1. Purpose

To outline the procedure for reporting and assessing temperature excursions for investigational products (IPs) used in clinical studies overseen by the Office of Sponsor and Regulatory Oversight (OSRO) in the Center for Cancer Research (CCR) in the National Cancer Institute (NCI) and evaluating potential risk to the study participant for continued use of the IP.

2. Scope

2.1. Temperature excursions occurring to IPs during storage and shipping are assessed to ensure that the IP has not lost purity, identity, quality, and/or content, and is acceptable for continued use by study participants.

3. Responsibilities

3.1. OSRO Pharmaceutical Management (OSRO PM) performs Sponsor oversight of IP, including review of submitted excursion documentation and assessment for acceptability and continued use in clinical studies.

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

3.3. Facilities managing the storage or shipping of IP used in CCR clinical trials are responsible for notifying OSRO PM of temperature excursions.

4. References

4.1. 504 Temperature Excursions of Investigational Product During Storage and Shipping

4.2. 501-S05 OSRO Guidelines for Investigational Product Management

4.3. 21 CFR Part 312 – Investigational New Drug Application

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

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 ICH E6(R3) Good Clinical Practice (GCP) draft Guidance for Industry (FDA), May 2023

5. Definitions

Refer to the OSRO Lexicon.

6. Procedure

6.1. The pharmacy or other study team staff at the IP storage facility or a site shipping or receiving an IP performs the following actions when a temperature excursion is discovered:

6.1.1. Place the IP in quarantine (separated from other IPs and clearly marked as not for clinical use).

6.1.2. Notify OSRO PM by completing F01-504-S01 Investigational Product Temperature Excursion Report and sending it to OSROStudyAgent@nih.gov.

6.2. F01-504-S01 Investigational Product Temperature Excursion Report completion includes but is not limited to the following information:

6.2.1. Identification of the controlled temperature storage unit or shipping container experiencing the temperature excursion

6.2.2. Date(s) of the excursion

6.2.3. Highest and/or lowest temperature recorded during the excursion

6.2.4. Duration of the excursion

6.2.5. Identification of the affected IP

6.2.6. Quantity of affected IP

6.2.7. Confirmation that the IP has been quarantined

6.2.8. Identification of affected protocols

6.2.9. Any temperature monitoring data and/or supporting information

6.2.10. All relevant information pertaining to temperature monitoring data and graphs

6.2.11. Information on previous temperature excursion(s) affecting the IP

6.2.12. A description of immediate actions taken to protect the affected IP

6.3. OSRO and SROS individuals unrelated to the Pharmacy Support task area (e.g., clinical monitor, quality auditor) that are made aware of an IP temperature excursion should inform ORSO PM as soon as possible, and with as much information as possible.

6.3.1. OSRO PM requests the pharmacy staff at the storage facility to complete F01-504-S01 Investigational Product Temperature Excursion Report.

6.4. OSRO PM reviews the form and supporting documentation for completeness and contacts the submitter for clarification, error correction and/or additional information as needed.

6.4.1. A receipt acknowledgment should be provided to the pharmacy within one (1) business day.

6.5. OSRO PM reviews available documentation (protocol, investigator's brochure (IB) or package insert (PI), pharmacy manual, product label, and stability information) for the associated IPs involved in the excursion.

6.6. OSRO PM, if needed, contacts the manufacturer/supplier and requests their opinion on the stability of the affected IP for continued use.

6.7. OSRO PM determines the acceptability of the IP for continued use in clinical studies. The decision is recorded on the submitted F01-504-S01.

6.8. If the IP is deemed acceptable for continued use, OSRO PM informs the facility holding the IP to remove it from quarantine and return it to clinical supply.

6.9. If the IP is deemed unacceptable for continued use, OSRO PM requests product disposition authorization from the study Principal Investigator and the manufacturer/supplier.

6.9.1. Once OSRO PM receives product disposition authorization, the facility holding the IP is instructed on the disposition determination and reminded to provide completed disposition documentation to the Sponsor.

6.10. OSRO PM submits the completed F01-504-S01 Investigational Product Temperature Excursion Report, supporting documentation, and correspondence to SROSTMF@tech-res.com for filing in the protocol-specific folder(s) of the electronic Trial Master File (eTMF).

6.11. For those instances when the storage facility submits a completed manufacturer/supplier's temperature excursion report form instead of F01-504-S01, OSRO PM at its discretion may accept this form in lieu of a completed F01-504-S01.

6.11.1. OSRO PM documents its decision on the manufacturer/supplier's report.

6.11.2. The signed report is uploaded to the eTMF per Step 6.10.

7. Associated Documents

7.1. F01-504-S01 Investigational Product Temperature Excursion Report

8. Change Summary

Revision Number	Effective Date	Description of Change
1	15JUL2024	New Document