1. Purpose

To outline the Office of Sponsor and Regulatory Oversight (OSRO) Sponsor approval process for dose escalation in protocols whose design includes dose escalation.

2. Scope

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2.1.1. Protocols developed by the Center for Cancer Research (CCR) investigators, with a dose escalation design, sponsored by CCR and overseen by OSRO are within scope.

3. Responsibilities

3.1. Principal Investigators are responsible for preparing a dose escalation report to justify a change in dosage.

3.2. OSRO approves dose change requests.

3.3. OSRO Sponsor and Regulatory Oversight Support (SROS) Contractor staff assist OSRO as needed.

4. References

4.1. 303 Interim Analysis Reporting Policy

5. Definitions

Refer to the OSRO Lexicon.

6. Procedure

6.1. Requirements for changing the investigational agent dosage.

6.1.1. The protocol must include a dose escalation scheme for the investigational agent.

6.1.2. Adverse events recorded up to the cut-off date must be provided.

6.1.3. Dose escalation criteria must be met.

6.1.3.1. The number of events contributing towards the criterion is typically the number of participants meeting the Dose Limiting Toxicity (DLT).

6.2. The Principal Investigator (PI) must provide a dose escalation report utilizing F01-303-S01 Dose Escalation Determination or equivalent report that includes all the items outlined in F01-303-S01 Dose Escalation Determination and submit it to OSRO Safety, NCIORSOSafety@mail.nih.gov.

6.3. OSRO reviews the submitted F01-303-S01 Dose Escalation Determination or equivalent report to determine if the current dose may be changed to the next protocol-defined level.

6.3.1. The decision is documented on F02-303-S01 Dose Escalation Decision Communication and emailed to the PI.

6.3.1.1. If the request is denied, an explanation and the information required to reevaluate the decision are provided.

6.3.2. OSRO sends the completed F01-303-S01 and F02-303-S01 to SROSTMF@tech-res.com for filing in the electronic Trial Master File (eTMF).

7. Associated Documents

7.1. F01-303-S01 Dose Escalation Determination

7.2. F02-303-S01 Dose Escalation Decision Communication

8. Change Summary

Revision Number	Effective Date	Description of Change
1	26May2022	New Document
2	03MAY2024	Step 4.1 – added hyperlink Step 5 – added hyperlink Step 6.3.2 – added Updated language and grammar as needed