

Title: Regulatory Documents

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REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
1.0	AUG-17-2020	Original version of document

1. INTRODUCTION AND PURPOSE

Lead Academic Organizations (LAOs) and Affiliated Organizations (AOs) are required to prepare, submit, and maintain essential regulatory documents throughout the duration of each study in accordance with Good Clinical Practice (GCP) guidelines. The purpose of this document is to provide regulatory document requirements for the Cancer Prevention Clinical Trials Network (CP-CTNet) developed by the National Cancer Institute (NCI), Division of Cancer Prevention (DCP). All regulatory documentation 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 requirements for LAOs and AOs concerning regulatory documents required per GCP.

3. REQUIRED ESSENTIAL SITE REGULATORY DOCUMENTS

DCP's list of required essential regulatory documents is provided below, followed by guidelines for completion of each document type.

1. [Form FDA 1572](#)
2. [Delegation of Tasks Log \(DTL\)](#)
3. [Principal Investigator \(PI\) Acknowledgement of Investigator's Brochure \(IB\) or Package Insert](#)
4. [NCI Biosketch](#)
5. [Professional Licensure](#)
6. [Financial Disclosure Form \(FDF\)](#)
7. [GCP Training Certification](#)
8. [Office of Human Subject Protections \(OHRP\) Assurance](#)
9. [Clinical Laboratory Improvement Amendments \(CLIA\) Certification](#)
10. [College of American Pathologists \(CAP\) Certification](#)
11. [Lab Normal Values \(LNVs\)](#)
12. [Central Institutional Review Board \(CIRB\) or Independent Ethics Committee \(IEC\) Approval](#)
13. [CIRB- or IEC-approved Informed Consent Document \(ICD\)](#)
14. [CIRB- or IEC-approved Patient/Recruitment Materials](#)
15. [Certificates of Translation](#) (if applicable)

In the CP-CTNet program, all investigators and study staff that are listed on the DTL are required to register in the [NCI Registration and Credential Repository \(RCR\)](#) as either Investigator (IVR), Non-Physician Investigator (NPiVR), or Associate Plus (AP), depending on their assigned tasks on the study. RCR provides a self-service online person registration application with electronic signature and submission capability. All study staff designated as IVR or NPiVR must provide the following documentation in RCR:

- Form FDA 1572
- NCI Biosketch

- FDF
- Professional Licensure (e.g., nursing, pharmacy, and/or medical)
- GCP training certification

All study staff designated as AP must provide the following documentation in RCR:

- NCI Biosketch
- FDF
- Professional Licensure (e.g., nursing, pharmacy, and/or medical)
- GCP training certification

The DCP regulatory contractor will access these forms in RCR. All other required essential site regulatory documents will be provided to the regulatory contractor by the LAO.

4. REQUIRED ESSENTIAL SITE REGULATORY DOCUMENTS GUIDELINES

4.1. Form FDA 1572

- a. DCP requires all investigators (IVR and NPIVR) conducting clinical investigations to provide accurate and current information on the Form FDA 1572.
- b. The regulatory contractor will download the Form FDA 1572 from RCR for IND submission and after drug shipment authorization (DSA), if information within the document has changed.
- c. Original Form FDA 1572 should be maintained in the local Investigator Site File. The DCP regulatory contractor will download the Form FDA 1572 from RCR and it will be reviewed and maintained for the sponsor's record.
- d. Instructions for the completion of the Form FDA 1572 are provided in RCR. Of note for CP-CTNet studies:

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

4.2. DTL (version 1.0, January 22, 2020)

- a. The DTL is the primary source for tracking staff who perform study-related duties. Each AO will provide a protocol-specific DTL listing all study staff members who are registered as IVR, NPIVPR, and AP. The DTL must be signed by each study staff member next to their designated task codes and the site PI.
- b. The DCP regulatory contractor will send a protocol-specific DTL in electronic format to the LAO when a protocol has received initial approval by DCP's CIRB. The regulatory contractor will list the protocol information as well as the site information, excluding the CTEP-Site ID. AOs will provide information for the remaining sections in the DTL.
- c. Tasks assigned to study staff must be appropriate for their level of training and qualifications.
- d. Tasks assigned to study staff listed on the DTL should be indicated as described below:

- Clinical Investigator (CI)
 - DTL Administrator (DTLA)
 - Agent Prescribing
 - Consenting Person
 - Eligibility Assessments
 - End Point Assessments
 - Enrolling Person/Treating Investigator
 - History and Physical (H&P) Assessments
 - IND Prescribing
 - Investigation Product Accountability
 - Pathology Lab Support
 - Patient Screening/Recruiting
 - Primary Study/Site Contact
 - Rave CRA
 - Rave Investigator
 - Regulatory Contact
 - RT/Imaging Support
 - Source Documentation Completion
 - Study-related Interventions
 - Toxicity Assessment
 - Unblinded Study Personnel
- e. 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 (except for a specific pharmacist who is compounding the study agent or monitoring compliance), fellows, and office staff who provide only ancillary or intermittent care. No regulatory documents are collected for these staff.
- f. The PI's signature or initials acknowledging the staff member's role may not precede the staff member's signature date. The end date for performance of the tasks should be entered when the staff member leaves the study.
- g. The signed DTL does not need to be an original.
- h. An updated DTL should be provided when a staff member changes responsibility or leaves or joins the study.
- i. LAOs will provide the DTLs to DCP's regulatory contractor who will review and maintain the documents for the sponsor's record. The DCP regulatory contractor will send the protocol-specific signed DTL to the Data Management, Auditing, and Coordinating Center (DMACC).

4.3. PI Acknowledgement of IB or Package Insert

- a. The PI at each site must sign an acknowledgement form stating that he/she has reviewed each version of the IB or package insert provided by DCP for each agent under investigation in the study.
- b. LAOs will provide the acknowledgement form to DCP's regulatory contractor who will review and maintain the documents for the sponsor's record.

4.4. NCI Biosketch

- a. An NCI Biosketch is required for all study staff who participate in the clinical investigation, including international sites. This includes all staff members listed on a DTL.
- b. Original documents with signatures and dates are not required, but documents should be current within two years of DSA. Document dates can be ascertained from the content of the NCI Biosketch.
- c. NCI Biosketches are updated annually for all study staff in RCR.
- d. If a staff member is added to the study after DSA, the NCI Biosketch must fall within two years of their initial date of involvement in the study.
- e. The NCI Biosketch should display the study staff's current affiliation and dates of involvement with the institution.
- f. LAOs and AOs should notify the regulatory contractor of any changes to the NCI Biosketch content.
- g. The DCP regulatory contractor will download the NCI Biosketch from RCR and it will be reviewed and maintained for the sponsor's record.

4.5. Current Professional Licensure

- a. Each study staff member listed on the DTL should provide the license number in RCR as applicable (NOT a 'controlled substance' license); exceptions include PhDs, study coordinators, etc. For international studies, the study staff member is required to provide a professional license.
- b. The staff member's name should match the Form FDA 1572 or NCI Biosketch and the license should be current.
- c. If the site is a government facility, investigators need to have current licensure but not necessarily from the same state as the facility. For example, Kansas City VA Hospital in Kansas City, MO may have investigators who are licensed in Kansas City, Kansas.
- d. The DCP regulatory contractor will download the professional licensure from RCR and it will be reviewed and maintained for the sponsor's record.

4.6. FDF

- a. The FDF must be signed and dated electronically by each investigator and study staff member listed on the DTL.
- b. Any revisions to the FDF should be updated annually in RCR.
- c. If any financial interests are indicated, they should be disclosed on the FDF Form in RCR.

- d. LAOs and AOs should notify the regulatory contractor of any changes to the FDF content.
- e. The DCP regulatory contractor will download the FDF from RCR and it will be reviewed and maintained for the sponsor's record.

4.7. GCP Training Certification

- a. GCP training certification is required for all personnel listed on the Forms FDA 1572 and/or the DTL Form.
- b. GCP training certificate will need to be uploaded into the RCR.
- c. Certification for CITI GCP training comes in two versions, FDA and ICH. The FDA version is preferred, though the ICH version is also acceptable.
- d. GCP training certification from NIH or the staff member's own institution is acceptable.
- e. Expiration of GCP training certification is based on the training provider/institution. Expiration dates should be listed on training certificates and should not exceed three years from date of completion.
- f. The DCP regulatory contractor will download the GCP training certificate from RCR and it will be reviewed and maintained for the sponsor's record.

4.8. OHRP Assurance

- a. All sites participating in federally funded studies are required to have Federal-wide Assurance (FWA).
- b. LAOs will provide the OHRP assurance to DCP's regulatory contractor who will review and maintain the documents for sponsor's record.

4.9. Current CLIA Certification

- a. The majority of labs have CLIA certification. The lab name and address should match the information on the Form FDA 1572 or DTL and the certification must be current.
- b. A Note-to-File (NTF), on institutional letterhead, signed by the PI/designee explaining the status of lab accreditation may be submitted in lieu of CLIA certification.
- c. New York and Washington State certifications are in the form of a CLP (Clinical Laboratory Permit).
- d. LAOs will provide the CLIA certification to DCP's regulatory contractor who will review and maintain the documents for the sponsor's record.

4.10. Current CAP Certification

- a. The lab name on the CAP certificate does not always match that on the Form FDA 1572/DTL or the CLIA certificate; however, the CLIA number should match. Not all sites are certified by CAP; if this is the case, a NTF, on institutional letterhead, should be provided.
- b. LAOs will provide the CAP certification to DCP's regulatory contractor who will review and maintain the documents for the sponsor's record.

4.11. Lab Normal Values

- a. A set of lab normal values (LNVs) is required for each lab listed on the Form FDA 1572/DTL. The LNVs should be from the correct lab and be current.

- b. LNVs for local and central labs (if applicable) should be updated every two years.
- c. LAOs will provide the lab normal values to DCP's regulatory contractor who will review and maintain the documents for the sponsor's record.

4.12. CIRB Approval

- a. CIRB approval of the protocol and model consent form is required; this is obtained from the DCP Protocol Information Office.
- b. The protocol version date for the model consent form approved by the CIRB must be included. If applicable and part of the institution's boilerplate language, a version date specific to the institution may be added to the consent form and does not need to match the CIRB version date prior to DSA.
- c. For international sites, protocol approval is required from the IEC only. The exception is for sites in US territories (e.g., Puerto Rico), which are overseen by the CIRB.
- d. According to CIRB policies and procedures, the local IRBs in the US give authority to the CIRB for review and approval of protocols. Collection of any local IRB acknowledgement letters for those sites that produce them will be managed by the LAOs, and submission to the DCP regulatory contractor is not required.

4.13. CIRB- or IEC-approved ICD

- a. CIRB (or IEC for international sites) approval must be provided for each ICD.
- b. CIRB or IEC approval must not have expired and the ICD version should match the approval memo.
- c. LAOs and AOs will utilize a local version of the ICD for patient enrollment that includes the ICD template language approved by the CIRB. If the institution has an approved stamp, the ICD with the incorporated template language should be stamped and provided.
- d. Local ICD version and date may be included if approved as part of the institutional boilerplate language and may be a different date than the protocol version date, as each institution has individual guidelines for versioning IRB submissions.

4.14. CIRB- or IEC-approved Patient/Recruitment Materials

- a. CIRB approval must be provided for patient/recruitment materials (drug diary, Quality of Life questionnaires, local advertising) for sites in the US or its territories. IEC approval must be provided for international sites.
- b. CIRB or IEC approval must not have expired and the patient/recruitment materials version should match the approval memo.
- c. Some LAOs and AOs will utilize a local version of the patient/recruitment materials. If the institution has an approved stamp, the final version should be stamped and provided.
- d. Patient/recruitment material versions and date may be included if approved as part of the institutional boilerplate language and may be a different date than the version date on the CIRB-approved document, as each institution has individual guidelines for versioning IRB submissions.

4.15. Certificates of Translation

- a. Certificates of Translations should be provided for all essential regulatory documents that are not written in English, including MLs, GCP training and laboratory accreditation certificates, LNVs, IRB or IEC approvals, ICDs, and Patient/Recruitment Materials.

5. LAO, AO AND DCP REGULATORY CONTRACTOR RESPONSIBILITIES

5.1. Document Submission for DSA

- a. Prior to forwarding regulatory documents to the LAO, an inspection of materials by the AO is recommended to reduce submission of expired, illegible, and invalid paperwork.
- b. Upon receipt from the AO, the LAO should forward regulatory documents to the DCP regulatory contractor, who will conduct a full quality review based on the criteria for each document type described in Section 4 of this SOP. As detailed above, except for documents downloaded from RCR by the regulatory contractor, all other regulatory documents should be submitted to the DCP regulatory contractor in electronic format at regulatory@ccsainc.com.
- c. Upon receipt of regulatory documents, DCP's regulatory contractor will confirm that each investigator providing a Form FDA 1572 is not listed on the FDA Disqualification Proceedings and Warning Letters websites.

FDA Disqualification Proceedings:

<http://www.accessdata.fda.gov/scripts/SDA/sdNavigation.cfm?sd=clinicalinvestigatorsdisqualificationproceedings&previewMode=true&displayAll=true>

Warning Letters:

<https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm>

- d. If an investigator is listed on either website, he/she may not participate in the study.
- e. DCP regulatory contractor will request the LAO to communicate any quality review comments and/or requests for revised documents to the submitting AO.
- f. When all essential regulatory documents have been received, reviewed, and approved, the DCP regulatory contractor will email a DSA to the DCP Protocol Information Office, LAO, AO, Medical Monitor, Scientific Monitor, Nurse Consultant, DMACC, and drug distributor (e.g., NCI repository contractor).

5.2. Document Submission for Non-accruing and Administrative Sites

- a. The following regulatory documents are required for non-accruing site activation if applicable:
 - Form FDA 1572
 - CIRB/IEC approval of the protocol (no ICD)
 - PI's NCI Biosketch, ML, FDF, and GCP training certification
 - IB Acknowledgment Form
 - OHRP Assurance

5.3. Document Submission During Course of Study

- a. Each LAO and AO is responsible for submitting updated regulatory documents throughout the duration of the study. All updated documents should be forwarded to the DCP regulatory contractor or updated in RCR with notification sent to the DCP regulatory contractor.
 - b. The following regulatory documents expire and require submission of updated versions:
 - Professional License
 - GCP training certification
 - LNVs
 - CLIA certification
 - CAP certification
 - OHRP Assurance
 - CIRB or IEC approval of protocol, ICD, and patient/recruitment materials
 - c. Regulatory documents that may require submission of updated versions due to changes in study staff and institutional information are the following:
 - Form FDA 1572
 - FDF
 - DTL
- 5.4. If an individual site study staff no longer performs study-related tasks, the end date can be added to the DTL for those study staff. The updated DTL is submitted to the DCP regulatory contractor, and the study staff can be removed from the Form FDA 1572 (if listed). Updated ML and GCP certificate will no longer be required once the signed DTL document with the end date has been provided to the DCP regulatory contractor. However, lab normal values and CAP/CLIA certifications need to be provided while the site remains open.

1. ADDITIONAL INFORMATION

Refer to the [CP-CTNet Acronym List](#) to see the description of commonly used acronyms in this SOP.

Please send questions and comments to the DCP Help Desk at:

1-844-901-4357

dcp helpdesk@dcpais.com

2. REFERENCES

- Delegation of Tasks Log Master Task List
- NCI Registration and Credential Repository – <https://ctepcore.nci.nih.gov/rcr/>

3. APPENDICES

- None