Protocol Review and Monitoring Committee Charter

1 Definitions

CCSG	Cancer Center Support Grant
CRLC	Clinical Research Leadership Committee
DSMC	Data and Safety Monitoring Committee
DSMP	Data and Safety Monitoring Plan
JIT	Just-in-Time; A submission process by the NIH or other grant funding mechanism which requires an investigator to submit documentation prior to approval as a qualification for the funding award.
MDG	Multidisciplinary Disease Group
NCI	National Cancer Institute
PI	Principal Investigator
PRMC	Protocol Review and Monitoring Committee
PRMS	Protocol Review and Monitoring System

2 Purpose

Protocol Review and Monitoring System (PRMS) responsibilities required for the Cancer Center Support Grant (CCSG) are carried out by the Sidney Kimmel Cancer Center (SKCC) Protocol Review and Monitoring Committee (PRMC). The purpose of this policy is to document the review processes undertaken by the PRMC.

The PRMC evaluates all clinical research protocols involving human subjects that have cancer related objectives. The committee is responsible for:

- Review of all new studies for scientific merit
- Ensuring that all the protocols have appropriate bio-statistical design to meet the objectives
- Assessing general feasibility, targeted annual accrual expectations, justification for accrual goals or prior accrual for similar population, and competing studies for each new clinical protocol
- Review adequacy of the suggested data and safety monitoring plan for each protocol
- Assigning risk according to the SKCC's Data and Safety Monitoring Plan (DSMP), and informing the SKCC Data and Safety Monitoring Committee (DSMC)
- Reviewing all protocol amendments that affect scientific merit
- Maintaining written records of all meetings
- Assessing accrual and scientific relevance for all open and enrolling studies annually which are not PRMC exempt
- Requesting corrective action plans for poorly accruing studies, and closing studies that do not meet accrual expectations

3 Responsible Personnel

The Associate Director of Clinical Research, PRMC Chair, PRMC Vice-Chair, PRMC Administrator, PRMC Manager, and PRMC Coordinator are responsible for the execution of the PRMC policies and procedures.

These policies and procedures are applicable to all SKCC Investigators conducting oncology-related research at the Sidney Kimmel Cancer Center.

4 PRMC Membership

4.1 Committee Composition

PRMC membership will include broad representation across medical disciplines in order to provide the highest quality study reviews. PRMC membership composition must maintain a minimum of 50% senior faculty (Associate Professor or higher). The Cancer Center Director and the Associate Director for Clinical and Translational Research shall appoint established researchers and senior cancer center members as the Chair and Vice-Chair of the Protocol Review and Monitoring Committee.

Potential PRMC members are identified by the current PRMC members, Associate Director for Clinical and Translational Research, and the PRMC Chairs; and presented for review by the Clinical Research Leadership Committee (CRLC) for approval. The CRLC evaluates potential members based on Senior/Junior faculty composition minimums, SKCC membership, representation from SKCC research programs, and representation from various disease specialties and disciplines. Revised membership rosters are forwarded to the Cancer Center Director for approval. At least annually and whenever membership changes, the Associate Director for Clinical and Translational Research and Clinical Research Leadership Committee (CRLC) will perform an assessment of the membership composition.

4.2 Member Expectations

There is no fixed term length to committee service. Members are expected to attend 75% of meetings annually. All non-chairing members are expected to provide at least 5 scientific reviews annually. PRMC Chairs evaluate member participation and performance annually and may revoke membership, at their discretion, if expectations are not met.

4.3 Member Onboarding

New members undergo orientation and training with the PRMC Chairs and PRMC Support Staff to review PRMC procedures, meeting format, and scientific review instructions. As part of new member onboarding, they will be assigned as a secondary reviewer for their first two reviews and paired with a more senior member. The senior reviewer will review the new member's review and give feedback on review quality.

4.4 Confidentiality

All PRMC members must sign a confidentiality agreement whereby they agree to maintain the confidentiality of all information revealed during the course of proceedings of the PRMC.

4.5 Leadership Development

To ensure continuity of the leadership, a small number (i.e. 1-3) of active members of the PRMC are mentored by the Chair and Vice-Chair and participate in standard operating procedure development, participate in the accrual monitoring subcommittee, and may serve as an Alternate Chair during meetings, if needed.

4.6 PRMC Meetings

The PRMC meets twice each month. The meetings are led by the PRMC Chair or Vice-Chair or an Acting Chair appointed by the Chair.

4.7 Member Anonymity

The identity of the PRMC members reviewing a particular study will remain anonymous to the submitter of the protocol and to the general TJU community unless the reviewer volunteers to initiate a discussion regarding the concerns and their expertise with the PI directly. Reviewers provide their comments to the PRMC Coordinator to relay them to the study team. The PI is expected to respond to inquiries from the assigned reviewers in a timely fashion and before the scheduled review, whenever feasible. If the submitting PI has questions or concerns about PRMC comments, they are asked to submit these questions to the PRMC Coordinator who will reach out to the appropriate committee member for clarification. The PRMC Coordinator will respond to the PI without revealing the identity of the reviewers. The PI, in collaboration with the research staff, is required to respond to any required changes that the PRMC may request for the submission post-PRMC review.

4.8 Conflicts of Interest

Committee members who are principal investigators or co-investigators on a study or who identify another potential conflict of interest (e.g., financial) may not serve as reviewers or vote. Additionally, Principal Investigators may not be present in the meeting room during the discussion or vote on their protocol.

4.9 Quorum

Meeting quorum is established once the following members are present:

- PRMC Chair (or Vice-Chair, if Chair is absent)
- One biostatistician member
- Two treating physician members
- Six additional committee members

5 Procedures

5.1 Submissions to PRMC

All submissions for new studies, scientifically significant amendments, and annual progress reports must be e-mailed to PRMC (PRMC@jefferson.edu) for review. Prior to PRMC review, all submissions first receive triage by the PRMC coordinator to ensure submission materials are complete and accurate; and ensure submissions go through the proper review processes, as described in this charter.

5.2 New Studies

All research studies involving human subjects that have cancer related objectives conducted at the SKCC must be submitted to the PRMC. All new study applications are triaged by the PRMC Coordinator to determine what level of review is appropriate. Studies may receive full committee or expedited review or may be given exemption, depending on specific criteria described below. The submission packet for a new study review includes the PRMC New Study Application, protocol, and if applicable: documentation related to the Protocol Facilitation Committee and Multidisciplinary Disease Group reviews.

5.2.1 New Study Review Process

5.2.1.1 Protocols Part of Grant Applications

If an investigator-initiated protocol is part of a grant application and is pending review, the Principal Investigator may request a "Just In Time (JIT) Grant Review" from PRMC. This administrative review process allows the PI to submit to the IRB prior to obtaining PRMC approval. This deviation from the standard process is intended to help investigators meet grant requirements, like obtaining IRB approval in a short timeframe. After the grant review outcome is determined, the protocol must come back to PRMC for determination of the appropriate level of review (i.e. expedited or full board) and the study must be approved by PRMC before it may be activated for enrollment. Investigators are expected to submit to PRMC within a reasonable timeframe of receiving a JIT notification.

5.2.1.2 Administrative Review / Exempt from PRMC Review

Protocols that are not applicable to Data Table 4 (DT4), and studies that are opening only at SKCC network or affiliate sites, may be exempt from PRMC review. These protocols are administratively reviewed and acknowledged by the PRMC coordinator. The following are examples of studies that may be exempt:

- Retrospective Research, i.e. retrospective chart review, studies using banked tissue, institutional registries, databases
- Serum and tissue banking protocols where there is no research objective or hypothesis
- Single subject compassionate use or emergency use protocols where there is no research objective
- Other non-hypothesis driven research
- NCI's National Clinical Trials Network (NCTN) studies opening only at SKCC network or affiliate sites

5.2.1.3 Expedited Review

Studies that qualify for Data Table 4 reporting and have been reviewed by an NCI approved scientific review committee may receive expedited review. Expedited reviews focus on prioritization, competing studies, and feasibility at that site. Reviews are completed by the PRMC Chair or Vice-Chair, who will determine the outcome or may defer to the committee for full review.

The following types of studies may receive expedited review:

- Peer-reviewed protocols supported by the various NIH mechanisms (e.g. R01s, U01s, U10s, P01s, P50s, etc.)
- Peer-reviewed protocols supported by other approved funding agencies (http://cancercenters.cancer.gov/documents/PeerReviewFundingOrganizations508C.pdf)
- Clinical research protocols approved by the NCI's Cancer Therapy Evaluation Program or the Cancer Control Protocol Review and Monitoring Committee. This includes NCI's National Clinical Trials Network (NCTN) sponsored studies.
- Multi-site institutional studies where TJU is a participating site and all of the following conditions are met:
    - The lead site is an NCI-designated (or comprehensive) cancer center with an approved PRMS
    - The PRMS of the lead site assumes responsibility for the full scientific review of the protocol

5.2.1.4 Full Review

Studies that do not meet criteria for exemption or expedited review will receive full committee review.

Full PRMC review focuses on the scientific merit and statistical design of the protocol, prioritization, competing studies, and feasibility at that site. Review criteria have been developed to assist reviewers and committee members in addressing all scientific aspects of a proposed study, including but not limited to:

- The study addresses a relevant scientific question
- The primary and secondary objectives are scientifically sound
- The study design is appropriate to meet the objectives
- The response criteria and endpoints are clearly defined
- The sample size is appropriate to answer the question, accrual goals are clearly stated and the patient population is sufficient to meet accrual goals
- The data and safety monitoring plan is appropriate
- The early stopping rules are adequate and clearly described
- The investigator has an appropriate plan for the inclusion and monitoring of women and minorities accrual

Non-interventional studies qualifying for full review will be assigned a scientific reviewer and a biostatistician. Interventional studies qualifying for full review will be assigned two scientific reviewers and a biostatistician. Reviews are documented on the appropriate review forms. Assigned reviewers must complete the appropriate review form prior to the PRMC meeting in order for the protocol to be discussed and voted on at the meeting.

5.2.2 New Study Review Outcomes

Once the new study review is completed, the PRMC Coordinator will prepare a review outcome notification that will be issued to the PI, relevant MDG Coordinator (if applicable), and Submitter. Additional individuals may be copied on notifications, as needed.

- Approved
    - The study is approved for eventual activation at TJU as submitted and with no additional comments. The PI will receive an approval letter.
- Contingent Approval
    - The study review results in concerns that require a PI response. PI will receive a letter requesting a written response to the concerns. Upon receipt of a successful response (as determined by the PRMC Coordinator, PRMC Chair, or the original reviewers, if necessary), the PI will receive a final approval letter.
    - If the PI does not respond to the concerns within 30 days, the study may be closed at the discretion of the PRMC Chair.
- Deferred
    - Significant revisions to the study are necessary. PI will receive a letter requesting a written response to the concerns for re-submission and re-review at a full committee meeting. Relevant MDG Committee Leaders (if applicable) will be copied on the notification.
    - If the PI does not address the concerns and re-submit to PRMC within 45 days, the study may be closed at the discretion of the PRMC Chair.
- Tabled
    - The committee cannot review the protocol at a scheduled meeting due to reviewer unavailability or other unforeseen circumstances. Tabled studies will be re-scheduled for review at the next scheduled meeting.
- Disapproved
    - The study does not satisfy the review criteria and is not approved for eventual activation at SKCC. PI will receive a letter with actions identified. Relevant MDG Committee Leaders (if applicable) will be copied on the notification.
    - A study may be disapproved if it was deferred twice and the concerns are not addressed adequately during the third review. Once disapproved, the study may not be resubmitted as is.

5.2.3 PRMC Prioritization Scores

Protocols that receive full or expedited review receive a score of low, medium, high based on feasibility, scientific merit, enrollment potential including from underrepresented populations, and biostatistical design.

5.3 Protocol Amendments

Protocols initially determined to be PRMC exempt do not require amendment review by PRMC. Amendments to NCTN sponsored protocols and Multi-site institutional studies conducted with an NCI-designated (or comprehensive) cancer center with an approved PRMS as a lead site also do not require PRMC review.

Protocol amendments and protocol clarifications that affect the principal elements of the original protocol, including but not limited to: study rationale, response criteria, eligibility criteria, objectives,

study design, treatment plan, sample size, stopping rules, safety evaluation changes or statistical plan, must be submitted to PRMC for review and approval. If changes in an amendment had already been submitted as a protocol clarification and had been approved, an amendment submission at a later date will be exempt from review. PRMC Coordinator is responsible to review and determine if changes were same as the protocol clarification submitted previously.

5.3.1 Amendment Review Process

The amendment submission packet includes the PRMC amendment application form, a summary of changes, clean revised protocol, a tracked protocol if available, and may include other supporting documentation. Submissions are reviewed as a whole packet. The review outcome will apply to all documents submitted, and to all changes contained within the Summary of Changes and clean, revised protocol document.

Amendments are reviewed by the PRMC Chair, Vice Chair, or Alternate Chair for review via an expedited review process. The PRMC Chair, Vice-Chair, or Alternate Chair has the prerogative to defer any amendment for full committee review.

5.3.2 Amendment Review Outcomes

After review by the PRMC Coordinator, PRMC Chair, Vice-Chair, or Alternate Chair, the PRMC Coordinator will either prepare a review outcome notification, or prepare the submission for full committee review, depending on the outcome.

PRMC coordinator will liaise the communication between reviewers and the PIs regarding any concerns with an amendment. Approval will not be granted until all concerns are satisfactorily addressed.

A review outcome notification for approval will be issued to the PI and study team. If there are suggestions provided with the amendment approval notification, they are recommendations only.

5.4 Annual Progress Reviews

The PRMC is responsible for monitoring the accrual and evaluating the scientific merit of all cancer related clinical research studies conducted at the SKCC. Evaluation of the scientific progress of the study, and how that fits into overall progress in that specific area of research, is important to ensure that the study is continuing to address an important scientific question.

Studies are monitored for progress and performance via Annual Progress Reviews. These reviews take place at least annually once a study is approved by the IRB and open to accrual for at least 6 months (includes any suspended period, if applicable). Protocols initially exempt from PRMC review do not require annual progress reviews by the PRMC.

The purpose of the annual progress review is to:

1. Evaluate major developments that occurred in the scientific area that affect the specific objectives of the study
2. Determine if sufficient progress is being made
3. Monitor changes in the study's priority

Annual progress submissions consist of a completed PRMC Annual Progress Application form and the current protocol. These documents must be submitted to PRMC prior to IRB expiration each year until the study is permanently closed to accrual.

5.4.1 Annual Progress Review Process

Annual progress submissions are reviewed by the PRMC Chair, Vice-Chair, or Alternate Chair through an expedited review process

The PRMC Chair, Vice Chair, or Alternate Chair has the prerogative to refer any annual progress submission for full committee review.

5.4.2 Annual Progress Review Outcomes

After review by the PRMC Coordinator, PRMC Chair, Vice-Chair, or Alternate Chair, the PRMC Coordinator will either prepare a review outcome notification, or prepare the submission for full committee review, depending on the outcome. Review outcome notifications are issued to the PI, Study Site Contact, and submitter.

5.5 Accrual Policy

The PRMS should have the authority to open protocols that meet the scientific merit and scientific priorities of the center and to terminate protocols that do not demonstrate scientific progress. Unique considerations may apply to studies of rare diseases, or targeted therapies, which often do not accrue rapidly.

See Protocol Review and Monitoring Committee Accrual Monitoring and Study Closure standard operating procedure document for details.

5.6 Activation Monitoring

All oncology studies that are not exempt during initial PRMC review are monitored for activation in a timely manner. It is important for studies to activate in a timely manner. Studies that have not activated within 9 months of PRMC approval shall be reviewed by the PRMC and may be subject to closure. As a courtesy, 6 months after initial PRMC approval, if a study has not yet activated, the PRMC will send an email to the Principal Investigator reminding them of the activation time expectation. After 9 months, if a study has not yet activated, the PRMC will email the Principal Investigator and study team, requesting information on the status of study activation in order for PRMC to review that study at their next meeting and determine whether the study should continue.

6 Document History

Version	Effective Date	Description of Change
1.1	07/09/2012	
1.2	11/16/2012	
1.3	04/23/2013	
1.4	10/31/2013	
1.5	05/28/2015	

1.6	7/25/2015	
2.0	11/03/2016	Updated to new SOP format; revised quorum; distinguished between exempt and expedited reviews; added requirements for annual progress reviews; simplified PRMC review outcomes; specified process for grant applications.
2.1	02/17/2017	Updated sections regarding full committee reviews, conflict of interest, committee membership, and time to activation.
3.0	08/24/2020	Updated Title to Protocol Review Committee Charter; revised sections including membership; criteria for full board and expedited review; submission requirements that are Data Table 4 non-applicable; annual progress report requirements; and modified study activation policy.
3.1	02/02/2022	Updated name of committee to Protocol Review and Monitoring Committee, updated chair for signature.
4.0	01/06/2023	Clarified language for research subject to PRMC review; updated PRMC membership selection, onboarding and participation requirements; revised PRMC exempt status for NCTN studies open only at SKCC affiliates and network sites, added a review process for studies in grant application processes.

7 Approval

Authors Joseph Curry, MD (PRMC Chair) and
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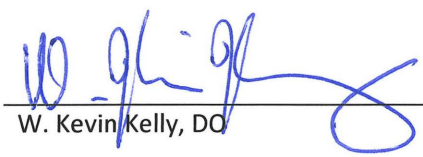
Associate Director for Clinical and Translational Research Approval  **Date of Signature** 5-22-2023
W. Kevin Kelly, DO

Does this document require review and approval from the SKCC Director or Deputy Director?

☑ **Yes** ☐ **No** **Initials** _____

SKCC Director/Deputy Director Approval  **Date of Signature** 5/18/23
Andrew Chapman, DO/Andrew Aplin, PhD