

## **Siteman Cancer Center Standing Data and Safety Monitoring Board** **Policies and Procedures, version 1.0**

### **Purpose**

A data and safety monitoring board (DSMB) is an independent advisory group responsible for safeguarding the interests of study participants, assessing the safety and efficacy of study procedures, and monitoring the overall conduct of the studies it reviews. A DSMB is expected to:

- Assess the overall utility of the trials it reviews based on study design and objectives
- Identify problems related to patient safety
- Identify any needs for additional data relevant to patient safety issues (and request these data from the study team)
- Review serious adverse events (SAEs) and all other patient safety data to determine possible safety measures (including pausing enrollment, revising the consent form, adding expanded safety monitoring or procedures, etc.)
- Consider the rationale for the continuation of each study it reviews and make a recommendation for or against continuation
- Draft meeting minutes summarizing key points of discussion, requests for additional information, response of investigators, and recommendations
- Communicate meeting outcomes to the study PI, who is then responsible for sharing the DSMB report and recommendations with the Quality Assurance and Safety Monitoring Committee (QASMC), Washington University IRB, and other participating institutions as applicable

The purpose of this document is to outline the policies and procedures of Siteman Cancer Center's standing data and safety monitoring board (standing DSMB), which is charged with reviewing trials that require a DSMB under the SCC institutional data and safety monitoring plan (found at <https://siteman.wustl.edu/research/clinical-research-resources/>) and are not otherwise reviewed by an independent board.

### **Membership**

The standing DSMB will have a faculty chair and will include faculty representatives specializing in medical oncology, radiation oncology, surgical oncology, pediatric hematology/oncology, and OB/GYN oncology. In addition, at least one biostatistician and one QASM staff member must be present for each meeting of the standing DSMB. Members of the standing DSMB must not be involved in the study for which they are providing monitoring services (refer to *Conflict of Interest*). Individuals will be invited to join the standing DSMB by the faculty chair.

A board member will be assigned as the primary reviewer for each study. The faculty chair is responsible for the conduct of the meetings and ensuring that all items requiring board review are addressed during each meeting. It is expected that the faculty chair will guide discussion with the ultimate goal of formulating a recommendation for each study reviewed (refer to *Meeting Outcomes*).

### **Meeting Frequency**

The standing DSMB will be scheduled to meet every 2 months (6 times annually) with meetings to occur or be canceled depending on whether reports have been received for review. At each

standing DSMB meeting that is convened, the board will review all submitted DSM reports. Frequency of individual DSM report review for each applicable trial will be dictated by PRMC at time of approval and may be adjusted by QASMC at the time of review. Should the need arise for urgent review of a protocol amendment or serious adverse event, the faculty chair may request an additional meeting or electronic review as needed.

### **Report Preparation**

The DSM report for the standing DSMB will be prepared by the study team with assistance from the study statistician. It is recommended that the QASMC report template be used for the DSM report. The DSM report must include:

- Study demographic information (HRPO #, title, list of primary team members, initial and most recent dates of approval, current study status)
- History of study (including summaries of substantive amendments, accrual suspensions and reasons, protocol exceptions, errors, and breaches of confidentiality)
- Study-wide target and actual accrual, as well as accrual by year by site (if applicable)
- Subject status by arm/cohort/dose level (cumulative and current)
- Protocol activation date(s)
- Protocol objectives and the number of participants who are evaluable each objective
- Early stopping rules and data describing whether the stopping rules have been met
- Interim analysis plans and the results of interim analysis (if applicable)
- Worst grade toxicity table separated by site (if applicable) and arm/cohort/dose level (if applicable)
- Participant-level response and survival data by arm/cohort/dose level (if applicable)
- Summary of specimen collection (percentage of participants who have had specimens collected at each required time point) (if applicable)
- Abstract submissions or publications
- Summary of recent literature that reports developments that may affect the safety of participants or the ethics of the study

The DSM report must be submitted to the QASM staff member supporting the standing DSMB at least 2 weeks prior to the DSMB meeting date. In addition to the report, a full copy of the current protocol and consent form must be attached.

### **Report Pre-Review**

The DSM report will be pre-reviewed by a QASMC staff member prior to agenda assignment. The QASMC staff member will confirm that the information presented in the report matches data available in OnCore, that the data in the report aligns with the protocol design, and that all fields are completed as required. Any concerns identified by the QASMC staff member will be communicated to the DSMB members prior to or at the time of the standing DSMB meeting.

### **Meeting Procedures**

The agenda for each standing DSMB meeting will be drafted by the QASM staff member responsible for that meeting. The agenda and meeting materials (including the DSM report(s)) must be provided to standing DSMB members at least 7 days prior to the meeting. A board member will be assigned as the primary reviewer for each study, which will be denoted on the agenda.

The standing DSMB will review the DSM report as well as formal interim analyses of the primary endpoint if available, reports of related studies (to determine whether the monitored study needs to be changed or terminated), and major proposed modifications to the study prior to their implementation. The report and any associated documents will be presented to the standing DSMB by the primary reviewer.

The standing DSMB is expected to identify problems relating to safety over the course of the study, including identifying any needs for additional data relevant to safety issues and requesting these data from the study investigators. At their meeting, they will consider the rationale for continuation of the study and make a recommendation for or against continuation of the trial, after which a vote will be held. A simple majority of members present passes a recommendation.

It is expected that all standing DSMB members will make every effort to attend every meeting (in person or remotely). However, quorum for voting is 2 uninvolved faculty (may include the DSMB chair) + 1 uninvolved statistician. Involved members, members with a financial conflict of interest, and the QASM staff member will not vote.

It is permissible for a study PI to attend the standing DSMB meeting, but s/he must not be present for voting. PI attendance is neither encouraged nor discouraged.

### **Meeting Outcomes**

After discussion of each study's DSM report, a recommendation will be made and voted on. Recommendations are:

- continue accrual with no changes
- continue accrual with changes
- suspend accrual until changes are approved
- close trial
- report results

A simple majority of members present passes a recommendation. Involved members and members with a financial conflict of interest will be asked to recuse themselves from voting; members with a financial conflict of interest may also be asked to excuse themselves from discussion of the report at the discretion of the faculty chair (refer to *Conflict of Interest*).

Meeting minutes will be drafted by the QASM staff member in order to summarize the key points of discussion and debate, requests for additional information, response of the investigators to previous recommendations, and the recommendations from the current meeting. If concerns are identified, the minutes will outline the concerns, the board's discussion of the concerns, and the basis for any recommendations the standing DSMB has made in response to the concerns. Any relevant conflicts of interest will be documented in the minutes, as well as member recusal.

The meeting outcome will be communicated to the study PI (refer to Appendix A), who is responsible for ensuring that the DSM report and DSMB recommendation are communicated to QASMC, the Washington University IRB, and other participating institutions (if applicable). The

meeting minutes will not be transmitted directly to the study PI but may be transmitted directly to QASMC upon request.

If the standing DSMB recommends that a study be changed or closed early for patient safety or efficacy reasons, the research team must act to implement the change as expeditiously as possible. In the event that the research team does not concur with the standing DSMB's recommendations, then the QASMC Chair must be informed of the reason for disagreement. The research team, QASMC Chair, and standing DSMB Chair will be responsible for reaching a mutually acceptable decision about the study.

### **Release of Outcome Data**

It is not recommended that outcome data be made available to individuals outside of the standing DSMB until accrual has been completed and all patients have completed study treatment.

The standing DSMB may approve the release of outcome data on a confidential basis to the PI for planning the preparation of manuscripts and/or to a small number of others for future trial planning purposes.

Any release of outcome data prior to the standing DSMB's recommendation for general dissemination of results must be reviewed and approved by the standing DSMB.

### **Confidentiality**

In general, no communication, either written or oral, of the deliberations or recommendations of the board will be made outside of the board except as provided for in this document and the QASMC policies and procedures. Each member of the standing DSMB must sign a statement of confidentiality when joining the board (refer to Appendix B).

### **Conflict of Interest**

A financial conflict of interest refers to situations in which it is reasonably determined a personal financial interest could directly and significantly affect the design, conduct, or reporting of research. (<https://research.wustl.edu/determining-and-managing-research-fcois-procedures/>) The PHS/NIH thresholds for financial interest will be followed:

- $\geq$  \$5,000 in remuneration from an entity in aggregate
- $\geq$  \$5,000 equity in any publicly traded entity
- Holding of any ownership interest or equity in a non-publicly trade entity
- Travel reimbursed or paid for on behalf of an investigator other than by government agency or institution of higher education
- Receipt of royalties/compensation related to intellectual property rights and interests
- An agreement with an entity that entitles an individual to future royalties related to intellectual property rights

Individuals invited to serve on the standing DSMB will disclose any potential conflicts of interest, whether real or perceived, to the appropriate institutional officials(s) in accordance with the institution's policies and self-report relevant COIs to the QASM staff member and Chair. Conflict of interest can include professional interest, proprietary interest, and miscellaneous interest. Potential conflicts which develop during a member's tenure on the standing DSMB must also be

disclosed. Decisions concerning whether individuals with potential conflicts of interest or the appearance of conflicts of interest may participate in the standing DSMB will be made in accordance with the institution's policies.

Before each meeting, when the agenda is distributed, the QASM staff member will ask all standing DSMB members to state whether they have developed any new conflicts of interest since the last meeting. If a new conflict is reported, the DSMB chair will determine if the conflict limits the ability of the standing DSMB member to participate in the discussion for each particular study and whether the member must recuse him/herself from reviewing any particular studies. Voting members directly involved with the conceptual design or analysis of a particular trial must excuse themselves from all DSMB discussion of that trial and must not receive the DSMB report related to that trial. In the event that the DSMB chair is potentially conflicted, the QASMC chair will make a final determination regarding participation in DSMB reviews and/or discussion in accordance with institutional policies.

## APPENDIX A: Template Notification

Month Day, Year

**Re: HRPO # - Study Title**

Dear PI's name,

On mm/dd/yyyy, the Siteman Cancer Center Standing Data and Safety Monitoring Board reviewed the above-mentioned protocol. The board members included a statistician xxxxxxxx, and the following physicians: xxxxxxxx, and xxxxxxxx. Study team members xxxxxxx and xxxxxxx were available to address any concerns.

The board reviewed all safety and data and voted x-x to continue accrual with no changes/continue accrual with changes/suspend accrual until changes are approved/close the trial/report results.

The board has the following comments/recommendations:

1. xxxxxxx
2. xxxxxxx
3. xxxxxxx.

Please let us know if you have any questions.

Sincerely,

Signature of standing DSMB chair

## **APPENDIX B: Confidentiality Agreement**

I understand that the activities of the Siteman Cancer Center Standing Data and Safety Monitoring Board involve access to confidential information related to research protocols and research subjects. My signature below documents my assurance that I shall not divulge to any other person or source any information to which I have had access consequent to my attendance at meetings of this board, review of materials for this board, or otherwise assisting with the functions of this board.

Signature: \_\_\_\_\_

Printed name: \_\_\_\_\_

Job title: \_\_\_\_\_

Department: \_\_\_\_\_

Date: \_\_\_\_\_