1. **Purpose**

To define the site essential regulatory documents required for a clinical study and the process used to obtain, 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) or 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 nonsignificant risk device (NSR) under OSRO oversight.

2.2. **Limitation**

2.2.1. Non-NIH clinical sites will not have permission to upload files to the CCROSRO-CSM SharePoint site. Only CCR staff responsible for essential regulatory document submission will have the appropriate CCROSRO-CSM SharePoint permission to upload.

3. **Responsibilities**

3.1. OSRO Operations Coordinator oversees the OSRO Clinical Monitoring process for essential regulatory document receipt, review, and archive.

3.2. OSRO Clinical Site Monitors prepare for, conduct and document the site essential regulatory documents review and outcome.

3.3. OSRO IND Regulatory team conducts and documents the IND/IDE pre-submission stage initial review of the original Form FDA 1572 or OSRO F01-406-S03, as applicable.

3.4. OSRO Clinical Site Monitors evaluate the documents provided by the site staff and determine if all essential regulatory documents are present and completed correctly.

3.5. The OSRO Director is responsible for reviewing written justification from Principal Investigators requesting a temporary waiver for Site Initiation Visit prerequisite essential regulatory documents review and acceptance.

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 list of required site essential documents is presented in 203 Clinical Trial Records Policy.

6.2. The CCR site point-of-contact will upload all pertinent essential regulatory documents to the protocol-specific folder created on the CCROSRO-CSM SharePoint site, under Protocols > Site Per-Protocol Essential Regulatory Documents for the purpose of document transfer from the clinical site to OSRO. Submission of documents may be one-time or staggered until all documents have been sent and the document inventory is deemed complete by OSRO Monitoring.

6.2.1. For multicenter studies, non-NIH site essential regulatory documents will be collected by the CCR study coordinating center point-of-contact and submitted to OSRO on behalf of each participating non-NIH clinical site.

6.3. OSRO Clinical Monitoring reviews the site essential regulatory documents received for completeness and compliance with applicable requirements.

6.3.1. If no issues are identified, the site essential document review will be deemed complete. The CCR site point-of-contact will be informed by email with copy sent to the study team.

6.3.2. If any issues or discrepancies are identified or additional documents are required, the CCR site point-of-contact will be informed by email with copy sent to the study team. Site essential document review status will remain incomplete pending resolution of all issues or receipt of missing documents.

6.3.3. For multicenter studies, communications will be sent to the CCR study coordinating center, essential regulatory documents point-of-contact.

6.4. During Interim and closeout monitoring visits, OSRO Clinical Monitoring reviews the onsite site essential regulatory documents (i.e., paper and electronic) per site established access procedures.

6.4.1. Any issues, discrepancies or additional documents that are required will be communicated to the site Staff during the end of visit meeting and noted as follow-up/action items in the monitoring visit report.

6.4.2. For NIH-based studies, OSRO Clinical Monitors will inform site staff that new or updated documents should be submitted to OSRO via upload to the protocol-specific folder located under Protocols > Site Per-Protocol Essential Regulatory Documents on the CCROSRO-CSM SharePoint site.
6.4.3. For multicenter studies, OSRO Clinical Monitors will inform site Staff that new or updated documents should be submitted to the CCR clinical coordinating center, study point-of-contact who will upload the documents to a site-specific subfolder under the protocol-specific folder located under Protocols > Site Per-Protocol Essential Regulatory Documents on the CCROSRO-CSM SharePoint site.

6.4.4. Site essential document review findings will be documented in monitoring visit reports as outstanding follow-up/action items until resolved.

6.4.5. If no issues are identified, the respective site monitoring report section will indicate none.

6.5. Essential regulatory document reviews occur at the following time points over the study’s lifecycle.

6.5.1. Receipt of Form FDA 1572 Statement of Investigator for IND submission
6.5.2. Receipt of OSRO F01-406-S03 Investigator Agreement for IDE submission
6.5.3. Prior to the Site Initiation Visit (SIV)
6.5.4. During Interim Monitoring Visits (IMV)
6.5.5. During the Close-out Visit (COV)

6.6. Review of the Form FDA 1572 Statement of Investigator for an IND submission, or of the OSRO F01-406-S03 Investigator Agreement for an IDE submission.

6.6.1. At the pre-submission stage, the initial review of the form for accuracy and completeness will be conducted by the OSRO IND Regulatory team.
6.6.2. Recorded information is cross-checked with information contained in the protocol.
6.6.3. Note: At the early development phase of the protocol, a protocol code number may not have been assigned. When the protocol is issued its code number, the Form FDA 1572 Statement of Investigator or the OSRO F01-406-S03 Investigator Agreement, as applicable should be updated to include the protocol code number.

6.7. Review of documents prior to the Site Initiation Visit.

6.7.1. All site essential regulatory documents are reviewed for compliance with applicable requirements.
6.7.2. Documents should be submitted to OSRO Clinical Monitoring 4 – 8 weeks prior to the anticipated SIV date to allow sufficient time for review and verification of information.
6.7.3. All issues or discrepancies related to site essential documents (per 6.1 above) must be resolved before scheduling of the Site Initiation Visit.

6.8.1. OSRO Clinical Monitoring will review for expired, new or updated documents (i.e., training records, medical licensure, laboratory certification, IRB Approval), IND Safety Updates/Serious Adverse Event (SAE) Reports, Site Non-Adherence Log entries, notes to the study file and correspondence.


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

6.10. Archiving essential regulatory documents.

6.10.1. Accepted essential regulatory documents will be archived on the CCROSRO-CSM SharePoint site in a protocol-specific folder.

6.10.2. For multicenter studies, documents will be archived in a site-specific subfolder under the Protocol-specific folder.

6.11. This document shall be reviewed periodically and updated as necessary.

7. Associated Documents

7.1. 203-S01-W01 Essential Regulatory Document Review

8. Change Summary

<table>
<thead>
<tr>
<th>Revision Number</th>
<th>Effective Date</th>
<th>Description of Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>09JAN2020</td>
<td>New Document</td>
</tr>
</tbody>
</table>
| 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. |