Weill Cornell Medicine Data and Safety Monitoring Committee (WCM DSMC) Charter

Confidential

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| --- | --- |
| **Protocol Sponsor** | Weill Cornell Medicine |
| **ClinicalTrials.gov ID** | [Clinicaltrials.gov ID] |
| **Study ID** | [IRB Number] |
| **Date of Charter** | [Date Charter issued] |

**APPROVAL SIGNATURES**

|  |  |  |
| --- | --- | --- |
|  |  |  |
| [DSMC Chair Full Name], [MCC/Cancer] DSMC Chair |  | Date |
| [PI Name], Principal Investigator |  | Date |

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# STATEMENT OF PURPOSE

The WCM DSMC serves as a monitoring entity for WCM investigator-initiated clinical trials to ensure subject safety, data validity and scientific merit of the study. The WCM DSMC’s guiding principles are as follows:

1. Studies differ substantially in complexity and risk and no pre-determined criteria can adequately meet the needs of all projects. Per the NIH, the level of monitoring required is commensurate with the size, complexity and risks identified for each specific study. Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. The frequency of review, the parties responsible for review and the scope of review will all vary among studies. In general, the higher the risk, the more frequent and intensive the monitoring must be.
2. Efforts must be made to characterize the risk, since the level of monitoring required is directly proportional to the risk of the study. Risk is determined by taking multiple factors into account, including, but not limited to: potential toxicities or adverse effects associated with study interventions, the involvement of vulnerable populations, and the complexity of the study design.
3. The methods and degree of compliance oversight that must be conducted for clinical trials is commensurate with the type of study and level of risk as assigned by the PI and approved by the WCM DSMC.

This Charter serves as the guiding document for the WCM DSMC’s actions and responsibilities. It describes the following:

* Composition and organization of the WCM DSMC
* Roles and responsibilities of the WCM DSMC and study stakeholders
* Purpose and timing of WCM DSMC meetings
* Communication between key study stakeholders

This WCM DSMC Charter is designed to comply with the following policies and guidelines regarding data and safety monitoring:

|  |  |
| --- | --- |
|  | **Policy/Guideline** |
| **NIH:** | * [Policy for Data and Safety Monitoring](http://grants.nih.gov/grants/guide/notice-files/not98-084.html)
* [Further Guidance for Phase I and Phase II Trials](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html)
 |
| **FDA:**  | * [Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees](http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127073.pdf)
 |

# WCM DSMC Organization

The WCM DSMC functions as an independent committee within the institution and consists of 2 sub-committees, shown in **Figure 1**.

*Figure 1. WCM DSMC Structure*



Each committee shall consist of no fewer than 5 voting members, each with varying scientific and clinical trials methodology expertise to competently review protocols under its purview. Ad hoc reviewers may be included in the event additional expertise is needed. [*Section 10*](#_Toc19290515) includes a list of Ad Hoc members involved in this study.

The members of the DSMC serve in an individual capacity and provide their expertise, including recommendations regarding the continuation, modification, or termination of any or all arms of a study. The Director of Human Research Protections & Compliance has administrative oversight of the WCM DSMC. Qualified members are appointed by the Assistant Dean of Human Research Compliance. The DSMC contact information is listed below:­­­­­­­­­­­­­­­­­­­­­­­­­­­­­­­­­­­­

Data and Safety Monitoring Committee

575 Lexington Avenue, 9th Floor

New York, New York 10065

E-mail: dsmc@med.cornell.edu

Detailed procedures for soliciting and appointing WCM DSMC members are explained in *Section 3. Organization* of the WCM Data and Safety Monitoring Committee Standard Operating Procedures (WCM DSMC SOP).

### MCC DSMC Chairs

MCC DSMC Chairs are selected from the MCC DSMC members and are responsible for the following:

1. Facilitate meeting discussions, assist in the development of the agenda, and ensure that the meeting minutes and recommendation(s) are appropriately documented
2. Ensure that voting takes place for each protocol
3. Review and approve the DSMC charter

### MCC Voting DSMC Members

DSMC members have the following responsibilities:

1. Regularly attend DSMC meetings
2. Assess trial objectives and design in an unbiased way and provide timely review and comments on all DSMC submissions, including new study reviews, periodic reviews and immediate reports
3. Assess risk and complexity of clinical trials submitted for review to determine appropriate level of data and safety monitoring
4. Evaluate, on an ongoing basis, clinical trial data and serious adverse event (AE) reports from all study sites for safety, data integrity, study conduct and progress, and, when appropriate, efficacy
5. Consider any additional information obtained outside of the trial that may have an impact on the safety or appropriateness of continuing the study
6. Where appropriate, consider pre-specified study performance criteria (e.g. early stopping rules), masked and, if necessary, unmasked reviews of all data prior to making decisions
7. Make the following recommendations for the study:
	1. Continue without modification(s)
	2. Continue with modification(s)
	3. Hold/Discontinue Study Arm or Study
	4. Terminate

### MCC DSMC Administrative Staff

Administrative staff from the Human Research Compliance Office act as the principal liaisons between the DSMC and Principal Investigators.

## Conflict of Interest

It is crucial that WCM DSMC members are objective and capable of unbiased assessments of the studies under the WCM DSMC’s purview to maintain subject safety and preserve the integrity of the study.

Voting member or ad hoc reviewers are considered to have a conflict of interest when any of the following apply:

* The individual is an investigator on the trial
* The individual has a direct interest in knowing or influencing trial outcome or has a financial or intellectual interest in the outcome of any studies under review.
* The individual serves as a DSMC member on another DSMC evaluating the same, related or competing product
* The individual is a biostatistician involved in the initial design and/or data analysis of the study

Additional details on assessing conflicts of interest can be found in *Section 4. Conflicts of Interest* of the WCM DSMC SOP.

In order to facilitate member declaration of conflicts of interest at DSMC meetings, the DSMC administrative staff will indicate known conflicts of interest on each meeting agenda, including those of DSMC members who are known to be co-investigators of or biostatisticians for studies under DSMC oversight. Members shall:

* Declare any conflicts of interest as defined in this document and in accordance with the Member Acknowledgment, and WCM Conflict of Interest Policy prior to agreeing to act as reviewer for a given study and during DSMC meetings, as needed; and
* Immediately notify the appropriate DSMC administrative staff when a new conflict arises.

In some cases, such as if a biostatistician on the DSMC helped to design the study, but will not look at data, a DSMC member may participate in a closed discussion of a study, but this member cannot vote.

In case of any question of conflict of interest, standards used by NIH in determining conflict of interest for advisory committee members and investigators shall apply.

# key stakeholders And RESPONSIBILTIES

The parties described in the Section 3 play essential roles in data and safety monitoring for the clinical study. The responsibilities of these groups and individuals are also described in this section.

## WCM DSMC

The WCM DSMC (General and MCC DSMC) is responsible for ensuring patient safety, proper study conduct, and data integrity by reviewing cumulative study data. To fulfill this responsibility, the WCM DSMC:

1. Recommends the level of monitoring appropriate to the needs of a protocol consistent with institutional requirements. If WCM DSMC oversight is needed, the DSMP needs to be approved by the WCM DSMC before it can serve as the monitoring entity.
2. Reviews cumulative study data and, if applicable, related study data to make recommendations whether the trial should:
	* Continue as originally designed,
	* Changed, or
	* Terminated
3. Provides feedback to the PI on proposed modifications affecting the study DSMP (e.g. termination, dropping an arm based on toxicity results or other reported trial outcomes, increasing target sample size).

### MCC DSMC

The MCC DSMC is the sub-committee of the WCM DSMC that oversees the safety monitoring of the cancer studies conducted by the Meyer Cancer. In addition to the WCM DSMC responsibilities outlined in section 3.1, the MCC DSMC also has the following responsibilities:

1. Setting the standards for all risk-based safety monitoring for WCM investigator-initiated, interventional trials.
2. Providing MCC leadership with its recommendations related to continuing, changing, or terminating the trial. A copy of this information will be provided to the MCC Director or designee.

## WCM DSMC Voting Members

All individual WCM DSMC members have the following responsibilities:

1. Attending WCM DSMC meetings regularly and participating in all decision item discussions.
2. Providing timely, objective and unbiased assessments of trial objectives and design on assigned WCM DSMC submissions.
3. Disclosing potential conflicts of interest.

### WCM DSMC Chair

In addition to the responsibilities of WCM DSMC Voting Members, WCM DSMC Chairs are also responsible for the following:

1. Leading WCM DSMC meetings.
2. Ensuring that a formal vote is taken for all discussion items for which voting by the full WCM DSMC is necessary.
3. Reviewing and approving the WCM DSMC Charter.

## Ad Hoc WCM DSMC Reviewers

Ad hoc WCM DSMC Reviewers are responsible for the following:

1. Providing timely, objective and unbiased assessments of trial objectives and design on assigned WCM DSMC submissions.
2. Disclosing potential conflicts of interest.

## WCM DSMC Administrative Staff

WCM DSMC Administrative Staff are responsible for the following:

1. Acting as principal liaisons between the WCM DSMC and Principal Investigator.
2. Pre-reviewing all submissions to the WCM DSMC prior to review by the WCM DSMC (reviewers and/or full Committee)
3. Assigning studies to WCM DSMC reviewers based on member expertise and conflicts of interest.
4. Maintaining WCM DSMC records
5. Assisting the WCM DSMC Chair with facilitating DSMC meetings, specifically:
	1. Assessing quorum
	2. Informing the Committee of known member conflicts of interest
	3. Drafting the MDL for all convened meetings
	4. Scheduling WCM DSMC meetings

## Principal Investigator (PI)

**The PI is responsible for the following:**

1. Oversight of all aspects of the clinical trial. The PI may delegate his or her responsibilities related to the conduct of the study. However, doing so does not relieve the PI’s responsibility of overseeing the study.
2. **Promptly submitting data relevant to data and safety monitoring to the WCM DSMC as stipulated by the study DSMP.**
3. **Notifying the WCM DSMC of any events fitting Immediate Reporting criteria.**
4. **Notifying the IRB and sponsor of WCM DSMC recommendations.**
5. **Obtaining WCM DSMC approval for any proposed changes to the study DSMP prior to implementation.**

## Protocol Review and Monitoring Committee (PRMC)

The Protocol Review and Monitoring Committee (PRMC) provides a scientific and statistical assessment of studies involving human subjects. The mission is to deliver feedback to investigators designed to improve the quality and impact of their project. All studies conducted at MCC require PRMC review.

## Weill Cornell Medicine Institutional Review Board (WCM IRB)

The WCM IRB's primary responsibility is to ensure that the rights and welfare of human subjects in research are protected. In doing so, the IRB must ensure that the human subject research is conducted ethically, and in compliance with Federal regulations, the requirements of applicable New York State and local law, and institutional policies and procedures.

The WCM IRB is an appropriately constituted group that has been formally designated to review and monitor research involving human subjects. In accordance with the Common Rule and FDA regulations, the IRB has responsibility for approving, modifying, and/or disapproving human subject research. The IRB also has the authority to suspend or terminate research in order to protect research subjects and for noncompliance with applicable rules and regulations.

# ****Other Stakeholders and Responsibilities****

## Cancer Clinical Trials Office (CCTO)

The Cancer Clinical Trials Office (CCTO) provides operational support for the clinical research activities of the Meyer Cancer Center. This centralized office is structured to provide disease program support across all cancer disciplines and in alignment with the MCC initiatives and disease management teams.  The CCTO provides regulatory, data management, research nursing, finance, and operational oversight and compliance. The CCTO provides quality assurance support through routine monitoring, as well as training in areas requiring improvement. Education is provided to new investigators and staff and continuing education is provided through various venues. The CCTO utilizes OnCore for clinical trials management and reporting.

The mission of the Cancer Clinical Trials Office (CCTO) of the Meyer Cancer Center (MCC) is to facilitate clinical trial activation and conduct in an efficient and compliant fashion. The CCTO specific aims are to:

* Provide a centralized service to ensure standardized processes and procedures for the activation and conduct of cancer clinical trials, including regulatory, data management, research nursing, oversight and compliance support;
* Compile protocol-related data through use of a Clinical Trials Management System in order to track and report to MCC leadership information on activation timelines, accrual and quality metrics;
* Conduct routine monitoring of study conduct, compliance and data accuracy, while providing quality improvement actions as required; and
* Ensure appropriate training and education for investigators and study team

## Medical Monitor

The Medical Monitor is responsible for providing independent safety monitoring. The Medical Monitor will review all AEs including grading, toxicity assignments, all other safety data and activity data observed in the ongoing clinical trial along with discussing relevant animal and toxicology studies and similar investigational agents. The Medical Monitor may recommend reporting of adverse events and relevant safety data not previously reported and may recommend suspension or termination of the trial.

# MEETINGS

The WCM DSMC shall meet in-person and/or by teleconference in accordance with the schedule outlined in the study DSMP. The WCM DSMC shall only deliberate once quorum is met. Procedures regarding the conduct of WCM DSMC meetings are described in *Section 5. Meetings* of the “WCM DSMC SOP.”

# COMMUNICATIONS

The PI will communicate with the WCM DSMC through WCM DSMC administrative staff, unless solicited directly by the WCM DSMC. Review outcomes and recommendations from the WCM DSMC will be sent to the PI according to procedures outlined in *Section 6. DSMC Submissions* of the WCM DSMC SOP. All WCM DSMC decisions will be deemed advisory to the PI, Institutional Review Committee, and other reporting entities.

Additional details concerning study-specific communications are outlined in [*Section 10. Study Specific Information*](#_Toc59462840) of this Charter.

#  CONFIDENTIALITY

All materials, discussions and proceedings of the DSMC are completely confidential. Members and other participants in DSMC meetings are expected to maintain confidentiality.

# ENDING WCM DSMC OVERSIGHT

The DSMC may recommend ending its oversight if new information is unlikely to become available that would useful for assessing whether the risks and/or benefits of the study will change. The following conditions may also prompt the WCM DSMC to assess whether its oversight should continue:

* WCM DSMC oversight will be ended administratively if the status of the study is noted as closed or completed by the IRB.

#  Revisions to the Charter

Section 9 of this charter must be reviewed at least annually. Revisions may be proposed by either the WCM DSMC or the PI. However, both parties must approve of all changes before any changes may be implemented.

# Study Specific Information:

[Only the information outlined in this section may be modified.]

## Ad-hoc DSMC reviewers [If Applicable]

|  |  |  |
| --- | --- | --- |
| **Name, Title** | **Affiliation** | **Specialties/Field(s) of Expertise** |
|  |  |  |

## STUDY-SPECIFIC COMMUNICATIONS

[Section 8.2 should be modified based on the needs of the study. The sub-sections below are examples.]

### Blinded Trials

For blinded trials, individual participant treatment assignments will not be revealed unless required for patient safety

### Individual or Multi-center Trials

Individual or multi-center results will not be revealed unless required for patient safety. The magnitude of treatment differences in efficacy will not be revealed unless required for patient safety

### Interim Study Findings

Interim study findings will be communicated in cases where modifications are recommended, the DSMC will require the PI to submit confirmation to the DSMC that the modification(s) have been made, or to submit a reason why the PI did not agree with the DSMC’s recommendation

### Study Termination

In the event that the DSMC recommends the trial be terminated, the DSMC shall provide the PI and IRB with its written recommendation. The rationale for termination may be based on the DSMC’s examination of study reports and data indicating that there is a significant increase in the risks to subjects, overwhelming data showing either effectiveness or futility, and/or lack of feasibility.

## [ADDITIONAL SECTIONS MAY BE ADDED AS NEEDED]

# APPENDICES

Appendix A: Data and Safety Monitoring Plan *[a distinct document using the DSMP template is needed for Cancer Studies. For General studies, either the protocol document or specific protocol section can be attached instead.]*

Appendix B: [General or MCC] DSMC Roster

Appendix C: WCM DSMC SOP

 **[Add additional attachments as needed, such as report templates, etc.]**