MARKEY CANCER CENTER CLINICAL RESEARCH ORGANIZATION STANDARD OPERATING PROCEDURES		
SOP No.: MCCCRO-P-002.00 **Revision:** N/A **Revision Date:** N/A **Effective Date:** July 1, 2017	**Title:** **Protocol Review and Monitoring Committee Functional and Administrative**	
Approval	**Signature**	**Date**
MCC Director		
MCC Associate Director of Clinical Translation		
MCC Medical Director of Clinical Research Organization		
MCC Director of Clinical Research Operations		

1. PURPOSE

a. The purpose of this document is to describe the responsibilities and processes of the Protocol Review and Monitoring Committee (PRMC) at the University of Kentucky (UK) Markey Cancer Center (MCC).
b. The purpose of the PRMC is to support the vision of the UK MCC by evaluating clinical trials to bring to our subjects and our community, thereby providing cancer patients from Kentucky and their families' access to the latest research in cancer prevention, cancer control, and cancer treatment.

2. SCOPE

a. This procedure applies to all UK MCC personnel.
b. This procedure applies to all clinical trials being proposed at the UK MCC and the Markey Cancer Center Research Network (MCCRN).

3. RESPONSIBILITIES

The PRMC has the authority of reviewing and approving new and continuing clinical cancer protocols for scientific merit prior to IRB submission, assigning a risk level, and approving amendments to open protocols. Open protocols initially approved by the PRMC will be submitted to the PRMC for continuing review prior to continuing review by the IRB to determine whether a study continues to have scientific merit and progress is being made through accruals. The PRMC also reviews amendments to protocols for scientific reasons and has the authority to terminate protocols for scientific reasons and poor progress and/or low accrual. Such reasons include, but are not limited to, the development of therapy which is superior to that proposed in the protocol or a change in the standard of care which is no longer reflected in the protocol. Clinical trials will be considered by the PRMC if they are Phase I, II, or Phase III National Cancer Institute (NCI) cooperative group trials, industry-sponsored, or institutional investigator-initiated clinical trials focusing on cancer prevention, cancer control, or cancer treatment that have been approved by the appropriate Clinical Care and Research Team (CCART).

4. PROCEDURES

a. Clinical trials will be considered by the PMRC if they are Phase I, II, or Phase III NCI cooperative group trials, industry-sponsored, or institutional investigator-initiated clinical trials focusing on cancer prevention, cancer control, or cancer treatment that have been approved by the appropriate CCART.
b. The committee meets regularly to review protocols.
c. New clinical trials will be slated for full committee evaluation and potential approval at any one PRMC meeting. The Chair of the PRMC makes the ultimate decision regarding trials accepted on the agenda.
    i. The Chair may call an ad-hoc committee meeting at any time to address issues of immediate concern.
d. Attendance by committee members is requested at all meetings, but it is understood and expected that other commitments will come up on occasion.
    i. If a committee member foresees that they will be unable to attend more than 50% of the meetings, that committee member has the responsibility of notifying the PRMC and should be considered for replacement.
    ii. Attendance will be taken at all scheduled meetings.
    iii. The PRMC Chair and Co-Chair are appointed by the Director of the MCC with the advice of the AD for Clinical Translation. The Director formally reviews the performance of the PRMC Chair and Co-Chair at least annually and has full discretion to replace these positions, with the advice of the senior leadership. The Chair and Co-Chair may also be reappointed for an additional term if performance merits.
    iv. To promote communication and timely resolution of issues, the PRMC encourages the PI of new protocols to be available in person or by phone at the time of review. PIs of IITs are required to be present; it is optional for other trials unless formally requested by the PRMC.
e. The PRMC Chair assigns reviewers and the PRMC Administrative Research Assistant will notify reviewers that they have been chosen as a reviewer. Protocols are reviewed by 2 clinicians, 1 biostatistician, and 1 clinical pharmacologist (when relevant). Reviewers are assigned protocols prior to the meeting prior to the meeting. This process is facilitated with the OnCore ePRMS software package. The PRMC Administrative Research Assistant assists reviewers and others with technical, logistical, and software issues.
f. The reviewers will access the protocol, the protocol submission information, including accrual estimates, and the standardized PRMC review form electronically. The review form will include date, protocol title, phase of study, sponsor information, protocol number, and PI name. The specific major review criteria are:
    1. Scientific significance.
    2. Feasible accrual goals (at least 3 subjects annually, with exceptions of tumors defined as by the NCI, complementary and not competitive with current protocols).
    3. Programmatically relevant to the specific CCART goals.
    4. Appropriate study design, including appropriate statistical analysis.
    5. Prioritization of protocol based on MCC prioritization of studies.
    6. Objectives/Hypothesis
    7. Eligibility criteria
    8. Treatment plan
    9. Measure of effect/endpoints
    10. Alignment with MCC mission/vision and catchment population.
    ii. The protocol and abstract will be available to all committee members for discussion at the PRMC meeting.

iii. A quorum of 9 members plus one biostatistician must be present for any PRMC vote.
iv. The primary clinical reviewer presents the trial to the committee and their evaluation of strengths and weaknesses of the protocol. This review is followed by input from the other reviewers as well as a representative from the feasibility review committee. During this process the committee considers and discusses all points for which they have a concern or criticism. The protocols can be rejected outright for major criteria flaws, requiring appeal and re-submission. The can also require the PI to address unclear issues and/or minor criticisms. Clarifications and minor issues may be reviewed and approved administratively by chair, co-chair, and/or other committee members as suggested by motion and vote. Acceptable protocols include satisfactory information for all review criteria, which include: soundness of eligibility criteria, competing protocols, procedure and clinical assessment practicality, adequacy of appendices for reporting results, and drug accountability.
v. Investigators are not allowed to be present during the protocol presentation and discussion; however, when available, they are invited in to address concerns raised by the committee. The investigators are then asked to leave for further discussion.
vi. After the discussion is complete, all committee members assign a PRMC score for the protocol prior to a motion and vote. If the protocol is approved, then the committee collectively assigns a PRMC score.

g. Handling protocols based on origination and prior scientific review:

h. All interventional investigator-initiated trials undergo a two stage process. A concept must be approved or disapproved by the PRMC. When the protocol is final, the protocol must undergo a full committee review. Pharmaceutical company-sponsored trials must undergo a full review. A full review consists of two physician reviewers, an oncology clinical pharmacologist pharmacist, and a statistician from the BBSRF. Exceptions to this two-stage review include those protocols that have had external peer-review (e.g. documented review and approval from another NCI designated cancer center PRMC). and at the discretion of the PRMC chair for exceptional protocols.

i. Protocols derived from a national cooperative group will have an expedited review by the PRMC Chair or designee after the CCART and FRC has completed its review. The results of the expedited review will be presented at the next PRMC meeting.

j. Non-interventional or observational screening, supportive care, basic science, diagnostic, health services research protocols may undergo expedited PRMC review by the PRMC Chair or designee.

k. Protocol Disposition: The PRMC may make the following decisions regarding a clinical trial: Approve, Disapprove, Changes Required-Administrative Review, Changes Required-Full Review, or Table. A final score is agreed upon by the full committee. For expedited reviews, a final score will be given by the PRMC Chair or designee (Table D).
    i. If the committee decides that changes require administrative or full review, these revisions need to be submitted within 30 days. If longer than one month is required, a request for an extension must be submitted in writing as well as a rationale for why the extension is needed to the PRMC Chair. Otherwise the study will be administratively disapproved.
    ii. All substantive comments brought up during consensus voting by the committee will be addressed before final approval by the PRMC Chair.
    iii. All correspondence must be kept in the Oncore ePRMS database and maintained in hard copy and electronic formats. Investigators must address all committee concerns as outlined in the disposition memo in a separate document and provide a clean protocol as well as a track changes protocol. All of the documents will be provided electronically and managed with OnCore.

iv. The PI may appeal a PRMC decision by addressing all the concerns in writing and asking the PRMC Chair to place this on the next available committee meeting. The investigators communication will be shared with the committee prior to the meeting and the investigator will be invited in to address the committee. The investigator will be excused once they have made their case so the committee can discuss the protocol and all communication (verbal and written). The appeal outcomes are determined by committee motion and vote with the disposition options being the same as a new protocol.

v. Expectations of committee members: All members present at the meeting are asked to score all new protocols and then vote on a motion as described above.

l. Abstention from protocol/amendment review or voting by committee members is accepted if the committee member has a conflict of interest and/or a lack of expertise in the scientific subject of the protocol.

i. i. In order to be unified with the University of Kentucky, the PRMC conflict of interest is determined by The UK Office of Sponsored Research Projects Administration definition. All faculty (all voting PRMC members) update this conflict of interest statement annually. There is very little change in their policy on a year to year basis and it is primarily focused on faculty and their immediate families interest and financial connection to a company.

ii. A committee member who is a PI on a study submitted to PRMC will be asked to recuse themselves from the review and voting process.

m. The PRMC will determine the level of safety monitoring required for each protocol on a case-by-case basis using the Risk Definition (Table A) as a guide.

i. For investigator-initiated trials that are determined to be of high risk, the DSMC will monitor subject safety monthly.

n. Open protocols initially approved by the PRMC will be submitted to the PRMC for continuing review prior to continuing review by the IRB to monitored continuously to determine if study continues to have scientific merit and progress is being made through accruals. A formal review is performed at least annually.

o. The PRMC has authority to close a study due to a change in practice or if and not sub mit it to the IRB for continuing review if accrual plan and/or scientific progress and performance is not being achieved (Table C).

p. The Vice Chair of the PRMC will review and approve scientific protocol amendments; those with minor changes are administratively evaluated for approved. Protocols with a major amendment (change is study design, change in inclusion/exclusion criteria, treatment, or data analysis) will have reviewers assigned to match the amendment. Disposition of protocols with major amendments will determined at a meeting by vote, similar to a new protocol. Major amendments to exempt protocols (e.g. cooperative group trials) will be reviewed administratively. , except those where there may be When there is a conflict of interest; in that case, the amendments will be reviewed by the Vice Chair or Chair will review the protocol (assuming they have no conflict of interest). In the rare situation that both the Chair and Vice Chair are conflicted of the PRMC, or in their absence, the Associate Director of Clinical Translation will review the amendment. The PRMC recommends amendments to or termination of a protocol for scientific reasons. Such reasons include:

i. The development of therapy which is superior to that proposed in the protocol.

ii. A change in the standard of care which is no longer reflected in the protocol.

q. The PRMC has the authority to terminate protocols for lack of study progress including poor accrual.

r. Committee assignment is as follows:

i. Physician members are chosen from the MCC and UK faculty.

ii. The Chair is appointed by the Director of the MCC.

iii. One of the voting members will serve as the Vice Chair appointed by the Chair. Committee members are appointed by the Chair and the ADCT and approved by the Director and serve three year terms. Ad-hoc members may be appointed by the Chair, as needed. There is no limit on the number terms a member may serve.

s. At least annually the PRMC will review its processes and receive training as needed from external sources, such as the cooperative groups or the NCI. The focus and need is determined by the preparation and review of the PRMC process by the external advisory board.

5. DOCUMENTATION REQUIREMENTS

a. PRMC memos and minutes will document committee discussion and decisions.
b. Email communication may provide documentation of discussions.

6. FORMS

a. Table A: Risk Definition Table
b. Table B: Study Risk Profile and Monitoring Requirements
c. Table C: Accrual Criteria for review
d. Table D: PRMC Scoring Rubric

7. REFERENCES

a. NCI Dictionary of Cancer terms (NCI Dictionary of Cancer Terms - National Cancer Institute)
b. University of Kentucky Markey Cancer Center Data and Safety Monitoring Plan
c. Data Safety and Monitoring Committee Administrative and Functional SOP No.: MCCCRO-D-00100
d. MCC Audit Committee Functional and Administrative Overview SOP: MCCQA-002.0
e. MCCRN Audit Overview SOP: MCCQA-003.0
f. Markey Cancer Center/IRB/ORI Coordination SOP: IRB C6.0400

8. REVISIONS HISTORY

Revision: N/A
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