## 1. Purpose

To establish and describe the Office of Sponsor and Regulatory Oversight's (OSRO) Investigational Product Stability Studies policy.

## 2. Scope

2.1. OSRO in the Center for Cancer Research (CCR), National Cancer Institute (NCI) shall establish and control the policy.

2.2. Investigators, research team members, other departmental personnel, and external NIH collaborators and contractors when working on studies conducted under a CCR-held Investigational New Drug (IND) application, Investigational Device Exemption (IDE), or supported by a CCR-held Master File under OSRO oversight shall comply with the policy.

2.3. Limitations

2.3.1. This policy does not apply to personnel working on 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.

2.3.2. Nothing in this policy will supersede NCI, National Institutes of Health (NIH) or Health and Human Services (HHS) requirements.

## 3. Responsibilities

3.1. The Center for Cancer Research Management is committed to providing resources to meet the requirements for implementing an Investigational Product Stability Studies policy within OSRO and supporting its continual improvement.

3.2. OSRO personnel are responsible for understanding and using the Investigational Product Stability Studies policy.

3.3. The OSRO Director is responsible for establishing and maintaining the Investigational Product Stability Studies policy.

3.4. OSRO Sponsor and Regulatory Oversight Support (SROS) Contractor staff assisting OSRO Functional Groups are responsible for understanding the Investigational Product Stability Studies policy.

## 4. References

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

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 ICH E6(R3) Good Clinical Practice (GCP) draft Guidance for Industry (FDA), May 2023

4.3. ICH Q1A(R2) Stability Testing of New Drug Substances and Products Guidance for Industry (FDA), November 2003

4.4. ICH Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products Guideline for Industry (FDA), July 1996

4.5. ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients Guidance for Industry (FDA), September 2016

4.6. 21 CFR Part 210 – Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General

4.7. 21 CFR Part 211 – Current Good Manufacturing Practice for Finished Pharmaceuticals

4.8. 21 CFR Part 312 Investigational New Drug Application

## 5. Definitions

Refer to the OSRO Lexicon.

## 6. Policy

6.1. OSRO Pharmaceutical Management shall take steps to ensure that investigational product (IP) is stable over the period of use (Reference 4.1) and only used within the current shelf-life (Reference 4.2).

Stability Studies for Investigational Products Manufactured by CCR

6.2. OSRO Pharmaceutical Management shall provide oversight to stability studies of IPs for which CCR is the manufacturer and the IND is under OSRO oversight.

6.2.1. Clinical trial protocols approved by OSRO beginning in 2024 will be required to have an accepted written stability study for the IP.

6.2.2. Stability studies for commercially available products are not required unless the product is converted or manipulated into a form which differs from the licensed product.

6.3. OSRO Pharmaceutical Management will assist principal investigators (PIs) design a stability study but shall not assume responsibility for managing the study, i.e., determining stability-indicating analytical procedures, setting acceptance limits, sourcing testing laboratories, requesting sample testing per predetermined time points, or trending stability data.

6.4. A stability study should include testing of those attributes of the IP that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy. Testing should cover, as appropriate, the physical, chemical, biological, and microbiological attributes, preservation content, and functionality (Reference 4.3 Section 2.2.5).

6.5. The written stability study should include:

6.5.1. Sample size and test intervals based on statistical criteria for each attribute examined to assure valid estimates of stability;

6.5.2. Storage conditions for samples retained for testing;

6.5.3. Reliable, meaningful, and specific test methods and their acceptance criteria;

6.5.4. Microbial stability and sterility assessment, when appropriate (Reference 4.4).

6.6. At a minimum, the stability study should include storage of the IP under temperature and humidity conditions proposed for the intended shelf-life of the IP.

6.7. Real-time stability testing should be conducted at a minimal frequency of every 3 months over the first year, every 6 months over the second year, and annually thereafter (Reference 4.3).

6.7.1. More frequent time points may be requested by OSRO Pharmaceutical Management.

6.8. The stability study should continue past the anticipated date of the final dosing of the final participant enrolled in the study.

6.9. PIs should ensure that IP batch sizes are appropriate to provide a sufficient quantity to support both the proposed participant dosing and the stability study and to provide reserve/retention samples for two (2) full specification analyses (Reference 4.5).

Stability Confirmation of Investigational Products Without or Past an Expiration Date

6.10. For IPs lacking sufficient stability data to allow setting an expiration date, test data should be obtained over the course of the clinical trial such as before and after participant dosing which shows that the IP has not undergone a significant change with respect to safety and efficacy.

6.10.1. A significant change in IP is defined as a 5% change in assay from its initial value or failure to meet the acceptance criteria for any assay.

6.10.2. Acceptable IP test results obtained within 6 months of participant dosing should be available for review by OSRO Pharmaceutical Management.

6.11. The use of a commercially available IP in a clinical trial past its expiration date is not permitted. A new lot should be obtained.

6.11.1. Exceptions may be permitted with justification and a statement from the manufacturer declaring that the expired lot is acceptable for use.

6.11.2. Test data indicating that the IP has not undergone a significant change in any stability indicating assay may be required by OSRO (see Step 6.10.1).

6.12. If the expired IP is not available commercially, then the following are required before OSRO will consider allowing continued usage.

6.12.1. Recent (within 6 months) test data indicating that the expired IP has not undergone a significant change in any stability indicating assay (see Step 6.10.1).

6.12.2. A report summarizing the release and stability test results from the expired IP lot and compared to the test results from all lots produced.

6.12.3. Confirmation that sufficient inventory exists to perform post-dosing testing.

6.13. OSRO Pharmaceutical Management and/or the OSRO Director authorization is required.

## 7. Change Summary

| Revision Number | Effective Date | Description of Change |
|---|---|---|
| 1 | 08NOV2023 | New Document |