1. Purpose

To establish and describe the Office of Sponsor and Regulatory Oversight's (OSRO) Final Clinical Study Reports (CSRs) for Studies under CCR-Held INDs/IDEs 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 a Non-Significant Risk device under OSRO oversight shall comply with the policy.

2.3. Limitations

2.3.1. Personnel are not bound to this policy when working on non-IND, IDE or NSR studies and/or no interdepartmental collaboration with OSRO as Sponsor 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. CCR Management is committed to providing resources to meet the requirements for implementing this policy within OSRO and supporting its continual improvement.

3.2. OSRO personnel are responsible for understanding the policy.

3.3. The OSRO Director is responsible for establishing and maintaining the policy.

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

3.5. OSRO Regulatory determines the type of final clinical study report that will be needed.

3.6. The Lead Principal Investigator (PI) is responsible for providing the final clinical study report to OSRO.

4. References

4.1. 21 CFR 312.64: Investigational New Drug Application – Investigator Reports

4.2. 21 CFR 314.50(d)(5): Applications for FDA Approval to Market a New Drug – Applications: Content and Format of an NDA: Technical Sections: Clinical Data Section

4.3. 21 CFR 601.2: Licensing: General Provisions – Applications for Biologics Licenses: Procedures for Filing

4.4. 21 CFR 812.150: Investigational Device Exemptions: Records and Reports – Reports

4.5. FDA Guideline for Industry: Structure and Content of Clinical Study Reports (July 1996)

4.6. Guideline for the Format and Content of the Clinical and Statistical Sections of an Application (FDA, July 1988)

4.7. Guidance for Industry: Submission of Abbreviated Reports and Synopses in Support of Marketing Applications (FDA, August 1999)

4.8. IDE Reports: Suggested Format for an IDE Final Report (FDA)

4.9. ICH Harmonised Tripartite Guideline E3: Structure and Content of Clinical Study Reports (Nov 1995)

4.10. F01-410 Clinical Study Report Instructions and Template

5. Definitions

Refer to the OSRO Lexicon.

6. Policy

6.1. Background

6.1.1. Under IND regulations 21 CFR 312.64(c), an investigator is required to provide the sponsor with an adequate final report shortly after completion of the investigator's participation in the investigation. Since CCR sponsors clinical trials that may be used to support a marketing application, OSRO will submit a final CSR to the Food and Drug Administration (FDA) for each study conducted under a CCR-held IND that meets the requirements per 21 CFR 314.50 or 21 CFR 601.2. FDA Guidances for Industry (see References 4.5, 4.6 and 4.7) specify that information on clinical investigations may be submitted in one of three types depending on the particular study characteristics: full study reports, abbreviated reports, or synopses. Regardless of which type of report is submitted, the final CSR should contain a summary of all safety information and should encompass all study objectives and endpoints.

6.1.2. Under IDE regulations 21 CFR 812.150 (a)(6), an investigator is required to provide the sponsor with a final report within 3 months after completion of the investigator's participation in the investigation. For a significant risk device, the regulation (21 CFR 812 .150(b)(7)) requires that a sponsor submit a final report to the FDA within 6 months after the completion or termination of the investigation. In the case of a device that is a Non-Significant Risk device, the sponsor shall submit a final report to all reviewing IRBs within 6 months after completion or termination of the investigation.

6.2. Implementation:

6.2.1. Full study reports should be submitted for IND studies that contribute to the evaluation of effectiveness for the proposed indication or that support information included in product labeling.

6.2.2. Abbreviated reports may be submitted for IND studies that are not intended to contribute to the evaluation of effectiveness or provide definitive information on the clinical pharmacology. The final CSR for studies with licensed products that are done to affect standard of care/practice of medicine, but do not support a change in product labeling, may be submitted

as an abbreviated report. Abbreviated reports should contain all the safety information required for a full study report.

6.2.3. Synopses can be submitted for IND studies that are not relevant to the evaluation of effectiveness or clinical pharmacology but that provide safety data. A manuscript with a summary of all safety information may be deemed appropriate for a synopsis if all protocol objectives/endpoints are presented in the manuscript. If the manuscript does not detail all objectives/endpoints or provide a summary of all safety information, an addendum to the manuscript that discusses the remaining objectives/endpoints, in addition to a summary of all safety information, may be necessary.

6.2.4. CCR's Requirements for the Type of Final Clinical Study Report

6.2.4.1. A Full CSR will be required for the following types of studies:

6.2.4.1.1. Phase 3 or 4 trials that are pivotal to licensure for the product or for a change in the product label.

6.2.4.1.2. Phase 2, 3, or 4 studies that may be used to support licensure or changes in the product label and

- Support efficacy/effectiveness,
- Different indications (stages of disease or different populations),
- Different dosage forms or regimens,
- Bioavailability and bioequivalence studies that compare performance or dosage to the proposed final dose.

6.2.4.2. An Abbreviated CSR will be required for the following types of studies:

6.2.4.2.1. Phase 2 expanded safety studies.

6.2.4.2.2. Phase 2 or 3 studies for indications for which marketing approval will not be sought.

6.2.4.2.3. Studies with licensed product that are done to affect standard of care/practice of medicine.

6.2.4.3. Synopsis or manuscript with additional information (in lieu of a CSR) will be required for the following types of studies:

6.2.4.3.1. Phase 1 safety studies

6.2.4.3.2. Early dose range studies to evaluate:

- Immunogenicity
- Tolerability
- Pharmacokinetics
- Challenge dose

6.2.4.3.3. Early route of administration studies

6.2.4.3.4. Exploratory studies of a purely scientific nature e.g. providing information about physiology

6.2.4.4. OSRO Regulatory will make the determination on which type of final CSR will be required.

6.2.5. Exemptions

6.2.5.1. The OSRO Director may exempt or modify the CSR requirement for studies completed or terminated with no or low enrollment.

6.2.5.2. No exemption will be granted for a study closed because of a safety signal. A CSR must be provided.

6.3. Format and Content of a Clinical Study Report

6.3.1. The CSR should be modeled on References 4.5 and 4.9.

6.3.2. The CSR for IDE studies should follow the FDA suggested format for an IDE final report in Reference 4.8.

6.3.3. For protocols with pharmacokinetic analysis, the Bioanalytical Sample Analysis Report will be included in the CSR Appendix for Documentation of Inter-Laboratory Standardization Methods and Quality Assurance Procedures, as described in Reference 4.9.

6.3.4. The CSR should include all clinical and statistical descriptions, presentations, and analyses for all endpoints. A clinical trial is not considered complete until the analysis of all endpoints is included in the CSR (including interim or Addendum CSR).

6.3.4.1. The PI will provide the CSR to OSRO within:

6.3.4.1.1. Nine (9) months following the last data point collected for the last participant supporting the primary and secondary objectives for IND studies.

6.3.4.1.2. Three (3) months following the last data point collected for the last participant supporting the primary and secondary objectives for IDE studies.

6.3.4.2. At a minimum, the CSR should include discussion of all primary and secondary endpoints, and all exploratory endpoints available in the timeframe established in Step 6.3.4.1.

6.3.4.3. If all endpoint data cannot be provided within the required timeframe established in Step 6.3.4.1, then the PI should provide within this timeframe, a plan for providing all missing endpoint data. OSRO Regulatory will determine whether an addendum CSR will be required and in what timeframe.

6.3.4.4. If study-specific endpoint data will not be available, for example, an immunological assay is listed in a protocol as an endpoint but was not performed, the PI will discuss with OSRO Regulatory the best path to select.

6.3.4.5. Data that are not generated as part of the study analysis, or not pre-defined in the protocol/Statistical Analysis Plan (e.g., assay data generated using future use specimens), should not be included in the CSR.

6.4. Refer to F01-410 Clinical Study Report Instructions and Template (Reference 4.10) for a recommended Word document for generating the CSR.

7. Change Summary

Revision Number	Effective Date	Description of Change
1	06JAN2020	New Document
2	14JAN2022	Biennial review Step 3.4 – added SROS Contractor Updated document language as required
3	09JAN2024	Biennial review Step 6.2.5 and sub steps on exemptions – added