1. Purpose

To establish and describe the Office of Sponsor and Regulatory Oversight's (OSRO) Independent Data and Safety Oversight 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 they are working on studies conducted under a CCR-held Investigational New Drug application (IND), 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 the Independent Data and Safety Oversight Policy within OSRO and supporting its continual improvement.

3.2. OSRO personnel are responsible for understanding and using the Independent Data and Safety Oversight Policy.

3.3. The OSRO Director is responsible for establishing and maintaining the Independent Data and Safety Oversight 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. 21 CFR 50.24 Protection of Human Subject: Exception from informed consent requirements for emergency research

4.3. Establishment and Operation of Clinical Trial Data Monitoring Committees, Guidance for Clinical Trial Sponsors (FDA), March 2006

4.4. NIH Policy for Data and Safety Monitoring, June 1998

4.5. NIH Policy, Further Guidance on a Data and Safety Monitoring for Phase I and Phase II Trials, June 2000

4.6. Policy of the NCI for Data and Safety Monitoring of Clinical Trials, September 2014 (for extramural studies only)

5. Definitions

Refer to the OSRO Lexicon.

6. Policy

6.1. Each clinical protocol will have an appropriate safety oversight plan. The plan will describe the safety oversight mechanism employed to review the safety data and efficacy data (if applicable) of the clinical trial.

6.2. The following guidelines will be employed to decide the appropriate safety oversight mechanism. The final determination on the mechanism will reside with the OSRO Director. The assignment will occur in priority order (i.e., if one trial meets the criteria of more than one type of oversight mechanism, the most stringent mechanism will apply).

6.2.1. Data and Safety Monitoring Board

6.2.1.1. Regulatory mandated: Emergency settings in which the informed consent requirement is excepted (21CFR50.24(a)(7)(iv)).

6.2.1.2. All randomized clinical trials of any phase.

6.2.1.3. IRB mandated independent Data and Safety Monitoring Board.

6.2.2. Safety Monitoring Committee

6.2.2.1. All clinical trials that include products for which CCR is the legal manufacturer.

6.2.2.2. IRB mandated independent safety monitoring committee.

6.3. The safety oversight mechanism will operate under an appropriate charter that would describe its operations, membership and meeting schedules and triggers.

6.4. The safety oversight mechanism provides recommendations to the Sponsor. In general, the Sponsor will follow the safety oversight mechanism recommendations. In case the Sponsor chooses not to follow the safety oversight mechanism recommendations, approval of the Clinical Director in CCR will be required.

7. Change Summary

Revision Number	Effective Date	Description of Change
1	03MAR2022	New Document
2	19APR2022	Step 2.3.1 – revised Step 6.2.2.3 – added
3	20DEC2022	Step 6.2.1.2 – revised Step 6.2.2.4 – added Step 6.2.3 – removed

Revision Number	Effective Date	Description of Change
4	11MAR2024	• Step 6.2.1.3. – removed "All clinical trials that include interim analysis as part of the trial design" and replaced with "IRB mandated independent Data and Safety Monitoring Board." • Step 6.2.2.1. – removed "All multi-center clinical trials." • Step 6.2.2.2. – removed "All clinical trials that include dose-escalation." • Step 6.2.2.3. – removed "All clinical trials that include a phase I design (or safety assessment) followed by a phase II design (or efficacy assessment) in the same protocol." • Step 6.2.2.4. – removed "All clinical trials that include halting rules which require independent evaluation on whether to continue enrollment in the trial." • Step 6.2.2.2 – added "IRB mandated independent safety monitoring committee."