OSRO SROS Essential Regulatory Document Group
Essential Regulatory Document Review Criteria

1. Introduction

This review criterion is provided to aid study teams in review of the site's essential documents for appropriateness and compliance. The document-specific review criteria are listed by document type or topic. Sections with specific documents are presented. Sites may organize their documents differently, but all pertinent study records must be in the site file and available for review by the CCR Office of Sponsor and Regulatory Oversight (OSRO) sponsor documentary oversight support services (SROS).

This document assumes that the study will be performed under a US IND and that the CCR Office of Sponsor and Regulatory Oversight (OSRO) will be the IND Sponsor.

A study file is established at the beginning of each study and kept updated throughout the life of the study. Study files must be maintained for a minimum of two years after a licensing application has been filed with the FDA, until two years have elapsed since the formal discontinuation of clinical development of the investigational product or to the time period stated in the Site-Sponsor agreement. The site must contact OSRO for authorization before destroying any study records.

According to the ICH guidelines Section 8: "Essential Documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents demonstrate the compliance of the investigator, sponsor, and monitor with the standards of GCP and with all applicable regulatory requirements…These documents are also the ones that are usually audited by the sponsor's independent audit function and inspected by the regulatory authority(ies) as part of the process to confirm the validity of the trial conduct and integrity of the data collected."

This document assumes that all documents will be provided via an electronic submission system and will be available in an electronic format unless specified otherwise.

Refer to the table of contents that follows for links to go directly to the location of the desired section.

Contents

2. Acronyms

AE	Adverse Event	**ERDG**	Essential Regulatory Documents Group	**IMV**	Interim Monitoring Visits
CAP	College of American Pathologists	**eTMF**	Electronic Trial Master File	**IND**	21 CFR Part 312 Investigational New Drug (Application)
CCR	Center for Cancer Research	**FAQ**	Frequently Asked Questions	**IRB**	21 CFR Part 56 Institutional Review Board
CLIA	Clinical Laboratory Improvement Amendments	**FD**	21 CFR Part 54 Financial Disclosure by Clinical Investigators	**LNR**	Laboratory Normal Ranges
COI	Conflict of Interest	**FDA**	Food and Drug Administration	**NSR**	Non-Significant Risk (Device)
COV	Close-Out Visit	**FWA**	Federalwide Assurance	**OSRO**	Office of Sponsor and Regulatory Oversight
CRFs	Case Report Forms	**GCP**	ICH E6 Good Clinical Practice	**PI**	Principal Investigator
CV	Curricula Vitae	**HSP**	21 CFR Part 50 Human Subjects Protections	**PII**	Personal Identifying Information
DOA	Delegation of Authority & Staff Signature Log	**IB**	Investigator's Brochure	**SAE**	Serious Adverse Event
DMP	Data Management Plan	**ICH**	International Conference on Harmonisation	**SIV**	Site Initiation Visit
eCRFs	Electronic Case Report Forms	**IDE**	21 CFR Part 812 Investigational Device Exemptions	**SROS**	Sponsor and Regulatory Oversight Support Services

3. References

E6(R2 GCP: Integrated Addendum to ICH E6(R1)

CCR Wiki - Office of Sponsor and Regulatory Oversight

- OSRO Policies
- OSRO SOPs
- OSRO Forms and Instructions

4. General Requirements

All document **File Names** must sufficiently describe the document's **Contents** and include **Version Control** (i.e., a version number and, or a version date).

A document transmittal form must be used if you choose to send your complete uncategorized file or if the file names do not include adequate information. The OSRO Transmittal Form types available on the CCR Wiki – OSRO section include:

- Pre-Site Initiation Visit (SIV) Essential Document Transmittal Form
- Interim Monitoring Visit (IMV) Essential Document Transmittal Form

All protocol-specific documentation must be consistent with the approved version of

- The corresponding protocol,
- The corresponding investigational product IBs or study product Package Inserts,
- IRB Approval documentation, and
- OSRO Clinical Trial Records Policy 203 requirements before, during, and after the study.

5. Federal Wide Assurance

Maintain a record of your Institutional Review Board's Federalwide Assurance number in the regulatory file. The expiration date of the Assurance number should be present on IRB documentation.

Search the following website to obtain this information: http://ohrp.cit.nih.gov/search/irbsearch.aspx?styp=bsc

Form FDA 1572 related notes:

- Section 1 – each facility listed must have an OHRP Federal Wide Assurance number assigned.
- Section 5 - the IRB name on the IRB approval document corresponds to the IRB name listed in Section 5.

The NIH IRBO documentation may be deferred.

6. Form FDA 1572

If the study is under a US IND, Form FDA 1572 is required. The Form FDA 1572 must be signed and dated by the Principal Investigator and include the names of all sub-investigators for the study and the location of all sites where the study will be conducted (all sites where participants will be examined). Be sure to complete Sections 1 – 11 of the Form.

The weblink to the current Form FDA 1572 is https://www.fda.gov/media/71816/download. Refer to the upper-right-hand header for the form's OMB Expiration Date. Keep all signed versions, with the newest in front, if kept in hard copy format. Previous versions of the Form FDA 1572 should not be used.

A new form must be completed when the following occurs:

- Change in Principal Investigator
- Change in address of study site
- Change in clinical laboratory
- Change in Institutional Review Board
- Addition of a new Sub-Investigator

Ensure that all sections are complete and that there are no significant typographical errors that may impact the interpretation or intended use of the information.

Section 1: The PI name corresponds (exact match not required) to the name on the CV. If included on the CV, suffixes such as "Jr." and "Sr." for the PI are on the Form FDA 1572. Credentials such as MD and Ph.D. are on the CV if listed on the Form FDA 1572. The complete physical mailing address is present. The PI is not currently listed as Debarred, Disqualified, or Restricted by the FDA.

Section 2: The appropriate box (usually the CV box) is checked.

Section 3: Name(s) and address(es) of all facilities where clinical investigation(s) will be conducted are listed. Name(s) and address(es) for receiving shipments of study products and supplies are listed. If the study is conducted at the address that is entered in Section 1, the name and address are also entered in Section 3. ("Same as above" or "See Section 1" is not acceptable)

Section 4: Must include the clinical laboratory and facilities/departments/laboratories generating study data supporting the primary or secondary endpoints. Name and complete address of the clinical laboratory location must be listed, as well as the names and addresses of facilities/departments/laboratories that support the safety and efficacy data defined in the Protocol (e.g., Central EKG reader, imaging lab/radiology, central clinical lab, other laboratories). If no clinical laboratories are used for the trial, "None" or "Not Applicable" is noted. (This section cannot be left blank.)

Section 5: The name and complete address of all IRBs (e.g., local IRB, single IRB per NIH policy, and central IRB) utilized for the study are listed.

Section 6: Names of all Sub-Investigators authorized by the PI to conduct significant participant assessments are listed. If there are no Sub-Investigators, "None" or "Not Applicable" is noted. Sub-Investigators are not currently listed as Debarred, Disqualified, or Restricted by the FDA.

Section 7: Must include the protocol number and list the full Protocol title as listed in the most recent version of the Protocol. The protocol number only is not enough.

Section 8: The appropriate box is checked for the clinical trial. For a combined Phase 1/2 investigation, the second box is checked. For a Phase 4 post-marketing clinical trial, the second box is checked, and Field 7 states that the study is a Phase 4 study.

Section 10: The typed or hand-written date is present for the PI listed in Section 1.

Section 11: A hand-written or electronic digital signature is present for the PI listed in Section 1. The handwritten or typed date and an electronic signature date must match. (Date format does not need to match)

7. Investigator Agreement/Investigator of Record

The OSRO Investigator Agreement for Investigational Device Exemption Form must be used for IDE/NSR only studies. The form includes instructions. All sections are complete, and there are no significant typographical errors.

Section 1: The Clinical Investigator's name is spelled correctly and corresponds (exact match not required) to the name on the CV. Suffixes such as "Jr." and "Sr." (or "II" and "III") for the Clinical Investigator are on the IoR if listed on the CV. Credentials such as MD and

Ph.D. are on the CV if listed on the IoR. A complete mailing address is present. The Clinical Investigator is not listed as Debarred, Disqualified, or Restricted by the FDA.

Section 2: Corresponding documents or information is provided.

Section 3: Name(s) and address(es) of all facilities where clinical investigation(s) will be conducted are listed. If the study is conducted at the address that is entered in Section 1, the name and address are also entered in Section 3

Section 4: Only clinical laboratory facilities need to be included. Research laboratories must be identified in the protocol, not on the IoR. Names and addresses of the clinical laboratories must be listed, and the names and addresses of laboratories that support the safety and efficacy data are defined in the Protocol. If clinical laboratories are not used for the trial, "None" or "Not Applicable" is noted.

Section 5: The name and complete address of all IRBs are listed.

Section 6: Names of all Sub-Investigators authorized by the Clinical Investigator to conduct significant participant assessments are listed. If there are no Sub-Investigators, "None" or "Not Applicable" is noted. Sub-Investigators are not listed as Debarred, Disqualified, or Restricted by the FDA.

Section 7: Must include the protocol number and list the full Protocol title as listed in the most recent version of the Protocol. The protocol number only is not enough.

Section 8: Complete with a Yes or No response. If yes, an explanation is provided.

Section 9: Clinical Investigator's Commitment Statement.

Section 10: The hand-written or electronic digital signature is present for the Clinical Investigator listed in Section 1. A hand-written or electronic date is present for the Clinical Investigator's signature.

8. Protocol Acceptance by OSRO

The IRB-approved protocol version (submitted for review before the site initiation visit and before site activation) must be consistent with/match the version referenced on the **OSRO Protocol Approval Memo**.

If the OSRO Protocol Approval Memo protocol version does not match, contact the SROS Essential Documents Group to confirm the status of the approval memo and the protocol version of the most recent OSRO-approved protocol.

9. Protocol Signature Page

The OSRO Form F01-202-S01 Protocol Signature Page must be completed for the Initial Protocol and all subsequent Protocol Amendment versions.

All sections are complete, there are no typographical errors, and the IRB has approved the protocol version.

The Protocol Signature Page includes the following:

- Protocol Number
- Protocol Version (Specify by Date, Number, or Letter)
- Type (Initial or Amendment should be selected)
- Site Name
- Full Name of the Principal Investigator
- The handwritten or electronic digital signature and a signature date are present for the PI.

10. Investigators Brochure and Package Insert

Files are observed by the Clinical Site Monitor, not collected.

IBs and Package Inserts are observed to confirm that the document version and the version date match the information listed on the IRB Approval Letter.

If the IRB Approval Letter doesn't list or include a reference to the study product IB (for unlicensed/not FDA approved products) or Package Insert (for licensed, FDA approved products), the SROS monitoring team will request confirmation that the document was submitted to the IRB.

Sites must ensure that their staff have access to the most current study product information.

Related note:

- When CCR is the manufacturer of an investigational product, refer to OSRO Policy 408 for the need for an IB.

11. Curriculum Vitae

CVs for all Principal Investigators listed in section 1 and section 6 Sub-Investigator(s) on the Form FDA 1572 are present in the documents submitted to the Sponsor eTMF.

Ensure the following for all CVs:

- The name of the Investigator is spelled correctly and corresponds to the name in Section 1 or Section 6 of the Form FDA 1572 (exact match not required).
- Indicates an affiliation to a location where the study will be conducted (noted in Section 3 of the Form FDA 1572).
- Shows the relevant education, experience, and training that qualifies the investigator for the study.
- The date of the CV is within four (4) years of the current date determined by the Investigator's 'signature date' on the CV or the embedded electronic signature date.
- There are no breaks in page numbering (if present).

12. Medical License

Effective April 1, 2023:

Professional licenses must be submitted for those physicians and nurses listed as clinical investigators on the Form FDA 1572 or Investigator Agreement for Investigational Device Exemption studies. This includes the Principal Investigator in section 1 and all Sub-Investigators listed in section 6 of the Form FDA 1572 or Investigator Agreement for Investigational Device Exemption studies. This requirement applies to those Protocols that receive an IRB approval dated after April 1, 2023. Medical licenses are required for physicians, unless physicians are delegated to a data analysis role on the DoA. Nurse Practitioner, Physician Assistant or Registered Nurse licenses are required as applicable.

- A copy of the current professional license or written confirmation from the state licensing board (information from a licensing board website is acceptable) should be provided.
- A professional license number and expiration date documented within the Staff member's CV is insufficient and will not be accepted.
- A physician working at a US military base may have a license issued from a state different than the state where the military base is located.
- The medical or nursing license expiration date is required.
- A physician working at a US military base may have a license issued from a state different than the state in which the military base is located.
- For a US investigator practicing in a Veterans Administration (VA) facility:
    - The license may be issued from a state different than the state in which the VA facility is located.
- ◦ The PI's name on the license must correspond with the name in Section 1 of Form FDA 1572 *or* Investigator Agreement for Investigation Device Exemption. ◦
- ◦ The Sub-I's name on the license must correspond with the name in Section 6 of Form FDA 1572 *or* Investigator Agreement for Investigation Device Exemption. ◦

- If a license is not provided (i.e., licensure is not required per VA policy), documentation of the VA policy provided by the investigator is present.
- For a PI that does not hold medical licensure, a copy of Sub-Investigator's medical license must be present.

Note: All active (excluding those in data analysis only) protocols on January 1, 2024, will be brought into compliance, i.e., the physicians and nurses listed as clinical investigators on the Form FDA 1572 or Investigator Agreement for Investigational Device Exemption studies will be collected, reviewed, and filed in the eTMF.

13. Financial Disclosure

See the CCR Wiki for posted financial disclosure form instructions.

If the outcome of the OSRO Evaluation of Required Financial Disclosure (F02-401-S01) indicates that the 'PI financial disclosure' is required, a Financial Disclosure Form (OSRO Form F01-401-S01) for the PI listed in Section 1 of the FDA Form 1572 must be completed and provided.

- If a financial conflict of interest is indicated, disclosure of the financial interest is required. The PI must include a statement specifying the disclosure statement date, investigator name, protocol #, nature and amount of the interest, and a description of the risk mitigation plan to minimize potential bias.

Related notes:

- The outcome of the Sponsor evaluation applies to all PIs participating in a multicenter study.
- Original, signed Financial Disclosure forms will remain at the site, stored separately from the site essential regulatory documents in a secure location; copies of signed and dated forms will be sent to OSRO as part of the required site essential documents.

14. Site IRB Approval

All IRB-approved materials will be reviewed for compliance with ICH GCP 8.2.7, necessitating the use of version control of all documents submitted for review by the IRB.

The IRB Approval (initial, contingent, continuing review) document must:

- List the full Protocol title listed in the Protocol; it may also contain the Protocol number. A Protocol number only without the title is not enough.
- Be on IRB letterhead with identifiers (e.g., name [abbreviations are acceptable], address) that correspond with the Form FDA 1572 of at least one of the participating investigators or sites. E-mail correspondence stating approval is not enough.

- Specify the study documents that were reviewed, such as:
    - Protocol with version number/date
    - Protocol Amendment(s) with version number/date
    - Informed Consent Form(s) with version number/date
    - If applicable, Informed Consent Form in a foreign language with required English Informed Consent Form or English translation included with version # or date
    - Written educational or study materials to be given to study participants (identified with version # or date)
    - Participant diary cards or memory aids with version # or date
    - Advertisement, recruitment materials with version number or date (note: not required for NIH clinical center-based protocols that use established NIH recruitment referral process and website announcements).
- Be dated, and dates of approval or duration of approval included (e.g., approved on [date], approval expiration on [date], or approved on [date] and in 12 months must be renewed).
    - If the renewal date is not listed, IRB documentation (e.g., Guidelines, Policies, or Memo) stating the IRB approval/renewal timeframe is included.
    - If the Protocol is dated, the approval date is after the Protocol version date.
- Be initialed or signed by the IRB Chairperson or authorized representative.
- For conditional/contingent approval with stipulations, IRB-issued documentation indicates that the PI responded, that the stated conditions were met and that the IRB final approval was granted.

Electronic IRB Systems, Submissions, Approvals

eIRB documentation (generated from electronic submission and approval systems) are most acceptable if all components listed above are present.

A view attachments or equivalent page listing the documents submitted for review by the IRB, including the following information, is acceptable. The list must include the following:

- Document name
- Version number and/or version date
- Version information must match the version information as it appears in the header/footer of the approved document

15. Multicenter Protocol Central or Single IRB

The IRB Approval documentation must:

- Be on the letterhead of the IRB of Record
- Acknowledge the Reliance Agreement between the relying IRB and the IRB of Record
- Include the names of participating institutions/clinical sites and applicable agreement date(s)
- Include the PI Name for each respective site named on the approval letter
- Contain site-specific documents and materials with corresponding version number/date for each respective site named on the approval letter

An IRB of Record approval may include language specifying documents that apply to all involved sites (i.e., Protocol Amendments).

A **conflict-of-interest assessment (COI) and institutional COI management plan** may be required for the non-NIH site PI by the IRB responsible for the review of a multicenter, single IRB protocol. If applicable, the documents must be submitted to the Sponsor eTMF.

16. Informed Consent Forms

All IRB-approved consent/assent/short forms will be reviewed for compliance with ICH GCP 8.2.7, necessitating the use of version control of all documents submitted for review by the IRB.

- All pages of the document are present
- The Protocol title is listed correctly if present
- The document is approved by the IRB
  - The document should have an approval stamp somewhere on the document or a notation present to indicate the IRB approval and effective approval date(s).
  - If the document does not contain an approval stamp or other approval notation, the IRB approval letter must specifically identify the document's approval and correctly match the version listed on the document.

For Informed Consent Forms:

- If state-specific and/or IRB-specific documents are required to be given to the participant during the informed consent process in addition to the study consent, these documents are present, e.g., the state of California requires the California Bill of Rights to be included with the consent.

17. IRB Roster

- NIH CCR sites - the NIH "Request for IRB Membership/Roster Information" memo is sufficient documentation.
- Non-NIH sites - the relevant IRB Roster must be provided.

18. Diary Cards or Memory Aids

A protocol-related Diary Card or Memory Aid may be a separate document or be contained in the IRB-approved protocol as a section or an appendix. If it is part of the protocol, this item would not be an essential applicable/collected and tracked document.

If the Protocol related Diary Card or Memory Aid is a separate document, it should be listed or referenced in the IRB Approval. And in this instance, the Protocol related Diary Card or Memory Aid must include version control, e.g., version # or version date.

19. Participant Information Sheet

This document may be part of the IRB-approved protocol as an appendix or attachment. If it is part of the protocol, this item would not be an essential applicable/collected and tracked document. If submitted as a separate document, it should be listed or referenced in the IRB Approval. And in this instance, it must include version control, e.g., version # or version date.

20. Participant Participation Card

This document may be part of the IRB-approved protocol as an appendix or attachment. This item would not be an essential applicable/collected and tracked document if part of the protocol. If submitted as a separate document, it should be listed or referenced in the IRB Approval. And in this instance, it must include version control, e.g., version # or version date.

21. Advertisements for Recruitment

Non-NIH site recruitment advertisements do not require submission to the Sponsor eTMF.

If part of the protocol as an appendix or attachment, it would not be an essential applicable/collected and tracked document. If submitted as a separate document, it should be listed or referenced in the IRB Approval. And in this instance, it must include version control, e.g., version # or version date.

22. Clinical Laboratory Credentials / Certification

If a **clinical laboratory is listed in Section 4** of the Form FDA 1572, CLIA certification or equivalent is required for each if there are multiple.

CLIA certificates are not required for the following:

- All labs in the state of Washington
- All Hospital labs in the state of New York (NY private practices require a CLIA)
- All Veteran Administration (VA) hospital labs

Related notes:

- State certifications or foreign country equivalent are required instead of CLIA certification
- As applicable, private inspection agency certificates (e.g., CAP, COLA) are present and current for each clinical laboratory listed in Section 4 of the Form FDA 1572.
- A private inspection agency certificate is needed for the CLIA Certificate of Accreditation
- A private inspection agency certificate is not needed for:
    - CLIA Certificate of Compliance
    - CLIA Certificate of Registration
    - CLIA Certificate of Waiver
    - CLIA Certificate for Provider-Performed Microscopy Procedures

23. Clinical Laboratory Normal Reference Ranges

The laboratory's name must be on the laboratory normal ranges (LNR) document, and consistent/matches the lab's name that appears in Section 4 of the Form FDA 1572.

- Current and updated reference ranges (as applicable) must be provided for each clinical laboratory in Section 4 of the Form FDA 1572.
- The current date is indicated on the LNR document. Acceptable dates include the following:
    - Start Date
    - Effective Date
    - Print the date on the document page
- If the laboratory address is indicated on the LNR, it corresponds to Section 4 of the Form FDA 1572 (an exact match is not required).
- The 'per protocol' laboratory test(s) LNRs are required.
- LNR documents are not required for laboratories not listed on the Form FDA 1572.

24. Clinical Site Delegation of Authority & Staff Signature Log

The **OSRO Clinical Site Delegation of Authority & Staff Signature Log (F01-203-S01)** is required for all studies under a CCR-held IND, IDE, and NSR Device Study. The Log may be completed and signed electronically in Adobe Acrobat via PIV access or printed and filled out by hand. Please see the **OSRO Delegation of Authority & Staff Signature Log FAQ document.**

Effective on July 17, 2023, the DOA Log (revision 3), must be completed electronically. Paper will not be accepted for new studies (requiring an SIV) moving forward. Starting on June 1, 2025, SROS will not accept any older version of the OSRO DOA Log.

The Log must include the following:

- List of names of all Site Staff, their respective roles (e.g., Principal Investigator, Sub-Investigator, Pharmacist, Study Coordinator, Data Manager, Regulatory Coordinator, Research Nurse, Research Laboratory Technician), and the significant study-related duties/tasks delegated by the PI using the Task Codes.
- All Staff listed on Form FDA-1572. Staff duties/tasks must remain within the scope of their professional licensure. Study-specific tasks may be added to the list of numbered task codes as needed.
- Staff duties/tasks delegated by the PI may not be performed if the Staff member's training documentation is unavailable.
- If revised version 3 of the Log is used, it must be completed electronically; a paper version of the Log using handwritten (wet) signatures will not be accepted. Individuals listed on the Log must provide an electronic 'certified' digital signature.
- Staff assigned a duty/task, e.g., Task Code 1. Obtain hand-written Informed Consent, that requires a handwritten wet signature and/or initials, must sign using a full signature and their initials for documentation of their handwriting and indicate an understanding of the responsibilities assigned.
- Staff assigned duties/tasks that do not require handwritten entries may provide an electronic 'certified' digital signature (in Adobe Acrobat) to indicate an understanding of the responsibilities assigned.
- Provide the Start Date for delegated study duties/tasks. If a Site Staff member's duties/tasks change, enter the End Date, then add a new line with their updated duties/tasks and Start Date.
- Provide the End Date when the individual no longer performs a delegated duty/task or participates in the study. If blank, this indicates that the duties/tasks were conducted until the completion of the study (Date of PI End-of-Study declaration).
- An entry for named Staff is not complete without the PI´s Initials and Date. By initialing the Start Date, the PI confirms that the Staff member is authorized, trained appropriately for the role, and qualified to perform the duties/tasks assigned. PI retains the overall responsibility for the conduct of the clinical trial, including delegated duties/tasks.
- Retain the current Log and all previous original Log versions in the site study file. Update the Log as personnel, roles, and/or study tasks change.

Completion instructions for the end-of-study:

- For a printed form, filled or signed by hand: If blank rows remain, draw a diagonal line through the blank section and mark NA, initial, and date.

- For an electronic form, fill and sign electronically: If blank rows remain, enter NA in each unused cell.
- After reviewing all entries for accuracy at the end of the study, the PI will sign and date the Log in the designated area for the End-of-Study declaration.

Related notes:

- Implementation of the OSRO delegation of authority log (F01-203-S01) is required for pre-SIV and active/open protocol statuses: Screening, Enrolling, and in Follow-Up.
- **A different delegation of authority log format confirmed by the SROS Monitor to include elements similar to the OSRO F01-203-S01 form may be used by non-NIH sites**

25. Site Staff Training Records

For all research team members on the FDA Form 1572 and Clinical Site Delegation of Authority & Staff Signature Log. A record of training is required. The training topics must include the following:

- Protocol (initial and all amendments)
- Human Subjects Protections (HSP)
- Good Clinical Practice (GCP) (completed/renewed within the last three years)
- Also, as applicable:
    - Dangerous Goods Handling or International Air Transport Association (IATA)
    - Other specialized procedures, e.g., study product preparation
    - Protocol-specific use of the EDC system for non-NIH PI and site Staff electronic data capture (EDC) system. Documentation must be provided before site activation.

Training record topics and dates should correspond to the individual's designated tasks and functions noted on the Clinical Site Delegation of Authority & Staff Signature Log **during the period the individual is an active member of the study team**.

Records should include the training date, title, and attendee's name or the individual's training Certificate of Completion with their name, date, and title of training.

26. Data Management Plan

The CCR main site must provide the Data Management Plan (DMP). An approved DMP is required for those protocols with an initial IRB approval after January 1, 2023.

27. Electronic Case Report Form (eCRF) Technical Specifications

The specifications document provided for the Sponsor eTMF must correspond to the IRB-approved protocol, version, and version date. A detailed supplement must be retained with the eCRF specifications if another protocol is referenced within the specification document. A record of the clinical study team's approval must also be included.

- If the blank annotated eCRFs are provided and accepted before the Site Initiation Visit, eCRF specifications are not required,
- If a multicenter protocol, the non-NIH sites are not required to provide eCRF specifications.

28. Blank Annotated Electronic Case Report Form (eCRF)

The blank annotated electronic case report form provided for the Sponsor eTMF must correspond to the IRB-approved protocol or protocol amendment, version, and version date. A record of the clinical study team's approval must also be included.

- The eCRF design/data fields must correspond to the protocol requirements. The protocol-specific CRF may not collect data that is not required per protocol.
- The blank annotated eCRFs must be reviewed and accepted before site activation.
- If a multicenter protocol, the non-NIH sites are not required to provide blank annotated eCRFs

29. ICF (signed) and Related Process

A signed, fully executed informed consent /assent form or re-consent is available in the participant's source records. Per each protocol amendment, IRB Approval re-consent may be required.

The methods and materials used in obtaining and documenting the participant's informed consent/assent / re-consent comply with E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1), section 4.8: Informed Consent of Trial Subjects, and Regulations: 21 CFR 312.62(b) and 21 CFR 812.140(a)(3)(i). Includes:

- Current IRB-approved version of ICF is used.
- All pages are present.
- Signature page includes all required signatures and signature dates.
- Appropriate type of informed consent process is used, e.g., for autonomous adults, minors, and adults who are or may be unable to consent
- Documentation of the informed consent/assent / re-consent process is present in the participant's source records.

30. Notes to the Study File

A note to the study file should include the following:

- Date written
- Name and title of the author
- Subject line with protocol #, topic/issue
- Description of the issue with dates/timeframe of occurrence and reason for the error, omission, discrepancy, or process/policy it aims to address
- Corrective action the site will perform to avoid similar issues in the future
- Effective date for corrective action, if different from the date written.

Notes to the study file should be:

- Filed in the site essential documents folder
- Made available to the Monitors reviewing the site's documents and procedures
- Submitted by the site Staff to the IRB, per IRB guidelines
- Submitted by the site Staff to the CCR Office of Sponsor and Regulatory Oversight (OSRO)
- It should be possible to authenticate the document as appropriate

31. Sponsor Correspondence

Protocol-specific correspondence should be retained in this section of the study file.

32. IRB Correspondence

Protocol-specific correspondence should be retained in this section of the study file. This should not include IRB Approval Letters.

33. Relevant Communications

This section of the study file should include significant site correspondence about the conduct of the study, e.g., with site staff, to/from collaborators, laboratories, ancillary institutional department personnel/management, and contracts.

34. Pharmacy Correspondence

Pharmacy monitoring visit communication and monitoring visit reports should be retained.

35. Pharmacy Logs

During the studies, pharmacy inventory, accountability, and temperature logs will be retained by the Pharmacy.

At the time of the monitoring Closeout Visit (COV), a **redacted** copy of the final/cumulative pharmacy logs must be submitted to the Sponsor eTMF.

36. Participant Screening and Enrollment Logs

Effective March 10, 2022, the OSRO Participant Screening and Enrollment Log is required for all protocols under a CCR-held IND, IDE, or considered an NSR device study. Please go to the CCR Wiki - OSRO Forms and Instructions and download, save, and fill in the information.

Related notes:

- The previous screening and enrollment logs should be retained in the site's essential regulatory documents file.
- All participants considered for this study must be listed (e.g., all participants you screened for this study).
- A study number or record number must be used on this list, and an ID Code list that links those numbers must be kept. For study purposes, records cannot be maintained by name or other personal (non-study) identifier. PII (e.g., names, addresses, and other personal identifying information that map to Study ID) should be stored on an ID Code list apart from study files. In this instance, the NIH MRNs to which access is restricted are allowed and may be captured on the log.
- Participants cannot be screened until they have signed an informed consent document or an IRB-approved screening consent.
- Be sure to note why a participant was not enrolled when applicable.