1. Purpose

To establish and describe the Office of Sponsor and Regulatory Oversight (OSRO) Clinical Site Activation 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 and other departmental personnel and external NIH collaborators and contractors when they are working on studies conducted under a CCR-held Investigational New Drug application (IND), Investigational Device Exemption (IDE), or a National Institutes of Health (NIH) Institutional Review Board (IRB)-approved protocol using a Non-Significant Risk (NSR) device under OSRO oversight or supported by a CCR-held Master File under OSRO oversight shall follow 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, NIH or Health and Human Services (HHS) requirements.

3. Responsibilities

3.1. CCR Management is committed to providing resources for the implementation of the Clinical Site Activation policy and supporting its continual improvement.

3.2. OSRO personnel are responsible for understanding the Clinical Site Activation policy.

3.3. OSRO Sponsor and Regulatory Oversight Support (SROS) Contractor staff assisting OSRO Functional Groups are responsible for understanding the Clinical Site Activation policy.

3.4. The OSRO Director is responsible for establishing and maintaining the Clinical Site Activation 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. 203 Clinical Trial Records Policy

4.3. 21 CFR Part 312.6 Investigational New Drug Application – Labeling of an investigational new drug

4.4. 21 CFR Part 812.5 Investigational Device Exemptions – Labeling of investigational devices

5. Definitions

Refer to the OSRO Lexicon.

6. Policy

6.1. The Office designation of OSRO shall refer both to the Office of Sponsor and Regulatory Oversight staff and the OSRO Sponsor and Regulatory Oversight Support contractor staff.

6.2. Investigators, research team members, and other departmental personnel will begin screening and enrollment of study participants only after the trial has been activated.

6.2.1. Only after the trial has been activated may an investigational study product be dispensed to study participants.

6.3. A clinical site will be activated after the following:

6.3.1. All pertinent agreements have been fully executed.

6.3.2. The IND is safe to proceed; IDE or NSR has been approved, as applicable.

6.3.3. The Sponsor safety monitoring plan has been approved.

6.3.4. The electronic Case Report Form (eCRF), blank and annotated, has been approved by the clinical study team and accepted by OSRO (not required for non-significant risk (NSR) device trials).

6.3.5. The Data Management Plan (DMP) has been approved by the clinical study team and accepted by OSRO (not required for non-significant risk (NSR) device trials).

6.3.5.1. An approved DMP is required for those protocols with an initial IRB approval after January 1, 2023.

6.3.6. Investigational Study Agent(s)/Product(s)/material(s) are available on site and are ready to be dispensed; the manufacturing facility is ready for production for just-in-time manufactured products and/or labeling requirements per federal regulations 21 CFR 312.6 (Reference 4.3) and/or 21 CFR 812.5 (Reference 4.4) are met.

6.3.7. A Site Assessment Visit (SAV) has been conducted per the Clinical Monitoring Plan (CMP).

6.3.7.1. SAV findings have been resolved, and the resolution is accepted by OSRO.

6.3.7.2. An SAV is not required for NIH sites as the SROS Clinical Site Monitoring team will maintain a master description of the facility and processes supporting studies conducted at the NIH Clinical Center and ancillary departments.

6.3.7.3. If a multicenter protocol, the NCI CCR coordinating center Point of Contact ensures that resolution is reached and accepted by OSRO.

6.3.8. The site's essential documents (per the OSRO 203 Clinical Trial Records Policy) have been reviewed and accepted by OSRO.

6.3.9. A Site Initiation Visit has been conducted per the protocol-specific CMP.

6.3.9.1. The SIV will be onsite unless otherwise approved by OSRO.

6.3.9.2. A quorum of Staff with delegated responsibility for protocol tasks/duties attended the SIV.

6.3.9.2.1. A quorum includes at least one Staff member responsible for each of the following roles:

- Principal Investigator
- Sub-Investigator that is a licensed physician
- Study Coordinator
- Data Manager
- Pharmacy Staff representative
- Non-Pharmacy Staff representative (if the study product is handled in an area outside of the pharmacy)
- Clinical Nursing representative

6.3.9.3. OSRO will confirm that no critical outstanding issues or action items are pending after the SIV.

6.3.9.3.1. If any outstanding issues or action items are critical, these must be adequately addressed and the resolution accepted by OSRO before the clinical site will be activated.

6.3.10. Study personnel have been trained on the protocol and study procedures.

6.3.10.1. The List of Participants in the SIV Report documents the Staff who attended the SIV and, as such, were trained on the IRB-approved protocol presented during the SIV.

6.3.10.1.1. If more than 8 weeks have lapsed between the SIV and site activation, protocol re-training by the study PI is required. Protocol re-training must be documented in the site Staff training records.

6.4. The site will be activated to implement the protocol version presented during the SIV.

6.4.1. Protocol amendment

6.4.1.1. If after the SIV and before site activation, a protocol amendment has been approved by the IRB, the following are required before the site will be activated:

6.4.1.1.1. OSRO must be notified in writing that the IRB has approved a protocol amendment.

6.4.1.1.2. All protocol amendment-related essential documents (per the OSRO 203 Clinical Trial Records Policy) must be submitted to the Sponsor eTMF for document review, and all required documentation must be accepted.

6.4.1.1.3. A record of PI training on the amendment for all Staff delegated duties/tasks on the Clinical Site Delegation of Authority, and Staff Signature Log (DOA) must be submitted to the Sponsor eTMF.

7. Change Summary

Revision Number	Effective Date	Description of Change
1	30Aug2019	New Document
2	05FEB2020	1. Added nonsignificant risk device to Section 2 Scope. 2. Added 203 Clinical Trial Records Policy to Section 4 References. 3. Revised the Site Initiation Visit prerequisites in Section 6 Policy.
3	18APR2022	Biennial Review Step 3.3 – added Section 4 – added hyperlinks Step 6.1 – added Step 6.5 – removed Updated document language as required Updated process due to addition of SROS Contractor services
4	30Jan2023	Revision of policy based on lessons learned Steps 4.3 and 4.4 – added Step 6.3 – expanded Step 6.4 – added
5	12FEB2024	Step 6.3.4 – added NSR Step 6.4.5 – added NSR Step 6.3.9.1 – added that the SIV will be onsite unless otherwise approved by OSRO.