

1. PURPOSE

1.1 This document describes the process to establish a Protocol Safety Review Team (PSRT), develop the charter, conduct the review, and document the subsequent recommendations for Division of Microbiology and Infectious Disease (DMID).

1.1.1 Protocol Specific Procedures (PSPs) or similar documents may be used to describe specific steps for a given protocol and are encouraged to ensure consistency in the process.

2. SCOPE

2.1 This document applies to clinical trials with a PSRT specified in the protocol when DMID is responsible for safety oversight (per DMID-SF-POL-00001). This includes clinical trials conducted under a DMID held Investigational New Drug Applications (IND)/Investigational Device Exemptions (IDE) or equivalent and other non-IND clinical trials.

3. DEFINITIONS

3.1 Protocol Safety Review Team (PSRT): An advisory group internal to a specific protocol to review safety data and additional protocol-specific information at pre-specified study milestones. This group is comprised of sponsor representatives, site investigators, and may include representatives of the Investigational Product (IP) developer.

For other definitions, see [DMID glossary](#).

4. RESPONSIBILITIES

4.1 The protocol team of a clinical trial determines the need of a PSRT and will determine the composition and function of the PSRT.

4.2 The Medical Monitor (MM) and Clinical Project Manager (CPM) will determine the need for Safety Oversight Committee (SOCS) Support.

4.3 The MM will lead the PSRT reviews.

4.3.1 Any activities in the PSRT SOP performed by the MM can also be conducted by the Medical Officer (MO).

5. PROCEDURE

5.1 PSRT Establishment

5.1.1 The protocol team will determine if a PSRT is an appropriate mechanism for safety review and oversight of the study in accordance with DMID-SF-POL-00001 (Safety Oversight in DMID Funded Clinical Research) and DMID-SF-POL-00003 (Safety Oversight for DMID-held IND Trials).

5.1.2 The protocol must contain the following information:

- PSRT responsibilities for reviewing trial safety data.
- Summary of the composition of the PSRT.

- Frequency of review and whether reviews are based on protocol timelines (e.g., Day 7), enrollment milestones (e.g., sentinel participants, cohort escalations), and/or ad-hoc events (e.g., halting rules).
- High-level description of the data provided to the PSRT for their review (e.g., adverse events, clinical labs, vital signs, etc.).
 - If a protocol includes blinded interventions, a PSRT can be used but can only review pooled blinded data.

5.2 Safety Oversight Committee Support (SOCS) Utilization

5.2.1 Studies using an independent safety oversight committee (e.g., Safety Monitoring Committee (SMC) or Data and Safety Monitoring Board (DSMB)) must involve SOCS to facilitate the transfer of information between the PSRT and the independent safety oversight committee. Otherwise, SOCS utilization is at the discretion of MM and CPM.

- If SOCS support is requested, the CPM will enter a Request for Service (RFS) or email the SOCS contractor at SOCS@dmidcroms.com to request PSRT support.

5.2.2 If SOCS is involved, the CPM will provide SOCS with the following:

- A near final protocol draft with finalized safety assessments (study days and data collected) and finalized PSRT information (Section 5.1.2).
- PSRT member contact information.

5.3 PSRT Charter Development

5.3.1 All DMID held IND/IDE trials utilizing a PSRT must develop and implement a PSRT charter. Non-IND trials can use a PSRT charter or include the PSRT information in other documents (e.g., Manual of Operations (MOP)).

- Any trial actively utilizing a PSRT prior to the effective date of this SOP may specify PSRT details in other documents if no charter was developed.
- DMID-SF-FORM-00003 is a recommended template for the PSRT charter and can be modified as needed.

5.3.2 The protocol team will determine and provide details regarding the following information to be included in the PSRT charter.

- PSRT composition and responsibilities.
- PSRT quorum: quorum is generally met with input from a minimum of 3 members (including at least 1 from the sponsor and at least 1 from the site(s)). Other definitions of quorum may be used.
- Data for review: what reports or types of data will be reviewed.
- Timing for review: frequency and triggers for review as noted in the protocol.
- Data format: the format of the documents for review.
 - The data reviewed must be captured in a way to preserve the data used during the review (e.g., live web-based reports are not sufficient as these change over time, but pdfs of live web-based reports are sufficient).
- Report sharing: Files can be shared through various platforms (e.g., email, share drive or cloud storage)

- Documentation of review: how the summary of the PSRT review and recommendations will be documented and where it will be stored (e.g., document library).
- 5.3.3 The PSRT Charter will be drafted by the MM or by SOCS.
- PSRT members and the CPM will review the charter and provide feedback prior to finalization and approval by the MM.
- 5.3.4 The signed charter will be stored in the CROMS Committee Management System (CMS) or Document Library.
- 5.4 Data Preparation and Distribution for PSRT Review
- 5.4.1 At the timepoint for PSRT review (per protocol), the Statistical and Data Coordinating Center (SDCC) will generate the reports as specified in the PSRT charter or protocol documents.
- The PSRT will use data in its current state, i.e., the data is not considered clean.
 - The PSRT should consider timelines for data entry, and plan PSRT report generation after the data has been entered by sites.
- 5.4.2 The SDCC will distribute the reports.
- If SOCS is utilized, SDCC will send reports to SOCS and copy DMID as applicable. SOCS will send reports to the PSRT per the charter.
 - If SOCS is not utilized, SDCC will distribute the report as defined in the PSRT Charter or protocol specific MOP (or other supporting documents).
- 5.5 Electronic PSRT Review
- 5.5.1 After the distribution of materials, PSRT members are requested to respond with their initial determination regarding safety and recommendations on next step(s) for the protocol. All email communications with member determinations are part of the final documentation to be stored.
- 5.5.2 When quorum for review (per charter) is met and if there are no safety concerns, the MM (or designee) will document the summary/conclusion of the PSRT review.
- See section 5.7 for procedures to document PSRT review.
 - Prior to completion of formal documentation, the MM or designee may notify the SDCC in writing (email) of the outcomes next steps (e.g., notify sites to open enrollment or continue IP administration) prior to completion of the PSRT form. If SOCS is utilized or if there is a SMC or DSMB, SOCS should be copied.
- 5.5.3 If there are safety concerns, the MM will determine the need for a teleconference review.
- MM will email the study team and SDCC with the next step(s) for reviews (Section 5.6).
- 5.5.4 Ad Hoc or Safety Concern Review (Teleconference Review)
- 5.5.5 The MM or other PSRT members may ask for an ad hoc review for any reason (e.g., safety concerns, complexity of the information reviewed, value of a collaborative review).
- 5.5.6 The MM will request from the SDCC any reports needed in addition to those generated for the routine review.
- If new reports are requested, the request should be sent to the Contracting Officer's Representative (COR) of the SDCC for approval. The COR will notify the SDCC of the additional request and timeline for delivery.

- SDCC will provide the reports according to section 5.4

5.5.7 The MM can use the SOCS contractor to coordinate and schedule the teleconference or the MM may schedule it directly.

5.6 PSRT Documentation

5.6.1 Following any PSRT electronic review or teleconference:

- The MM will complete the PSRT form (or equivalent) which documents at minimum the name of reviewers, type of data reviewed, summary of relevant findings, and recommendations.
- DMID-SF-FORM-00004 is a recommended template for the PSRT form.
- An email notification is sufficient for the SDCC to reopen the trial for enrollment. The email notification is part of the documentation sent to SOCS for final storage.

5.6.2 The MM or designee will ensure SOCS is provided with all relevant PSRT documents for storage.

6. REFERENCES

6.1 DMID-SF-POL-00001 - Safety Oversight in DMID Funded Clinical Research.

6.2 DMID-SF-POL-00003 - Safety Oversight for DMID-held IND Trials.

6.3 DMID-SF-FORM-00001 - PSRT Charter Template.

6.4 DMID-SF-FORM-00002 - PSRT Review Form Template.

6.5 [FDA Code of Federal Regulations \(CFR\) Title 21: Part 312 and 812](#)

6.6 [ICH E6\(R2\) Good Clinical Practice: Section 5.16 and 5.18](#)

6.7 [EMA Guidelines: EMA/INS/GCP/856758/2018 Guidelines on GCP Compliance](#)

7. APPENDICES

7.1 Not applicable

8. REVISION HISTORY

8.1 This is the original version of this procedure.

9. ADDITIONAL INFORMATION

9.1 Document Lead: OCRA Safety

9.2 Posting externally: Yes