. DMASC provides training during the SIM based on the DMASC responsibilities outlined in the CP-CTNet TMPL02 *Study Initiation Meeting Report Template*. The LAO coordinates with DMASC (via DMASC_SIM_CP-CTNet@frontierscience.org) before scheduling the SIM to ensure that DMASC trainers are available to present at the SIM.

    2.2. Prepare meeting materials and distribute them to participants.

    2.3. Confirm with the DCP Regulatory Contractor (via regulatory@ccsainc.com) that all or most of the essential records are on file and complete for each accruing LAO and AO.

3. Conduct the SIM:

    3.1. Complete an attendance record to document the name, institutional affiliation, and study role for all meeting participants. Maintain the original attendance record in the LAO essential records file and provide a copy to accruing LAO and AO staff for their records.

    3.2. Record the meeting.

    - Store the SIM recording on a preferred secure internal storage system.
    - Share the SIM recording with the accruing LAOs and AOs, DCP, and DMASC.
    - Share the SIM recording with relevant LAO and/or accruing LAO and AO staff who missed the original SIM (e.g., due to scheduling conflicts, new accruing LAO or AO staff added after the SIM was conducted, etc.).

    3.3. Document items that are identified as action items or that require follow-up.

    3.4. Review the action items with the meeting participants prior to concluding the meeting.

    3.5. Complete the *CP-CTNet Study Initiation Meeting Report*, including a description of action items.

    - Distribute the completed report via email to the accruing LAOs and AOs, DCP, and DMASC within 15 business days of the meeting.

      Note: If accruing LAO or AO follow-up of action items is required, the updated CP-CTNet TMPL02 *Study Initiation Meeting Report* with the follow-up items addressed must be returned to the LAO Coordinator within 30 business days upon receipt of the completed report.

    - Document the resolution of all action items in the CP-CTNet TMPL02 *Study Initiation Meeting Report* prior to participant enrollment and forward the updated CP-CTNet TMPL02 *Study Initiation Meeting Report* to the accruing LAOs and AOs, DCP, and DMASC.

4. Maintain an attendance record for LAO and/or accruing LAO and AO staff who reviewed and signed off on the training included in the SIM. The DMASC Audit team verifies that the appropriate documentation for SIMs is available during DMASC quality assurance audits.

6. DOCUMENTATION REQUIREMENTS

The LAO is responsible for maintaining the following documentation related to the SIM: attendance record, meeting agenda, *CP-CTNet Study Initiation Meeting Report*, SIM recording, and any other related communications (e.g., resolution of action items). This documentation must be readily accessible and may be requested by DCP, the DCP Regulatory Contractor, and/or the DMASC Audit team at any time during the duration of the study. The accruing LAOs and AOs must file the completed CP-CTNet TMPL02 *Study Initiation Meeting Report* in their essential records file.

Note: Documented evidence of training should be present for all accruing LAO and AO staff listed on the DTL. This includes staff that attended the SIM, as well as staff that did not attend the SIM. Accruing LAO and AO staff that did not attend the SIM should contact their LAO to determine the acceptable training methods for the given study (e.g., a documented review of the original SIM recording, self-training, etc.),

7. SIMS FOR NEW ACCRUING LAOS OR AOS ADDED TO EXISTING STUDIES

The LAO is responsible for determining the best way to convey important SIM information to accruing LAOs or AOs that are added to a study after the initial SIM is conducted. The LAO considers the training needs of each new accruing LAO or AO while determining the agenda and format for conveying this SIM information (e.g., via a full-length SIM, an abbreviated SIM with limited presenters and presentations, a documented review of the original SIM recording, etc.). The DMASC Audit team verifies that the appropriate documentation (as outlined in section 6 *Documentation Requirements*) for SIMs for new accruing LAOs or AOs added to an existing study is available during DMASC quality assurance audits.

8. ADDITIONAL INFORMATION

Please send questions and comments to DMASC_SIM_CP-CTNet@frontierscience.org.

9. 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.

Resource	ID	Location
CP-CTNet Study Initiation Meeting Agenda Template	Template	Program Resources
CP-CTNet Study Initiation Meeting Report Template	TMPL02	Program Resources
Accruing LAO and AO Activation	SOP 01-03	Program Resources

10. APPENDICES

1. None

Title: Accruing LAO and AO Activation

Document ID: CP-CTNet SOP 01-03

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REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
7.0	FEB-24-2026	Added section 4 *Required Steps for Study Activation.* Updated section 6 *Confirmation of Accruing LAO or AO Activation* and section 7 *Accruing LAO or AO Activation to a Protocol Amendment* to highlight that LAOs should maintain confirmation of site activation tracking lists for each accruing LAO and AO. Updated section 7 *Accruing LAO or AO Activation to a Protocol Amendment* to clarify LAO responsibilities when a protocol amendment is approved after a study is closed to accrual. Updated section 8 *Protocol Training Requirements* to include additional information regarding the use of an email-based documentation method and the appropriate procedure for accruing LAOs and AOs to follow to document an institutional policy on protocol and/or protocol amendment training that differs from the CP-CTNet policy. Updated DMACC to DMASC and the name of SOP 01-01 throughout the document. Made minor editorial updates throughout the document.
6.0	FEB-07-2025	Updated section 6 *Accruing LAO or AO Activation to a Protocol Amendment* to highlight that a protocol deviation must be completed if a participant is not enrolled to the same protocol version they are consented to. Added section 7 *Protocol Training Requirements*. Made minor editorial updates throughout the document.
5.0	AUG-13-2024	Updated section 6 *Accruing LAO or AO Activation to a Protocol Amendment* to reflect the updated protocol amendment implementation process for CP-CTNet studies. The updates indicate that (1) LAOs should not send a protocol amendment to the accruing LAOs and AOs until it has been implemented in the database, which is confirmed by DMACC via email, (2) accruing LAOs and AOs cannot enroll any participants to a protocol amendment until their site receives notification from DMACC, and (3) participants must be enrolled in Stars to the same protocol version that they are consented to.
4.0	JAN-26-2024	Updated the document to clarify the approval and document submission requirements for accruing LAO and AO activation. Replaced the term "site" with “accruing LAOs and AOs” (as appropriate) throughout the document.
3.0	FEB-21-2023	Added section 3 Definitions and updates to procedures throughout document.
2.0	JAN-06-2022	Major rewrite of entire SOP.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

The purpose of this document is to provide accruing Lead Academic Organization (LAO) and Affiliated Organization (AO) activation requirements for Cancer Prevention Clinical Trials Network (CP-CTNet) studies. Accruing LAO or AO activation means an accruing LAO or AO can enroll participants and enter data for a given study.

The following must be in place for an accruing LAO or AO to be activated to a study:

1. The study has received final approval from the Division of Cancer Prevention (DCP).
2. The study setup in the Medidata Rave Electronic Data Capture (EDC) system is completed by the Data Management, Auditing, and Statistical Center (DMASC).
3. The study implementation in the Stars registration/randomization system has been completed by DMASC. Stars is the web-based enrollment system hosted at DMASC and is used to pre-screen, screen, and enroll participants to a study.
4. The LAO has confirmed to DMASC that the accruing LAO or AO has met all accruing LAO and AO activation requirements (refer to CHK001 *CP-CTNet Accruing LAO and AO Activation Checklist for LAOs* for additional information).

The steps for activating an accruing LAO or AO can begin prior to database and systems setup being completed by DMASC. Each accruing LAO and AO must meet several requirements, including receipt of local Institutional Review Board (IRB) acknowledgement, submission of documents to the DCP Regulatory Contractor, registration of appropriate staff to the National Cancer Institute (NCI) Registration and Credential Repository (RCR), etc. (refer to SOP 01-01 *Essential Records Submission for Sponsor's Trial Master File* for additional information). The accruing LAO's or AO's site open date (site activation date) is the date that DMASC sends a ***Confirmation of Site Activation*** email to the LAO, the accruing LAO or AO, the DCP Study Team (Medical Monitor (MM), Nurse Consultant (NC), and Scientific Lead (SL)), the DCP Regulatory Contractor, and DCP PIO. If multiple accruing LAOs and/or AOs are participating in a study, each accruing LAO and/or AO may have a different site open date, depending on when requirements are met.

LAOs are responsible for study oversight, including conducting Study Initiation Meeting(s) (SIM(s)), assisting accruing LAOs and AOs with meeting all regulatory and documentation requirements before activation at their accruing LAO or AO, and informing DMASC when an accruing LAO or AO meets all requirements for activation.

2. SCOPE

This document details the requirements and steps for LAOs, accruing LAOs and AOs, and DMASC that must be completed before activating an accruing LAO or AO to begin enrollment onto a study.

3. DEFINITIONS

Term	Definition
AO	Affiliated Organization
CIRB	Central Institutional Review Board
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DSA	Drug Shipment Authorization

Term	Definition
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
GCP	Good Clinical Practice
GDSP	Genomic Data Sharing Policy
IBC	Institutional Biosafety Committee
IND	Investigational New Drug
IRB	Institutional Review Board
LAO	Lead Academic Organization
M-SOP	Manual of Standard Operating Procedures
MM	Medical Monitor
NC	Nurse Consultant
NCI	National Cancer Institute
PID	Participant Identification Number
PIO	Protocol Information Office
PSU	Protocol Status Update Form
RCR	Registration and Credential Repository
SIM	Study Initiation Meeting
SL	Scientific Lead
SOP	Standard Operating Procedure
SSW	Study Specific Worksheet
SVAR	System Variable Attribute Report

4. REQUIRED STEPS FOR STUDY ACTIVATION

1. The study has met all DCP requirements for final approval. Please refer to the DCP Notice of Study Approved on Hold letter to see the specific items marked as needed to be resolved (e.g., receipt of CIRB approval, IND acceptance by FDA, regulatory documents received, agent availability/supply resolved, biomarker report accepted, SVAR/eCRFs completed and approved by DCP, SIM performed, budget finalized and approved, GDSP approved, etc.).
    1.1. At least one accruing LAO or AO has received DSA and has contracts and/or subcontracts in place, and the agent is available for shipment.
2. DCP PIO prepares a DCP Final Study Approval letter and sends it to the LAO and DMASC.
3. DMASC emails the LAO to notify them that the study has been implemented in Stars and Medidata Rave, and is ready to open for enrollment and data entry once the accruing LAOs and AOs are ready.
4. The LAO submits the PSU to DCP PIO to indicate that the study is active.
5. DCP PIO emails the LAO to acknowledge receipt of the PSU, which indicates that DCP PIO submitted the PSU to the CIRB.
    5.1. The LAO is responsible for notifying the accruing LAOs and AOs that the study is active.
    5.2. All accruing LAOs and AOs may now submit their SSWs to the CIRB.

5. REQUIRED STEPS FOR ACCRUING LAO OR AO ACTIVATION

The process of accruing LAO or AO activation involves the accruing LAO or AO meeting all regulatory requirements, as well as accruing LAO or AO users having appropriate access to Stars (including all applicable modules) and Medidata Rave. An accruing LAO or AO cannot be activated or begin pre-screening, screening, and enrolling participants to a study until they receive a ***Confirmation of Site Activation*** email from DMASC. This email indicates that an accruing LAO or AO has met all requirements for activation and now has permissions to begin pre-screening, screening, and enrolling participants to a study. The date that DMASC sends the ***Confirmation of Site Activation*** email is the accruing LAO's or AO's site open date.

The LAO is responsible for ensuring all requirements for accruing LAO and AO activation are met. CHK001 *CP-CTNet Accruing LAO and AO Activation Checklist for LAOs* is provided as a guideline. There is no need to submit the checklist to DMASC. These requirements include:

1. All regulatory approvals are in place (e.g., CIRB, local IRB, SSW, IBC, in-country approvals for international sites (if applicable)), and the DCP Regulatory Contractor has collected all necessary regulatory documents (refer to SOP 01-01 *Essential Records Submission for Sponsor's Trial Master File* for additional information).
2. Contracts/sub-contracts are in place.
3. The LAO conducted the SIM(s) onsite or virtually with the accruing LAOs and AOs who are named as "Accrual Organizations" for the study (refer to SOP 01-02 *Study Initiation Meeting* for additional information).
4. If applicable, Drug Shipment Authorization has been received and agent availability is confirmed onsite.
5. The LAO Coordinator or designee accessed the CP-CTNet DMASC Portal Gateway to proxy-request appropriate access for accruing LAO or AO staff based on their study role, and DMASC has granted access. There are several study roles that may be requested within the Portal Gateway and the most common applications associated with the requested study role are selected by default. The available study roles include Audit System User, Clinical Research Coordinator, DCP Staff, LAO Staff, Medical Monitor, Pharmacist, Scientific Lead, and Site Investigator. For more information about the CP-CTNet DMASC Portal Gateway account registration process, refer to USRMAN02 *Public Website and Portal Gateway Overview and User Registration Guide*.
    - 5.1. DMASC User Support processes each access request within two days. DMASC User Support (UserSupport_CP-CTNet@frontierscience.org) is available to assist with any questions.
6. DMASC contacted the LAO Coordinator or designee to confirm the name(s) and email address(es) of the personnel at the LAO who have permission to reserve PIDs for each accruing LAO and AO (usually the LAO Coordinator).
    - 6.1. DMASC User Support processes each access request within two days.
    - 6.2. The LAO must access the Reserve PIDs module in Stars to reserve PIDs for a given accruing LAO or AO before that accruing LAO or AO can enroll participants. For more information about the process that LAOs follow to reserve PIDs in Stars, refer to USRMAN01 *CP-CTNet Stars User Guide*, QKREFGD02 *Summary of Enrollment Process*,

and the Reserving Participant IDs for CP-CTNet video tutorial that is available on the *Stars* dashboard item page on the CP-CTNet DMASC Portal Gateway.

7. The LAO sent an email to DMASC, confirming that the accruing LAO or AO has met all activation requirements.

6. CONFIRMATION OF ACCRUING LAO OR AO ACTIVATION

1. Once DMASC receives notification from the LAO that an accruing LAO or AO has met all activation requirements outlined in Section 5 above and the study has been implemented in Stars and Medidata Rave, DMASC then activates the accruing LAO or AO in the Protocol Approval module in Stars.
2. DMASC sends a ***Confirmation of Site Activation*** email to the LAO, the accruing LAO or AO, the DCP Study Team (MM, NC, and SL), the DCP Regulatory Contractor, and DCP PIO to indicate that the accruing LAO or AO is officially open to accrual in Stars and the accruing LAO or AO may now begin pre-screening, screening, and enrolling participants to the study.
3. The LAO and accruing LAO or AO file this email in their electronic or paper essential records binder for the study.
4. The LAO also maintains a tracking list which includes the initial activation date for each accruing LAO and AO.
5. After pre-screening its first participant, a newly activated accruing LAO or AO should update the CP-CTNet AQuIP Recruitment Journal in Medidata Rave with the site open date, which is the date that the accruing LAO or AO was activated to the study as per the ***Confirmation of Site Activation*** email sent by DMASC.

7. ACCRUING LAO OR AO ACTIVATION TO A PROTOCOL AMENDMENT

Depending on the nature of the protocol amendment and whether or not the study is still open to accrual, all the steps involved in the initial activation of an accruing LAO or AO may not need to be followed when activating an accruing LAO or AO to a protocol amendment. For example, new or revised contracts are generally not required (unless a new accruing LAO or AO is added), additional or updated regulatory documents may not be needed (e.g., in the case of an administrative protocol amendment), etc.

For protocol amendments that are approved when a study is open to accrual:

Note: DMASC implements the CIRB- and DCP-approved protocol amendment in Medidata Rave (if needed) concurrently with the steps below.

1. DMASC implements the CIRB- and DCP-approved protocol amendment in Stars. During the protocol amendment process, both the initial and amended versions are in Stars, and accruing LAOs and AOs continue to enroll under the initial version until they are activated to the amended version.
    1.1. To ensure that all necessary study-wide protocol amendment implementation steps are completed before accruing LAOs and AOs begin implementing the protocol amendment at their sites, the LAO should not send the protocol amendment to the accruing LAOs and AOs until it has been implemented in Stars.
    1.2. Once the protocol amendment has been implemented in Stars, DMASC sends an email to the LAO indicating that the protocol amendment has been implemented in Stars, and is ready to open for enrollment once the accruing LAOs and AOs are ready.

1.3. Once that email is received, the LAO then sends the CIRB- and DCP-approved protocol amendment to the accruing LAOs and AOs.

2. The LAO confirms that all necessary accruing LAO or AO activation requirements have been met for the protocol amendment (refer to CHK001 *CP-CTNet Accruing LAO and AO Activation Checklist for LAOs* for additional information).

3. Once the accruing LAO or AO has met all protocol amendment activation requirements, the LAO sends a confirmation email to DMASC.

4. Once DMASC receives a confirmation email from the LAO, DMASC activates the accruing LAO or AO to the protocol amendment in the Protocol Approval module in Stars. This is required before the accruing LAO or AO can use any updated eligibility checklists in Stars or apply/enact any modifications included in the protocol amendment.

5. DMASC sends a ***Confirmation of Site Activation to Protocol Amendment*** email to the LAO, the accruing LAO or AO, the DCP Study Team (MM, NC, and SL), and the DCP Regulatory Contractor to indicate that the accruing LAO or AO is officially open to accrual to the protocol amendment in Stars and the accruing LAO or AO may now begin pre-screening, screening, and enrolling participants to the protocol amendment.

   5.1. Accruing LAOs and AOs cannot enroll any participants to a protocol amendment until their site receives a ***Confirmation of Site Activation to Protocol Amendment*** email from DMASC.

   Note: Participants must be enrolled in Stars to the same protocol version that they are consented to. A protocol deviation must be completed if a participant is not enrolled to the same protocol version that they are consented to (refer to SOP 02-02 *Reporting Protocol Deviations* for additional information).

6. The LAO and accruing LAO or AO file this email in their electronic or paper essential records binder for the study.

7. The LAO also maintains a tracking list which includes every protocol amendment activation date for each accruing LAO and AO.

For protocol amendments that are approved when a study is closed to accrual:

Note: DMASC implements the CIRB- and DCP-approved protocol amendment in Medidata Rave (if needed) concurrently with the steps below. However, the protocol amendment is not implemented in Stars when the study is closed to accrual.

1. The LAO sends the CIRB- and DCP-approved protocol amendment to the accruing LAOs and AOs.

2. The LAO confirms that all necessary accruing LAO or AO activation requirements have been met for the protocol amendment (refer to CHK001 *CP-CTNet Accruing LAO and AO Activation Checklist for LAOs* for additional information).

3. Once the accruing LAO or AO has met all protocol amendment activation requirements, the LAO sends a *Confirmation of Site Activation to Protocol Amendment* email to the accruing LAO or AO and copies the DMASC Data Management Team (via DataManagement_CP-CTNet@frontierscience.org) and the DMASC Audit Team (via Audit_CP-CTNet@frontierscience.org) for informational purposes only.

4. The LAO and accruing LAO or AO file this email in their electronic or paper essential records binder for the study.
5. The LAO also maintains a tracking list which includes every protocol amendment activation date for each accruing LAO and AO.

8. PROTOCOL TRAINING REQUIREMENTS

All accruing LAOs and AOs participating in a CP-CTNet study must ensure that all current and new relevant staff at their site have documented evidence of training on the current version of the protocol and any subsequent protocol amendments. Training on protocol amendments after a study is closed to accrual is based on the needs of the protocol. If training is not required for a specific protocol amendment, then the LAO should document the reason that it is not required in a study-wide note to file.

Accruing LAOs and AOs are responsible for tracking the training of the staff at their site. The SIM attendance and report constitute protocol training. However, accruing LAOs and AOs may also use TMPL03 *CP-CTNet Training Confirmation Log for Accruing LAOs and AOs*, which is a resource for accruing LAOs and AOs to document training activities. Accruing LAOs and AOs can use this to document training that is conducted at their site (e.g., protocol amendments, new procedures, etc.). Some examples of when to use this training log include, but are not limited to, onboarding a new study coordinator or co-investigator if they were not able to participate in a SIM for their initial protocol training, self-training for a new protocol amendment, or pharmacist self-training on a new pharmacy manual, etc. Use of this training log is not required, as accruing LAOs and AOs may elect to document training using their own process (e.g., an electronic or paper institutional sign-off log) or an email-based documentation method.

If an accruing LAO or AO documents training via email, then the protocol amendment and/or other documentation should be attached to an email that details the changes made to each document in the body of the email. Once the individual that received the email with the protocol amendment and/or other documentation completes the training, they must forward the original email to a designated individual at their accruing LAO or AO indicating that the email and associated documents were received, reviewed, and acknowledged. The designated individual at the accruing LAO or AO saves the training-related emails that they receive and tracks who has been trained at their site.

Note: If an accruing LAO or AO has their own institutional policy on protocol and/or protocol amendment training that differs from the CP-CTNet policy stated above, then they should document this policy in a note to file and send it to DCP for approval. The accruing LAO or AO should also forward the institutional SOP where this is documented to DCP with the note to file. The approved note to file and institutional SOP should be forwarded to the LAO and DCP Regulatory Contractor for filing in the electronic or paper essential records binder for the study.

Protocol training documentation is required per GCP and will be reviewed during audits.

9. ADDITIONAL INFORMATION

Please send questions and comments to DataManagement_CP-CTNet@frontierscience.org.

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.

Resource	ID	Location
CP-CTNet Program Guidelines	Reference	Program Resources
CP-CTNet Accruing LAO and AO Activation Checklist for LAOs	CHK001	Program Resources
CP-CTNet Stars User Guide	USRMAN01	Program Resources
CP-CTNet Training Confirmation Log for Accruing LAOs and AOs	TMPL03	Program Resources
Essential Records Submission for Sponsor's Trial Master File	SOP 01-01	Program Resources
NCI Registration and Credential Repository	Application	CTEPcore.nci.nih.gov
Protocol Status Update Form	Form	Program Resources
Public Website and Portal Gateway Overview and User Registration Guide	USRMAN02	Program Resources
Reporting Protocol Deviations	SOP 02-02	Program Resources
Study Initiation Meeting	SOP 01-02	Program Resources
Summary of Enrollment Process	QKREFGD02	Program Resources

11. APPENDICES

None

Title: Reporting Serious Adverse Events

Document ID: CP-CTNet SOP 02-01

Version: 7.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
7.0	FEB-24-2026	Updated section 4 *Responsibilities for Reporting SAEs* to indicate that accruing LAOs and AOs should reference section 13 *Reporting Adverse Events* of the study protocol to ensure that the event meets SAE reporting requirements for that particular study. Updated the *DCP Serious Adverse Event Report Form* and the *Serious Adverse Event Report Form: Instructions for Completion and Submission* links to reflect the new URLs. Updated the DCP regulatory contractor's extension and DMACC to DMASC throughout the document.
6.0	FEB-07-2025	Updated the *Algorithm to Assess a Potential Unanticipated Problem* link to reflect the new URL.
5.0	JAN-26-2024	Updated the text and flowchart to include the notification procedures for Protocol PIs, the CIRB, and CNTs. Minor updates were made throughout the document.
4.0	FEB-21-2023	Added section 3 Definitions, minor clarifications on timelines for reporting SAEs.
3.0	DEC-02-2021	Updated SAE definition and reporting requirements to be consistent with FDA guidance, updated response to queries in Appendix I.
2.0	SEP-10-2020	Clarified inpatient hospitalization, updated DCP Regulatory Contractor phone number, clarified query response submittal, updated contact information in Appendix I.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

Investigators, Co-Investigators, Coordinators, and designees at Cancer Prevention Clinical Trials Network (CP-CTNet) accruing Lead Academic Organizations (LAOs) and Affiliated Organizations (AOs) are responsible for the proper and timely reporting of all serious adverse events (SAEs) that occur during the conduct of a study.

For all SAEs, the accruing LAO or AO where the SAE occurred is responsible for reporting the SAE to the Division of Cancer Prevention (DCP) Medical Monitor (MM) and DCP Regulatory Contractor's Safety Department by phone or email within 24 hours of knowledge and on the *DCP Serious Adverse Event Report Form* within 48 hours of knowledge. The accruing LAO or AO must also report the SAE to the Protocol Principal Investigator (PI) and LAO Coordinator. The Food and Drug Administration (FDA) or other regulatory authority, and/or the pharmaceutical sponsor, may also have other reporting requirements.

For Cross-Network Trials (CNTs), in addition to the above, the accruing LAO or AO where the SAE occurred must also send the *DCP Serious Adverse Event Report Form* to the Lead LAO Coordinator and Collaborating LAO Coordinator within 48 hours of knowledge (see REFGD06 *Cross-Network Trials Guidelines* for more information).

Note: The DCP protocol numbering convention for CP-CTNet CNTs is INT, which stands for "inter-network trial" (e.g., INT21-05-01).

An SAE is defined by the Code of Federal Regulations (CFR) as any untoward medical occurrence associated with the use of a drug in humans that, at any dose, has one or more of the following outcomes:

1. Death.
2. A life-threatening adverse event:
    2.1. Per FDA regulations, a life-threatening adverse event places the participant at immediate risk of death. It does not include an adverse event that, had it occurred in a more severe form, might have caused death.
3. Inpatient hospitalization or prolongation of existing hospitalization:
    3.1. The FDA does not define what constitutes inpatient hospitalization. The National Cancer Institute (NCI), DCP uses admission or stay (including emergency room) equal to or greater than 24 hours as the definition of hospitalization. Exceptions are hospitalization for treatment of a pre-existing condition (unless the condition increased in severity on study), outpatient surgery, planned/elective procedures, and procedures described in the protocol (e.g., pharmacokinetic sampling, surgery). These events ***should not*** be reported by the Investigator/Co-Investigator on the *DCP Serious Adverse Event Report Form* even if the hospital stay is equal to or greater than 24 hours.
    3.2. In contrast, an event occurring during <u>any</u> hospitalization, even during protocol-defined procedures, that prolongs the hospitalization or has another serious outcome should be considered an SAE and reported by the Investigator/Co-Investigator on the *DCP Serious Adverse Event Report Form*. The DCP MM, DCP Regulatory Contractor's Safety Department, Protocol PI, and LAO Coordinator should also be notified by phone or email.
4. A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.

5. A congenital anomaly or birth defect.
6. Important medical events that may not result in death, are not life-threatening, and do not require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the other outcomes listed above.

    6.1. FDA's examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

2. SCOPE

This document details the responsibilities of the CP-CTNet accruing LAO and AO Investigators, Co-Investigators, Coordinators, and designees regarding the reporting of SAEs, including initial reporting, follow-up, and documentation.

3. DEFINITIONS

Term	Definition
AO	Affiliated Organization
CFR	Code of Federal Regulations
CIRB	Central Institutional Review Board
CNT	Cross-Network Trial
Collaborating LAO	An LAO that is involved in a CNT that has oversight responsibilities for its own accruing LAO and AOs
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
FDA	Food and Drug Administration
INT	Inter-Network Trial or INT is the DCP protocol numbering convention for CP-CTNet trials (e.g., INT21-05-01).
IRB	Institutional Review Board
LAO	Lead Academic Organization
Lead LAO	An LAO that takes primary responsibility for the administrative aspects of the CNT and has oversight responsibilities for its own accruing LAO and AOs
M-SOP	Manual of Standard Operating Procedures
MM	Medical Monitor
NCI	National Cancer Institute
PI	Principal Investigator
PT	Pacific Time Zone
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
UP	Unanticipated Problem

4. RESPONSIBILITIES FOR REPORTING SAEs

Investigators, Co-Investigators, Coordinators, and designees at each accruing LAO and AO will report SAEs as follows:

1. Contact the DCP MM (phone and email as listed in the protocol), DCP Regulatory Contractor's Safety Department (phone: 650-691-4400 x140 and email: safety@ccsainc.com), Protocol PI (phone and email as listed in the protocol), and LAO Coordinator within 24 hours of knowledge of the SAE, and communicate the following information:
    - 1.1. Participant ID.
    - 1.2. Date and time of SAE onset.
    - 1.3. Date and time the accruing LAO or AO was notified about the SAE by the study participant or other person(s).
    - 1.4. Name of the person who is reporting the SAE.
    - 1.5. Call-back phone number and email.
    - 1.6. Accruing LAO or AO at which the participant is enrolled.
    - 1.7. DCP protocol number.
    - 1.8. Title of protocol.
    - 1.9. Suspected drug (if any).
    - 1.10. Description of SAE, including attribution to the investigational agent.
2. Email a copy of the completed *DCP Serious Adverse Event Report Form* to the DCP MM (email as listed in the protocol) and DCP Regulatory Contractor's Safety Department (safety@ccsainc.com) within 48 hours of knowledge of the SAE. The information must be entered into the Word form; the form should then be signed with a wet ink or electronic signature, scanned (as needed), and emailed. For guidance or assistance, the DCP Regulatory Contractor's Safety Department may also be reached by phone at 650-691-4400 x140 during regular business hours (PT).
    - 2.1. Reference section 13 *Reporting Adverse Events* of the study protocol to ensure that the event meets SAE reporting requirements for that particular study.
    - 2.2. Reference the *Serious Adverse Event Report Form: Instructions for Completion and Submission* for assistance in completing the *DCP Serious Adverse Event Report Form*.
    - 2.3. Ensure that an Investigator or Co-Investigator for the accruing LAO or AO where the SAE occurred signs the form.
    - 2.4. Forward the completed form to the Protocol PI and LAO Coordinator. For CNTs, also forward the completed form to the Lead LAO Coordinator and Collaborating LAO Coordinator (see REFGD06 *Cross-Network Trials Guidelines* for more information).
3. Comply with all institutional requirements and all CIRB requirements related to the reporting of SAEs. Specifically, if an SAE meets the definition of an UP (i.e., requires expedited reporting to the FDA or manufacturer as a safety report [serious, unexpected, and related to a study agent]), then it needs to be reported to the CIRB by the Signatory Institution PI at the accruing LAO or AO where the SAE occurred (see SOP 02-02 *Reporting Protocol Deviations* for more information). In addition to CIRB requirements, UPs must be reported to the accruing LAO's or AO's local IRB per local requirements.
    - 3.1. Accruing LAOs and AOs must discuss UPs with the DCP Study Team, Protocol PI, and LAO (or Lead and Collaborating LAOs for CNTs) prior to CIRB submission.

3.2. The Signatory Institution PI or designee should share a copy of the UP CIRB submission with the DCP Study Team.

4. Respond to any queries from the DCP Regulatory Contractor's Safety Department.
5. When applicable (e.g., revised information, new follow-up information), complete a follow-up report using the previously submitted *DCP Serious Adverse Event Report Form* as soon as additional information is available. The Investigator or Co-Investigator should also sign and date each follow-up report.
6. Send follow-up reports to the following:
   6.1. DCP Study Team.
   6.2. DCP Regulatory Contractor's Safety Department.
   6.3. Protocol PI.
   6.4. LAO Coordinator.
   6.5. Lead LAO Coordinator and Collaborating LAO Coordinator if the study is a CNT.
7. Comply with the instructions listed in the protocol regarding the length of time for follow-up of an SAE.

5. DOCUMENTATION REQUIREMENTS

1. Each accruing LAO and AO will retain in their study files a copy of each *DCP Serious Adverse Event Report Form*, supporting documentation, and communication related to the reporting of the SAE. All participant identifiers should be redacted from copies of the supporting documentation.
2. The LAO Coordinators and/or designees will retain in the LAO study files a copy of each *DCP Serious Adverse Event Report Form*, supporting documentation, and communication related to the reporting of the SAE from all accruing LAOs and AOs.
3. The Protocol PI will retain in the study Trial Master File a copy of each *DCP Serious Adverse Event Report Form*, supporting documentation, and communication related to the reporting of the SAE from all accruing LAOs and AOs.
4. For CNTs, the Lead LAO Coordinator and/or designees will retain in the LAO study files a copy of each *DCP Serious Adverse Event Report Form*, supporting documentation, and communication related to the reporting of the SAE from all accruing LAOs and AOs. The Collaborating LAO Coordinator and/or designees will retain in the LAO study files a copy of each *DCP Serious Adverse Event Report Form*, supporting documentation, and communication related to the reporting of the SAE from their accruing LAO and all of their AOs.

6. ADDITIONAL INFORMATION

Questions related to the reporting of SAEs may be directed to the DCP Regulatory Contractor's Safety Department at safety@ccsainc.com.

7. 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.

Resource	ID	Location
Algorithm to Assess a Potential Unanticipated Problem	Website	ncicirb.org

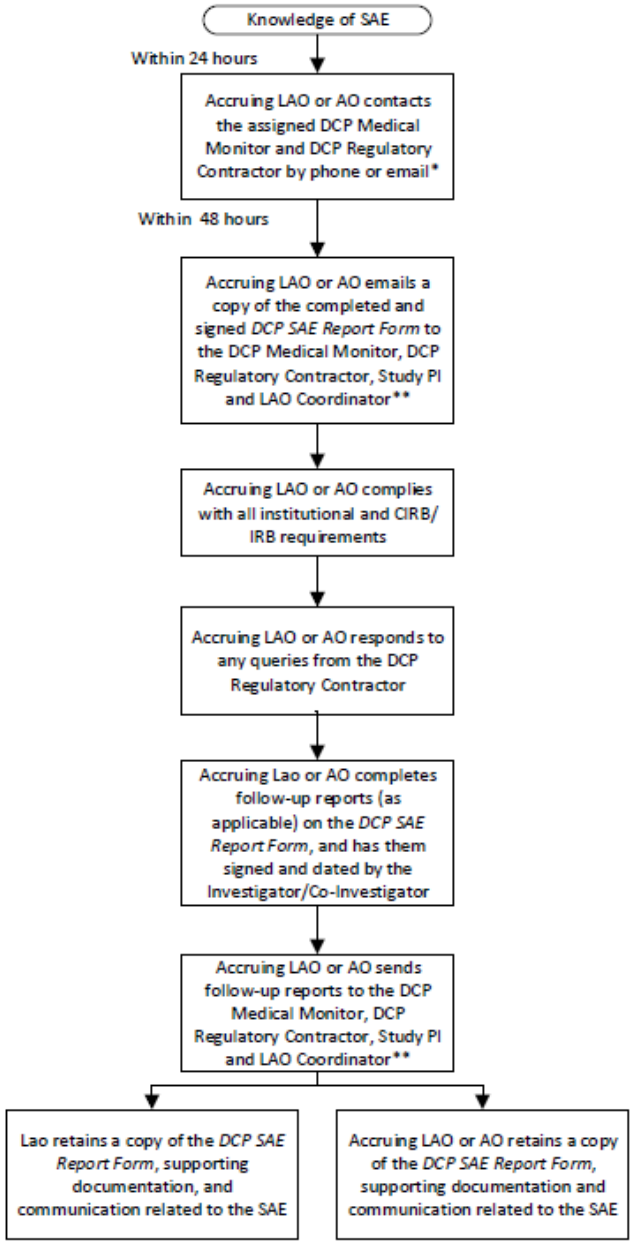
Resource	ID	Location
Cross-Network Trials Guidelines	REFGD06	Program Resources
DCP Serious Adverse Event Report Form	Form	Program Resources
Reporting Protocol Deviations	SOP 02-02	Program Resources
Serious Adverse Event Report Form: Instructions for Completion and Submission	Reference	Program Resources

8. APPENDICES

1. Appendix I – Reporting Serious Adverse Events

Appendix I

Reporting Serious Adverse Events (SAEs)



*Contact Information:
DCP Medical Monitor: Refer to the phone number and email address as listed in the protocol
DCP Regulatory Contractor: phone (650-691-4400 x140), e-mail (safety@ccsainc.com)

**For Cross-Network Trials (CNTs), the accruing LAO or AO must send the SAE and follow-up reports to both the Lead LAO Coordinator (LAO Coordinator at the Lead LAO) and Collaborating LAO (LAO Coordinator at the accruing LAO's or AO's LAO).

Title: Reporting Protocol Deviations

Document ID: CP-CTNet SOP 02-02

Version: 6.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
6.0	FEB-24-2026	Updated Section 4 *Responsibilities for Prompt Reporting of Protocol Deviations* to include a timeframe for reporting protocol deviations in Medidata Rave and to clarify that LAO Administrative Teams should query the *Minor or Moderate/Major* protocol deviation grade question if the grade provided by the accruing LAO or AO does not align with the protocol deviation grade definitions included in the question's help text. Made updates throughout the document to reflect the updated *CP-CTNet Protocol Deviation Notification* eCRF. Updated DMACC to DMASC throughout the document.
5.0	FEB-07-2025	Updated the *Algorithm to Assess a Potential Unanticipated Problem* and *Algorithm to Assess Potential Noncompliance* links to reflect the new URLs. Minor editorial edits and clarifications were made.
4.0	JAN-26-2024	Updated the text to include a timeframe for reporting PDs in Rave, the updated DCP MM/NC review process, and the notification procedures for Study PIs, the CIRB, and CNTs. Major updates were made throughout the document to clarify the protocol deviation reporting and review workflow.
3.0	FEB-21-2023	Added information to Section 6 to clarify that the LAO Administrative Team is responsible for monitoring protocol deviation trends at their accruing LAO and AOs. Updated the protocol deviation grade definitions. Minor editorial edits were made as well.
2.0	JUL-11-2022	Major rewrite of entire SOP to reflect the updated protocol deviation reporting and review procedure in Medidata Rave.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

A protocol deviation is any noncompliance with the study design and/or procedures of a Division of Cancer Prevention (DCP)- and Central Institutional Review Board (CIRB)-approved protocol. Protocol deviations may result from the actions of the study participant, the Investigators, or the clinical staff conducting the study.

Investigators, Coordinators, and designees at accruing Lead Academic Organizations (LAOs) and Affiliated Organizations (AOs) are responsible for recording and reporting protocol deviations as soon as they are identified.

Note: DCP does not allow any protocol waivers or exceptions for the enrollment of a participant in violation of protocol inclusion/exclusion criteria.

2. SCOPE

This document details the responsibilities of the Investigators, Coordinators, and designees at accruing LAOs and AOs regarding the reporting of protocol deviations, as well as the responsibilities of the LAO Administrative Teams and DCP Study Teams (Medical Monitors (MMs), Nurse Consultants (NCs), and Scientific Leads (SLs)) regarding the review of protocol deviations.

3. DEFINITIONS

Term	Definition
AE	Adverse Event
AO	Affiliated Organization
CIRB	Central Institutional Review Board
CNT	Cross-Network Trial
Collaborating LAO	An LAO that is involved in a CNT that has oversight responsibilities for its own accruing LAO and AOs.
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DM	Data Manager
DMASC	Data Management, Auditing, and Statistical Center
eCRF	Electronic Case Report Form
ICF	Informed Consent Form
INT	Inter-Network Trial. The DCP protocol numbering convention for CP-CTNet CNTs begins with INT (e.g., INT21-05-01).
IRB	Institutional Review Board
LAO	Lead Academic Organization
LAO Administrative Team	The LAO Coordinator and other LAO staff at the Lead LAO and each Collaborating LAO that provide oversight for their own accruing LAO and AOs.
Lead LAO	An LAO that takes primary responsibility for the administrative aspects of a CNT and has oversight responsibilities for its own accruing LAO and AOs.
M-SOP	Manual of Standard Operating Procedures
MM	Medical Monitor
NC	Nurse Consultant
NCI	National Cancer Institute

Term	Definition
OTC	Over The Counter
PI	Principal Investigator
PID	Participant Identifier
SAE	Serious Adverse Event
SL	Scientific Lead

4. RESPONSIBILITIES FOR PROMPT REPORTING OF PROTOCOL DEVIATIONS

Investigators, Coordinators, and designees at accruing LAOs and AOs report protocol deviations using the *CP-CTNet Protocol Deviation Notification* eCRF in Medidata Rave (Rave) within 14 calendar days of awareness of the protocol deviation.

1. Protocol Deviation Entry:

    1.1. The accruing LAO or AO where the protocol deviation originated must comply with all institutional, CIRB, and international requirements related to reporting protocol deviations (as applicable).

    1.2. To start the process of entering a protocol deviation into Rave, the accruing LAO or AO uses the Add Event dropdown on the participant's patient page and selects "Protocol Deviation Notification" to add the *CP-CTNet Protocol Deviation Notification* eCRF to the record of the participant who is impacted by the protocol deviation.

    - The accruing LAO or AO completes the first section of the *CP-CTNet Protocol Deviation Notification* eCRF (up to and including the "By checking this box, I confirm that the site investigator has reviewed this form" field). The help text associated with each field on the eCRF can be used to assist with completing the eCRF. Help text in Rave is accessed by clicking the question mark icon next to the associated field on the eCRF.

    1.3. Only one protocol deviation per PID should be recorded on a single eCRF.

    - If another protocol deviation occurs for the same participant, a separate *CP-CTNet Protocol Deviation Notification* eCRF should be added and completed.
    - If the same protocol deviation occurs for two (2) to nine (9) participants, a separate *CP-CTNet Protocol Deviation Notification* eCRF should be added and completed for each PID.
    - If the same protocol deviation occurs for 10 or more participants, the information for all participants can be documented on one *CP-CTNet Protocol Deviation Notification PDF*, which is available on the CP-CTNet DMASC public website. The completed PDF should be sent to the DMASC DMs via DataManagement_CP-CTNet@frontierscience.org. The DMASC DMs route the PDF for LAO Administrative Team and DCP Study Team review and enter the protocol deviations into the database on behalf of the accruing LAO or AO, LAO Administrative Team, and DCP Study Team.
        - Each PID and associated date that each protocol deviation occurred must be noted on the PDF.
        - DCP does not require prior approval or a Note to File.

1.4. Rave automatically sends the LAO Administrative Team an email indicating that there is a protocol deviation to be reviewed.

Note: For CNTs, Rave automatically sends the DMASC DMs an email notification that there is a protocol deviation to be reviewed, and the DMASC DMs forward the email to the appropriate LAO Administrative Team.

2. LAO Administrative Team Review:

2.1. As a function of their oversight role, the LAO Administrative Team (LAO Coordinator and/or designee(s)) is responsible for reviewing protocol deviations reported by their accruing LAO and AOs. For CNTs, the LAO Administrative Team at the Lead LAO and each Collaborating LAO is responsible for reviewing protocol deviations reported by their own accruing LAO and AOs (see REFGD06 *Cross-Network Trials Guidelines* for more information).

2.2. The LAO Administrative Team verifies the accuracy and completeness of the *CP-CTNet Protocol Deviation Notification* eCRF, and confirms that appropriate details were provided and the eCRF was completed according to the help text.

Note: The LAO Administrative Team should query the *Minor or Moderate/Major* protocol deviation grade question if the grade provided by the accruing LAO or AO does not align with the protocol deviation grade definitions included in the question's help text. For example, if a protocol deviation related to an eligibility violation is graded as *Minor*, then the LAO Administrative Team should query this question and advise the accruing LAO or AO to change the grade to *Moderate/Major*. See the Protocol Deviation Grade Definitions section below for more information.

2.3. If queries are required, the LAO Administrative Team selects "Yes" for the "Does LAO review require queries?" field and enters the query/queries into Rave.

2.4. The accruing LAO or AO responds to the query/queries directly in Rave. The accruing LAO or AO addresses each query by either correcting the data and providing a reason for correction, or by indicating that the data are correct and providing an explanation. In order to facilitate timely review, the DMASC DMs email the LAO Administrative Team if they see, as part of their routine data management activities, that the accruing LAO or AO has addressed the query/queries, but the query response(s) have yet to be reviewed by the LAO Administrative Team.

- Queries should be addressed by accruing LAOs and AOs within 14 calendar days. See REFGD03 *CP-CTNet Master Data Management Plan* for more information.

2.5. The LAO Administrative Team logs into Rave to review the accruing LAO's or AO's query response(s). The LAO Administrative Team can re-query, if necessary. Once the query/queries are resolved, the LAO Administrative Team changes their response for the "Does LAO review require queries?" field from "Yes" to "No."

2.6. If there are no queries, or once the query/queries from the LAO Administrative Team are resolved, the LAO Administrative Team checks the "LAO Review Complete" box and saves the eCRF.

3. DCP MM/NC Review:

3.1. The DCP MM/NC reviews minor (grade 1) protocol deviations on/near the 1st of each month. For minor protocol deviations where the LAO Administrative Team review is complete, the DMASC DMs enter what is already in Rave into the *CP-CTNet Protocol*

Deviation Notification PDF, send the PDF to the DCP MM/NC, and ask that the DCP MM/NC complete their review on this PDF within 10 business days of receipt. If the same protocol deviation is entered into Rave for more than one participant per study, DMASC may combine these protocol deviations on the same PDF to streamline the DCP MM/NC review.

Note: This is different from the procedure outlined in Section 1.3 above for the initial reporting of the protocol deviation by the accruing LAO or AO (i.e., using this PDF to report the same protocol deviation for 10 or more participants).

3.2. The DCP MM/NC reviews moderate (grade 2)/major (grade 3) protocol deviations in real time. For moderate/major protocol deviations where the LAO Administrative Team review is complete, the DMASC DMs enter what is already in Rave into the *CP-CTNet Protocol Deviation Notification PDF*, send the PDF to the DCP MM/NC, and ask that the DCP MM/NC complete their review on this PDF within 10 business days of receipt. If the same protocol deviation is entered into Rave for more than one participant per study, DMASC may combine these protocol deviations on the same PDF to streamline the DCP MM/NC review.

Note: This is different from the procedure outlined in Section 1.3 above for the initial reporting of the protocol deviation by the accruing LAO or AO (i.e., using this PDF to report the same protocol deviation for 10 or more participants).

3.3. The DCP MM/NC reviews each *CP-CTNet Protocol Deviation Notification PDF*.

3.4. If queries are required, the DCP MM/NC sends them to the DMASC DMs via email (DataManagement_CP-CTNet@frontierscience.org), and the DMASC DMs proxy enter the queries into Rave on behalf of the DCP MM/NC. The DMASC DMs indicate that each query is from the DCP MM/NC in the query text.

3.5. The accruing LAO or AO responds to the query/queries directly in Rave. The accruing LAO or AO addresses each query by either correcting the data and providing a reason for correction, or by indicating that the data are correct and providing an explanation.

- Queries should be addressed by accruing LAOs and AOs within 14 calendar days. See REFGD03 *CP-CTNet Master Data Management Plan* for more information.

3.6. The DMASC DMs provide the accruing LAO's or AO's query response(s) and updated *CP-CTNet Protocol Deviation Notification PDF*, if necessary, to the DCP MM/NC via email. The DCP MM/NC works with the DMASC DMs to re-query, if necessary.

3.7. If there are no queries, or once the query/queries from the DCP MM/NC are resolved, the DCP MM/NC completes the "For DCP MM/NC Use Only" section on the *CP-CTNet Protocol Deviation Notification PDF*.

3.8. The DCP MM/NC sends each completed *CP-CTNet Protocol Deviation Notification PDF* to the DMASC DMs via email (DataManagement_CP-CTNet@frontierscience.org).

Note: If the same minor protocol deviation occurs consistently within an accruing LAO or AO or across accruing LAOs and AOs, then the DCP MM/NC may determine the grade of the protocol deviation(s) to be moderate (grade 2)/major (grade 3). This protocol deviation grade escalation may need to be reported to the CIRB as potential serious or continuous noncompliance. The DCP MM/NC indicates whether CIRB notification is recommended as part of their review. See Section 5 CIRB Requirements for Reporting Protocol Deviations below for more information.

3.9. The DMASC DMs enter the DCP MM/NC review into Rave, check the "DCP MM/NC Review Complete" box, and save the eCRF. Rave automatically sends an email to the accruing LAO or AO study staff with the *Clinical Research Coordinator - IVRS* role in Rave, LAO Administrative Team, and DMASC DMs to indicate that the protocol deviation has been finalized.

3.10. The accruing LAO or AO reviews the completed "For DCP MM/NC Use Only" section of the eCRF.

3.11. There are two optional fields in the "For Site Use Only (Optional)" section at the bottom of the eCRF. Per the accruing LAO's or AO's protocol deviation policy, the accruing LAO or AO can confirm that the accruing LAO or AO Investigator acknowledges the DCP MM/NC review. Per the LAO's request, the accruing LAO or AO can also provide the date that the CIRB was notified if CIRB notification was recommended by the DCP MM/NC.

3.12. The review process for the protocol deviation is complete.

5. CIRB REQUIREMENTS FOR REPORTING PROTOCOL DEVIATIONS

1. The Signatory Institution PI is responsible for reporting all required protocol deviations that occur at their accruing LAO or AO to the CIRB (see algorithms linked below). In addition, these protocol deviations should be reported to the study PI, LAO Administrative Team, and DCP Study Team prior to CIRB submission. For CNTs, these protocol deviations should be reported to the study PI, Lead LAO Administrative Team, Collaborating LAO Administrative Team, and DCP Study Team prior to CIRB submission (see REFGD06 *Cross-Network Trials Guidelines* for more information).
2. The LAO Administrative Team is responsible for reporting any study-wide issues or protocol deviations to the CIRB (see algorithms linked below). For CNTs, the Lead LAO Administrative Team is responsible for reporting any study-wide issues or protocol deviations to the CIRB (see algorithms linked below) (see REFGD06 *Cross-Network Trials Guidelines* for more information).
3. The following protocol deviation categories must be reported to the CIRB via the IRB Manager:
   3.1. Serious or continuous noncompliance:
      - Further details regarding whether a protocol deviation is reportable as serious or continuous noncompliance may be found on the NCI CIRB webpage: Algorithm to Assess Potential Noncompliance.

   3.2. Unanticipated problem:
      - Further details regarding whether a protocol deviation is reportable as an unanticipated problem may be found on the NCI CIRB webpage: Algorithm to Assess a Potential Unanticipated Problem.
4. The DCP MM/NC indicates whether CIRB notification is recommended as part of their review of each protocol deviation.
5. In addition to CIRB requirements, protocol deviations (including those not reportable to the CIRB) must be reported to the accruing LAO's or AO's local IRB as per local requirements.
6. The Signatory Institution PI or LAO Administrative Team should share copies of the CIRB submissions with the DCP Study Team (if possible).

6. PROTOCOL DEVIATION TRENDS

The LAO Administrative Team is responsible for monitoring protocol deviation trends at their accruing LAO and AOs. As trends are identified, the LAO Administrative Team should notify the study PI, DCP Study Team, and DMASC of the trend, and maintain consistent communication about any corrective and/or preventative action(s) implemented to address the identified trend (as needed). For CNTs, the LAO Administrative Team at the Lead LAO and each Collaborating LAO is responsible for monitoring protocol deviation trends at their own accruing LAO and AOs. As trends are identified, the LAO Administrative Team should notify the study PI, Lead LAO Administrative Team (if identified by the Collaborating LAO Administrative Team), DCP Study Team, and DMASC of the trend, and maintain consistent communication about any corrective and/or preventative action(s) implemented to address the identified trend (as needed) (see REFGD06 *Cross-Network Trials Guidelines* for more information). Protocol deviation trends and the LAO oversight of these trends are reviewed during DMASC quality assurance audits.

The Data Listing Report in Rave can be used by the LAO Administrative Team to help monitor and identify protocol deviation trends. This report is useful for reviewing/downloading bulk data reported on the *CP-CTNet Protocol Deviation Notification* eCRF for all participants in a selected study. The LAO Administrative Team can run this report at any time. For more information on generating Rave reports, please refer to QKREFGD01 *Medidata Rave Reports* and USRMAN03 *Rave Reports Resource Guide for the CP-CTNet Project*.

The DMASC DMs also send a Cumulative Protocol Deviation Report for each study to the LAO Administrative Team and DCP Study Team on/near the 1st of each month.

7. ADDITIONAL INFORMATION

Please send questions and comments to DataManagement_CP-CTNet@frontierscience.org.

8. 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.

Resource	ID	Location
Algorithm to Assess a Potential Unanticipated Problem	Reference	ncicirb.org
Algorithm to Assess Potential Noncompliance	Reference	ncicirb.org
CP-CTNet DMASC Website	Website	cp-ctnet-dmasc.org
CP-CTNet Master Data Management Plan	REFGD03	Program Resources
CP-CTNet Protocol Deviation Notification PDF	Form	Program Resources
Cross-Network Trials Guidelines	REFGD06	Program Resources
IRB Manager	Application	nci.my.irbmanager.com
Medidata Rave Reports	QKREFGD01	Program Resources
Rave Reports Resource Guide for the CP-CTNet Project	USRMAN03	Program Resources

9. APPENDICES

1. Appendix I - Protocol Deviation Grade Definitions and Category Descriptions

Appendix I

Protocol Deviation Grade Definitions and Category Descriptions

Protocol Deviation Grade Definitions:

1. **Grade 1/Minor:** No meaningful effect on the integrity or reliability of research data and no meaningful risk to participant rights or safety.
2. **Grade 2/Moderate:** Has the potential to affect the integrity or reliability of research data or poses potential risk to participant rights or safety.
3. **Grade 3/Major:** Will affect the integrity or reliability of research data or will affect participant rights or safety. This includes all deviations related to inclusion/exclusion criteria, deviations related to data necessary for primary endpoints, and deviations related to data necessary for key secondary endpoints.

Protocol Deviation Category Descriptions:

1. **AE/SAE Reporting:** Any adverse or serious adverse event that was not reported.
2. **Biospecimen:** Tissue, blood, urine: Any deviation impacting biospecimen collection, integrity (processing/storing), and/or analysis (both pre- and post-intervention).
3. **Concomitant Medication:** Any OTC/prescription drug that is prohibited per protocol.
4. **Consent Procedures:** Any deviation from compliance with Human Subject Protection regulations including any deviation from ICF version, signature/date/other requirements.
5. **Eligibility:** Any deviation related to eligibility (inclusion/exclusion criteria).
6. **Pre-Intervention Procedures:** Any deviation related to pre-intervention procedures (other than biospecimen- and eligibility-related deviations).
7. **Schedule: Incomplete Visit Assessment/Call:** Some or part of visit assessment/call was not completed (other than biospecimen-related deviations).
8. **Schedule: Missed Visit Assessment/Call:** Visit assessment/call did not occur (other than biospecimen-related deviations).
9. **Schedule: Out of Window Visit Assessment/Call:** Visit assessment/call not held within study designated time points (other than biospecimen-related deviations).
10. **Study Drug Accountability:** Any deviation related to study drug requirements for example pharmacy documentation, study drug integrity, distribution, administration error by study staff, or missing study drug.
11. **Study Drug Administration:** Any deviation related to participant not taking drug per protocol.
12. **Documentation Error:** An error or absence in documenting any research related activity.
13. **Removal from Study Error:** Deviation related to erroneous removal of participant from study.

Title: System Variable Attribute Report (SVAR) and Electronic Case Report Form (eCRF) Development

Document ID:	CP-CTNet SOP 02-03
Version:	6.0
Version Date:	February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
6.0	FEB-24-2026	Updated section 4 *Responsibilities* to remove the DCP Regulatory Contractor from the eCRF Review Team and to add an updated link to more information on CDE standards. Updated DMACC to DMASC throughout the document.
5.0	AUG-13-2024	Updated section 4 *Responsibilities* to include LAO, eCRF Review Team, and DCP Study Team SVAR review timelines, and to clarify that the study build is completed within 30 business days of the date of the SVAR approval letter.
4.0	JUL-13-2023	Major updates to entire document.
3.1	FEB-21-2023	Title change – formerly “Electronic Case Report Form Development.”
3.0	AUG-02-2022	Addition of Definition and References sections, major rewrite of section 4, replaced original Appendix I with current Appendix I.
2.0	JUN-07-2021	Major updates to entire document.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

Electronic Case Report Forms (eCRFs) are developed to collect and record the data required to answer the research question(s) for a specific protocol, to create the study build in the Medidata Rave clinical database management system, and to serve as a description of the expected content of the final dataset for the study.

The System Variable Attribute Report (SVAR) Template is a customizable tool that is used to create or revise protocol-specific eCRFs. The SVAR Template contains both mandatory and recommended content, and should be used as the basis for developing the protocol-specific eCRFs.

eCRFs should be created to collect data in a consistent manner to assure quality, completeness, and accuracy of the final data sets, and to ensure that data collection is done in compliance with Good Clinical Practice (GCP), the standards for National Cancer Institute (NCI) Common Data Elements (CDEs), and federal regulations, including but not limited to 21 CFR Part 11 and the Health Insurance Portability and Accountability Act (HIPAA).

2. SCOPE

This document details the responsibilities of the Principal Investigators (PIs), Lead Academic Organization (LAO) Coordinators, and designees regarding the creation of eCRFs for new and amended protocol submissions.

3. DEFINITIONS

Term	Definition
CDE	Common Data Element
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
eCRF	Electronic Case Report Form
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
LAO	Lead Academic Organization
M-SOP	Manual of Standard Operating Procedures
MDS	Minimum Data Set
NCI	National Cancer Institute
PI	Principal Investigator
PIO	Protocol Information Office
SVAR	System Variable Attribute Report

4. RESPONSIBILITIES

DMASC is responsible for drafting eCRFs for each new protocol submission and any applicable amended protocol submissions. The PI, LAO Coordinator, and/or designee is responsible for reviewing and approving these eCRFs and collaborating with DMASC to ensure that these eCRFs accurately reflect the protocol and contain all necessary data elements for data collection, analysis, and reporting.

1. Procedures for SVAR development include:

1.1. DMASC begins drafting the study-specific SVAR after DMASC receives the first Approval on Hold letter for the protocol from PIO.

1.2. The *CP-CTNet SVAR Template*, including instructions for use of the SVAR, is posted on the CP-CTNet DMASC public website. The SVAR Template is a spreadsheet used to create the study-specific SVAR. The study-specific SVAR should document all questions and data elements required for a given protocol.

- Each tab in the SVAR represents an eCRF and contains questions, their corresponding attributes (e.g., field length, response value, data type), and other additional elements. The columns in each eCRF tab include the following:
  - Change Indicator
  - Question Name
  - Data Type
  - Field Length (including decimal places, if applicable)
  - Field Type
  - Valid Values
  - Field Help Text
  - MDS Field?
  - MDS Collection Table
  - Site Comments
  - DMASC Comments
  - Curator Comments
  - caDSR Public ID: Version
  - caDSR Definition
  - caDSR Representation (Value Domain Public ID)
- The SVAR Template contains “generic” eCRFs that can be used across CP-CTNet studies, if applicable. Generic/standard fields on each eCRF tab that should not be changed across studies are highlighted gray. Fields that can be modified according to a study’s protocol are not highlighted gray. Notes to the Study Build Team may be included at the top of each eCRF tab and serve as a guide for modifying these fields.
- Study-specific eCRFs can be designed and added to the SVAR.
- The SVAR also includes the Schedule of Forms, which describes which eCRFs should be completed at each visit/event according to the protocol, an MDS Checklist to identify MDS fields, and a Versions tab used to track each version of the protocol and SVAR.

1.3. The Versions tab of the SVAR should contain the protocol version number and date as well as the SVAR version number and date.

- The initial draft of the SVAR is version 1.0. It remains version 1.0 while DMASC and the LAO work on it until it is sent out for initial eCRF Review Team review.

- During the review process, if minor updates (e.g., spelling, grammar, minor formatting updates) are made, the SVAR is not up-versioned. If major updates (e.g., adding/removing eCRFs) are made, the SVAR is up-versioned by a whole number (e.g., 2.0 → 3.0).
- When a protocol amendment receives final approval, the SVAR must be updated (as needed) and up-versioned. Subsequent versions are incremented by .1 (e.g., 4.1, 4.2, 4.3, etc.) and remain this version number throughout the review process.
- Each version is tracked in the Versions tab of the SVAR.

  Note: The version date of the SVAR is not required to match the version date of the protocol and informed consent form.

1.4. After DMASC receives the first Approval on Hold letter for the protocol from PIO and drafts the initial SVAR, DMASC sends this draft to the LAO. The LAO should follow the SVAR review process as outlined in CP-CTNet REFGD03 *Master Data Management Plan for Lead Academic Organizations and Affiliated Organizations*.

- When sending the initial draft of the SVAR to the LAO, DMASC can request to schedule a meeting with the LAO to discuss the SVAR. This meeting can occur before or after LAO review of the initial draft of the SVAR, depending on LAO preference.
- The LAO is given two weeks for their initial review. If their initial review requires more time, the LAO should be in weekly contact with DMASC to provide updates.

1.5. The LAO reviews the SVAR to ensure all information specified in the protocol is captured on an eCRF. DMASC tracks any changes based on LAO comments in the appropriate tab of the SVAR. These tracked changes are removed before the SVAR is sent out for initial eCRF Review Team review.

1.6. Once the DMASC Data Management team and LAO determine the SVAR is ready for wider review, the DMASC Data Management team submits the SVAR to the eCRF Review Team (CDE Curators and DMASC Statisticians) for their initial review, along with the current version of the protocol. The eCRF Review Team is given one week for their initial review.

- The CDE Curators confirm compliance with CDE standards. Information regarding these standards is available on the caDSR Wiki website. The CDE Curators work with DMASC and the LAO to ensure all questions and valid values are CDE-compliant.

  Note: The DMASC Statisticians review the protocol for internal consistency and share any comments with the DMASC Data Management team as part of this process. The DMASC Data Management team then relays these comments to the LAO and/or DCP Study Team on behalf of the DMASC Statisticians so that the comments can be considered by the PI. If the DMASC Statisticians have no comments on the protocol or SVAR, they email the DMASC Data Management team to confirm the completion of their review.

1.7. The eCRF Review Team sends any comments they have to DMASC. DMASC works with the LAO, if needed, to resolve the comments. If revision is required, DMASC tracks any updates in the appropriate tabs of the SVAR and summarizes the updates in a Change Memo, as needed. The SVAR is revised and resubmitted until the eCRF Review Team finds the SVAR to be acceptable.

1.8. Once the SVAR is found to be acceptable by the eCRF Review Team, DMASC removes any tracked updates. Once DMASC receives the CIRB Approval letter for the protocol from PIO, DMASC submits the SVAR to the DCP Study Team for their initial review, along with the current version of the protocol. The DCP Study Team is given one week for their initial review. If their initial review requires more time, the DCP Study Team should notify DMASC.

1.9. The DCP Study Team sends any comments they have to DMASC. DMASC works with the LAO and eCRF Review Team, if needed, to resolve the comments. If revision is required, DMASC tracks any updates in the appropriate tabs of the SVAR and summarizes the updates in a Change Memo, as needed. The SVAR is revised and resubmitted until the DCP Study Team grants approval.

1.10. Once DCP Study Team approval is granted, DMASC notifies PIO and sends the final SVAR to them. PIO sends DMASC an SVAR approval letter. PIO also notifies the LAO and provides them with the final SVAR and SVAR approval letter for their records.

1.11. Once the SVAR approval letter is received from PIO, DMASC builds the study in Medidata Rave using the final SVAR. DMASC completes the study build within 30 business days of the date of the SVAR approval letter.

2. The SVAR may be revised due to protocol amendments. When DMASC receives a protocol amendment from PIO, they review the protocol amendment and determine if any updates are needed to the SVAR.

2.1. If no updates are needed, only the Versions tab of the SVAR are updated to reflect the updated protocol version. This updated SVAR is then sent to PIO per step 1.10 above.

2.2. If updates are needed, DMASC tracks any updates in the appropriate tabs of the SVAR and summarizes the updates in a Change Memo. The revised SVAR and Change Memo are submitted to the LAO, followed by the eCRF Review Team, followed by the DCP Study Team for their review. Approval of the revised SVAR follows the same steps as noted above (LAO, eCRF Review Team, DCP Study Team).

3. The SVAR may also be revised to address administrative issues at the site and/or to address site errors. If an update is identified by the LAO, they should contact the DMASC Data Management team (DataManagement_CP-CTNet@frontierscience.org) with details.

5. DOCUMENTATION REQUIREMENTS

Each LAO is responsible for maintaining the following documentation in their files:

1. Current CP-CTNet REFGD03 *Master Data Management Plan for Lead Academic Organizations and Affiliated Organizations* and any related documents that reflect the current data collection practices for each protocol.
2. The approval letter from DCP regarding all approved SVARs for each protocol.
3. All approved SVARs for each protocol.

6. ADDITIONAL INFORMATION

Please send questions and comments to DMASC at: DataManagement_CP-CTNet@frontierscience.org

7. 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.

Resource	ID	Location
caDSR Wiki	Website	wiki.nci.nih.gov
CP-CTNet Master Data Management Plan for Lead Academic Organizations and Affiliated Organizations	REFGD03	Program Resources
CP-CTNet SVAR Template	Template	Program Resources
CP-CTNet DMASC public website	Website	cp-ctnet-dmasc.org

8. APPENDICES

1. Appendix I: CP-CTNet SVAR Change Memo

Appendix I

CP-CTNet SVAR Change Memo

Protocol Number	
Protocol Title	
Protocol Version Number and Date	
SVAR Version Number and Date	

SVAR **[version number]** dated **[version date]** has been updated to **[include brief summary of updates]**. The updates made are outlined below. Tabs highlighted **[color]** in the SVAR include these updates. Tabs highlighted **[color]** in the SVAR include comments for the CDE Curators.

Tab Name	Change

Title: Participant Recruitment, Retention, Adherence, and Reporting Requirements

Document ID: CP-CTNet SOP 02-04

Version: 7.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
7.0	FEB-24-2026	Updated DMACC to DMASC throughout the document.
6.1	FEB-21-2025	Minor update to the examples of demographic data listed in section 4 *AQuIP Tools and Procedures*, subsection 4 *Systems to Record Accrual Information*.
6.0	AUG-13-2024	Updated section 4 *AQuIP Tools and Procedures*, subsection 2 *AQuIP Toolkit* to clarify that DCP Study Team review of accruing LAO- or AO-specific participant-facing recruitment materials is not required for institution-specific forms that are not study-specific. Updated section 4 *AQuIP Tools and Procedures*, subsection 4 *Systems to Record Accrual Information* to reflect that LAOs now have edit permissions for the *CP-CTNet AQuIP Recruitment Journal - Site-Specific Events* eCRF. Made minor updates throughout the document.
5.0	JAN-26-2024	Updated to clarify the process for submitting study-wide and accruing LAO- or AO-specific participant-facing recruitment materials for typical trials and CNTs. Additional minor clarifying updates were made throughout the document.
4.0	JUL-13-2023	Added detail about accruing LAO and AO responsibilities when completing the *CP-CTNet AQuIP Recruitment Journal - Site-Specific Events* eCRF, clarified the section on recruitment materials and protocol submissions, added detail about the RRA plan, and made other clarifying updates throughout the document.
3.0	FEB-21-2023	Made editorial modifications to clarify procedures.
2.0	SEP-20-2021	This version of the SOP includes updated information about CP-CTNet procedures, resources, and eCRFs used to collect AQuIP-related data. Proofing and formatting updates were applied throughout the SOP.
1.0	AUG-17-2020	Original version of the document.

1. INTRODUCTION AND PURPOSE

The Cancer Prevention Clinical Trials Network (CP-CTNet) Participant Recruitment, Retention, Adherence, and Reporting Requirements Standard Operating Procedure (SOP) pertains to the National Cancer Institute (NCI) Division of Cancer Prevention's (DCP's) Accrual Quality Improvement Program (AQuIP) and the required CP-CTNet Data Management, Auditing, and Statistical Center (DMASC) systems for recording accrual information. The overall purpose of AQuIP is to facilitate efficient implementation of clinical trials through well-planned and carefully monitored participant accrual. AQuIP supports NCI DCP's mission to lead, conduct, and support cancer research across the nation, advance scientific knowledge, and help all people to live longer, healthier lives, while ensuring proper stewardship of public funds.

AQuIP is a multi-component, continuous quality improvement program that entails systematic study- and site-specific recruitment planning with data-driven accrual rate goals and detailed real-time reporting of accrual activity and actual recruitment rates. Frequent monitoring and analysis of accrual data enables a better understanding of performance factors and continuous identification of opportunities for modification of study characteristics and outreach methods.

2. SCOPE

This document provides information for Investigators and Coordinators of Lead Academic Organizations (LAOs) as well as accruing LAOs and Affiliated Organizations (AOs) regarding planning, implementing, monitoring, and adjusting participant recruitment, retention, and adherence (RRA) strategies as well as documenting recruitment-related information. AQuIP RRA planning covers the enrollment trajectory from study design, to accruing LAO and AO selection, to identification of potential participants (pre-screening) through first contact, consent, screening, enrollment, and start of study intervention. Detailed instructions for completing the RRA Plan are embedded in the fillable PDF planning form. All activities should be consistent with Good Clinical Practice (GCP).

3. DEFINITIONS

Term	Definition
AO	Affiliated Organization
AQuIP	Accrual Quality Improvement Program
CIRB	Central Institutional Review Board
CNT	Cross-Network Trial
Collaborating LAO	An LAO that is involved in a CNT that has oversight responsibilities for its own accruing LAOs and AOs.
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DM	Data Manager
DMASC	Data Management, Auditing, and Statistical Center
eCRF	Electronic Case Report Form
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
INT	Inter-Network Trial or INT is the DCP protocol numbering convention for CP-CTNet trials (e.g., INT21-05-01).
LAO	Lead Academic Organization

Term	Definition
Lead LAO	An LAO that takes primary responsibility for the administrative aspects of the CNT and has oversight responsibilities for its own accruing LAOs and AOs.
M-SOP	Manual of Standard Operating Procedures
NCI	National Cancer Institute
PI	Principal Investigator
PIO	Protocol Information Office
RRA	Recruitment, Retention, and Adherence
SOP	Standard Operating Procedure

4. AQUIP TOOLS AND PROCEDURES

AQuIP provides LAOs as well as accruing LAOs and AOs with six complementary tools. ***All tools are available on the CP-CTNet DMASC Public Website and Portal Gateway***:

1. RRA Plan: A comprehensive fillable PDF planning form.
    1.1. Use the RRA Plan to formulate and document study- and site-specific plans for ensuring appropriate recruitment, retention, and adherence for each study.
    1.2. Each study RRA Plan includes site-specific strategies for each accruing LAO and AO (as developed in consultation with each accruing LAO and AO PI and Coordinator for implementation by each accruing LAO and AO).
    1.3. The planned enrollment of participants from underrepresented racial and ethnic populations must be defined and justified.
        - Refer to the RRA Plan for additional recommendations regarding the specific plan of action to enroll and retain diverse participants.
    1.4. RRA Plans are submitted with the first revision (e.g., version 2.0) of the protocol.
    1.5. The RRA Plan is revised per DCP recommendation, if needed.
    1.6. The approved RRA Plan is distributed to each accruing LAO and AO by the LAO.
2. AQuIP Toolkit: A user-friendly library of recruitment resources including a recruitment instruction manual, templates for recruitment materials, media templates, and an image library that may be used by recruitment staff.
    2.1. Recruitment materials include items designed to inform potential participants or referral sources about a specific study in the form of letters, brochures, telephone scripts, advertisements, websites, social media announcements, videos, and other modes of communication.
    2.2. Policies and guidance related to submission of recruitment materials are included in the AQuIP Toolkit.
    2.3. Recruitment materials, including their content and mode of communication, intended for presentation to potential participants (at the public-level or participant-level) must be approved by DCP and the CIRB.
        - All study-wide and accruing LAO- or AO-specific participant-facing recruitment materials should be submitted by LAOs to the DCP Study Team for approval prior to CIRB submission. This includes any participant-facing recruitment materials that are

only applicable to one accruing LAO or AO which are unique or have significantly changed from analogous study-wide CIRB-approved materials (e.g., a phone script with significantly different wording from the study-wide CIRB-approved phone script), but not those which have been updated to only add institutional contact information. This does not apply to institution-specific forms that are not study-specific (e.g., HIPAA forms, instructions regarding the institution's protocol compensation procedures, parking instructions, etc.).

- If an LAO needs additional clarification about whether accruing LAO- or AO-specific participant-facing recruitment materials should be reviewed by DCP for approval prior to CIRB submission, they should contact their DCP Study Team.

- For CNTs, accruing LAO- or AO-specific participant facing recruitment materials should be submitted to the Collaborating LAO (the accruing LAO's or AO's LAO) for review and submission to DCP. The Lead LAO (has primary responsibility for the administrative aspects of the CNT and has oversight responsibilities for its own accruing LAOs and AOs) should be copied on each email correspondence related to the accruing LAO- or AO-specific participant-facing recruitment materials (see REFGD06 *Cross-Network Trials Guidelines* for more information).

  Note: The DCP protocol numbering convention for CP-CTNet CNTs is INT, which stands for "inter-network trial" (e.g., INT21-05-01).

2.4. Recruitment materials require distribution plans when submitted for CIRB review.

- The protocol document should NOT reference or include recruitment materials, as they are not considered a required component of the protocol submission.
  - However, if this guidance is not followed, and the protocol document refers to recruitment materials, those materials must be submitted as a separate part of the same protocol submission for DCP and CIRB approval.
  - If the protocol document refers to recruitment materials that are not included in the protocol submission, the CIRB tables those protocols until those materials are submitted. For more information about CIRB requirements for submission of recruitment materials, refer to the CIRB SOPs.

2.5. Recruitment materials may be submitted for DCP review and approval, in order to proceed to CIRB review, any time after the protocol and other associated documents are submitted/approved.

- Recruitment materials* are submitted to DCP for review through PIO (nci_dcp_pio@mail.nih.gov). Once the materials are approved by DCP, PIO forwards the materials to the CIRB for review.
  - *Different types of recruitment materials for the same study may be submitted to DCP for review via PIO simultaneously, or at different times. However, every effort should be made to consolidate submissions.

3. Training and Resources: A library of recorded webinars as well as links to additional clinical trial resources and accrual support tools to aid LAOs as well as accruing LAOs and AOs in their ongoing research staff training responsibilities.

4. Systems to Record Accrual Information:

   4.1. The Stars registration/randomization system (Stars) is the system that accruing LAOs and AOs use to obtain *Pre-Screen ID*, *Screening ID*, and *Participant ID* assignments for Pre-Screening, Screening, and Enrollment, respectively. Stars is also used to generate participant records in the Medidata Rave (Rave) clinical database. Please see USRMAN01 *CP-CTNet Stars User Guide* for more information.

   4.2. Rave is the Electronic Data Capture system that holds the clinical database that accruing LAOs and AOs use to enter participant-level and site-specific recruitment information.

   4.3. Participant-level recruitment information is entered into several Rave eCRFs during the participant's enrollment trajectory, including the *CP-CTNet Pre-Screening Form*, *CP-CTNet Screening Form*, *Demography, Intervention Administration*, *Registration*, and *Off Study* eCRFs (as applicable). Participant-level recruitment information includes:

   - Strategies used to identify and/or contact and inform each study candidate in order to track the implementation and effectiveness of recruitment strategies for each individual.
   - Reasons that individual study candidates do not proceed to the next stage of the enrollment process – in order to identify study components or recruitment strategies that may be modified to improve accrual.
   - Participant demographic data including race, ethnicity, sex, date of birth, and zip code – in order to determine if the characteristics of the potential participant pool change at each stage of the enrollment process (e.g., pre-screening, first contact, consent, screening, enrollment, and start of study intervention). Please see the *AQuIP Guide to the Enrollment Trajectory: I-SCORE 2023* brochure for more information about the participant enrollment trajectory.

   4.4. Site-specific and study-wide recruitment information, referred to as CP-CTNet AQuIP Recruitment Journal data, is entered into the CP-CTNet AQuIP Recruitment Journal in Rave and is intended to chronicle the "life story" of the study.

   - The CP-CTNet AQuIP Recruitment Journal in Rave includes eCRFs that are used to enter CP-CTNet AQuIP Recruitment Journal data.
   - Examples of these data (events, conditions, or efforts (with dates of occurrence) that may, or are expected to, affect accrual (either positively or negatively)) include the following:
     - Protocol amendments, study agent updates, availability of new recruitment strategies or materials, holidays, staffing issues, and any activities, events, situations, clinic conditions, and/or efforts at a particular accruing LAO or AO or all accruing LAOs and AOs (as opposed to those that affect an individual participant).
   - *Study-wide* recruitment information refers to the subset of CP-CTNet AQuIP Recruitment Journal data that may be, or is expected to be, associated with accrual changes at all accruing LAOs and AOs (e.g., protocol amendments, study agent updates, national holidays, Protocol PI changes, etc.) and is entered and maintained (with the date of occurrence) in the *CP-CTNet AQuIP Recruitment Journal - Study-Wide Events* eCRF by DMASC.
     - DMASC receives information about study-wide events from several sources, including event notification emails from the LAOs and/or DCP Study Teams, study

active notifications, protocol amendment notifications, protocol status update documents, protocol submission worksheets and documents, agent calls, and study staff changes/turnover notifications (as applicable).

- Accruing LAOs and AOs can view, but not edit, study-wide recruitment information on this eCRF.

- *Site-specific* recruitment information refers to the subset of CP-CTNet AQuIP Recruitment Journal data that may be, or is expected to be, associated with accrual changes at a single accruing LAO or AO and is entered and maintained (with the date of occurrence) in the *CP-CTNet AQuIP Recruitment Journal - Site-Specific Events* eCRF by the accruing LAO or AO where the event occurred. Accruing LAOs and AOs are responsible for regularly updating the *CP-CTNet AQuIP Recruitment Journal - Site-Specific Events* eCRF and should include any site-specific events that may affect recruitment (either positively or negatively) for their accruing LAO or AO. Accruing LAOs and AOs and are not responsible for entering study-wide recruitment information.
  - Accruing LAOs and AOs should add a new log line on the *CP-CTNet AQuIP Recruitment Journal - Site-Specific Events* eCRF for each site-specific *Study Event*.
  - The first site-specific *Study Event* that should be added for each accruing LAO and AO is “A3 - Site Open (provide date in *Event Description*).” The *Study Event Start Date* and *Study Event End Date* should be the date that the accruing LAO or AO was activated to the study based on receipt of the ***Confirmation of Site Activation*** email sent by DMASC.
  - Anytime the accruing LAO or AO is activated to an amendment, the site-specific *Study Event* “A29 - Amendment Activated at Accrual Site” should be entered in a new log line. The *Study Event Start Date* and *Study Event End Date* should be the date that the accruing LAO or AO was activated to the amendment based on receipt of the ***Confirmation of Site Activation to Amendment*** email sent by DMASC.
  - An *Event Description* should always be entered to provide more detail about the selected event.
  - Since the events added to this eCRF are site-specific, the *AOs Affected* dropdown should always be completed. The selected accruing LAO or AO should match the CP-CTNet AQuIP Recruitment Journal that is being updated.
  - LAOs are responsible for ensuring that their accruing LAOs and AOs add site-specific events (if any) to the *CP-CTNet AQuIP Recruitment Journal - Site-Specific Events* eCRF. In order to assist the LAOs with this responsibility, DMASC sends monthly CP-CTNet AQuIP Recruitment Journal email reminders to each LAO.

    Note: LAOs have edit permissions for the *CP-CTNet AQuIP Recruitment Journal - Site-Specific Events* eCRF for their accruing LAOs and AOs. LAOs may elect, but are not required, to enter and edit site-specific CP-CTNet AQuIP Recruitment Journal data on behalf of their accruing LAOs or AOs.

    Note: Documentation and training materials for Stars and Rave can be found in the Stars and Rave sections of the CP-CTNet DMASC Portal Gateway.

5. AQuIP Accrual Tracking and Monitoring Reports: This set of data analytics and visualizations is produced by DMASC based on real-time accrual data entered into Stars and Rave by accruing LAO and AO staff. The reports provide visual goals and motivation for timely accrual as well as a basis for monitoring accrual rates by DCP, LAO staff, and accruing LAO and AO staff, facilitate prompt identification of improvement opportunities, and provide guidance for responsive interventions to address shortfalls in accrual. The CP-CTNet AQuIP Recruitment Journal events are reported on the AQuIP Accrual Tracking and Monitoring Reports to illustrate associations (if any) with accrual changes.
6. AQuIP Think Tank: A group of CP-CTNet representatives (including DCP) with expertise in clinical trial management and coordination, assembled as a community of practice to facilitate discussion of real-world clinical trial implementation challenges and solutions, collaboratively identify knowledge and training gaps, and provide practical feedback to DCP leadership.

5. AQUIP DOCUMENTATION, REPORTING, AND OVERSIGHT REQUIREMENTS

1. Data should be entered on a continual basis, and all required data fields should be completed.
    1.1. Data are reviewed carefully by DMASC staff, who aggregate the data, perform data integrity checks, and send data queries back to the accruing LAOs and AOs.
    1.2. Each accruing LAO and AO is responsible for entering data and resolving data queries within 14 calendar days.
2. An escalation process is defined for data and/or query responses that are overdue:
    2.1. If an accruing LAO or AO has not responded to requests for overdue data/queries, DMASC escalates to the LAO. If there is no resolution, the LAO escalates to DCP, keeping DMASC in copy.
    2.2. If an LAO has not responded to requests for overdue data/queries for their accruing LAO or AOs, DMASC escalates to DCP.
3. DCP, DMASC, and LAOs (as applicable) work with accruing LAOs and AOs to determine the reason for the delinquency and create a plan to address the issue and prevent further issues.
4. DMASC generates monthly AQuIP Accrual Tracking and Monitoring Reports.
    4.1. The LAOs provide oversight of accrual and participant-level and site-level recruitment information documentation for their respective accruing LAOs and AOs to assure timely and accurate data entry.
    4.2. The LAOs must review and proactively evaluate the study-specific AQuIP Accrual Tracking and Monitoring Reports and distribute the reports to their accruing LAOs and AOs.
    4.3. The LAOs must assure that the recruitment impediments, strategic corrective actions, and favorable factors are well-documented via accruing LAO and AO CP-CTNet AQuIP Recruitment Journal event entries.
    4.4. DCP may require additional recruitment barrier analysis and a corrective action plan for review by the DCP Medical Monitor, Nurse Consultant, and Scientific Lead, and approval by DCP leadership. Depending on the recruitment issues, interventions for improvement are devised and/or study design modifications or discontinuation are considered.

Please send questions and comments to DataManagement_CP-CTNet@frontierscience.org.

6. 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.

Resource	ID	Location
AQuIP Guide to the Enrollment Trajectory: I-SCORE 2023	Brochure	Program Resources
CIRB SOPs	SOP	ncicirb.org
CP-CTNet Stars User Guide	USRMAN01	Program Resources
Cross-Network Trials Guidelines	REFGD06	Program Resources
RRA Plan	Form	Program Resources

7. APPENDICES

1. None

Title: Policy on Standard Operating Procedures

Document ID: CP-CTNet SOP 02-05

Version: 6.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
6.0	FEB-24-2026	Updated section 5 *M-SOP*, subsection 3 *M-SOP Training/Sign-off* to clarify that M-SOP training may also be documented using an electronic or paper institutional sign-off log or an email-based documentation method. Additional information regarding the use of an email-based documentation method was added for consistency across LAOs, accruing LAOs, and AOs. Minor editorial updates and clarifications were made throughout the document. Updated DMACC to DMASC throughout the document.
5.0	FEB-07-2025	Minor editorial updates and clarifications were made throughout the document.
4.0	JAN-26-2024	Updated the M-SOP release schedule from up to three times per year to up to two times per year. Updated the DTL descriptions based on the updated DTL Master Task List. Minor updates were made throughout the document. Updated the document title.
3.0	JUL-13-2023	Updated to clarify that LAO staff should review and sign off on the M-SOP. Updated the links to documents hosted on the DCP website to ensure that documents download as expected.
2.0	FEB-21-2023	Total re-write to reflect implementation of the M-SOP.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

The Cancer Prevention Clinical Trials Network (CP-CTNet) Standard Operating Procedures (SOPs) are written standard procedures that describe the responsibilities of staff from the Division of Cancer Prevention (DCP), the Data Management, Auditing, and Statistical Center (DMASC), Lead Academic Organizations (LAOs), accruing LAOs, and Affiliated Organizations (AOs).

The CP-CTNet SOPs are maintained as one master manual, referred to as the Manual of Standard Operating Procedures (M-SOP). The M-SOP is located on the *Program Resources* page on the CP-CTNet DMASC public website.

2. SCOPE

This document details the responsibilities of DCP, DMASC, LAOs, accruing LAOs, and AOs throughout the CP-CTNet SOP creation, update, review, training/sign-off, and amendment process.

3. DEFINITIONS

Term	Definition
AE	Adverse Event
AERS	Adverse Event Reporting System
AO	Affiliated Organization
CP-CTNet	Cancer Prevention Clinical Trials Network
CRA	Clinical Research Associate
CRF	Case Report Form
CTEP	Cancer Therapy Evaluation Program
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DTL	Delegation of Tasks Log
H&P	History and Physical
IND	Investigational New Drug
LAO	Lead Academic Organization
M-SOP	Manual of Standard Operating Procedures
PI	Principal Investigator
QA	Quality Assurance
SOP	Standard Operating Procedure

4. SOP CREATION, UPDATE, AND REVIEW

1. Creation and Update:

1.1. The first iteration of a CP-CTNet SOP is written by DCP and DMASC.

1.2. The draft SOP is then reviewed by the LAOs, as applicable. Each LAO determines the reviewer(s).

1.3. The draft SOP is then sent to the CP-CTNet Steering Committee for final approval.

1.4. DMASC integrates the approved individual SOP into the M-SOP. Any new or updated individual SOPs will be documented in the M-SOP's revision history table alongside the M-

SOP version number and effective date. See the Versioning section below for more information about M-SOP and individual SOP versioning.

1.5. Any new or updated individual SOPs are included as part of the next M-SOP release. See the Release Frequency section below for more information.

1.6. The M-SOP is posted to the Program Resources page on the CP-CTNet DMASC public website.

1.7. The new or updated individual SOPs become effective within five business days after DMASC sends an announcement email to DCP and the LAOs indicating that a new version of the M-SOP is available. The LAOs then forward the announcement to their accruing LAOs and AOs.

2. Review:

2.1. All SOPs require review by DCP and DMASC annually, and ad hoc, with the latest version superseding earlier versions. The annual review is formally performed by DMASC. Every January, a new version of the M-SOP will be released if any changes were made to the individual SOPs during the annual review.

2.2. All changes to SOPs made during the annual and ad hoc reviews are sent to DCP for review and approval before they are finalized and integrated into the M-SOP. The changes from the annual and ad hoc reviews are announced to the network as part of one of the M-SOP releases (up to two times per year). See the Release Frequency section below for more information.

2.3. LAO and CP-CTNet Steering Committee review is requested for major changes to individual SOPs.

2.4. The LAOs discuss the M-SOP with their accruing LAOs and AOs annually, and each time the M-SOP is released (up to two times per year), to ensure understanding.

5. M-SOP

After individual SOPs are created, reviewed, and finalized, they are integrated and maintained within the M-SOP by DMASC. The M-SOP contains all current CP-CTNet SOPs in one file, which is posted to the *Program Resources* page on the CP-CTNet DMASC public website. The M-SOP includes a clickable table of contents to allow for quick navigation to individual SOPs. DMASC releases the M-SOP up to two times per year (e.g., January and June) if there have been updates to individual SOPs since the last release of the M-SOP. See the Release Frequency section below for more information. Each M-SOP release includes all new, existing, and updated CP-CTNet SOPs, with a *CP-CTNet M-SOP Acknowledgement Sign-Off Log*.

Note: The M-SOP does not include related documentation (e.g., reference guides, quick reference guides, templates, forms, etc.). All related CP-CTNet documentation is updated as needed and is publicly available on the *Program Resources* page on the CP-CTNet DMASC public website.

1. Release Frequency:

1.1. DMASC, in collaboration with DCP, releases the M-SOP with relevant individual SOP changes up to two times per year to alleviate constant SOP updates.

- If an individual SOP is updated after the M-SOP is released, that individual SOP is included as part of the next M-SOP release.

- It is possible that individual SOPs may require updates outside of the release schedule (up to two times per year), as procedures change, or new processes are added. If an individual SOP containing major or time-sensitive changes requires an expedited update and cannot wait until the next M-SOP release, the plan of action is determined collaboratively by DCP and DMASC.

1.2. For each M-SOP release, DMASC sends an announcement email to DCP and the LAOs indicating that a new version of the M-SOP is available, and the LAOs then forward the announcement to their accruing LAOs and AOs.

- The LAOs distribute the most recent version of the M-SOP to any new accruing LAOs and AOs at the time that they join the network.

1.3. Each LAO, accruing LAO, and AO is responsible for obtaining documented evidence of training/sign-off on the M-SOP initially and on every M-SOP version for relevant staff at their site. See the M-SOP Training/Sign-off section below for more information about the relevant staff that are required to be trained on/sign off on the M-SOP.

1.4. All LAOs, accruing LAOs, and AOs should maintain the most recent version of the M-SOP on file at their site.

1.5. If there are no updates to individual SOPs prior to an M-SOP release, then the M-SOP is not released and DMASC sends a notification to LAOs indicating that there are no changes to the M-SOP. LAOs notify their accruing LAOs and AOs that there are no changes to the M-SOP. No additional action is needed from DCP, DMASC, LAOs, accruing LAOs, or AOs.

2. Versioning:

2.1. The entire M-SOP is assigned a version number, starting at version 1.0, which is increased by a whole number each time the M-SOP is released to the network. If no SOP updates have occurred since the last release, the M-SOP version will not change until the next release containing an SOP update.

2.2. Individual SOPs also maintain their own cover tracking sheet and revision history table to track historical changes made to individual SOPs.

2.3. The M-SOP version date is the same or later than the last updated individual SOP date (e.g., the SOP with the most recent date).

- For example, if an individual SOP was updated on 02/28/2023, the M-SOP has a version date of 02/28/2023 or later.

3. M-SOP Training/Sign-off:

3.1. All LAO staff need to review and be trained on/sign off on the M-SOP as part of their oversight of their accruing LAOs and AOs. Accruing LAO and AO staff that are listed on the DTL with the task names listed below are required to review and be trained on/sign off on the M-SOP as well. The M-SOP does not apply to the other DTL task names.

- Agent/Intervention Prescribing: Responsible for writing an order for a patient that is an agent or intervention.
- Site PI: Investigator at the site responsible for signing the DTL for a given protocol, and with overall responsibility for the study conduct at the site.
- Consenting Person: Person having responsibility for consent.

- Eligibility Assessments: Verification of eligibility.
- End Point Assessment: Assess study endpoints.
- Enrolling Person/Treating Investigator: Investigator having responsibility for subject treatment (e.g., Enrolling investigator).
- H&P Assessments: Conducts physical exam and assessments.
- Patient Screening/Recruiting: Responsible for screening and recruiting of subjects.
- Primary Study/Site Contact: The point of contact for the study.
- Rave CRA: Rave write access; responsible for data management and uploads of Central Monitoring documents; and using Rave CTEP - AERS safety reporting tools.
- Rave Investigator: Investigator assigned to sign-off on the CRFs in Rave.
- Regulatory Contact: Site staff responsible for regulatory submissions and maintaining essential records.
- Source Documentation Completion: Responsible for collecting data on study-related assessments.
- Study-Related Interventions: Responsible for coordinating and/or administering study-related interventions and procedures.
- Toxicity Assessment: Assesses AEs.
- Unblinded Study Personnel: Study personnel responsible for handling, preparing, and labeling study agents to ensure blinded study randomization is protected at the site. A copy of the pharmacy's plan or SOP for unblinded study personnel to be included in the site Trial Master File. At a minimum, one of the listed personnel must be the Shipping Designee at the drug shipment site.

3.2. The above staff are trained on/sign off on the M-SOP initially and on every M-SOP version regardless of if the modification affects their task(s) or not.

3.3. Each LAO, accruing LAO, and AO must ensure that all current and new relevant staff at their site have documented evidence of training/sign-off on all applicable M-SOP versions by:

- Collecting signatures from the relevant staff on the *CP-CTNet M-SOP Acknowledgement Sign-Off Log*; or
- Using their own process (e.g., an electronic or paper institutional sign-off log) which must clearly document the M-SOP version, relevant staff name, and date of signature, and be outlined in a site-specific SOP; or
- Using an email-based documentation method.
    - If training is documented via email, then the M-SOP should be attached to an email that details the changes made to the M-SOP in the body of the email. Once the individual that received the email with the M-SOP completes the training, they must forward the original email to a designated individual at their site indicating that the email and associated M-SOP were received, reviewed, and acknowledged. The designated individual at the site saves the training-related emails that they receive

and tracks who has been trained at their site. The saved emails and tracking method are retained in the appropriate essential records binder/file.

3.4. LAOs, accruing LAOs, and AOs must be able to provide documented evidence of training/sign-offs for their staff and their site-specific SOP (if applicable) upon request, as this documentation is reviewed during DMASC QA audits.

3.5. LAOs, accruing LAOs, and AOs may determine how to collect documented evidence of training/sign-offs for their staff within their site.

- LAOs may provide guidance to their accruing LAOs and AOs about how to collect documented evidence of training/sign-offs for their staff within their site. However, LAOs should not dictate for a given study how accruing LAOs and AOs should collect documented evidence of training/sign-offs on the M-SOP. This allows each accruing LAO and AO to have a consistent way of collecting documented evidence of training/sign-offs on the M-SOP across studies.

6. AMENDING SOPS DUE TO LOCAL INSTITUTIONAL POLICY

1. CP-CTNet SOPs are to be adopted by the LAOs, accruing LAOs, and AOs as written unless they are in direct conflict with local institutional policy. If this is the case, the LAO may amend the applicable SOPs only after obtaining written approval from DCP.
2. If LAOs, accruing LAOs, and/or AOs need to amend individual SOPs to comply with local institutional policy, the LAO:

2.1. Collects all LAO, accruing LAO, and AO amendment requests and electronically submits them as a package to DMASC (Documentation_CP-CTNet@frontierscience.org). DCP and DMASC review the package.

- The submission package includes:
  - A cover letter requesting the changes to the SOPs, including rationale for the requested changes.
  - The ‘clean’ copy of the revised SOPs with the ‘Site Version Date’ in the footer.
  - The ‘tracked changes’ copy of the revised SOPs with the ‘Site Version Date’ in the footer.

2.2. Communicates DCP’s decision regarding the amended SOPs to all applicable LAO, accruing LAO, and AO staff.

2.3. Adds the ‘Effective Site Version Date’ and ‘This SOP has been amended in compliance with local institutional policy.’ to the footer of the amended SOPs once approved by DCP.

2.4. Distributes the DCP-approved amended SOPs to all applicable LAO, accruing LAO, and AO staff for their use.

2.5. LAOs, accruing LAOs, and AOs should maintain all approved SOPs that are revised based on local institutional policy on file at their site.

2.6. Individual SOPs that have been amended to meet local institutional policy are not included in the M-SOP or posted on the CP-CTNet DMASC public website.

7. ADDITIONAL INFORMATION

Please send questions and comments to Documentation_CP-CTNet@frontierscience.org.

8. 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.

Resource	ID	Location
CP-CTNet DMASC Public Website	Website	cp-ctnet-dmasc.org
CP-CTNet M-SOP Acknowledgement Sign-Off Log	Log	Program Resources
DCP Delegation of Tasks Log	Form	prevention.cancer.gov

9. APPENDICES

None

Title: Biospecimen Submission Requirements

Document ID: CP-CTNet SOP 02-06

Version: 6.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
6.0	FEB-24-2026	Added clarifying information about submitting biospecimens to DMASC for inclusion in the VSR. Updated DMACC to DMASC and made minor editorial updates throughout the document.
5.0	FEB-07-2025	Made minor editorial updates throughout the document.
4.0	JAN-26-2024	Updated to reflect the new version of the *CP-CTNet Material Transfer Manifest*. Made minor updates throughout the document.
3.0	FEB-21-2023	Added Section 3 Definitions and updated FNLCR contact information.
2.0	SEP-10-2020	Added that shipments to FNLCR are confirmed upon receipt.
1.0	AUG-17-2020	Original version of the document.

1. INTRODUCTION AND PURPOSE

As described in each protocol and laboratory manual, the Lead Academic Organizations (LAOs), accruing LAOs, and Affiliated Organizations (AOs) are responsible for collecting, processing, storing, and shipping Cancer Prevention Clinical Trials Network (CP-CTNet) study biospecimens to the appropriate laboratories for biomarker and/or other analyses. Any remaining biospecimens after completion of analyses and other study-related activities are required to be shared with the research community for any research participants that provided consent for future use of research biospecimens. These biospecimens may be submitted to the Frederick National Laboratory for Cancer Research (FNLCR) for storage and distribution to the community for investigational use.

2. SCOPE

This document details the responsibilities of the LAOs regarding biospecimen collection, processing, storage, and shipment to FNLCR. These responsibilities may be delegated to the accruing LAOs and AOs as described in each protocol and laboratory manual.

3. DEFINITIONS

Term	Definition
AO	Affiliated Organization
BSI	Biological Specimen Inventory
CP-CTNet	Cancer Prevention Clinical Trials Network
DSS	Data Submission System
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
FDA	Food and Drug Administration
FNLCR	Frederick National Laboratory for Cancer Research
LAO	Lead Academic Organization
LDMS	Laboratory Data Management System
M-SOP	Manual of Standard Operating Procedures
NCI	National Cancer Institute
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
VSR	Virtual Specimen Repository

4. PROCEDURES

1. Requirements for study-specific biospecimen management, including collection, processing, storage, and shipment, are defined in Section 12 of each protocol. Further details may be found in the laboratory manual for each study.
2. Biospecimen inventory data are sent to DMASC through LDMS or DSS for inclusion in the VSR website.
3. Required storage and distribution of biospecimens after the end of a study may be managed by FNLCR.
    3.1. Biospecimens designated for centralized storage and distribution must be confirmed as consented for future use ***prior*** to shipping these biospecimens to FNLCR. Any

biospecimens that are lacking this consent should ***not*** be shipped to FNLCR and should be destroyed per institutional guidelines.

3.2. An electronic item-level FORM001 *CP-CTNet Material Transfer Manifest* is to be submitted prior to shipment of any biospecimens to FNLCR. For studies using DMASC's LDMS, the LAO, accruing LAO, or AO may reach out to DMASC at ldmsinfo@frontierscience.org for assistance with any LDMS-related questions that come up while preparing the Manifest.

3.3. The ***minimum data items required*** for each biospecimen submitted are listed below. Additional data may be required and/or requested depending on the specialized needs of the study, protocol requirements, and/or the material group(s) of the biospecimens being submitted.

- BSI ID
- Study ID
- Material Type
- Current Label
- Label Status
- Volume
- Volume Estimate
- Volume Unit

3.4. The shipper or designated representative must provide a signature and date within the Manifest to verify that all biospecimens listed on the Manifest have been reviewed as consented for future use.

4. The Manifest should be submitted to FNLCR at NCI-FrederickCSPBPTLStaff@mail.nih.gov and to DCP at NCIDCP-CTNetBiospecimens@mail.nih.gov at least 48 hours prior to shipping the listed biospecimens.

4.1. When the LAO, accruing LAO, or AO is ready to ship the biospecimens, they should contact FNLCR. A pre-shipment webinar will be held by FNLCR with the institution responsible for shipment, to discuss the specifics of the study's biospecimen collection, review supply, and shipment instructions, and develop a timeline for related tasks and activities. Supplies and related materials will be provided by FNLCR to ensure the proper packaging and transportation of biospecimens to FNLCR.

5. Supplies are provided by FNLCR for frozen, chilled, and room temperature shipments, as required. The supplies will include packaging, instructions, points of contact, shipping address, and prepaid courier documents.

5.1. Biospecimens should be shipped with a copy of the Manifest and a packing slip in each package. The shipping address for these materials is noted on the Manifest and in #5 below. Details regarding completion of the Manifest and packing slip will be reviewed during the pre-shipment webinar with the responsible institution.

5.2. All shipments to FNLCR are confirmed when they arrive (e.g., condition, temperature, # of boxes, # of vials, etc.).

6. The FNLCR Head of Bioprocessing and Trial Logistics is responsible for general oversight of this process, laboratory administration, shipping supplies, and biospecimen database inquiries:

BioProcessing Laboratory

Attn: Norma Diaz/CP-CTNet
4600 Wedgewood Blvd
Suite K
Frederick, MD 21703
(301) 228-4200
NCI-FrederickCSPBPTLStaff@mail.nih.gov

5. ADDITIONAL INFORMATION

Please send questions and comments regarding this SOP to ldmsinfo@frontierscience.org.

6. 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.

Resource	ID	Location
CP-CTNet Material Transfer Manifest	FORM001	Program Resources

7. APPENDICES

None

Title: Unblinding Participants

Document ID: CP-CTNet SOP 02-07

Version: 5.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
5.0	FEB-24-2026	Updated DMACC to DMASC throughout the document. Updated the name of SOP 04-02 to *Study Closeout* throughout the document. Added a link to v20 of the *DCP CP-CTNet Chemoprevention Protocol Template* in section 7 *References*.
4.0	FEB-07-2025	Added Appendix I *Study Unblinding Data Requirements* and made minor associated edits throughout document.
3.0	AUG-13-2024	Added information regarding non-emergency unblinding during the study, clarified the full study unblinding workflow (DMACC to the LAOs to the accruing LAOs and AOs), replaced references to Study Investigator with PI, and made minor editorial updates throughout document.
2.0	JAN-26-2024	Replaced references to sites with accruing LAOs and AOs and made minor editorial updates throughout document.
1.0	FEB-21-2023	Original version of document.

1. INTRODUCTION AND PURPOSE

This document provides guidelines for unblinding participants enrolled in Cancer Prevention Clinical Trials Network (CP-CTNet) studies that involve randomization with blinded treatment assignment.

2. SCOPE

This document details the responsibilities related to unblinding participants for staff at Lead Academic Organizations (LAOs), accruing LAOs, Affiliated Organizations (AOs), the Division of Cancer Prevention (DCP), and the Data Management, Auditing, and Statistical Center (DMASC).

3. DEFINITIONS

Term	Definition
AO	Affiliated Organization
CIRB	Central Institutional Review Board
CMDMRU	Co-Manager of the Data Management and Reporting Unit
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DM	Data Manager
DMASC	Data Management, Auditing, and Statistical Center
DOB	Date of Birth
DSMB	Data Safety Monitoring Board
IEC	Independent Ethics Committee
IRB	Institutional Review Board
LAO	Lead Academic Organization
M-SOP	Manual of Standard Operating Procedures
MDS	Minimum Data Set
MM	Medical Monitor
NC	Nurse Consultant
PI	Principal Investigator
PID	Participant Identifier
SL	Scientific Lead
SOP	Standard Operating Procedure
Study Team	Comprised of the DCP MM, DCP NC, DCP SL, LAO staff, and DMASC staff

4. CATEGORIES AND REASONS FOR UNBLINDING

1. Unblinding by DMASC

    1.1. Full study unblinding at the end of the study takes place when all data forms have been keyed into the database for all participants, data cleaning has been completed including resolution of any outstanding data queries (this includes MDS queries), and the study team has declared the study dataset to be complete (refer to SOP 04-02 *Study Closeout* for additional information). On a date predetermined by the study team, the DMASC CMDMRU provides each LAO with the unblinded treatment assignments for all participants enrolled in the study at its accruing LAO and each of its AOs.

1.2. Non-emergency unblinding during the study, as requested by the LAO PI or Protocol PI, takes place as needed and should be approved by the DCP MM. Additional information regarding non-emergency unblinding during the study is included in section 5.2 below.

2. Unblinding by the Accruing LAO or AO Pharmacist of Record

2.1. Emergency unblinding of individual participants takes place when the information is needed for the immediate medical management of a participant. Guidelines for emergency unblinding can be found in section 8.9 of each study protocol.

5. PROCEDURES

1. Full Study Unblinding at the End of the Study

1.1. During the preparation of the study closeout timeline, the study team should confirm the plan for unblinding the participants. Before unblinding the participants can take place:

- The unblinding date should be determined in advance by the study team along with the study closeout timeline.
- The DMASC DM should send a draft unblinding memo to the study team for review and for the addition of any study-specific language the study team wishes to include.
- All data forms need to be keyed, all data needs to be cleaned, and the study team needs to declare the study dataset to be complete (refer to SOP 04-02 *Study Closeout* for additional information).

1.2. The DMASC CMDMRU prepares unblinding lists for each accruing LAO and AO. See Appendix I *Study Unblinding Data Requirements* for additional information.

1.3. On the date predetermined by the study team, the DMASC CMDMRU securely emails each LAO the unblinding memo and unblinding lists for the participants from its accruing LAO and each of its AOs. The DMASC CMDMRU should copy the DCP MM, NC, and SL on this email.

1.4. Each LAO distributes the unblinding memo and appropriate unblinding lists to its accruing LAO and each of its AOs.

1.5. Each Accruing LAO and AO PI or designee informs their participants of their assigned study treatment. Any participant-facing material(s) that the Accruing LAO or AO PI or designee decides to use to inform their participants of their assigned study treatment must be approved by the CIRB.

2. Non-Emergency Unblinding During the Study

2.1. In the rare circumstance where the LAO PI or Protocol PI requests the unblinding of a cohort of participants or the full study during the study (e.g., need to know the assigned study treatment in order to amend the study design), the LAO PI or Protocol PI should provide clear rationale for this request and email the DCP MM for approval. The LAO PI, Protocol PI, DCP NC, DCP SL, LAO Statistician, DMASC Statistician, and DMASC DM should be copied on this email.

2.2. Once approved by the DCP MM, the DMASC CMDMRU who is not assigned to the study prepares the requested unblinding lists and securely emails them to the individuals that the LAO PI or Protocol PI requested.

2.3. If this unblinding was not outlined in the study protocol, the accruing LAO(s) and/or AO(s) should submit a protocol deviation for each participant who was unblinded (refer to SOP 02-02 *Reporting Protocol Deviations* for additional information).

3. Emergency Unblinding of Individual Participants

3.1. In the rare circumstance where an Accruing LAO or AO PI or designee determines that there is an immediate medical need to know the assigned study treatment of an individual participant (per section 8.9 of each study protocol), the Accruing LAO or AO PI or designee contacts the Accruing LAO or AO Pharmacist of Record to obtain the assigned study treatment.

3.2. Within 24 hours, the Accruing LAO or AO PI or designee must document the reason for emergency unblinding and send the protocol number, PID, and reason for unblinding to the CIRB, IEC, and/or local IRB (as applicable) as well as the LAO PI, Protocol PI, DCP MM, DCP NC, DCP SL, LAO Statistician, DMASC Statistician, DMASC DM, and DSMB (if applicable).

3.3. There must be written documentation of the communication regarding the unblinding request from the Accruing LAO or AO PI or designee to the Accruing LAO or AO Pharmacist of Record, and from the Accruing LAO or AO Pharmacist of Record back to the Accruing LAO or AO PI or designee, preferably at the time of the initial request/response, but if that is not feasible, then at least within 24 hours. This written documentation should be stored in the essential documents file at the accruing LAO or AO.

6. ADDITIONAL INFORMATION

Please send questions and comments to DataManagement_CP-CTNet@frontierscience.org.

7. 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.

Resource	ID	Location
DCP CP-CTNet Chemoprevention Protocol Template V18 April 2025	Template	Program Resources
DCP CP-CTNet Chemoprevention Protocol Template V20 January 2026	Template	Program Resources
Study Closeout	SOP 04-02	Program Resources
Reporting Protocol Deviations	SOP 02-02	Program Resources

8. APPENDICES

1. Appendix I - Study Unblinding Data Requirements

Appendix I

Study Unblinding Data Requirements

1. All randomized participants are to be unblinded, regardless of whether or not they actually received the assigned study treatment. DMASC will provide the unblinding lists in PDF file format.
2. The following data are included in the unblinding lists:
    - 2.1. Protocol
    - 2.2. PID
    - 2.3. Treatment ID
    - 2.4. Sex
    - 2.5. DOB
    - 2.6. Randomization Date
    - 2.7. Treatment Description
    - 2.8. Start of Treatment Date
    - 2.9. End of Treatment Date
    - 2.10. Report Generated Date

Title: Site (LAO/AO) Preparations for Quality Assurance Audits

Document ID: CP-CTNet SOP 03-02

Version: 5.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
5.0	FEB-24-2026	Updated DMACC to DMASC, essential documents to essential records, and source documents to source records throughout the document. Updated the name of SOP 01-01 to *Essential Records Submission for Sponsor's Trial Master File*.
4.0	AUG-13-2024	Major updates to sections 1 *Introduction and Purpose*, 4 *Scope of a DMACC Quality Assurance Audit*, 5 *Scheduling*, 6 *Site Coordinator Responsibilities for LAO and AO*, and 7 *Responsibilities for LAO Only* to align with REFGD15 *CP-CTNet DMACC Auditing Plan*. Added Appendix I *Investigator Site File of Essential Documents Tip Sheet*.
3.0	FEB-21-2023	Major updates to all sections.
2.0	SEP-30-2021	Added scheduling timelines as well as changed 10% of participants or a minimum of 7 (it previously said 25%), added information about the risk assessment tool.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

The National Cancer Institute (NCI)/Division of Cancer Prevention (DCP) requires Quality Assurance (QA) audits of clinical trials data and processes at each Lead Academic Organization (LAO) and Affiliated Organization (AO). Audits are conducted by the Cancer Prevention Clinical Trials Network (CP-CTNet) Data Management, Auditing, and Statistical Center (DMASC).

Auditing is an independent quality assurance function for systematic evaluation of trial processes and documents to determine whether trial-related activities are conducted, and data are recorded, analyzed, and accurately reported according to the protocol, the sponsor's Standard Operating Procedures (SOPs), relevant Good Clinical Practice (GCP) guidelines, applicable regulatory requirements, federal regulations, and National Institutes of Health (NIH)/NCI/DCP policies. Audits are performed by DMASC on a routine and ad hoc basis and are a snapshot in time of the CP-CTNet sites' compliance with program requirements.

The specific purpose of the auditing program is as follows:

1. Verify investigator compliance with GCP, the protocol and all regulatory requirements.
2. Ensure participant safety, rights, and well-being.
3. Document the accuracy of data submitted to Medidata Rave, the Stars registration/randomization system, and DCP.
4. Verify adherence to CP-CTNet policies and procedures.
5. Provide site staff with resources for a more thorough understanding of regulatory requirements, GCP, data collection, and data management practices, as necessary.

Auditing also provides the opportunity for LAOs, AOs, DCP, and DMASC to work together to identify areas for systemic and policy-level improvements to increase both efficiency and compliance, to better ensure the protection of human subjects, and to enhance the quality and integrity of CP-CTNet clinical trials. Additionally, audits provide sites with the opportunity to address any questions or concerns about CP-CTNet processes or related issues.

The major objectives of the audit program are to ensure compliance with GCP, the protocol and all federal and regulatory requirements, to verify accurate recording and reporting of study data that could affect the interpretation of primary study endpoints, and to ensure participant safety. The four main components reviewed during an accruing LAO/AO audit are:

1. Essential records.
2. Policy, procedure, and site operations.
3. Pharmacy and drug accountability.
4. Participant study charts.

Routine Quality Assurance Audits

1. An accruing site (AOs and accruing LAOs) is eligible for audit once they have enrolled a minimum of three (3) participants to a CP-CTNet protocol. Site selection for a DMASC quality assurance (QA) audit is determined by risk analysis performed by the audit team, along with input from the DCP Study Team and LAO as outlined in REFGD15 *CP-CTNet DMASC Auditing Plan*.

For-cause Audits

1. A for-cause audit is a repeat audit of the same network protocol at the same accruing LAO or AO. For-cause audits are not routinely performed and must be requested by the DCP Study Team, and/or recommended by the auditor or the LAO in response to a specific concern.

LAO Oversight Audits

1. The major objectives of an LAO oversight audit are to ensure LAO oversight is performed according to SOP 03-03 *LAO Oversight Activities*. LAO oversight audits are performed through review of various documentation and communications.

2. SCOPE

This document details the responsibilities of the LAO and AO Site Coordinators and Principal Investigators (PIs) regarding the conduct of a QA audit.

3. DEFINITIONS

Term	Definition
AE	Adverse Event
AO	Affiliated Organization
APIW	Annual Principal Investigator Worksheet
AQuIP	Accrual Quality Improvement Program
ASIW	Annual Signatory Institution Worksheet
CAP	College of American Pathologists
CIRB	Central Institutional Review Board
CLIA	Clinical Laboratory Improvement Amendments
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DSMC	Data Safety and Monitoring Committee
DSMP	Data and Safety Monitoring Plan
DTL	Delegation of Tasks Log
EMR	Electronic Medical Record
FWA	Federal wide Assurance
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICD	Informed Consent Document
ID	Identifier
IEC	Independent Ethics Committee
IRB	Institutional Review Board
LAO	Lead Academic Organization
M-SOP	Manual of Standard Operating Procedures
MM	Medical Monitor
NC	Nurse Consultant
NCI	National Cancer Institute

Term	Definition
PD	Protocol Deviation
PI	Principal Investigator
QA	Quality Assurance
RRA	Recruitment, Retention, and Adherence
SAE	Serious Adverse Event
SDV	Source Data Verification
SL	Scientific Lead
SOP	Standard Operating Procedure
SSW	Site Specific Worksheet
SVAR	System Variable Attribute Report

4. SCOPE OF A DMASC QUALITY ASSURANCE AUDIT

The scope of the DMASC QA audit includes but is not limited to:

1. Investigator Site File of Essential Records: See Appendix I *Investigator Site File of Essential Records Tip Sheet* for more information.
    1.1. Well organized, current, and complete in accordance with SOP 01-01 *Essential Records Submission for Sponsor's Trial Master File*.
    1.2. RCR status is "active" for current applicable staff members on the DTL.
2. Site Operations, Policy, and Procedure review:
    2.1. Assurance of participant confidentiality.
    2.2. Documentation of training and qualifications of staff (general and protocol specific).
    2.3. Documentation of regular communication:
        - Between LAOs and AOs.
        - LAO dissemination of DCP, DMASC, CIRB, and DCP Regulatory Contractor communications to AOs as appropriate.
        - LAO communication of AO generated questions, concerns, issues to DCP, DMASC, CIRB, and DCP Regulatory Contractor as appropriate.
    2.4. Protocol compliance:
        - 100% adherence to eligibility criteria
        - Deviations from the protocol are identified and reported in compliance with SOP 02-02 *Reporting Protocol Deviations*.
        - Serious or continuous noncompliance and unanticipated problems are reported to the CIRB, local IRB, and DSMC in compliance with the policies and procedures specified by each entity.
    2.5. Participant recruitment, retention, adherence (RRA), and reporting is in compliance with SOP 02-04 *Participant Recruitment, Retention, Adherence, and Reporting Requirements*.
        - The RRA Plan developed for the protocol (provided by the LAO) is being followed.

- Documentation of accrual efforts (pre-screening and screening) in Stars is complete and current.
- Accrual rates are on target.
- The AQuIP recruitment journal in Medidata Rave (Rave) is current and complete and documents events, situations, conditions, or efforts that may have an impact (either positive or negative) on accrual at the site.

2.6. The clinical evaluations and procedures described in the protocol are complete for each participant and are performed in accordance with the methods and within the timeframe specified for each.

2.7. Study visits and interim contacts are complete and performed within the specified timeframe.

2.8. The collection of clinical labs and biospecimens for endpoints analysis is complete.

- Biospecimens are collected, labeled, inventoried, processed, stored, and submitted for endpoint analysis (or analyzed on-site) as specified by the protocol.

2.9. Off-agent and off-study criteria are adhered to.

2.10. Criteria for dose modification of study agent are followed.

2.11. AEs are assessed and reported accurately, completely, and in a timely fashion.

2.12. Serious adverse events are correctly identified and reported within 24 hours of knowledge of the event.

3. Pharmacy/Drug Accountability:

3.1. Storage is secure and environmental conditions (such as temperature) are monitored and maintained within the parameters specified in the study protocol.

- Any excursions from the protocol-specified storage conditions are documented.

3.2. Study agent accountability records are maintained, are current, available for review, and include:

- Study agent order receipts.
- An accurate physical inventory of dispensed, un-dispensed and returned study agent.
- A record of per participant study agent dispensing and returns documenting:
  - Institution Name.
  - Protocol name and number.
  - Agent name, dose form, and strength.
  - Participant initials, study ID number and, when applicable, randomization number.
  - Date and quantity dispensed to participant.
  - Date and quantity returned by participant.
  - Manufacturer, lot number, and expiration date, if applicable.
  - Balance Forward/Balance.
  - Recorder’s initials.

- An accurate account of final study agent disposition (either returned to the supplier or destroyed on-site as specified in the study protocol).
- Measures are in place to ensure study agent is dispensed only upon receipt of a prescription or written orders from an authorized prescriber and dispensed only to a registered study participant.

4. Participant Case Review:
    4.1. Informed consent.
    4.2. Inclusion/Exclusion Criteria.
    4.3. Investigational agent compliance (administration, dose modification, etc.).
    4.4. AE/SAE reporting.
    4.5. General data management quality (e.g., timely, complete, and accurate Rave data entry and query response).
    4.6. Participant-specific AQuIP data (strategies, reasons not enrolled, etc.).
    4.7. Protocol deviation identification and reporting.
    4.8. Concomitant medication documentation and reporting.
    4.9. Specimen collection, processing, storage, shipment.
    4.10. Secure record storage.
    4.11. A minimum of three (3) participant charts per protocol/per site are selected for participant chart review. For single arm or blinded studies, 100% source data verification is performed for the first two participants and the additional chart(s) to be audited during the visit are randomly selected by the DMASC statistician. In addition, all SAE reports are reviewed.
    4.12. For unblinded randomized studies, 100% source data verification is performed for the first two participants randomized to an intervention arm. The additional cases to be audited during the visit are randomly selected from either arm by the DMASC statistician. All SAE reports are reviewed.
    4.13. Source data verification for the remaining participant cases selected for review are targeted. The level of targeted source data verification is determined by the risk level assigned to the protocol by the DCP reviewers during the initial protocol review.

5. SCHEDULING

Prior to contacting an AO regarding scheduling an audit, the LAO is notified so that they can notify the AO and reiterate the purpose of the audit and inform them that the DMASC Clinical Trials Auditing Unit will be contacting them soon.

A “Request to Schedule Audit” email is sent six (6) weeks in advance to the Organization Investigator(s) listed on the protocol. One or more additional key study staff members, who the LAO identifies as being study staff likely to be responsible for coordinating the audit at the site, is copied on the email. The “Request to Schedule” includes:

1. Desired date range for conducting the audit.
2. Anticipated length of time to complete the audit.

3. Request for a brief site operations meeting with the PI and key study staff on the first day of the audit.
4. Request to schedule a pharmacy visit (if applicable).
5. Request for a 30-minute "summary of findings" meeting with the PI and key study staff at the end of the final day of the audit. The DCP MM, SL, and NC for the protocol as well as LAO staff members are invited to participate by phone/video.

An "Audit Confirmation" email and agenda is sent to the site once a date for the audit is agreed upon. The agenda includes the list of participant cases selected for review during the audit.

6. SITE COORDINATOR RESPONSIBILITIES FOR LAO AND AO

1. Collaborate with the auditor(s) to identify a mutually agreeable date for the on-site or remote audit to allow maximum participation by site staff.
2. Acknowledge receipt of the confirmation email, confirming the date and objectives of the audit.
3. Communicate audit logistics and objectives to site and pharmacy staff.
4. If on-site, ensure that adequate workspace is available for the auditor(s) during the visit.
5. Ensure all relevant materials are available for review. This should include:
    5.1. All essential records (including communication files).
    5.2. A signed ICD for each individual registered to the study (enrolled and screen failures).
    5.3. Complete source records (or copies) for participants selected for case review, including eligibility checklists, medical records, laboratory data and requisition forms/specimen manifests or log including specimen IDs and tracking information (if applicable), worksheets, questionnaires etc.
        - If an EMR system is used, the auditor(s) may be granted access to the system, or the records may be printed for review by the auditor(s). A staff member should be available to assist with the system if necessary.
    5.4. When sending source records for review during a remote audit, ensure all participant identifiers are removed per your local policies.
    5.5. SAE documentation and PDs (refer to SOP 02-01 *Reporting Serious Adverse Events* and SOP 02-02 *Reporting Protocol Deviations* for requirements).
    5.6. Logs and documentation for enrollment, screening, and monitoring/auditing visits.

    Note: For remote/virtual audits, the auditor contacts the site coordinator in advance to arrange for access to the documentation, and/or relevant electronic systems.
6. Ensure all entries in Rave (the database of record) are current, complete, and accurate and any data queries received to date are addressed.
7. Communicate any institution-specific policies to the auditors in advance of the audit (visitor policies, Covid-19 policies, vaccine requirements, etc.).

7. RESPONSIBILITIES FOR LAO ONLY

The LAO is responsible for documenting its oversight activities and maintaining copies of protocol-specific communications in its essential records file. The LAO should provide documentation to support performance of the following:

1. Tracking the receipt of regulatory documents from accruing LAO/AO(s) and submission of those documents to the DCP Regulatory Contractor.
2. Method(s) of communicating information to accruing LAO/AO(s). Examples include meeting minutes, email documentation, or an active website link.
3. Tracking staffing changes, accrual and retention patterns, PDs, SAEs, data entry, research specimen tracking, and query resolution at accruing LAO/AO(s).
4. Accruing LAO/AO(s) are trained on the most current CP-CTNet SOPs.
5. Accruing LAO/AO staff are trained on the current protocol.
6. 100% review of the signed ICDs obtained for all individuals screened for study participation as indicated in SOP 03-03 *LAO Oversight Activities*.
7. SDV of participant charts for accruing LAO/AOs as indicated in SOP 03-03 *LAO Oversight Activities*.
8. For studies deemed to be high risk per the *Protocol Risk Assessment* tool by the DCP protocol review team, 100% review and confirmation of eligibility **prior** to randomization/enrollment for all sites seeking to enroll a study candidate on a protocol deemed “high risk” by the DCP Study Team. The risk level assigned to a protocol is documented on the Consensus Review of the first submission of a protocol to DCP for review.

Provide the following documents:

1. SVAR Worksheets for each CIRB-approved version of the protocol.
2. All versions of the LAOs DCP-approved DSMPs including the time frame during which each was in effect.

8. DOCUMENTATION REQUIREMENTS

1. The Audit Team creates an Audit Report in the Audit System housed on the CP-CTNet DMASC Portal Gateway. The report contains a list of action items that must be addressed by the site.
2. The report is opened to the Director of the DMASC Clinical Trials Auditing Unit for review/approval within 15 business days of the audit.
3. Access is then granted to the DCP Study Team for review.
    3.1. The DCP Study Team has eight (8) business days to review and comment on the report.
4. Upon completion of DCP review (or after eight (8) business days - whichever is sooner), access to the report is granted to the site.
5. The LAO or AO Site Coordinator responds to all action items identified during a QA audit within thirty (30) calendar days of receipt of the report to respond to the audit findings using the *Action-Item Site Response Form*.
    5.1. This response indicates either resolution of the action item or include a corrective action plan with a projected resolution date.
    5.2. For items with a projected resolution date, the CP-CTNet auditor follows up on those items every thirty (30) days until all items are resolved.
    5.3. The reports are reviewed by the DMASC Director of the Clinical Trials Auditing Unit and a DCP study representative.

5.4. Once all items are resolved, the final Audit Report is signed by the Organization Investigator.

6. If the site does not respond within the thirty (30) calendar day timeframe, an auditor contacts the site to help remedy any issues delaying the response.

6.1. If the site does not respond to or resolve the issue within seven calendar days, the auditor documents the site's noncompliance in an email to the site, with DCP representatives copied, and records this as a major violation in the Audit Report.

9. ACTION-ITEM RESPONSE FORM

1. To avoid any potential pitfalls during preparation of the Site Action-Item Response Form, the following should be considered:

1.1. Document every step of corrective and preventative action implementation (documentation of root cause analysis, development of new procedures, any training, etc.).

1.2. Specify the timeframe for completion of the corrective and preventive actions.

2. Adherence to and implementation of the agreed upon corrective and preventive action is critical and may be the scope of a future audit.

3. Sites are requested to review the Audit Reports and record agreement or disagreement with each audit finding. If you do not agree, a reason and if applicable, additional supporting documentation should be provided to the auditor.

3.1. For example, if the findings cited no evidence of hematologic values or radiotherapy treatment in the patient's chart, but values exist or radiation was given, it is necessary to send copies of the reports, which confirm the values or treatment. Any supporting documentation provided to the auditor must be anonymized prior to sending.

4. The auditor follows up with the site to obtain necessary confirmatory documentation. If the PI confirms the documentation is not available, the PI or designee should flag the data as unconfirmed in Rave. If these data are related to eligibility criteria, inability to provide appropriate documentation may render the participant ineligible.

5. If the audit of individual participant source records indicates data have been entered incorrectly in Rave, and the PI agrees with this assessment, the site makes the appropriate changes to the database based on the Audit Report.

6. Sites should retain all audit reports and correspondence available for future audits (e.g., in Regulatory Binder or protocol Trial Master File).

7. All Audit Reports and Site Action-Item Response Forms are distributed to:

- LAO PI and Site Coordinator
- AO PI and Site Coordinator (as applicable)
- Per protocol DCP MM
- Per protocol DCP SL
- DCP NC

8. Any Audit Reports that identify major deficiencies within the site are also accessible to:

- DCP Program Director

- DCP Program Official

Note: The Audit Team also notifies the DCP Regulatory Contractor of any unreported or misreported SAEs.

10. ADDITIONAL INFORMATION

Please send questions and comments to the DMASC at Audit_CP-CTNet@frontierscience.org.

11. 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.

Resource	ID	Location
CP-CTNet DMASC Auditing Plan	REFGD15	Program Resources
Essential Records Submission for Sponsor's Trial Master File	SOP 01-01	Program Resources
LAO Oversight Activities	SOP 03-03	Program Resources
Participant Recruitment, Retention, Adherence, and Reporting Requirements	SOP 02-04	Program Resources
Protocol Risk Assessment to Determine the Level of Targeted Source Data Verification During a CP-CTNet Audit	REFGD17	Program Resources
Recruitment, Retention and Adherence Plan	Form	Program Resources
Reporting Protocol Deviations	SOP 02-02	Program Resources
Reporting Serious Adverse Events	SOP 02-01	Program Resources

12. APPENDICES

1. Appendix I: Investigator Site File of Essential Records Tip Sheet.

Appendix I

Investigator Site File of Essential Records Tip Sheet

This tip sheet includes a list of the essential records that should be included in the Investigator Site File and are reviewed during DMASC QA audits.

1. All CIRB/IEC approved versions of the protocol and ICDs.
2. All CIRB approvals:
    2.1. CIRB Final Approval.
    2.2. CIRB Approval of Amendment Reviews.
    2.3. CIRB Approval of Continuing Reviews.
    2.4. Other study specific CIRB approvals (translations, patient materials, unanticipated problems, etc.).
3. All IEC approvals (international sites)
4. All Local IRB approvals/acknowledgements.
5. All approved Informed Consent versions.
6. HIPPA forms template.
7. ASIW: CIRB Approval of the Annual Signatory Institution Worksheet About Local Context.
8. APIW: CIRB Approval of the Annual Principal Investigator Worksheet.
9. SSW: CIRB Approval of the Study-Specific Worksheet.
10. CLIA certificates.
11. CAP certificates.
12. Laboratory Normal Values.
13. FWA with expiration.
14. Delegation of Tasks Log (current and previous DTLs).
15. DMASC *Confirmation of Activation* emails for initial activation and any amendments.
16. Drug Shipment Authorization Email.
17. Site Initiation Meeting Report.
18. Protocol training documentation.
19. All versions of the Investigator Brochure and acknowledgement(s) signed by the Investigator.
20. M-SOP Signoff logs.
21. Study wide Note to Files.
22. Local Notes to File applicable to study conduct.

Title: Lead Academic Organization Oversight Activities

Document ID: CP-CTNet SOP 03-03

Version: 7.0

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REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
7.0	FEB-24-2026	Updated section 4 *LAO Roles and Responsibilities*, subsection 2 *Study Initiation Meetings and Targeted Training of Accruing LAO and AO Staff* to clarify that accruing LAOs and AOs are responsible for tracking the training of the staff at their site. Updated section 4 *LAO Roles and Responsibilities,* subsection 5 *Documentation Requirements* to reference maintaining confirmation of site activation tracking lists for each accruing LAO and AO. Updated section 4 *LAO Roles and Responsibilities,* subsection 6 *Informed Consent Document Review and Confirmation of Eligibility* to clarify that accompanying source documents should be kept with the signed eligibility checklist at the enrolling site. In addition, this subsection was updated to add that the protocol audit risk level is now included in the protocol and that if a protocol deviation is reported for an eligibility violation on a study deemed to be low or intermediate risk, then the LAO must review and confirm eligibility for three additional participants to ensure participant safety. Finally, this subsection was updated to add that the LAO should maintain a tracking sheet documenting their informed consent document reviews and confirmations of eligibility. Updated section 4 *LAO Roles and Responsibilities*, subsection 8 *Study Agent* to include pharmacy oversight activities as per the protocol audit risk level and to provide details on the frequency of review. Updated DMACC to DMASC throughout the document.
6.0	AUG-13-2024	Clarified that documented protocol and study procedure training is needed for all staff members at accruing LAOs and AOs in section 4 *LAO Roles and Responsibilities,* subsection 2 *Study Initiation Meetings and Targeted Training of Accruing LAO and AO Staff.* Updated section 4 *LAO Roles and Responsibilities,* subsection 6 *Informed Consent Document Review and Confirmation of Eligibility* to (1) change the “moderate” protocol risk level to “intermediate” to match the terminology used in DMACC REFGD09 *Protocol Risk Assessment to Determine the Level of Targeted Source Data Verification During a CP-CTNet Audit,* (2) clarify that participants must be enrolled in Stars to the same protocol version that they are consented to, (3) add LAO review of informed consent documents that are updated as a result of protocol amendments, and (4) add that LAO review and confirmation of eligibility for low or intermediate risk studies must be performed within two weeks of enrollment/randomization.
5.0	JAN-26-2024	Updated to highlight the difference between Lead vs. Collaborating LAOs on CNTs and to highlight that UPs and SCNCs should be discussed with DCP prior to CIRB submission.
4.0	JUL-13-2023	Updated to highlight that LAO staff should review and sign off on the M-SOP. The links to documents hosted on the DCP website were updated to ensure that documents download as expected.

Version	Effective Date	Summary of Changes
3.0	FEB-21-2023	Added section 3, Definitions, and removed reference to REFGD07.
2.0	JUN-13-2022	Extensive rewrite of the SOP to provide specific guidance on the roles and responsibilities associated with LAO oversight of accruing LAOs and AOs.
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

A Cancer Prevention Clinical Trials Network (CP-CTNet) Lead Academic Organization (LAO) manages and assumes responsibility for its network protocols on behalf of the Division of Cancer Prevention (DCP). The LAO Principal Investigator (PI) is responsible for the routine quality control monitoring of the conduct of network protocols at their accruing LAO and Affiliated Organizations (AOs). Any time an LAO is accruing at its own site, the accruing LAO is treated the same as an AO and is subject to the same selection criteria and oversight. The same holds true for a CP-CTNet Cross-Network Trial (CNT) in which an LAO is participating as an accruing site.

Note: The DCP protocol numbering convention for CP-CTNet CNTs is INT, which stands for "inter-network trial" (e.g., INT21-05-01).

It is the responsibility of the LAO to provide the infrastructure necessary to oversee and support study activities performed by its accruing LAO and AOs to ensure that they are conducted, recorded, and reported in compliance with the current approved protocol version, REFGD03 *CP-CTNet Master Data Management Plan*, the Data and Safety Monitoring Plan (DSMP), CP-CTNet Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) as described in *E6(R3) Good Clinical Practice: Integrated Addendum to ICH E6(R1)*, and any additional applicable regulations (e.g., in-country requirements for AOs that reside outside of the United States (US), etc.). The LAO PI may delegate specific tasks associated with this oversight to qualified personnel; however, the LAO PI retains overall oversight responsibility for accruing LAOs and AOs.

As per *E6(R3) Good Clinical Practice: Integrated Addendum to ICH E6(R1)*, clinical trial quality assurance consists of "all those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s)", while quality control includes "the operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled." In CP-CTNet, quality control monitoring is performed remotely (e.g., LAO staff are not expected to travel to their accruing LAOs and AOs to conduct study monitoring visits), and in complement with data management and quality assurance auditing conducted by the Data Management, Auditing, and Statistical Center (DMASC). The DCP Study Team and DCP Regulatory Contractor also support the LAO with certain aspects of its routine quality control monitoring.

2. SCOPE

This document details the specific responsibilities of LAO PIs and/or designees in relation to the oversight of study activities for their respective accruing LAOs or AOs.

3. DEFINITIONS

Term	Definition
AE	Adverse Event
AO	Affiliated Organization
AQuIP	Accrual Quality Improvement Program
CIRB	Central Institutional Review Board
CNT	Cross-Network Trial
Collaborating LAO	An LAO that is involved in a CNT that has oversight responsibilities for its own accruing LAOs and AOs.
CP-CTNet	Cancer Prevention Clinical Trials Network

Term	Definition
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DSMP	Data and Safety Monitoring Plan
DTL	Delegation of Tasks Log
eCRF	Electronic Case Report Form
GCP	Good Clinical Practice
ICH	International Council for Harmonization
INT	Inter-Network Trial or INT is the DCP protocol numbering convention for CP-CTNet trials (e.g., INT21-05-01).
IRB	Institutional Review Board
LAO	Lead Academic Organization
Lead LAO	An LAO that takes primary responsibility for the administrative aspects of the CNT and has oversight responsibilities for its own accruing LAOs and AOs.
M-SOP	Manual of Standard Operating Procedures
NCI	National Cancer Institute
PD	Protocol Deviation
PI	Principal Investigator
PIO	Protocol Information Office
RCR	Registration and Credential Repository
SAE	Serious Adverse Event
SCNC	Serious or Continuing Non-Compliance
SDV	Source Data Verification
SIM	Study Initiation Meeting
SOP	Standard Operating Procedure
UP	Unanticipated Problem

4. LAO ROLES AND RESPONSIBILITIES

LAO oversight of its accruing LAO and AOs begins with careful site selection, assistance with the collection of the essential records required to open a study at an accruing LAO or AO, conducting a SIM, and additional targeted training of accruing LAO or AO study staff. It continues with frequent communication to ensure that the study is progressing in accordance with the planned timeline and accrual goals. During the active phase of the study (e.g., pre-screening/recruitment, screening, enrollment, study intervention, and follow-up), the LAO provides routine quality control monitoring that focuses on the protection of the rights and well-being of the study participants, compliance with the protocol, GCP, and regulatory guidance, complete, accurate, and timely entry of study data, PD and AE reporting, investigational product management, and research specimen management. LAO oversight ends with study closeout at each site.

Note: For CNTs, multiple LAOs participate and have different roles and responsibilities based on if they are a Lead LAO or a Collaborating LAO. The Lead LAO takes primary responsibility for the administrative aspects of the CNT and has oversight responsibilities for its own accruing LAO and AOs. Each Collaborating LAO involved in the CNT has oversight responsibilities for its own accruing LAO and AOs, but not for the cross-network administrative aspects of the CNT. See REFGD06 *Cross-Network Trials Guidelines* and QKREFGD18 *Roles and Responsibilities for CP-CTNet Cross-*

Network Trials for more information on the roles and responsibilities of Lead LAOs vs. Collaborating LAOs.

1. **Site Selection**: The addition of an accruing LAO or AO to an LAO's roster is subject to approval by the DCP CP-CTNet Director. The *Guidelines for Modifications to a Lead Academic Organization Roster* reference document describes the process for submitting a request for approval of an accruing LAO or AO. When vetting an accruing LAO or AO for addition to the roster, the LAO should consider whether:

    1.1. The accruing LAO or AO Investigator has adequate qualifications and resources to conduct the study safely and properly.

    1.2. The accruing LAO or AO has adequate staffing for protocol implementation throughout the duration of the study.

    1.3. The accruing LAO or AO staff has the ability and expertise to:

    - Create, submit, track, organize, and store the regulatory documents for the study.
    - Identify, recruit, pre-screen, consent, screen, and enroll eligible study candidates, and document these efforts using the Stars registration/randomization system at each stage of the enrollment process.
    - Meet the accrual goals for their site within the specified timeframe.
    - Conduct study visits as outlined in the protocol schedule of events and complete any additional participant contacts within the required window.
    - Conduct protocol-required assessments and procedures with study participants within the required window.
    - Complete protocol-required assays (if applicable).
    - Maintain accurate, complete, and up-to-date source data, records, and other study records.
    - Provide the LAO with access to participant source records and other documents for the purposes of remote monitoring oversight.
    - Assess, document, track, and report AEs as specified in the protocol.
        - See *DCP Baseline and Adverse Event (AE) Reporting Guidelines* for more information.
    - Identify and report deviations from the protocol.
        - See SOP 02-02 *Reporting Protocol Deviations* for more information.
    - Enter study and AQuIP data into Medidata Rave completely, accurately, and within the required timeframes. Medidata Rave is the clinical trials data management system used for all CP-CTNet studies.
        - See SOP 02-04 *Participant Recruitment, Retention, Adherence, and Reporting Requirements* for more information.
    - Respond to data queries within the required timeframes.
    - Handle and dispense study agent in full compliance with the protocol, GCP, and institutional, state, and in-country regulations.

- Track the receipt, use, return, and final disposition of study agent(s) as specified by the protocol, and in compliance with GCP and institutional, state, and in-country regulations regarding the use and handling of prescription medications.
- Collect, process, store, track, and submit any protocol-required specimens using a virtual specimen repository or other equivalent specimen tracking system.
- Perform and report the results of any tests and/or assays if required by protocol.

1.4. The accruing LAO or AO has adequate facilities to:

- Conduct study visits, as outlined in the protocol schedule of events, in a safe, clean, private, and professional space supplied with any equipment and materials required to perform study visits and protocol-required assessments and procedures.
- Access and enter data into Medidata Rave through a secure interface.
- Securely store regulatory documents, participant study source records, and other study records and limit access to those materials to study personnel and individuals with oversight responsibilities.
- Store the study agent(s) in accordance with the recommended conditions and monitor those conditions throughout the course of the study.
- Store the study agent(s) securely and limit access to authorized staff and those responsible for oversight.
- Store the study agent(s) separately from any commercially available supply of the same agent.
- Process and store study specimens in accordance with the protocol and ship (when required) in accordance with regulations covering the transportation of biohazardous materials.
- Complete any protocol-required tests and/or assays.

2. **Study Initiation Meetings and Targeted Training of Accruing LAO and AO Staff**:

2.1. The LAO is responsible for conducting a SIM in compliance with SOP 01-02 *Study Initiation Meeting*. This includes recording the SIM and sharing the SIM recording with accruing LAO and AO staff who were unable to attend the meeting, new staff at existing accruing LAOs and AOs, and staff at new accruing LAOs and AOs.

- DMASC participates in the preparation process for each SIM by working with the LAO Coordinator to develop a study-specific training topic list, and provides training during the SIM based on the DMASC responsibilities outlined in TMPL02 *CP-CTNet Study Initiation Meeting Report Template*. The LAO should coordinate with DMASC (via DMASC_SIM_CP-CTNet@frontierscience.org) before scheduling the SIM to ensure that DMASC trainers are available to present at the SIM.

2.2. DMASC provides supplemental training on various CP-CTNet procedures and systems. The LAO is responsible for ensuring that all accruing LAO and AO staff are aware of any required or recommended trainings. The LAO is also responsible for ensuring that all accruing LAO and AO staff have completed any required trainings. See REFGD12 *Training Registration Guide* for information about registering for CP-CTNet training sessions.

2.3. The LAO is responsible for ensuring that applicable training materials have been disseminated to the accruing LAO and AO staff members, including new staff members at existing accruing LAOs and AOs and staff members at new accruing LAOs and AOs. All applicable staff members must be appropriately trained on the protocol (including any protocol amendments) and study procedures. Training must be documented. Accruing LAOs and AOs are responsible for tracking the training of the staff at their site.

Note: Recorded attendance during the SIM constitutes initial training on the protocol and study procedures.

Note: Accruing LAOs and AOs may use TMPL03 *CP-CTNet Training Confirmation Log for Accruing LAOs and AOs*, their own process (e.g., an electronic or paper institutional sign-off log), or an email-based documentation method to document subsequent training. If an accruing LAO or AO documents training via email, then the protocol amendment and/or other documentation should be attached to an email that details the changes made to each document in the body of the email. Once the individual that received the email with the protocol amendment and/or other documentation completes the training, they must forward the original email to a designated individual at their accruing LAO or AO indicating that the email and associated documents were received, reviewed, and acknowledged. The designated individual at the accruing LAO or AO saves the training-related emails that they receive and tracks who has been trained at their site. See SOP 01-03 *Accruing LAO and AO Activation* for more information.

2.4. The LAO is responsible for ensuring that re-training is provided if performance or compliance issues are identified at an accruing LAO or AO. Upon request, DMASC can assist the LAO by developing trainings on topics identified as being an issue.

3. **Communication**: The LAO acts as the main line of communication between the accruing LAOs and AOs and DCP, DMASC, and the DCP Regulatory Contractor.

3.1. The LAO PI and/or designee(s) is responsible for:

- Communicating information regarding changes to procedures, the availability of new and revised policies on the CP-CTNet DMASC Public Website and Portal Gateway, and announcements from DMASC and DCP to accruing LAOs and AOs in a timely and systematic manner.
    - See SOP 02-05 *Creating, Reviewing, and Amending Standard Operating Procedures* for more information.

  Note: All LAO staff are responsible for reviewing and signing off on the M-SOP to ensure that they are familiar with all network policies and can provide appropriate oversight of their accruing LAOs and AOs in accordance with these policies.

- Distributing all relevant information about the protocol and study operations to accruing LAO and AO staff, including CIRB protocol approval notifications and the associated approved materials and documents, continuing review approvals, pending protocol amendments, CIRB protocol amendment approval notifications and the associated materials and documents, and any additional details about pending and final decisions.

- Conducting regularly scheduled conference calls with accruing LAOs and AOs and the DCP Study Team to review AQuIP data and recruitment and/or retention strategies, discuss study progress including relevant AEs, track staffing resource or facility changes at the accruing LAOs and AOs, and identify and address areas of concern.

Documentation of these calls should include the preparation of an agenda of topics prior to the call and the distribution of meeting minutes after the call.

- Developing electronic mail distribution lists (e.g., listserv, contact list) for immediate dissemination of important information from DCP, DMASC, and DCP contractors.
- Requesting that accruing LAO or AO staff send questions about protocol implementation and other protocol-specific issues to the LAO Coordinator so that they may reply or search for solutions in a consistent manner across sites.
- Developing an appropriate file structure for saving electronic communications to accruing LAOs and AOs to ensure that they can be readily retrieved (e.g., a communications folder). This includes the communications listed above and documentation related to agreements or significant discussions regarding study administration, PDs, study conduct, and AE reporting. Specific documentation may include emails, agendas, and meeting minutes. The communications that should be saved in the LAO's essential records file are described below in section 4.

4. **Essential Records**:

4.1. The LAO is responsible for ensuring that the accruing LAO or AO understands and is compliant with the collection, completion, and submission of regulatory documents required for CP-CTNet studies as described in SOP 01-01 *Essential Records Submission for Sponsor's Trial Master File* and QKREFGD18 *Roles and Responsibilities for CP-CTNet Cross-Network Trials*.

4.2. The DCP Regulatory Contractor is responsible for maintaining the Trial Master File of essential records required for each CP-CTNet study. They conduct a thorough review of the regulatory documents submitted for this file. However, to avoid delays, the LAO is asked to do a quick review of documents received from the accruing LAO or AO to ensure that the correct version of the document has been used, all fields have been completed, and the document is signed and dated, prior to forwarding those documents to the DCP Regulatory Contractor.

4.3. The LAO should assist the accruing LAO or AO with understanding the Cancer Therapy Evaluation Program (CTEP) Identity and Access Management System (IAM) and provide guidance, as needed, with the use of the NCI Registration and Credential Repository (RCR). However, the LAO is not responsible for collecting, reviewing, or tracking any of the documents collected through the RCR system (e.g., the Statement of Investigator (Form FDA 1572), Financial Disclosure Form, NCI Biosketch, GCP Training Certification and Professional Licensure).

- If the LAO would like to help a site expedite the completion of those documents, or if the drug shipment authorization is being held up by missing documents, the DCP Regulatory Contractor provides a list of the outstanding documents to the LAO.

4.4. The LAO is not responsible for maintaining a "shadow file" of regulatory documents, however, a system for documenting the receipt of non-RCR regulatory documents from the accruing LAO or AO and transmission of those documents to the DCP Regulatory Contractor should be in place to ensure complete and timely collection and submission of those documents.

4.5. The LAO is responsible for ensuring that the accruing LAO or AO is maintaining an essential records file and that the file is organized, current, complete, and available for

quality assurance auditing by DMASC and/or inspection by regulatory authorities. This file may be electronic or paper based.

Note: The RCR serves as the official repository for the Financial Disclosure Form, NCI Biosketch, GCP training certificate, and professional licensure. Copies of these documents do not need to be maintained in the accruing LAO's or AO's essential records file.

4.6. The LAO should provide guidance to the accruing LAO or AO to help comply with local and/or foreign (as applicable) institutional requirements regarding the local IRB ceding to the CIRB, study activation/closeout, filing of protocol amendments, submission of UPs and SCNCs to the CIRB, and reporting of SAEs.

Note: UPs and SCNCs should be discussed with the DCP Study Team prior to CIRB submission.

- See SOP 02-01 *Reporting Serious Adverse Events* and SOP 02-02 *Reporting Protocol Deviations* for more information.

4.7. The LAO is responsible for reporting staffing changes at the LAO-, accruing LAO-, and AO-level to the DCP Regulatory Contractor and DMASC (Admin_CP-CTNet@frontierscience.org) as per REFGD13 *CP-CTNet Responsibilities for Personnel Changes*, and ensuring these changes are documented on the site's DTL.

- The DCP Regulatory Contractor ensures that new staff have completed their required documents in the RCR and stops tracking documents in the RCR for staff that are no longer associated with the study.
- DMASC updates the CP-CTNet Contact List as changes are reported.

  Note: A PI change at the LAO-, accruing LAO-, or AO-level must be reported to PIO with an accompanying protocol amendment to reflect this change.

5. **Documentation Requirements**:

5.1. The LAO is responsible for documenting its oversight activities and maintaining copies of protocol-specific communications in its essential records file. These records should be readily accessible, and may be requested by DCP, the DCP Regulatory Contractor, and/or DMASC at any time during the conduct of the study. Types of documentation include:

- Reports regarding protocol implementation and operations, and other major issues or changes.
- Documents that describe progress, barriers, and outcomes in 'Notes to File' as necessary.
- Communications from DCP, DMASC, the DCP Regulatory Contractor, and the accruing LAO or AO.
- Documents to support the tracking of the receipt of regulatory documents from the accruing LAO or AO and the forwarding of those documents to the DCP Regulatory Contractor.
  - For more information, see SOP 01-01 *Essential Records Submission for Sponsor's Trial Master File*.
- Confirmation of site activation tracking lists that include the initial activation date and every protocol amendment activation date for each accruing LAO and AO.

- For more information, see SOP 01-03 *Accruing LAO and AO Activation*.

- Documents to support methods of communicating information to the accruing LAO or AO as listed in section 3 (e.g., meeting minutes, email documentation, or an active website link).
- Documents to support methods of tracking staffing changes, accrual and retention patterns, PDs, SAEs, data entry, research specimen tracking, and query resolution at the accruing LAO or AO.
  - For more information, see SOP 03-02 *Site Preparations for Quality Assurance Audits*.

6. **Informed Consent Document Review and Confirmation of Eligibility**:

6.1. The LAO is responsible for the review of 100% of the signed informed consent documents obtained for all individuals screened for study participation. This includes screen failures, all enrolled participants, and any re-consents. At a minimum, the following elements should be addressed as part of the LAO review:

- Informed consent was obtained prior to the conduct of any study-specific procedures.
- The correct version was used.

  Note: The informed consent document version should match the protocol version that the participant is enrolled to in Stars.

- The individual who obtained the informed consent was delegated that authority.
- The document was correctly signed and dated by all parties (including co-signers and/or witnesses, if required).

6.2. For any informed consent documents that were updated as the result of a protocol amendment, the LAO is responsible for reviewing the informed consent document content and confirming that the boilerplate language is correct. The DCP Regulatory Contractor performs this review for the initial informed consent document, but all subsequent informed consent documents must be reviewed by the LAO.

6.3. To help ensure participant safety, all eligibility checklists require a two-person review and sign off at the accruing LAO or AO **prior** to entry of the checklist data into Stars. One of these two parties must be a registered Investigator or Non-Physician Investigator for the protocol in the NCI RCR and be delegated the *Eligibility Assessments* task on the DTL. The names of the two parties are typed into Stars. The signed eligibility checklist (wet signature or electronic) and accompanying source records are kept at the enrolling site and serve as source records for the confirmation of eligibility.

6.4. The protocol audit risk level, which is documented on the Consensus/Concurrence Review form and in the protocol, should be reviewed during the SIM, as per TMPL02 *CP-CTNet Study Initiation Meeting Report Template*.

- For studies deemed to be high risk by the DCP protocol review team per the Protocol Audit Risk Assessment Tool, 100% review and confirmation of eligibility of all participants is required by the LAO **prior** to enrollment of each eligible participant at the accruing LAO or AO.

- For studies deemed to be low or intermediate risk by the DCP protocol review team per the Protocol Audit Risk Assessment Tool, review and confirmation of eligibility of the first two participants enrolled at each accruing LAO or AO, at minimum, is required by the LAO. The review and confirmation of eligibility should take place as soon as possible, but no later than two weeks following enrollment/randomization. Review and confirmation of eligibility beyond the first two participants enrolled at each accruing LAO or AO is at the discretion of the LAO based upon the performance of the accruing LAO or AO, complexity of the eligibility criteria for the given protocol, and/or any other factors the LAO believes warrant continuing review and confirmation of eligibility. If a protocol deviation is reported for an eligibility violation, then the LAO must review and confirm eligibility for three additional participants to ensure participant safety.

Note: LAO oversight, as described in Section 6.4, does not apply to international sites where data sharing is prohibited.

6.5. The LAO should maintain a tracking sheet documenting their informed consent document reviews and confirmations of eligibility. This tracking sheet is reviewed during DMASC quality assurance audits.

7. **Quality Control Monitoring and Management of Study Data**: The Stars registration/ randomization system is used by accruing LAOs and AOs to pre-screen, screen, and enroll participants onto CP-CTNet studies and to generate associated *Pre-Screen*, *Screening*, and *Participant IDs* (see USRMAN01 *CP-CTNet Stars User Guide* for more information). Medidata Rave is used by sites to enter study data, record study pre-screening and screening efforts, and record site-level AQuIP recruitment journaling situations or events that may impact study recruitment efforts. The LAOs and DMASC Data Managers work together to ensure the quality and integrity of study data. This section outlines the LAO's roles and responsibilities for the quality control monitoring and management of study data and provides information about how DMASC Data Managers support these efforts.

7.1. eCRFs: DMASC Data Managers take the lead in the creation of eCRFs for each CP-CTNet study. The LAO is responsible for reviewing the eCRF data fields and ensuring that all data elements are included as per protocol requirements.

7.2. Study Accrual: The LAO is responsible for the oversight of accruing LAO and AO study recruitment efforts, including:

- Ensuring that accruing LAO and AO recruitment efforts are accurately and completely documented in Stars and Medidata Rave.
    - This includes identifying the protocol-specific pre-screen eligibility criteria that define the study target population and ensuring that accruing LAOs and AOs enter data on all individuals who meet those criteria and are reviewed for potential study participation, regardless of whether they agree to participate or are found to be eligible for the study. Instructions for the selection and documentation of the protocol-specific pre-screen eligibility criteria may be found in the *Recruitment, Retention, and Adherence Plan* template.
- Tracking participant enrollment in relation to accruing LAO- or AO-specific accrual targets.

- Checking the CP-CTNet AQuIP Recruitment Journal in Medidata Rave to ensure that accruing LAOs and AOs are accurately and completely documenting any site-specific factors that affect or could potentially affect accrual at their site.
- Reviewing recruitment and/or retention strategies with the accruing LAO or AO (as appropriate) to meet accrual targets.

7.3. DMASC Data Management: A DMASC Data Manager is assigned to each CP-CTNet study. DMASC Data Managers manage the data entered into Medidata Rave on an ongoing basis. DMASC data management includes:

- Pre-programmed edit checks for specific data fields which trigger an automated query when a required data field is left blank or non-conformant data are entered (e.g., a word entered in a numeric data field, an inappropriate number of letters or digits entered, or a value entered that falls outside of a specified range).
- Ensuring that data entry in Medidata Rave is complete, accurate, and timely by checking eCRFs for completeness, cross-checking eCRFs for consistency and accuracy, and cross-checking data entry against protocol-specified study contact and procedure windows.
- Manual entry of queries when data entry is incomplete or appears inconsistent with network data entry policies and procedures, protocol requirements, or with data entered on other eCRFs.
- Informing LAOs when outstanding data issues are identified and requesting that they follow up with the accruing LAO or AO. DMASC sends monthly query reports to LAOs for each of their studies, which include any outstanding queries or data issues. These reports serve as a reminder that queries and data issues should be addressed by the accruing LAO or AO within 14 calendar days.

7.4. While DMASC manages the aspects of data entry described above, the LAO maintains the overall responsibility for participant safety and the integrity of study data, which includes:

- Reviewing monthly query reports from DMASC and assuring that the accruing LAO or AO addresses those queries correctly and within the required time frame.
- Running and reviewing additional Medidata Rave reports to ensure that the accruing LAO or AO is performing as expected. Information about the Medidata Rave reports available to assist with accruing LAO and AO oversight is available in QKREFGD01 *Medidata Rave Reports* and USRMAN03 *Rave Reports Resource Guide for the CP-CTNet Project*.
- SDV: DMASC Data Managers do not have access to participant source records, therefore, it is the responsibility of the LAO to perform 100% SDV on a minimum of the first two participants enrolled per protocol at each accruing LAO or AO to ensure that data entry is accurate, complete, and verifiable and study processes and procedures are being conducted in accordance with the protocol. The focus and amount of SDV on subsequent participants should be determined by the LAO based on the accruing LAO's or AO's performance, the LAO's DCP-approved DSMP, and any protocol-specific data or safety concerns.
    - The accruing LAO or AO should be instructed to upload or share source records in a manner that is 21 CFR Part 11-compliant for review by the LAO.

- The LAO staff responsible for performing SDV are granted the *LAO Staff* role in Medidata Rave and can enter manual SDV-related queries for their accruing LAOs and AOs directly in Medidata Rave for the duration of each study. This allows for consistency in the presentation of queries to the accruing LAOs and AOs and a unified audit trail of queries and responses.
- To avoid conflicting or overlapping queries, manual query entry by the LAO should be limited to variances from source data. Any other type of data entry error or discrepancy detected during SDV should be brought to the attention of the DMASC Data Manager assigned to the study who generates the appropriate query. See REFGD01 *CP-CTNet Source Record Guide* and REFGD03 *CP-CTNet Master Data Management Plan* for more information.

Note: LAOs should document and save any communications with accruing LAOs and AOs that are not entered directly into Medidata Rave.

- Ensuring timely reporting of AEs and treatment-related morbidity information, including the reporting of SAEs. The LAO is responsible for the safety of all study participants and should routinely monitor the AE data entered into Medidata Rave and ensure that the protocol PI and DCP Study Team are notified of any concerning trends, unexpected events, or SAEs.
  - Accruing LAOs and AOs should be routinely asked about AEs during regularly scheduled study calls and encouraged to contact the LAO immediately with any questions or concerns about AEs and reminded of the steps to take should a participant experience an SAE. The LAO should assist the accruing LAO or AO with the reporting of SAEs.
  - See *DCP Baseline and Adverse Event (AE) Reporting Guidelines* and SOP 02-01 *Reporting Serious Adverse Events* for more information.
- Ensuring that PDs are reported according to SOP 02-02 *Reporting Protocol Deviations*.
- Ensuring that the data/assessments/specimen collection required for study endpoints are present.
- Ensuring that research specimen management is consistent and adequate at the accruing LAO or AO and includes the use of a research specimen tracking system or tracking log.
  - A research specimen tracking log includes basic elements applicable to the protocol, such as the type of research specimen, specimen number, date and time of collection and shipping, and storage location.
- Developing a corrective action plan when issues are identified.
- Informing DMASC of any data issues that are identified during routine quality control monitoring activities. The LAO retains the overall responsibility for its accruing LAO's and AOs' data entry performance.
  - LAOs may email the DMASC data management group email address (DataManagement_CP-CTNet@frontierscience.org) as data issues are identified. To enable DMASC to triage questions efficiently, the following information should be included in the email subject heading: protocol number and question topic.

8. **Study Agent**: The LAO is responsible for ensuring that the accruing LAO or AO is handling the study agent in accordance with the protocol, GCP, any state and/or in-country regulations, and the network guidelines listed below.

    8.1. In general, pharmacy oversight will be risk-based (i.e., in accordance with the protocol audit risk level) and may be performed on-site or remotely.

    - For high-risk studies:
        - 100% of accruing LAOs and AOs meeting the accrual threshold (≥3 participants) will be audited by DMASC. LAO monitoring of these pharmacies will not be necessary as DMASC audits include a pharmacy review.
        - Pharmacies for accruing LAOs and AOs not meeting the accrual threshold (≥3 participants within six months of opening) will be monitored by the LAO.
            - Follow-up LAO pharmacy monitoring will be conducted at least every three years, as appropriate and in consultation with the DCP Study Team and LAO.
            - LAO pharmacy monitoring outcomes will be reviewed by DMASC during LAO audits.
    - For low- or intermediate-risk studies:
        - ≥50% of accruing LAOs and AOs meeting the accrual threshold (≥3 participants) will be audited by DMASC. LAO monitoring of these pharmacies will not be necessary as DMASC audits include a pharmacy review.
        - Pharmacies for other accruing LAOs and AOs will be monitored by the LAO after a site has reached the accrual threshold (≥3 participants), or within six months of opening, whichever comes first.
            - Follow-up LAO pharmacy monitoring will be conducted at least every three years, as appropriate and in consultation with the DCP Study Team and LAO.
            - LAO pharmacy monitoring outcomes will be reviewed by DMASC during LAO audits.
    - This oversight may be accomplished remotely by requesting copies of relevant SOPs from the accruing LAO or AO pharmacy, requesting reports of temperature excursions, conducting an interview with the accruing LAO or AO pharmacist, and/or reviewing drug accountability logs for those participants selected for SDV. For blinded studies, the accruing LAO or AO pharmacy should be able to send blinded/redacted drug accountability logs upon request.

    8.2. The accruing LAO or AO should:

    - Document the receipt of study agent from the supplier.
    - Store study agent securely, limit access to authorized personnel, monitor storage conditions to ensure they remain within protocol-specified ranges for temperature and/or humidity, and store study agent separately from any commercially available supply of the same agent.
    - Ensure supply of study agent is sufficient by maintaining an inventory.
    - Ensure study agent is dispensed only to eligible study participants and in the amount and dose specified in the protocol.

- Document the dispensing of study agent to a participant and the amount of unused study agent returned by the participant. An accruing LAO or AO should use its institution's drug accountability logs or system to document drug distribution, return, inventory, etc.
- Instruct participants in the proper use, handling, storage, and return of their study agent.
- Document the final disposition of unused study agent in accordance with the protocol. If institutional policy or state and/or in-country regulations preclude final disposition in the manner described in the protocol, the accruing LAO or AO should document the variance in a 'Note to File' saved with its essential records file and the LAO should notify the repository and DCP Study Team.

5. ADDITIONAL INFORMATION

DMASC is a resource for LAO, accruing LAO, and AO staff. Please contact the DMASC email support groups below for questions or guidance:

Category	Email Support Group
Data Entry in Medidata Rave / Data Management / Protocol	DataManagement_CP-CTNet@frontierscience.org
Audit	Audit_CP-CTNet@frontierscience.org
Registration / Randomization	Enrollment_CP-CTNet@frontierscience.org
Access to Systems (e.g., Portal Gateway, Stars, Medidata Rave, Audit System)	UserSupport_CP-CTNet@frontierscience.org
Contact Management	ContactAdmin_CP-CTNet@frontierscience.org
Documentation	Documentation_CP-CTNet@frontierscience.org
Education and Training	Training_CP-CTNet@frontierscience.org
Administrative	Admin_CP-CTNet@frontierscience.org

6. 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.

Resource	ID	Location
Accruing LAO and AO Activation	SOP 01-03	Program Resources
CP-CTNet Protocol Risk Assessment Form	FORM003	Program Resources
CP-CTNet Master Data Management Plan	REFGD03	Program Resources
CP-CTNet Responsibilities for Personnel Changes	REFGD13	Program Resources
CP-CTNet Source Record Guide	REFGD01	Program Resources
CP-CTNet Stars User Guide	USRMAN01	Program Resources

Resource	ID	Location
CP-CTNet Study Initiation Meeting Report Template	TMPL02	Program Resources
CP-CTNet Training Confirmation Log for Accruing LAOs and AOs	TMPL03	Program Resources
Cross-Network Trials Guidelines	REFGD06	Program Resources
CTEP Identity and Access Management	Application	CTEPcore.nci.nih.gov
DCP Baseline and Adverse Event (AE) Reporting Guidelines	Reference	Program Resources
DCP Delegation Task Log Master Task List	Reference	Program Resources
Essential Records Submission for Sponsor's Trial Master File	SOP 01-01	Program Resources
Good Clinical Practice: Integrated Addendum to ICH E6(R1)	E6(R3)	FDA.gov
Guidelines for Modifications to a Lead Academic Organization Roster	Reference	Program Resources
Medidata Rave Reports	QKREFGD01	Program Resources
NCI Registration and Credential Repository	Application	CTEPcore.nci.nih.gov
Participant Recruitment, Retention, Adherence, and Reporting Requirements	SOP 02-04	Program Resources
Policy on Standard Operating Procedures	SOP 02-05	Program Resources
Protocol Risk Assessment to Determine the Level of Targeted Source Data Verification During a CP-CTNet Audit	REFGD17	Program Resources
Rave Reports Resource Guide for the CP-CTNet Project	USRMAN03	Program Resources
Recruitment, Retention, and Adherence Plan	Template	Program Resources
Reporting Protocol Deviations	SOP 02-02	Program Resources
Reporting Serious Adverse Events	SOP 02-01	Program Resources
Roles and Responsibilities for CP-CTNet Cross-Network Trials	QKREFGD18	Program Resources
Site Preparations for Quality Assurance Audits	SOP 03-02	Program Resources
Study Initiation Meeting	SOP 01-02	Program Resources
Training Registration Guide	REFGD12	Program Resources

7. APPENDICES

None

Title: Instructions for Accruing LAO and AO Closeout

Document ID: CP-CTNet SOP 04-01

Version: 4.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
4.0	FEB-24-2026	Updated DMACC to DMASC, essential documents to essential records, and source documents to source records throughout the document. Updated the name of SOP 01-01 to *Essential Records Submission for Sponsor's Trial Master File*.
3.0	FEB-07-2025	Added that the LAO should contact the DMACC Auditors and DCP to see if there are any unresolved findings or pending action items from previous audits in Section 4 *Roles and Responsibilities*. Clarified that Independent Ethics Committees apply to international sites in Section 4 *Roles and Responsibilities* and Section 5 *Documentation Requirements*. Made minor editorial updates throughout the document.
2.0	JAN-26-2024	Complete rewrite of the document to delineate the accruing LAO and AO responsibilities versus the LAO responsibilities in relation to closeout and to clarify closeout for cross-network trials. Added Section 3 *Definitions* and a table to Section 7 *References*.
1.0	AUG-17-2020	Original version of the document.

1. INTRODUCTION AND PURPOSE

Cancer Prevention Clinical Trials Network (CP-CTNet) accruing Lead Academic Organizations (LAOs) and Affiliated Organizations (AOs) are responsible for meeting all study obligations as part of their closeout. The accruing LAO and AO closeout process ensures that all study-related activities have been accurately reconciled, documented, and reported. This process takes approximately three months from the initial decision to initiate closeout, but may take longer if there are unforeseen delays.

As part of its monitoring responsibilities, the LAO ensures that closeout activities for its accruing LAO (as applicable) and AOs are completed for each study after all study activities are complete, or at the discretion of the Division of Cancer Prevention (DCP). For cross-network trials (CNTs), each participating LAO is responsible for the closeout activities of its accruing LAO (as applicable) and each of its AOs. The accruing LAO or AO closeout activities may be done onsite or remotely at the discretion of the LAO in consultation with the DCP Medical Monitor (MM).

In accordance with SOP 04-02 *Study Closeout*, the Data Management, Auditing, and Statistical Center (DMASC) Auditors audit the study closeout process that occurs at each LAO. Once all accruing LAOs (as applicable) and AOs have been closed out, DMASC then audits the LAO oversight of the accruing LAO and AO closeout process. This can be done as part of the LAO oversight audit and may include a high-level review of the accruing LAO (as applicable) and AO closeout Standard Operating Procedures (SOPs), reports, checklists, etc.

2. SCOPE

This document details the responsibilities of LAOs, accruing LAOs, and AOs regarding the conduct of closeout activities and outlines the information and materials that accruing LAOs and AOs are expected to prepare and provide to the LAOs for closeout.

3. DEFINITIONS

Term	Definition
Accruing LAO	A department within the LAO that contributes accrual to the study. Acts as an AO for the study.
AO	Affiliated Organization
CIRB	Central Institutional Review Board
CNT	Cross-Network Trial
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DM	Data Manager
DMASC	Data Management, Auditing, and Statistical Center
FDA	Food and Drug Administration
INT	Inter-Network Trial. The DCP protocol numbering convention for CP-CTNet CNTs begins with INT (e.g., INT21-05-01).
IRB	Institutional Review Board
LAO	Lead Academic Organization. This organization is responsible for study oversight of its accruing LAO (as applicable) and AOs.
MM	Medical Monitor
NCI	National Cancer Institute

Term	Definition
PI	Principal Investigator
SOP	Standard Operating Procedure

4. ROLES AND RESPONSIBILITIES

1. Before accruing LAO or AO closeout:

1.1. The LAO is responsible for initiating and overseeing the accruing LAO or AO closeout process after:

- All participants enrolled at the accruing LAO or AO have completed study-related activities; and
- All data for the accruing LAO or AO are entered into Medidata Rave and all outstanding data discrepancies are resolved. This is confirmed by the DMASC DMs via an email to the LAO once all data for the accruing LAO or AO are cleaned. If the LAO has any questions about this process, they may contact the DMASC DMs via email (DataManagement_CP-CTNet@frontierscience.org).
    - The LAO then completes a final review and makes the final determination that all data for the accruing LAO or AO are entered into Medidata Rave and all outstanding data discrepancies are resolved.

Note: The accruing LAO or AO, DCP, or the LAO may elect to close the accruing LAO or AO early if the accruing LAO or AO fails to accrue participants or is faced with other issues that may necessitate closure (e.g., PI leaving the accruing LAO or AO with no replacement, change in staffing status, budget constraints, etc.).

- The accruing LAO or AO, DCP, or the LAO may initiate the closeout process. Once the process is initiated, the LAO informs DCP of the pending closure and works with the accruing LAO or AO to perform the closeout activities.
- If the accruing LAO or AO has received study agent, study agent return or disposal must be handled as outlined in the protocol, pharmacy manual, and/or other study documents.

Note: If a proposed accruing LAO or AO has not been activated, accruing LAO or AO closeout activities are not required.

- The LAO sends a letter to the accruing LAO or AO (with a copy to the DCP Study Team, DMASC, and the DCP Regulatory Contractor) stating that the accruing LAO or AO was not activated; therefore, accruing LAO or AO closeout activities are not required.

  Note: If the accruing LAO or AO is removed from the study, then the protocol cover page must be updated, and a protocol amendment must be submitted to the CIRB.

1.2. Regulatory documents collected by the LAO for the accruing LAO or AO are managed as directed by the LAO and/or as required by institutional policy.

- The DCP Regulatory Contractor manages essential records that have been submitted to them by the accruing LAO or AO.

1.3. The LAO should contact the DMASC Auditors and DCP to see if any audit activities are required (e.g., participant chart review, regulatory/essential records check, pharmacy

review, etc.) or if there are any unresolved findings or pending action items from previous audits.

2. During accruing LAO or AO closeout:

2.1. **Accruing LAO or AO Responsibilities:** The accruing LAO or AO is responsible for completing all applicable local closure activities included in CHK002 *CP-CTNet Accruing LAO and AO Closeout Checklist* and should work with the LAO as needed.

2.2. **LAO Responsibilities:** The LAO is responsible for verifying that the accruing LAO or AO completed all applicable local closure activities included in CHK002 *CP-CTNet Accruing LAO and AO Closeout Checklist* in a timely manner. For CNTs, each participating LAO is responsible for the closeout activities of its accruing LAO (as applicable) and each of its AOs. Once all accruing LAOs (as applicable) and AOs have been closed out, DMASC then audits the LAO oversight of the accruing LAO and AO closeout process. This can be done as part of the LAO oversight audit and may include a high-level review of the accruing LAO (as applicable) and AO closeout SOPs, reports, checklists, etc. Additional LAO responsibilities include:

- If the study is closing to accrual, notify the DMASC DMs via email (DataManagement_CP-CTNet@frontierscience.org) that all accruing LAOs and AOs for the study should be closed to accrual in Stars, the registration/randomization system for CP-CTNet.
    - If a specific accruing LAO or AO is closing to accrual but the study remains open to accrual, notify the DMASC DMs via email (DataManagement_CP-CTNet@frontierscience.org) that the specific accruing LAO or AO for the study should be closed to accrual in Stars.
- Notify the DCP Regulatory Contractor of accruing LAO or AO closure and confirm that there are no outstanding essential records prior to the accruing LAO or AO closing the study with the local IRB, CIRB, and/or Independent Ethics Committee for international sites.
- Maintain records of communication with each accruing LAO or AO to verify that appropriate support and oversight was provided to the accruing LAO or AO during the closeout process (as needed).
- Ensure that CHK002 *CP-CTNet Accruing LAO and AO Closeout Checklist* is completed and signed by the accruing LAO or AO Coordinator, accruing LAO or AO PI, and LAO staff.

5. DOCUMENTATION REQUIREMENTS

Each accruing LAO and AO is responsible for maintaining all study records in a secure manner, including source records, laboratory data, pharmacy documents, regulatory documents, and study communications. See REFGD03 *CP-CTNet Master Data Management Plan* for more information.

1. Study records must be accessible for inspection by authorized NCI/DCP representatives, DMASC Auditors, the local IRB, the CIRB and/or Independent Ethics Committee for international sites, FDA personnel, and/or any drug company supporting the study.
2. If the study is conducted outside of the United States or United States territories, additional requirements may apply that are specific to the country of the AO participating in the study.

3. The study records must be maintained and accessible as specified in the protocol.

6. ADDITIONAL INFORMATION

Please send questions and comments to Documentation_CP-CTNet@frontierscience.org.

7. 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.

Resource	ID	Location
CP-CTNet Accruing LAO and AO Closeout Checklist	CHK002	Program Resources
CP-CTNet Master Data Management Plan	REFGD03	Program Resources
Essential Records Submission for Sponsor's Trial Master File	SOP 01-01	Program Resources
Study Closeout	SOP 04-02	Program Resources

8. APPENDICES

None

Title: Study Closeout

Document ID: CP-CTNet SOP 04-02

Version: 2.0

Version Date: February 24, 2026

REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
2.0	FEB-24-2026	Updated DMACC to DMASC and source documents to source records throughout the document.
1.0	FEB-07-2025	Original version of document.

1. INTRODUCTION AND PURPOSE

This Standard Operating Procedure (SOP) presents guidance and procedures regarding study closeout for Cancer Prevention Clinical Trials Network (CP-CTNet) studies. Study closeout takes place once (1) all accruing Lead Academic Organizations (LAOs) and Affiliated Organizations (AOs) have been closed out as per SOP 04-01 *Instructions for Accruing LAO and AO Closeout* and (2) a study has been designated as Completed or Administratively Completed. See CHK003 *CP-CTNet Study Closeout Checklist* for the specific tasks that must be completed as part of study closeout.

2. SCOPE

This SOP details the responsibilities of the LAOs, accruing LAOs, AOs, Division of Cancer Prevention (DCP), and Data Management, Auditing, and Statistical Center (DMASC) regarding study closeout procedures.

3. DEFINITIONS

Term	Definition
AO	Affiliated Organization
Administratively Completed	The protocol has been completed prematurely (e.g., due to poor accrual, insufficient drug supply). The trial is closed to further accrual and all participants have completed protocol treatment. (Equivalent to the clinicaltrials.gov status definition of "Terminated").
CIRB	Central Institutional Review Board
Closed to Accrual, Participants Still on Treatment/Intervention	The protocol has been closed to participant accrual. Participants are still receiving therapy/intervention. (Equivalent to the clinicaltrials.gov status definition of "Active, Not Recruiting").
Closed to Accrual, All Participants Have Completed Treatment/Intervention	The protocol has been closed to participant accrual. All participants have completed therapy/intervention, but participants are still being followed according to the primary objectives of the study. No additional investigational agents are needed for this study. (Equivalent to the clinicaltrials.gov status definition of "Active, Not Recruiting").
Completed	The protocol has been closed to accrual, all participants have completed therapy, and the study has met its primary objectives.
CP-CTNet	Cancer Prevention Clinical Trials Network
DCP	Division of Cancer Prevention
DMASC	Data Management, Auditing, and Statistical Center
DSS	Data Submission System
eCRF	electronic Case Report Form
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FDAAA/IRB Completed	The study has concluded normally; participants are no longer being examined (including any long-term follow-up) or treated (i.e., last participant's last visit has occurred) and analysis of data has been completed. The FDAAA/IRB Completed date must be on or after the Completed date. (Equivalent to the clinicaltrials.gov status definition of "Completed").
FNLCR	Frederick National Laboratory for Cancer Research

Term	Definition
HIPAA	Health Insurance Portability and Accountability Act
IMS	Information Management Services, Inc. (DCP Contractor)
IND	Investigational New Drug
IRB	Institutional Review Board
LAO	Lead Academic Organization
LDMS	Laboratory Data Management System
MDS	Minimum Data Set
MM	Medical Monitor
NC	Nurse Consultant
NDA	New Drug Application
OHRP	Office for Human Research Protections
PI	Principal Investigator
PIO	Protocol Information Office
PSU	Protocol Status Update
SL	Scientific Lead
SOP	Standard Operating Procedure
Study Team	Comprised of the DCP MM, DCP NC, DCP SL, LAO staff, and DMASC staff
SVAR	System Variable Attribute Report

4. PROCEDURES

1. LAO Responsibilities

   - Conduct accruing LAO and AO closeout visits. All accruing LAOs and AOs must be closed out prior to submitting the PSU Form with a status of Completed or Administratively Completed indicated. See SOP 04-01 *Instructions for Accruing LAO and AO Closeout* for additional information.
   - Work with DMASC on database cleaning and lock (see additional details in the *DMASC Responsibilities* section below). The Medidata Rave database should be cleaned and locked prior to submitting the PSU Form with a status of Completed or Administratively Completed indicated.
   - Inform PIO that the study is completed by submitting the PSU Form with a status of Completed or Administratively Completed indicated.
   - Send a notification to the accruing LAOs and AOs that the study is completed.
   - Ensure that the remaining biospecimens are submitted to the FNLCR. See SOP 02-06 *Biospecimen Submission Requirements* and the *CP-CTNet Material Transfer Manifest* for additional information.
   - Work with DCP and DMASC on final dataset and documentation submission to DCP (see additional details in the *DMASC Responsibilities* section below). The LAO is responsible for submitting data collected outside of the database of record (see *Appendix I: Final Dataset and Documentation Requirements* for additional information).
   - After receipt of the final dataset from DMASC, the LAO Statistician (or the DMASC Statistician in the case of a cross-network trial) analyzes the data.

2. DCP Responsibilities

    - Initiate and work with the LAO and DMASC on final dataset and documentation submission to DCP (see additional details in *DMASC Responsibilities* section below).

3. DMASC Responsibilities

    - Database cleaning and lock: This process ensures a complete and accurate database for analyses. DMASC reviews the data and works with the LAO to ensure that all outstanding data are submitted (either through Medidata Rave or through the LDMS, DSS, etc.), all queries (including MDS queries) are resolved, all accruing LAO and AO PIs have signed off on the Verification eCRF in Medidata Rave for all participants, and the DCP Study Team has been notified that the data are ready to be locked.
    - Study unblinding: Treatment/intervention assignments are to be unblinded for all participants on blinded treatment/intervention studies. See SOP 02-07 *Unblinding Participants* for additional information.
    - Final dataset and documentation submission to DCP: The final datasets and documentation must be submitted to IMS within 180 calendar days of the date of status change to Completed or Administratively Completed on the PSU Form. Final biomarker data and biomarker and other laboratory study analyses may be submitted at a later date with prior approval by the DCP MM and SL (see *Appendix I: Final Dataset and Documentation Requirements* for additional information).
        - Once DCP receives the PSU Form from PIO with a status of Completed or Administratively Completed indicated, DCP generates an email to the DMASC Data Management team (DataManagement_CP-CTNet@frontierscience.org) and IMS (youngm@imsweb.com and MabieJ@imsweb.com), with the LAO PI, LAO Coordinator, and study PI copied, requesting that the data be submitted to IMS within 180 days of study completion (or the next business day if it falls on a weekend or holiday).
        - If needed, IMS sets up a meeting with DMASC, the LAO PI, the LAO Coordinator, and/or the study PI to discuss the data that will be submitted.
        - Once DMASC submits the data to IMS, IMS prepares it for posting.
        - IMS sends the data to the DCP MM, NC, and SL for review and approval. DCP may ask the LAO PI to review and approve the data as well. IMS requests that the data be reviewed within 30 days.
        - Once the DCP MM, DCP NC, DCP SL, and LAO PI (as applicable) give their approval, the data are retained by IMS until the study is published.
        - Once the study is published, IMS reaches out to the CP-CTNet Program Director for approval to make the data public.

          Note: If the study fails to publish, IMS will still make the data public upon approval from the CP-CTNet Program Director.
        - Once the CP-CTNet Program Director provides approval, IMS makes the data public and notifies the LAO PI, LAO Coordinator, study PI, and DMASC.

5. DOCUMENTATION REQUIREMENTS

Each accruing LAO and AO is responsible for maintaining all study records, including source records, laboratory data, pharmacy documents, regulatory documents, and study communications, in a secure manner. PIO maintains both electronic and hard copies of the protocols.

Clinical records for all participants, including eCRFs and source records (containing evidence of study eligibility, history and physical findings, laboratory data, results of consultations, etc.), CIRB records, and other regulatory documents will be retained by the accruing LAO or AO PI in a secure storage facility in compliance with HIPAA, OHRP, and FDA regulations and guidance, as well as DCP requirements, unless the standard at the accruing LAO or AO is more stringent. DCP requires that the records for all CP-CTNet studies be retained at the accruing LAO or AO for at least three years after the completion of the research. The records for all studies performed under an IND will be retained, at a minimum, for two years after the approval of an NDA. DCP will be notified prior to the planned destruction of any materials. The records should be accessible for inspection and copying by authorized persons of the FDA. If the study is done outside of the United States, applicable regulatory requirements for the specific country participating in the study also apply.

6. ADDITIONAL INFORMATION

Please send questions and comments to DataManagement_CP-CTNet@frontierscience.org.

7. 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.

Resource	ID	Location
Biospecimen Submission Requirements	SOP 02-06	Program Resources
Clinicaltrials.gov	Website	Clinicaltrials.gov
CP-CTNet Material Transfer Manifest	Template	Program Resources
CP-CTNet Study Closeout Checklist	CHK003	Program Resources
IMS Collaborative Portal	Website	Applications.prevention.cancer.gov
Instructions for Accruing LAO and AO Closeout	SOP 04-01	Program Resources
Unblinding Participants	SOP 02-07	Program Resources

8. APPENDICES

Appendix I: Final Dataset and Documentation Requirements

Appendix I

Final Dataset and Documentation Requirements

General Guidelines

1. Digital submission of the deliverables listed below is required.
    - All deliverables should be submitted via the IMS Collaborative Portal for CP-CTNet datasets and documentation at https://applications.prevention.cancer.gov/portals/dcp/.
    - All final dataset and documentation deliverables should be uploaded to the study-specific "Final Data" folder as appropriate.
    - A completed *Final Dataset and Documentation Deliverables Summary* should be submitted with the deliverables.
    - All deliverables should be organized for submission as a single zip file.
2. The final datasets and documentation must be submitted to IMS within 180 calendar days of study completion.
    - Final biomarker data and biomarker and other laboratory study analyses may be submitted at a later date with prior approval by the DCP MM and SL.

Deliverables

1. Final MDS Report
    - The final MDS Report should be prepared from the locked data for the study.
    - The final MDS Report should be submitted with the study-specific datasets so that the final MDS Report can be replicated.
2. Study-specific datasets and documentation
    - Datasets are required for all clinical data, biomarker data, and other study-specific data used for analyses.
    - Datasets should be a copy of the final, complete, cleaned, audited, and locked data used for analysis.
    - Each dataset should include any descriptive and/or administrative information considered pertinent to the subsequent use of these data.
    - Simple one-way frequencies and/or univariates of the variables in each dataset should be provided so that the integrity of the data transfer can be checked.
3. Data are to be submitted as either SAS datasets or .CSV files.
4. The datasets should be organized by eCRF, with each eCRF having its own dataset.
    - For data collected outside of the database of record (e.g., study-specific questionnaires that are not included in Medidata Rave, final biomarker data, biomarker and other laboratory study analyses, etc.), the LAO is responsible for submitting these data as individual datasets or spreadsheets.
        - Data obtained from a source other than a Medidata Rave eCRF should be identified in the dataset. The source of these data should be specified.

5. Documentation of the analysis and/or analytic code or programs should be submitted with the dataset(s) so that the published study results can be replicated.
6. The latest approved versions of the protocol and SVAR as well as the data dictionary XML file, eCRF Completion Guide, and Annotated Print Matrix should be submitted with the datasets. The version number and/or version date should be noted within each document.