



## **PCORI Policy on Data and Safety Monitoring Plans for PCORI-Funded Research**

Approved July 1, 2016

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## Overview

This Policy outlines the requirements of the Patient-Centered Outcomes Research Institute (PCORI) for data and safety monitoring related to research funded by PCORI, including:

- Role of IRBs and Governmental Agencies;
- PCORI's Role as Funder;
- Definitions;
- Data and Safety Monitoring Plans;
- Appointment and Membership of Data and Safety Monitoring Boards;
- Principles, Structure, and Meetings of Data and Safety Monitoring Boards; and
- Reporting to PCORI.

## Role of IRBs and Governmental Agencies; PCORI's Role as Funder

This Policy does not usurp the role of Institutional Review Boards (IRBs) or other monitoring or regulatory bodies with jurisdiction over a particular research study. Awardee institutions and investigators participating in PCORI-funded research must meet all reporting and related obligations imposed by law or monitoring bodies (e.g., fulfilling obligations of IRBs and governmental agencies such as the Food and Drug Administration ["FDA"]).

In developing Data and Safety Monitoring Plans (DSMP) and establishing Data and Safety Monitoring Boards (DSMB) consistent with this Policy, PCORI research awardees should ensure that PCORI's role as a funder of the research study is accurately described. Under the terms and conditions of PCORI's funding of research studies, the research awardee is responsible for the conduct of the research study, including fulfilling applicable regulatory requirements (e.g., FDA) and requirements of IRBs and human subject research obligations. Thus, to the extent either the DSMP or DSMB refers to PCORI, PCORI should be reflected as the funder of the study, not the sponsor.

The awardee institution is responsible for ensuring that PCORI, as the funder of the research study, is informed in a timely manner of reporting relating to and recommendations, decisions, findings, actions, and steps taken emanating from DSMP activities, including to or from any sponsor, any DSMB, IRB, the FDA, or other monitoring or regulatory bodies, consistent with this Policy.

PCORI may, in its discretion, withhold or terminate funding for failure to comply with this Policy.

## Definitions

A Data and Safety Monitoring Plan (DSMP) is a specific oversight and monitoring plan designed for a research study and research team to ensure the safety of human subjects and the integrity of data collected. Elements that may be part of a DSMP include, among others, a description of adverse event reporting procedures and a statement of how frequently the data will be monitored. As described below, depending on the nature of a research study, a DSMP may also include the establishment of a Data and Safety Monitoring Board.

A Data and Safety Monitoring Board (DSMB) is an independent committee of experts responsible for reviewing research study data on an ongoing basis to ensure the safety of study subjects and validity and integrity of the data. Among other things, the DSMB may review interim outcomes and evidence of



adverse events to make recommendations to the Principal Investigator (PI) and the awardee institution on whether a research study should be continued, altered, or terminated.

## Data and Safety Monitoring Plans

PCORI requires the awardee institution of a research study that involves human subjects and that is funded by PCORI to ensure that there is a DSMP for the research study that is commensurate with the research study's potential risks, target study subject population, nature, size, scope, and complexity.

The DSMP for PCORI-funded research must be approved by the applicable IRB.

PCORI requires the DSMP to include the appointment of a DSMB in the instances discussed below in this Policy.

The DSMP must fulfill the following minimal requirements:

- Identify the entity, group, or individuals that will monitor the research study. Monitoring may be conducted in various ways or by various individuals or groups. Depending upon the potential risks, target study subject population, nature, size, scope, and complexity of the research study effort, data monitoring may be performed by the PI, an independent monitoring group, a DSMB, or another appropriate individual or body. For studies with no more than minimal risk, monitoring by the PI and the IRB may suffice; for greater than minimal risk studies and in the situations described below in this Policy, a DSMB is required.
- Describe the procedures for:
  - monitoring study safety;
  - minimizing research-associated risk;
  - protecting the confidentiality of participant data;
  - identifying, reviewing, and reporting adverse events and unanticipated problems to the applicable IRB(s), FDA, and any other applicable governmental agencies or other monitoring bodies, consistent with legal requirements and requirements of the IRB; and
  - for multi-site studies, the procedures for ensuring compliance with the DSMP and requirements for reporting across research study sites.

## Appointment and Membership of Data and Safety Monitoring Boards

PCORI requires DSMPs for PCORI-funded research to include the appointment of a DSMB by the awardee institution when a DSMB is appropriate given the research study's potential risks, target study subject population, nature, size, scope, and complexity, as determined by an IRB or regulatory agency (e.g., FDA).

Additionally, even if not required by an IRB or regulatory agency, the awardee institution and/or PCORI may determine that it is appropriate for a DSMB to be appointed, such as when:

- The research study involves a high-risk intervention;
- The research study includes a vulnerable research subject population or others that are disadvantaged or may be particularly subject to coercion; and/or
- The research study is a multi-center trial or otherwise includes a research network.



### DSMB Membership

Members of the DSMB must be independent of the research study, with no vested interest in a specific treatment or therapy being studied and must not include the study investigators or other members of the research study team. DSMB membership must fulfill the following requirements:

- All DSMB members must be properly trained in the DSMB's purpose, proceedings, and roles;
- Each DSMB must have an executive secretary who is not otherwise involved in the research study or with the research study team;
- Each DSMB must have a Chair;
- The DSMB must include members who generally have expertise in biostatistics, epidemiology, clinical trials, bioethics, and key subject areas involved in the research;
- PCORI strongly recommends the inclusion of a patient or family representative who is independent of the research study to serve on the DSMB;
- In general, DSMB members should be appointed for a term that coincides with the duration of the research study;
- When specialized expertise is needed for a short period of time, ad hoc members may also be appointed to the DSMB with shorter terms of service; and
- PCORI staff will not serve as members of the DSMB and will not have voting rights on the DSMB.

## Principles, Structure, and Meetings of the Data and Safety Monitoring Board

### Principles for the Conduct of the DSMB

PCORI expects DSMBs to be structured and to function in accordance with this Policy. The essential elements of the DSMB must be included in the DSMP. PCORI expects all DSMBs appointed for PCORI-funded research studies to operate consistent with the following principles:

- DSMBs are independent and operate without undue influence from any interested party, including study investigators, other members of the research team such as patient research partners, and PCORI staff;
- DSMBs protect the interests of research study subjects and ensure that they are not exposed to undue risk;
- As the DSMB deems appropriate for the research study, DSMBs must have access to "unmasked" data (meaning that DSMB members know which subjects are in which treatment group) during the course of a research study;
- DSMBs are encouraged to review unmasked interim analyses of research study data as appropriate for the research study. If a DSMB decides to remain masked for a certain period of time, rigorous stopping rules should be outlined at the onset of the research study and documented in the DSMB's charter;
- Access to any unmasked data must be limited to DSMB members and a small group of additional individuals who are to be determined at the onset of the research study. Typically, the additional individuals will include data coordinating center (DCC) staff directly involved in the analyses, including statistician(s) who are overseeing the analysis. Details may vary by research study; and
- DSMBs should have access to external evidence that could inform the research study. These types of evidence could include recent publications from the research study and information about similar ongoing research studies.



### Structure and Management of DSMB

DSMBs must be structured and managed to fulfill the requirements of this Policy, including the following:

- DSMBs must:
  - Have a charter that has been approved by the DSMB and that meets the requirements of this Policy;
  - Approve the study protocol, including the DSMP, informed consent template, reporting templates for data to be presented to the DSMB, and anything else the DSMB may wish to see before a research study begins enrollment;
- Minutes of all DSMB meetings must be taken that summarize the topics discussed and list all DSMB recommendations. All meeting minutes must be signed by the DSMB Chair. After each DSMB meeting, throughout the active phase of a research study, the lead investigators must arrange for a summary of DSMB recommendations to be sent to each participating IRB;
- DSMB meeting minutes or meeting summaries and the follow-up plans of the lead investigators must be submitted to the DSMB members within the timeline specified in the DSMB charter; and
- The DSMB is expected to have a Conflict of Interest (COI) policy and/or plans for identifying and monitoring and/or managing COIs. COIs for DSMB members must be reviewed and managed appropriately.

### Format of DSMB Meetings and Attendance of PCORI Program Staff

DSMB meetings are generally expected to have the following different sessions: an open session; a closed session (for DSMB members only); and an executive session. As the funder of the research, PCORI is interested in the progress and work of the DSMB that is overseeing the research study, but PCORI will not have a formal representative on the DSMB. The expected role of PCORI staff for each session is as follows.

- Open session
  - The issue of who may attend open sessions of the DSMB should be addressed in the DSMB charter;
  - PCORI program staff may attend the DSMB open sessions, unless the DSMB Chair decides that the presence of PCORI staff may inhibit free and open discussion, or compromise or appear to compromise the DSMB's independence; and
  - PCORI program staff should be informed of upcoming DSMB open session meetings at least one to two weeks in advance, and receive the appropriate meeting materials at the same time as the DSMB members.
- Closed session
  - It is generally expected that PCORI staff will not attend closed sessions of the DSMB. The DSMB Chair, in his or her discretion, may invite PCORI staff to attend all or part of a closed session of the DSMB.
- Executive session
  - It is generally expected that PCORI staff will not attend executive sessions of the DSMB. The DSMB Chair, in his or her discretion, may invite PCORI staff to attend all or part of an executive session of the DSMB.



## Reporting to PCORI

The awardee institution must keep PCORI informed in a timely manner of reporting relating to and actions taken emanating from DSMP activities, including to or from any sponsor, any DSMB, IRB, the FDA, or other monitoring or regulatory bodies, consistent with this Policy.

### Documenting IRB Approval

Awardee institutions must provide documentation of any new and continuing IRB approvals relating to the research study as addressed in the awardee institution's research funding contract Milestones and/or upon request by PCORI.

### Reporting to PCORI on Approval of any DSMB Charter

Awardee institutions must report on the adoption or approval of any DSMB Charter by any IRB and/or the DSMB as addressed in the Milestones or upon request by PCORI.

### Interim Progress Reports

In their Interim Progress Reports submitted to PCORI, awardee institutions must (among other requirements) include a summary of any significant data and safety monitoring issues that occurred since the previous reporting period, including:

- a summary of any reports submitted to the sponsor, a DSMB, an IRB, the FDA, or other regulatory or oversight body about unanticipated problems involving risks to subjects or others relating to the research study (e.g., adverse events, deviation from approved protocol that places subjects at increased risk of harm, data breach, procedural or medication error) that were reported since the previous PCORI reporting period; and
- a summary of any significant decisions, findings, recommendations, actions, and directions of a DSMB, IRB, the FDA, or any other regulatory or oversight body relating to the research study since the previous PCORI reporting period.

### Accelerated Reporting to PCORI Relating to Serious Unanticipated Problems

Awardee institutions must fulfill all reporting obligations relating to any serious unanticipated problems (e.g., serious adverse events, serious safety issues, or other serious problems) relating to the research study that are required by the sponsor, DSMB, IRB, the FDA, or other applicable regulatory or oversight body.

As the funder of the research study, PCORI expects to be kept informed of reporting about and actions relating to serious unanticipated problems relating to the research study. Thus, notwithstanding the interim reporting obligations described above, awardee institutions must notify PCORI promptly, but no later than 10 days after:

- reporting any serious unanticipated problems (e.g., serious adverse event, serious safety issue, or other serious problem) relating to the research study to the sponsor, DSMB, IRB, the FDA, or other regulatory or oversight body; and
- Any decision, finding, recommendation, action or direction of a DSMB, IRB, the FDA, or any other regulatory or oversight body relating to any serious unanticipated problems (e.g., serious adverse event, serious safety issue, or other serious problem).

### Provision of Documents and Materials Relating to DSMP upon PCORI Request

Upon request by PCORI, awardee institutions must provide PCORI with copies of documents and/or materials relating to the DSMP, such as minutes of open sessions of the DSMB.



Submission of Information to PCORI

All information, reports, notifications, materials and documents must be submitted to PCORI by email to [fundedpfa@pcori.org](mailto:fundedpfa@pcori.org) or as otherwise directed by PCORI.

History

*Approved by PCORI on July 1, 2016*