1. Purpose

To describe the process for managing planned/prospective deviations 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. Limitation

2.2.1. 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. The OSRO Director approves or denies requests for planned deviations.

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

3.3. Principal Investigators are responsible for requesting a planned deviation according to this SOP and obtaining IRB approval before initiating the deviation.

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.

6. Procedure

6.1. Planned deviations to clinical protocols are permitted only in rare circumstances. Planned deviations should not be used to compensate for inadequate planning. Only one (1) participant should be involved in the planned deviation.

6.2. Requests for a planned deviation must be made by the Principal Investigator (PI), documented on F01-104-S05 Clinical Protocol Planned Deviation Request, and submitted to the OSRO Director via the OSROConsultation@nih.gov e-mail address.

6.3. To be considered a planned deviation, the change must meet the following criteria.

6.3.1. The change must mitigate a risk to the participant.

6.3.2. The change must involve an unpredictable situation.

6.3.3. The change must not cause a meaningful change to the protocol.

6.3.4. The impacted participant must remain eligible to be included in the analysis of the protocol data.

6.4. The PI must explain how the proposed deviation meets each of the required criteria.

6.5. After signing the F01-104-S05, the PI emails the form to the OSRO Director via the OSROConsultation@nih.gov e-mail address.

6.6. The OSRO Director reviews the request and records their approval/denial decision on F01-104-S05.

6.7. The OSRO Director notifies the PI of the decision within 3 business days of receiving the F01-104-S05 from the PI.

6.8. IRB approval of the planned deviation is required before enactment.

6.9. The protocol should be amended expeditiously to address the deficiency which caused the need for a planned deviation.

6.10. No further deviations for the same primary event will be granted.

6.11. OSRO will maintain a list of all approved planned deviation requests on an OSRO Wiki page. This list will summarize the reasons for requesting a planned deviation and proposed mitigation.

6.11.1. PIs are encouraged to review the list when writing a protocol and incorporate mitigation strategies into the protocol.

6.11.2. No planned deviation will be approved if it already appears on the list.

7. Associated Documents

7.1. F01-104-S05 Clinical Protocol Planned Deviation Request

8. Change Summary

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