1. Purpose

To provide the process for recognizing incidents that require a corrective or preventive action (CAPA) at clinical sites participating in Center for Cancer Research (CCR)-held Investigational New Drug application (IND), Investigational Device Exemption (IDE) or Non-Significant Risk Device (NSR) studies and assessing the action for effectiveness.

2. Scope

2.1. Studies conducted under a CCR-held IND, IDE or NSR are monitored for incidents requiring a CAPA.

2.2. Limitations

2.2.1. The Office of Sponsor and Regulatory Oversight (OSRO) CAPA system for managing CAPAs within the OSRO Quality Management System is not in scope for this procedure.

2.2.2. Clinical sites are governed by their own CAPA procedures for identifying, investigating, documenting, and tracking incidents requiring a CAPA.

3. Responsibilities

3.1. Clinical Monitors provided by the OSRO Sponsor and Regulatory Oversight Support (SROS) Services contractor will notify an OSRO Operations Coordinator of significant and/or pervasive findings of non-compliance which may require a CAPA.

3.2. The Sponsor requests CAPA from clinical sites in case of significant noncompliance.

3.3. The Sponsor reviews clinical site CAPA reports for the ability of actions to correct or prevent the reoccurrence of the incident.

4. References

4.1. 104 Corrective and Preventive Action Policy

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

4.3. ICH E6(R3) Good Clinical Practice (GCP) draft Guidance for Industry (FDA), May 2023

4.4. 21 CFR Part 50 Protection of Human Subjects

4.5. 21 CFR Part 56 Institutional Review Boards

5. Definitions

Refer to the OSRO Lexicon.

6. Procedure

6.1. As sponsor of CCR clinical studies, OSRO is responsible for monitoring clinical sites in the conduct of clinical trials in compliance with an Institutional Research Board (IRB) approved protocol, International

Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP), Federal Regulations, and Human Subjects Protection.

6.2. Significant noncompliance issues that would require CAPA at clinical sites

6.2.1. Examples include but are not limited to the following if judged to be persistent or significant:

- Failure to meet per protocol eligibility criteria
- Failure to follow the Informed Consent Process and adequately document the process
- Breach in confidentiality, privacy
- Significant deviations from the IRB approved protocol
- Inadequate documentation of Study Team Member training and qualifications
- Significant deviations from the data management plan
- Inadequate source documentation
- Non-adherence to Good Clinical Practice (GCP)
- Non-adherence to Serious Adverse Event (SAE) reporting requirements
- Deviations from the Investigational Product manufacturing, shipping, storage, or dose preparation and administration requirements

6.3. If a noncompliance that significantly affects or has the potential to significantly affect human subject protection or reliability of trial results is discovered, then a CAPA should be documented.

6.4. SROS Monitoring notifies OSRO Operations of suspected incidents.

6.5. The OSRO Operations Coordinator reviews the incident.

6.5.1. If any conditions listed in Step 6.2 are true, then the Principal Investigator (PI) is notified of the finding and a request for a CAPA is made by the OSRO Operations Coordinator.

6.5.1.1. The recommended due date is 2 weeks from the date of request.

6.6. The clinical site uses its internal procedure for documenting CAPAs.

6.6.1. If the clinical site does not have a template in which to document the CAPA, then the site should be referred to the CCR CAPA template available on the OSRO Wiki page, Forms and Instructions - Forms and Instructions - CCR Wiki (cancer.gov).

6.7. The completed CAPA report is provided to the OSRO Operations Coordinator.

6.8. Upon receiving the CAPA report, the Sponsor assesses the incident and the site's actions for correcting the incident and/or preventing it from reoccurring.

6.8.1. If the site's actions are judged insufficient, then the PI is notified and requested to update the actions and submit the updated CAPA report within 2 weeks.

6.9. If the Sponsor deems it necessary, a root cause analysis may be performed.

6.9.1. Recommendations from the root cause analysis are provided to the PI.

6.10. The completed CAPA report and root cause analysis (if applicable) are shared with SROS Monitoring who will monitor the clinical site for effective control of the incident.

6.11. The site-provided CAPA report and the OSRO root cause analysis (if performed) are archived by SROS in the electronic Trial Master File

6.12. If the PI does not provide an acceptable CAPA report in reasonable time, then follow the noncompliance escalation process given in Step 7.2.

7. Associated Documents

7.1. CCR CAPA template

7.2. 104-S04-W01 Clinical Site Noncompliance Workflow

8. Change Summary

Revision Number	Effective Date	Description of Change
1	15OCT2021	New Document
2	06SEP2023	Biennial review Step 4.3 – added new reference Step 5 – added hyperlink Step 6.6.1 – added Step 6.8.1 – added Step 6.11 – revised Steps 7.1 & 7.2 – added Updated language as needed