1. Purpose

To outline the procedure for reporting safety information related to clinical trial study interventions submitted to the Office of Sponsor and Regulatory Oversight (OSRO). The intent is to ensure that all Investigational New Drug application (IND) and Investigational Device Exemption (IDE) Sponsor safety reporting obligations to the U.S. Food and Drug Administration (FDA) are met.

2. Scope

2.1. This SOP applies to studies conducted under a Center for Cancer Research (CCR)-held IND, IDE, or Non-Significant Risk Device (NSR), or supported by a CCR-held Master File under OSRO oversight.

2.2. Limitation

2.2.1. This procedure does not apply to CCR clinical studies when OSRO is not serving as Sponsor.

3. Responsibilities

3.1. OSRO Safety is responsible for prompt evaluation of Serious Adverse Event Reports and notification to Principal Investigators, the Protocol Support Office, and Study Agent companies that a report has been submitted.

3.2. OSRO Regulatory is responsible for filing documentation with the FDA within time limits.

3.3. The OSRO Director is responsible for reviewing and approving FDA MedWatch Form 3500A.

3.4. Clinical Study personnel are responsible for notifying OSRO Safety of adverse events within 24 hours of learning of the event and providing current and background information related to the event.

3.5. OSRO Safety through the OSRO Sponsor and Regulatory Oversight Support (SROS) are responsible for notifying collaborators and distributing assessed SAE cases.

3.6. OSRO SROS contractor staff assist OSRO Functional Groups as needed.

4. References

4.1. 301 Serious Adverse Events Reporting

4.2. ICH E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry (FDA), March 2018

4.3. FDA Guidance for Industry: Safety Reporting Requirements for INDs and BA/BE Studies, December 2012

4.4. 21 CFR 312.32 – Investigational New Drug Application – IND Safety Reporting

4.5. 21 CFR 812.150 – Investigational Device Exemption – Reports

5. Definitions

Refer to the OSRO Lexicon.

6. Procedure

6.1. Adverse events must be reported to the FDA within specific time limits. The general process flow is shown in Step 9.1. The serious adverse events (SAE) process workflow is shown in Step 9.2.

6.1.1. Suspected and Unexpected, Serious Adverse Reactions (SUSARs) use an expedited reporting path of either 7 or 15 calendar days.

6.1.2. Non-SUSARs use a non-expedited reporting path.

6.1.3. Unanticipated adverse device effects (UADEs) are reported within 10 working days.

6.2. The Clinical Study Team completes the SAE reporting form for each serious adverse event and submits it to OSRO Safety within 24 hours of learning of the event.

6.2.1. For an initial report submission, the SAE reporting form must be accompanied by participant baseline history and physical examination documents, laboratory test results, concomitant medications, and diagnostic testing report(s).

6.2.2. For a follow-up report submission, the SAE reporting form must be accompanied by associated medical records related to the new SAE information.

6.2.3. Any personally identifiable information (PII) on supporting documentation must be redacted.

6.2.4. Each page of supporting documentation must show the protocol number and participant identification number (PID).

6.3. SROS Safety reviews the submitted documentation for completeness, makes an initial event assessment, enters the case into the Safety database, communicates with the study team and collaborators as required and notifies the OSRO Medical Monitors.

6.4. The OSRO Medical Monitor reviews and approves the case narrative prepared by SROS Safety and makes final decision on the SAE type to determine the reporting pathway.

6.4.1. In cases where the Medical Monitor changes the attribution of the study intervention from that assessed by the PI, the Medical Monitor will discuss the change and rationale with the PI. The PI will be contacted by e-mail and by a phone call.

6.4.2. SUSARs and UADEs are reported on an FDA MedWatch Form 3500A (IND Safety Report).

6.4.3. All other events are reported on a CIOMS[1] form.

6.5. For SUSARs and UADEs, the OSRO Director reviews the FDA MedWatch Form 3500A, focusing on the summary, sponsor assessment and conclusion, and an analysis of similar events.

6.5.1. If approved, the report is sent to OSRO/SROS Regulatory for FDA submission.

6.5.2. If not approved, the report is returned to SROS Safety for editing.

6.5.3. If the OSRO Director is unavailable, then an OSRO Medical Monitor may approve the FDA MedWatch Form 3500A.

[1] Council for International Organizations of Medical Sciences

6.6. OSRO/SROS Regulatory notifies OSRO Safety of the date on which the FDA MedWatch Form 3500A was submitted to the FDA.

6.7. FDA MedWatch Form 3500A and CIOMS forms are distributed to relevant parties by SROS Safety.

6.8. All safety events and associated documents are archived in the Safety database and/or electronic Trial Master File (eTMF) as applicable.

7. Associated Documents

7.1. F01-301-S01 Serious Adverse Event Report Form

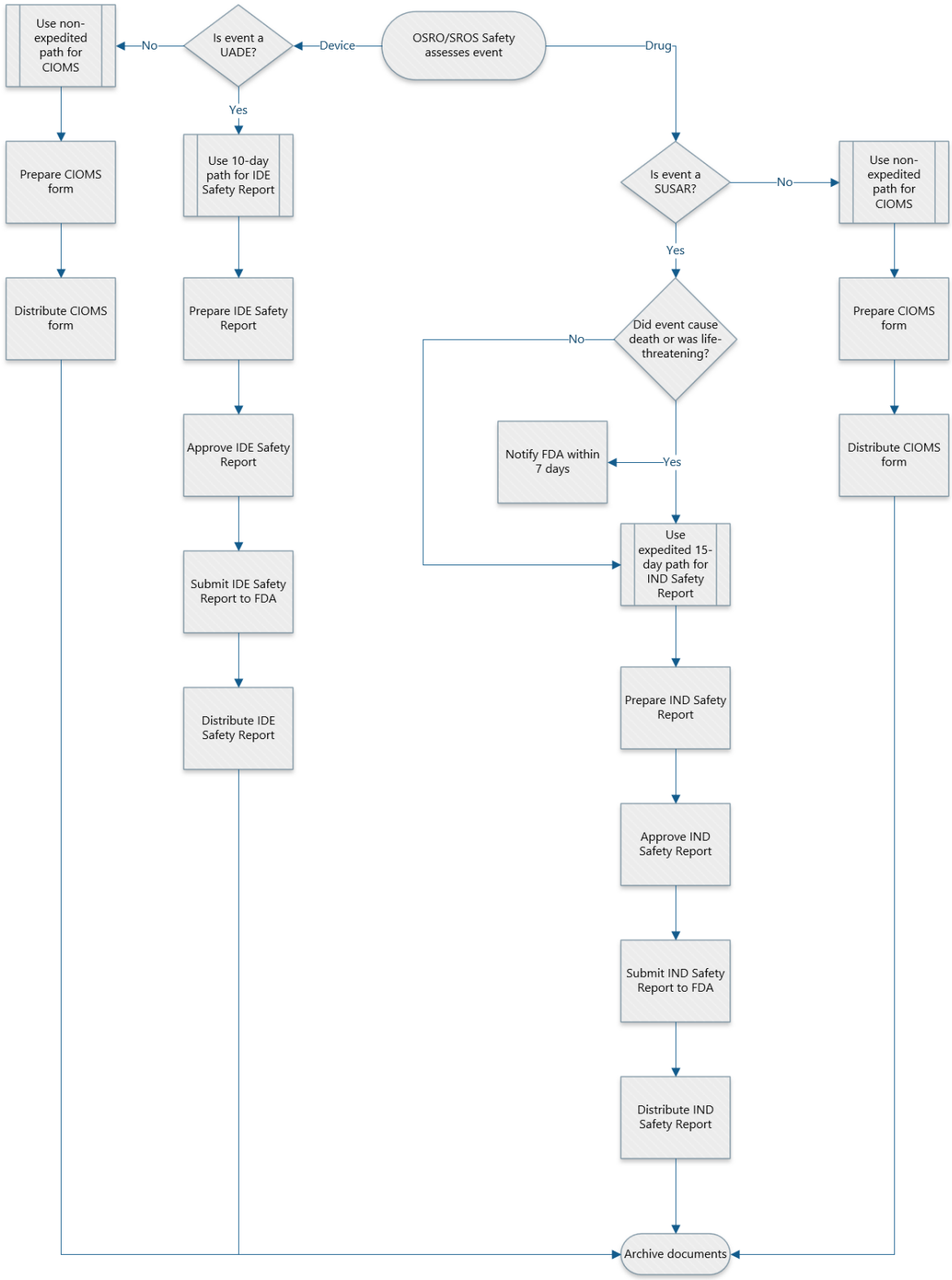
7.2. FDA MedWatch Form 3500A, available at https://www.fda.gov/media/69876/download

8. Change Summary

Revision Number	Effective Date	Description of Change
1	04FEB2020	New Document
2	12DEC2022	Step 2.1 – added Non-Significant Risk Device (NSR) Step 3.2 – removed Step 3.5 – added Section 4 – added hyperlinks Procedure rewritten to capture SROS Safety activities Steps 7.1 – 7.6, 7.8 – removed Sections 1,4,6 – added IDE
3	31JAN2024	Step 6.4.1 – added

9. Appendices

9.1. General process workflows for drug and device adverse event reporting.



9.2. SAE Process workflow showing responsible parties.