SOP#: PM-6	**Guidelines for the Development and Maintenance of Regulatory Files/Binders**
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NCI Clinical Director Signature:	James Gulley Digitally signed by James Gulley Date: 2022.05.19 07:47:25 -04'00'

POLICY

It is the responsibility of the Principal Investigator to create and maintain a regulatory binder or file of essential documents for each study (both interventional and observational) and ensure compliance with applicable regulations and guidelines, including the Code of Federal Regulations, Good Clinical Practice, and National Institutes of Health policies. This task may be delegated, and the Delegation of Tasks Log must reflect this action.

Essential documents are maintained in electronic form, except for those documents that require a written signature (e.g., Delegation of Tasks/Signature log, Monitoring log, etc.).

SCOPE

All studies conducted by a Principal Investigator in the Center for Cancer Research are subject to the requirements of the SOP with the exception of those in which the Office of Sponsor and Regulatory Oversight (OSRO) serves as the monitoring entity. For those studies, please refer to OSRO Policy 203: Clinical Trial Records Policy – see Resources.

For studies that transition from CCR monitoring to OSRO monitoring, please refer to the OSRO SOP for maintaining documents from the point of transition going forward.

Additional information on requirements for multicenter studies for which CCR is a participating site is addressed in a separate SOP.

PURPOSE

The purpose of this standard operating procedure (SOP) is to provide consistent processes/procedures to be followed for essential documents management/maintenance. Essential documents serve to ensure the compliance of the investigator with the standards of good clinical practice (GCP) and with all applicable regulatory requirements. These documents are generated throughout the various stages of a study, including, before the study begins, during the conduct of the study, and after completion or termination of the study.

RESOURCES

- CCR Office of Sponsor and Regulatory Oversight Policy website
    - Policy 203: *Clinical Trial Records Policy*
- 21 CFR 312.62, Investigator record keeping and record retention
- 21 CFR 812.140, Records
- Frequently asked questions, Statement of Investigator (1572)
- International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), Efficacy Guidelines website
    - E6 Good Clinical Practices (R2), Section 8, Essential Documents for the Conduct of a Clinical Trial
- NIH Records Management Schedule website
- Individual schedules are available here

PROCEDURES

STEP 1: Develop Regulatory Files for Each Study

Essential documents are maintained in electronic form and the regulatory file outline and nomenclature established by the Center for Cancer Research (CCR) Protocol Support Office (PSO) will be used. For each study that is activated, an electronic file folder is created by the PSO Manager. The file is located in the CCR Regulatory Files folder, in hierarchical subfolders for the PI's branch/program, the PI's name then the study number

The electronic regulatory file will serve as the official file and will be retained in accordance with the records schedule outlined in Step 3: Record Retention.

In cases where a Sponsor/collaborator requires that original documents be sent to them, it is acceptable to keep a scanned copy in the electronic regulatory file. All documents will be kept in the electronic record, and any hard copies will be considered a "convenience" copy should the research team elect to retain them.

The electronic records are kept on a secure, limited access server that is backed up daily. All files are kept confidential to ensure conformity to principles of confidentiality and human subjects protections. If the research team elects to keep a convenience copy, then all paper files need to be kept in a secure location such as in a locked cabinet or room.

STEP 2: Maintain Regulatory Files for Each Study

The following documents (all versions) should be collected and filed in the regulatory file if applicable to the study. Documents should be collected before study initiation/recruitment begins as well as throughout the study.

The following documents will be maintained by PSO Manager:

Note: For documents submitted in iRIS, please include submission form and application as applicable with approval/acknowledgement documents

- FDA Form 1572 (IND studies only) or investigator agreement (IDE studies only). Though new labs, testing facilities and sub-investigators **may** be recorded in real time on 1572s, it is not necessary to update and sign the document until a change requiring an FDA submission (e.g., PI change) is made.

  For CCR sponsored studies, individuals listed on the 1572 should also be listed as KSP. PI's name on 1572 needs to match with current CV. Please consult with other sponsors for their guidelines.
- Investigator's Brochure if applicable to the study (IND studies only with approval from the manufacturer)
- Drug package inserts if applicable to study
- Device package insert if applicable to study
- IRB approved initial Protocol and subsequent Protocol Amendments (filed by amendment approval date), including the IRB approvals
- IRB approved initial Informed Consent Form(s) and subsequent amendment approvals (filed by amendment approval date), including the IRB approvals if applicable to study
- Advertisements, participant educational materials, including IRB approval letter
- Other IRB approved submissions, including SPP/KSP lists, study status updates, study closures
- Translated informed consent forms (if applicable) and corresponding certificate of translation (if applicable) (filed by amendment approval date)
- Continuing review report and approvals OR Progress Report and acknowledgement correspondence from the IRB
- Unanticipated Problem, deviation and non-compliance reports submitted to and reviewed by the OHSRP Office of Compliance, including IRB outcome letter
- IND Safety reports received from Sponsor/manufacturer (even if they are not submitted to the OHSRP Office of Compliance as an Unanticipated Problem)
- Radiation Safety Committee (RSC) submission and approval, as applicable
- IRB membership roster for the reviewing IRB, updated as needed. Keep historical copies of all rosters. If the reviewing IRB does not provide a roster, documentation of the IRB's position should be saved in the file.
- Federal-Wide Assurance (FWA) Number for the reviewing IRB
- Principal Investigator and Associate Investigator CVs, signed and dated and current within 2 years of the time the investigator begins their participation in the study. No additional CVs will be required for CCR-led studies not under IND/IDE; however, Sponsor (e.g., OSRO) may have additional requirements.

- Laboratory certification (e.g., CLIA, CAP, or other applicable certificates) (update when the certificate expires, keep all historical copies). CLIA documentation for non-military labs may be found here.

  Note: The Research Coordinator MUST notify the PSO Manager when a new lab or testing facility is being used for protocol-directed assessments. The PSO Manager will secure the lab certification for non-military, US-based labs.
- Range of normal values for NIH laboratories
- Sponsor and/or manufacturer correspondence
  - Note: PI will send all sponsor/manufacturer correspondence to the PSO Manager if PSO staff member not included on the correspondence.
- Additional required authorization/approvals of protocol and amendments (e.g., Institutional Biosafety Committee)
- Additional required periodic committee review approvals/minutes (e.g., Data and Safety Monitoring Board, Safety Monitoring Committee, Independent Monitoring Committee)
- General training certificates (i.e., HSP, GCP)
- Other documents that may be required by a Sponsor such as financial disclosures and medical licenses. In that case, keep all copies in the file, even those that have expired. Note: For CCR sponsored studies which are not monitored by OSRO as well as non-IND/IDE studies – medical licenses are not required
- Documentation of study closure
- Protocol signature page(s) for original protocol and each amendment, if required
- Notes to file as applicable

The Research Coordinator will forward the following documents to the PSO Manager for saving in the electronic file:

- Range of normal values for reference laboratory (for each non-NIH lab used in the study)
  - Make copy of lab result, redact personally identifiable information, add study number and unique ID, scan and save to file entitled “Lab Normals and Certification” using the appropriate nomenclature. Laboratory certification for US military, or non-US labs should also be requested from patient and provided to the PSO.
- Redacted subject screening log and enrollment log[a]
- Redacted subject identification code list
- Delegation of tasks/signature log[a]
- Monitor visit log[a]

- Deviation log
    - If the CCR PDTS is used, a copy of the final log may be added at the end of the study unless needed at an interim IMV for external monitors to CCR (e.g., pharmaceutical collaborator).
- Monitoring reports and all relevant correspondence, including site initiation visit, interim monitoring visits and close-out visit reports. Pre- and post-visit letters from the monitor are included in the regulatory files. The Research Coordinator must copy the PSO Manger on all monitoring correspondences.
- Sponsor correspondence if PSO Manager not copied on email/letter
- Serious Adverse Event Reports sent to the Sponsor and/or Manufacturer, and other SAE reports required per protocol
- Relevant communication other than site visits (letters, meeting notes, etc.)
- Record of retained body fluids/tissue samples (if applicable)
- Protocol specific training records – including amendment training for active staff at each amendment and initial training for any AI(s) added after the SIV/ most recent amendment approval
- Notes to file as applicable

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a. Any log that requires a signature will be maintained initially as a paper copy by the Research Coordinator. It is recommended that these be periodically scanned to pdf and saved in the electronic folder to become part of the official file.

The following documents will be retained in the Clinical Center Investigational Drug Control Unit during the study:

- Drug accountability forms and shipping records

After the study closure is approved by the IRB, these forms and records will be saved in the electronic folder to become part of the official file.

STEP 3: Record Retention

All essential documents will be maintained in this file for the duration of the study and for the designated time requirement (i.e., FDA, ICH, NIH) after study closure. As the official regulatory file is kept electronically, the PSO will maintain the electronic file. Records must be kept for the longest applicable period for record retention as per the NIH Intramural Research Records Schedule and FDA Regulations.