1. Purpose

To describe the system for managing non-adherence reports to clinical protocols for which the Office of Sponsor and Regulatory Oversight (OSRO) oversees.

2. Scope

2.1. This SOP applies to studies conducted under a Center for Cancer Research (CCR)-held Investigational New Drug application (IND), Investigational Device Exemption (IDE) or Non-Significant Risk Device (NSR) under OSRO oversight.

2.2. This SOP applies to any non-adherence/noncompliance/deviation to an approved protocol and related procedures, the use of controlled (validated or qualified) equipment, and physical monitoring excursions (e.g., temperature, relative humidity, and room pressure).

2.3. Reports of non-adherence to Good Clinical Practices (GCP) and the Title 21 Code of Federal Regulations (CFR) are governed by this procedure.

2.4. Limitation

2.4.1. This procedure does not apply to studies that are not under a CCR-held IND, IDE, or is an NSR device study and/or when no OSRO oversight or interdepartmental collaboration is required.

3. Responsibilities

3.1. OSRO Operations oversees site-reported non-adherences.

3.2. OSRO Sponsor and Regulatory Oversight Support (SROS) Contractor staff reviews and tracks all non-adherences submitted by clinical sites.

3.3. Clinical study staff are responsible for documenting non-adherences after discovery.

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. All applicable Codes of Federal Regulations for GCP, cGMP and GLP.

5. Definitions

5.1. Refer to the OSRO Lexicon.

5.2. The terms non-adherence, noncompliance and deviation have the same meaning and may be used interchangeably.

6. Procedure

6.1. Clinical study staff should report any non-adherence in a clinical trial protocol, GCP or protocol-specific procedural requirement on the part of a participant, the Investigator, or the study site staff inclusive of site personnel performing procedures or providing services in support of the clinical trial.

6.2. Any non-adherence discovered by SROS Clinical Monitors is noted as an observation and discussed with the study staff.

6.3. CCR site protocol non-adherence events are documented in the CCR Protocol Deviation Tracking System (PDTS). See Section 6.7.

6.4. External site protocol non-adherence events are documented in F01-104-S02 Site Protocol Non-Adherence Log. See Section 6.8.

6.5. Each non-adherence is reported to the site's Institutional Review Board (IRB) per its guidelines.

6.6. Each non-adherence is documented in the participant's source records.

6.7. Method #1 – Documentation using PDTS – For CCR sites

6.7.1. CCR clinical site staff use the PDTS to document protocol non-adherence events.

6.7.2. The URL is https://PDTS.ccr.cancer.gov.

6.7.3. Study staff enter individual non-adherences/deviations per protocol into the system.

6.7.4. OSRO staff or designee with access to the PDTS may run and download reports.

6.7.5. SROS Clinical Monitors will obtain PDTS reports of site non-adherences.

6.8. Method #2 – Documentation using F01-104-S02 Site Protocol Non-Adherence Log – For non-CCR sites

6.8.1. Study staff use F01-104-S02 Site Protocol Non-Adherence Log to document protocol non-adherence events.

6.8.2. A working copy of the Log shall be maintained for each protocol by the study site.

6.8.2.1. The working copy should be named using the convention, <protocol number> <PI's last and first names> OSRO Site Protocol Non-Adherence Log.xlsx.

6.8.2.2. The working copy should be stored in the site's essential regulatory documents folder for the protocol.

6.8.3. Each protocol's F01-104-S02 Site Protocol Non-Adherence Log should be emailed to OSROMonitoring@mail.nih.gov on the first business day of the month.

6.8.4. All F01-104-S02 Site Protocol Non-Adherences Logs received by OSROMonitoring@mail.nih.gov are forwarded to the SROS Monitoring Group.

6.8.5. Submitted Logs are archived by the SROS Monitoring Group.

7. Associated Documents

7.1. F01-104-S02 Site Protocol Non-Adherence Log

8. Change Summary

Revision Number	Effective Date	Description of Change
1	24OCT2019	New Document
2	15APR2022	Biennial Review Rewrite of procedure to include use of the SROS Contractor and the CCR PDTS.
3	01MAY2024	Biennial Review Step 2.4.1 – revised to clarify language