1. Purpose

To outline the protocol close-out or closure process. In most instances, the protocol is considered closed after the finalization of the clinical study report post-database lock.

2. Scope

2.1. Center for Cancer Research (CCR) clinical trial protocols conducted under the Office of Sponsor and Regulatory Oversight (OSRO) oversight are within the scope.

2.2. The close-out process includes confirming that all activities at all locations associated with the clinical trial are appropriately reconciled, recorded, and reported at the end of the clinical trial in accordance with the protocol, relevant SOPs, and applicable regulatory and Good Clinical Practices (GCP) guidelines and a final clinical study report has been submitted to the Food and Drug Administration (FDA).

3. Responsibilities

3.1. The Principal Investigator (PI) oversees the conduct of the protocol and determines when per-protocol criteria for closure have been met. As appropriate, the PI notifies the Sponsor and the Institutional Review Board (IRB).

3.1.1. For multicenter protocols, the CCR PI will determine when per-protocol criteria for closure of the site(s) and the protocol closure have been met, respectively. As appropriate, in a multicenter protocol, the site PI will notify the IRB when site monitoring closeout occurs, and the CCR PI will notify the Sponsor when the protocol meets criteria for closeout.

3.2. The Sponsor conducts an ongoing assessment of study progress and if determined that the study should be suspended for any issues that may undermine the integrity of the clinical trial or for futility, then, the study will be terminated/closed early.

3.3. OSRO Operations confirms that all applicable study and regulatory requirements have been fulfilled at the conclusion of the clinical study.

3.4. OSRO Sponsor and Regulatory Oversight Support (SROS) contractor staff assist OSRO Functional Groups as needed.

3.5. SROS Study Information Office (SIO) manages the protocol closure process.

4. References

4.1. 205 Clinical Site Monitoring Policy

4.2. 410 Final Clinical Study Reports for Studies under CCR-held INDs or IDEs Policy

4.3. 205-S03 Clinical Site Closure

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

4.5. 21 CFR Part 312 Investigational New Drug Application

4.6. 21 CFR Part 812 Investigational Device Exemptions

5. Definitions

Refer to the OSRO Lexicon.

6. Procedure

6.1. Once all clinical trial sites have been closed per 205-S03 Clinical Site Closure (Reference 4.3), OSRO initiates the protocol closure process.

6.1.1. SROS SIO completes the SROS Protocol Closure Checklist to confirm that the protocol is ready for closure.

6.2. The following requirements must be met (as applicable to the study) before a protocol may close. In case of administrative protocol closure, go to Step 6.3.

6.2.1. The pharmacy Close-Out Visit has been conducted and the investigational product disposition completed. Investigational product accountability records have been monitored, retrieved, and posted to the Sponsor eTMF.

6.2.2. The study Investigational Device Exemption (IDE) or Non-significant Risk (NSR) device or assay product records have been monitored, retrieved, and posted to the Sponsor eTMF. Study device disposition has been completed.

6.2.3. Imaging product records have been monitored, retrieved, and posted to the Sponsor eTMF. Imaging product disposition has been completed.

6.2.4. The Center for Cellular Engineering (CCE) investigational product accountability records have been monitored, retrieved, and posted to the Sponsor eTMF. Investigational product disposition has been completed.

6.2.5. Research biological samples collected from participants who have withdrawn their consent have been destroyed.

6.2.6. Serious adverse events have been closed and reported to the FDA.

6.2.7. Clinical trial status has been updated in ClinicalTrials.gov.

6.2.8. Study results have been submitted to ClinicalTrials.gov.

6.2.9. A final clinical study report has been prepared. Note: the report must be submitted to the FDA no later than the next submission of the Investigational New Drug application (IND) annual report.

6.2.10. Acknowledgement of study closure issued by the IRB has been received.

6.3. Protocols may be closed prematurely or administratively with the OSRO Director's approval. Certain standard protocol closure requirements (Step 6.2) may be unfeasible to meet. OSRO communicates to SROS SIO those requirements which will be omitted.

6.4. OSRO Operations conducts the final review of SROS confirmation that all action items have been completed and that all applicable study and regulatory requirements have been fulfilled.

6.5. SROS SIO prepares form F01-205-S04 Protocol Closure Notification for the protocol.

6.6. The OSRO Director signs the F01-205-S04.

6.6.1. The protocol is deemed officially closed after the F01-205-S04 is signed.

6.7. SROS SIO emails the signed F01-205-S04 to the PI and copies the Protocol Support Office (PSO), the OSRO Director, OSRO Monitoring, OSRO Regulatory, OSRO Safety, SROS Essential Regulatory Documents Group (ERDG), SROS Monitoring, SROS Safety, SROS Regulatory, SROS Medical Writing, SROS Project Management, and SROS SIO.

6.8. SROS SIO updates the Sponsor eTMF by uploading the signed F01-205-S04, setting the protocol status to closed, and archiving the study.

6.9. OSRO Regulatory may submit a request to the FDA to withdraw the IND after the protocol is officially closed by OSRO.

7. Associated Documents

7.1. F01-205-S04 Protocol Closure Notification

7.2. SROS Protocol Closure Checklist

8. Change Summary

Revision Number	Effective Date	Description of Change
1	19SEP2022	New Document
2	21AUG2024	Complete rewrite of process Step 3.5 – added Step 4.3 – added Step 7.1 & 7.2 – added