1. Purpose

To define the site essential regulatory documents required for a clinical trial and the process used to collect, review and archive them.

2. Scope

2.1. This SOP applies to clinical studies conducted under a Center for Cancer Research (CCR)-held Investigational New Drug application (IND), Investigational Device Exemption (IDE) under Office of Sponsor and Regulatory Oversight (OSRO) oversight, or a National Institutes of Health (NIH) Institutional Review Board (IRB)-approved protocol using a Non-Significant Risk device (NSR) under OSRO oversight.

3. Responsibilities

3.1. OSRO Operations oversees the clinical monitoring process for essential regulatory document receipt, review, and archive.

3.2. The OSRO Sponsor and Regulatory Oversight Support (SROS) Contractor assists OSRO as needed.

3.3. The SROS Essential Regulatory Documents Group (ERDG) and/or Clinical Monitoring reviews site-submitted essential regulatory documents for completeness and ensures that all required documents are present.

3.4. The OSRO Director is responsible for reviewing written justification from Principal Investigators requesting any deviation from pre-Site Initiation Visit clinical trial records requirements.

4. References

4.1. 203 Clinical Trial Records Policy

4.2. 205 Clinical Site Monitoring Policy

4.3. 206 Site Activation Policy

4.4. ICH E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry (FDA), March 2018

5. Definitions

Refer to the OSRO Lexicon.

6. Procedure

6.1. The Office designation of OSRO shall refer both to the Office of Sponsor and Regulatory Oversight staff and the OSRO Sponsor and Regulatory Oversight Support contractor staff.

6.2. The required site essential documents list is provided in Reference 4.1.

6.3. Site essential regulatory document reviews occur per the Clinical Monitoring Plan (CMP). The following time points over a clinical study's life cycle are review points.

6.3.1. Documents for IND/IDE submissions (Step 6.5)

6.3.2. Prior to the Site Initiation Visit (SIV) (Step 6.6)

6.3.3. During Interim Monitoring Visits (IMV) (Step 6.7)

6.3.4. During the Close-out Visit (COV) (Step 6.8)

6.3.5. IRB Approved Protocol Amendment (Step 6.9)

6.3.6. Ad Hoc (Step 6.10)

6.4. The CCR site point-of-contact uploads all pertinent essential regulatory documents to the applicable electronic document system, including the eTMF.

6.4.1. For multicenter studies, non-NIH site essential regulatory documents may be submitted directly to SROS ERDG by the site or collected by the CCR study coordinating center and submitted to SROS ERDG on behalf of each participating non-NIH clinical site.

6.4.2. Documents containing no Personally Identifiable Information (PII) may be sent via an alternate method (e.g., email) as a last resort, with prior approval of OSRO.

6.4.3. A Coordinating Center Communication Plan for Multicenter Clinical Trials, F01-208-S01 should be completed for all multicenter studies.

6.5. IND/IDE essential regulatory documents.

6.5.1. The OSRO Regulatory team requires the following documents for an IND or IDE submission.

- Form FDA 1572 Statement of Investigator for an IND submission
- F01-406-S03 Investigator Agreement for an IDE submission
- IRB approved Informed Consent Form
- Study protocol
- PI Curriculum Vitae (CV)

6.5.2. Following completion of the Sponsor's protocol review process, the SROS Protocol Review Coordinator or designee uploads the finalized study protocol and Informed Consent Form(s) to the eTMF.

6.5.3. The site regulatory coordinator uploads the completed Form FDA 1572 Statement of Investigator (IND submission) or F01-406-S03 Investigator Agreement (IDE submission) and the PI's CV to the eTMF.

6.5.3.1. The site regulatory coordinator notifies the SROS ERDG by email after all required documents have been uploaded.

6.5.4. The SROS ERDG reviews the submitted documents for accuracy and completeness.

6.5.4.1. Recorded information is cross-checked with information contained in the protocol.

6.5.4.2. The site is contacted about any issues or discrepancies in the documents.

6.5.5. When all queries are resolved, the SROS ERDG files the accepted documents in the eTMF and notifies the OSRO Regulatory Team and the Protocol Support Office (PSO) that the documents are available.

6.5.6. The OSRO Regulatory Team downloads the IND/IDE essential regulatory documents, as needed.

6.6. Prior to the Site Initiation Visit (SIV), site essential regulatory documents are submitted to the SROS ERDG.

6.6.1. Documents should be submitted 4 – 8 weeks prior to the anticipated SIV date to allow sufficient time to review and verify the clinical trial records.

6.6.2. SROS ERDG reviews the submitted site essential regulatory documents for completeness and compliance with applicable requirements.

6.6.3. If no issues are identified, the essential document review is deemed complete.

6.6.3.1. The Principal Investigator (PI) is notified by email with a copy sent to the study team.

6.6.4. If any issues or discrepancies are identified or additional documents are required, the CCR site point-of-contact is notified by email with a copy sent to the study team.

6.6.4.1. Site essential document review status remains incomplete pending resolution of all issues or receipt of missing documents.

6.6.4.2. All issues or discrepancies related to site essential regulatory documents must be resolved before the SIV is conducted unless otherwise approved by the Sponsor.

6.6.5. For multicenter studies, emails are sent to the CCR study coordinating center to request essential regulatory documents.

6.7. During Interim Monitoring Visits, SROS Clinical Monitoring and/or ERDG reviews onsite site essential regulatory documents per site-established access procedures.

6.7.1. SROS Clinical Monitoring and/or ERDG inspects for expired, new, or updated documents which include training records, medical licensure, laboratory certifications, IRB Approvals, IND Safety Updates/Serious Adverse Event (SAE) Reports, Site Non-Adherence Log entries, notes to the study file and correspondence.

6.7.2. Source records stored outside of the Clinical Research Information System (CRIS) that contain PII, are sent by the site via Secure Email File Transfer (SEFT) to the monitor(s) listed in the confirmation letter.

6.7.2.1. Source records include medical records, outpatient clinic records, diagnostic reports, and site research records required for medical history/source documentation review and eCRF data verification.

6.7.3. Any issues, discrepancies, or additionally required documents are communicated to the site staff during the monitoring visit and/or at the closing meeting.

6.7.3.1. Findings are noted as follow-up/action items in the monitoring visit report until resolved.

6.7.3.2. For NIH-based sites, new or updated documents are submitted to SROS ERDG via upload to the eTMF.

6.7.3.3. For multicenter studies, new or updated documents are submitted to SROS ERDG via upload to the eTMF.

6.7.4. If no issues are identified, the site monitoring visit report will indicate that no issues were found.

6.8. Review of documents at the Close-Out Visit.

6.8.1. All site essential regulatory documents are reviewed for compliance with applicable requirements.

6.9. IRB Approved Protocol Amendment

6.9.1. When a protocol is amended, a document review is performed for any essential regulatory documents updated as a result of the amendment.

6.10. Ad Hoc

6.10.1. Additional essential regulatory document reviews may be performed as circumstances warrant.

6.11. Archiving essential regulatory documents.

6.11.1. Accepted essential regulatory documents are archived in the eTMF.

7. Associated Documents

7.1. 203-S01-W01 Essential Regulatory Document Review

7.2. Form FDA 1572 Statement of Investigator

7.3. F01-406-S03 Investigator Agreement for an IDE submission

7.4. F01-208-S01 Coordinating Center Communication Plan for Multicenter Clinical Trials

8. Change Summary

Revision Number	Effective Date	Description of Change
1	09JAN2020	New Document
2	05FEB2020	1. Added nonsignificant risk devices to Section 2 Scope. 2. Added step that the initial reviews of Form FDA 1572 Statement of Investigator and F01-406-S03 Investigator Agreement will be conducted by the IND team at the pre-submission stage (Step 6.6.1). 3. Added step that all issues or discrepancies related to site essential documents must be resolved before scheduling the Site Initiation Visit (Step 6.7.3). 4. Removed Section 9 Appendix 1. The Essential Regulatory Documents are listed in 203 Clinical Trial Records Policy.
3	18APR2022	1. Biennial Review 2. Document name changed from Essential Regulatory Documents Required for a Clinical Study to Clinical Trial Site Essential Regulatory Documents. 3. Complete rewrite of procedure due to addition of SROS Contractor services.
4	01MAY2024	Biennial Review Step 3.1 – removed “Coordinator” Step 6.5.5 – added PSO Step 6.6.4.2 – changed “before confirming the SIV date” to “before the SIV is conducted” Section 7 – added hyperlinks