Cancer Protocol Review Committee (CPRC) Charter

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Mission

The mission of the Cancer Protocol Review Committee (CPRC) is to improve oncology research by providing guidance and expertise to investigators in the development of high-quality and impactful research studies that demonstrate high standards of scientific rigor.

Overview

The purpose of the CPRC at the Masonic Cancer Center-University of Minnesota (MCC) is to provide rigorous evaluation of scientific merit, feasibility, prioritization, and progress of all cancer-related research involving human subjects at the University of Minnesota. Protocols must receive CPRC approval or minor stipulated approval prior to IRB review.

- Within the MCC, the CPRC has the sole authority to authorize activation of clinical studies. They are responsible for ongoing review of open protocols, including accrual, protocol amendments, and scientific relevance, and has sole authority to close trials for these reasons.
- The CPRC reviews all University of Minnesota cancer-related protocols including investigator-initiated trials (IIT), University Consortium, National Clinical Trials Network, and industry-sponsored studies.
- MCC leadership committee appoints CPRC committee chairs. Committee members may be selected by the MCC leadership and/or CPRC Chairs for expertise in a broad range of disciplines.
- The CPRC is co-chaired by Brenda Weigel, MD, MSc and Rachel Isaksson Vogel, PhD. The MCC Clinical Trials Office (CTO) provides operational support and management of the committee.
- The responsibilities of the CPRC are distinct from those of the Data and Safety Monitoring Council (DSMC), which has oversight of subject safety monitoring, clinical trial monitoring, and auditing.

CPRC Review Scope

The CPRC reviews cancer and tobacco related protocols at the University of Minnesota. The types of review and protocols eligible for those reviews are as outlined below.

The CPRC determination of clinical research is exclusive from an IRB's definition. While IRBs may make a determination of exemption for some research, there is no equivalent exemption determination for the CPRC. Therefore regardless of whether IRB review is required, CPRC review is required for all research categories listed below.

1. The CPRC reviews all cancer-related hypothesis-driven clinical research studies including:
    a. **Patient-oriented research**: This type of research is conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator directly interacts with human subjects. Patient-oriented research includes:
        i. Studies of mechanisms of human disease
        ii. Studies of therapies or interventions for disease
        iii. Clinical trials
        iv. Studies to develop new technology related to disease
    b. **Epidemiological and behavioral studies**: Studies among cancer patients and healthy populations that involve no intervention or alteration in the status of the participants, e.g. surveillance, risk assessment, outcome, environmental, and behavioral studies.
    c. **Health services research**: Protocols designed to evaluate the delivery, processes, management, organization, or financing of health care.
    d. **Minnesota Cancer Clinical Trials Network (MNCCTN) protocols**, when applicable
        i. If any MNCCTN protocol is not subject to review by another Comprehensive Cancer Center's scientific review, it will be reviewed by the CPRC regardless of which sites are planned for protocol activation.
2. The CPRC does not review:
    a. Protocols that do not require patient consent.
    b. Single subject or compassionate use protocols without research objectives.
    c. In vitro protocols utilizing human tissues that cannot be linked to a living individual (e.g. specimen banking studies).
    d. Retrospective chart or retrospective data review protocols.
    e. Protocols involving only populations outside the University of Minnesota (with the exception of MNCCTN studies).
        i. This includes Fairview Community Health studies that will not be implemented at Clinics and Surgery Center or UMMC-F hospitals.
    f. Non-cancer research protocols.
        i. These protocols may be reviewed by the CPRC if the study will be managed by the MCC Clinical Trials Office.

ii. If a protocol's only cancer-related aims/objectives are exploratory, it is not considered a cancer-related protocol.

Committee Composition

The CPRC is composed of members with scientific expertise in medical oncology, hematology, blood and marrow transplant, pediatrics, epidemiology, pharmacology, radiation oncology, radiology, and cancer control and prevention, to encompass the portfolio of cancer related research conducted at the University of Minnesota. Chairs of the committee are appointed by MCC Executive Leadership.

Conflict of Interest Management

CPRC members will be recused from decision-making discussions during reviews of any trial in which they are Principal Investigator or investigator initiated trials in which they are a Co-Investigator.

Initial Review Process & Policies

Schedule

1. The CPRC meets twice monthly, on the first and third Tuesdays.
2. Submission deadlines are 14 calendar days prior to the scheduled meeting.
3. Applications will not be assigned to an agenda until all required documentation has been submitted.
4. Meeting agendas will generally prioritize protocols in the order they were received.
    a. Note: Meeting a submission deadline does not guarantee a spot on the corresponding agenda, but the committee will include as many submissions as possible (regardless of submission date) based on reviewer availability.
5. Protocols applicable for Administrative, Cede, or Exempt review are not assigned to an agenda.

CPRC Submission

1. Submission deadlines and applications are posted on the CPRC website.
2. All applications (except Exempt and studies not requiring OnCore entry) are submitted via the Electronic Protocol Review and Monitoring System (ePRMS) in OnCore.
    a. Please review the ePRMS Submission Guideline document on the CPRC website for instructions on submission and OnCore access.
3. Required documentation is listed within each application located on the CPRC website.

Types of Initial Reviews

1. **Full Review**
    a. Study types:
        i. Interventional
        ii. Ancillary/correlative studies

b. Review Process:
    i. Reviewed at a committee meeting by 2 clinical reviewers and 1 biostatistician reviewer.
    ii. Review results sent within 5 business days after the meeting.

2. **Administrative Review**
    a. Study types:
        i. Observational trials
        ii. Trials involving healthy participants
    b. Review Process:
        i. Reviewed by 1 clinical reviewer and 1 biostatistician reviewer.
        ii. Review results are expected within 5-10 business days from submission.

3. **Cede Review**
    a. Study types: Interventional, ancillary/correlative and observational protocols that are either:
        i. Approved by the NCI's Cancer Therapy Evaluation Program (CTEP) or the Cancer Control Protocol Review Committee.
        ii. Multi-site investigator initiated trials (IITs) where UMN is a participating site and the lead site is an NCI-designated Cancer Center whose Protocol Review and Monitoring System (PRMS) has approved the study.
            1. As part of the NCI Cancer Center Support Grant (CCSG), which designates Comprehensive Cancer Centers, the NCI will either state that the committee is fully approved until the next competitive renewal or it will state that there were concerns with committee conduct and grant conditional approval.
            2. If a site's scientific review committee does not have full approval by the NCI, we cannot cede scientific review to them and must perform our own scientific review at UMN before the trial can be activated.
        iii. M Health Fairview-managed protocols open in community (non-UMN) clinics via the Minnesota Cancer Clinical Trials Network (MNCCTN)
            1. As these protocols will be routed for CPRC review by MNCCTN, separate submissions for CPRC review from Fairview will be ceded to the MNCCTN review and acknowledged by the CPRC.
    b. Review Process:
        i. Applications reviewed by the Committee Manager.
        ii. Acknowledgment letters expected within 5 business days from submission.

4. **Exempt Review**
    a. Study types:
        i. Protocols that meet the criteria to be Exempt by the IRB.
    b. Review Process:
        i. Reviewed by a CPRC Chair.
        ii. Review results are expected within 5 business days from submission.
        iii. All studies are given the review outcome of "study may proceed" with no requirement to respond to reviewer comments prior to activation.

Discussion

The Chair or committee member designee leads a comprehensive discussion of a protocol with the committee including but not limited to all of the following:

1. Evaluation of Scientific Merit: The committee considers the scientific relevance, validity, justification of the hypothesis, completeness of the protocol, adequacy of the study design, biostatistical plan, subject availability, and feasibility of study completion in the proposed time-period.
2. Prioritization of Protocols: (if applicable) The committee considers competing protocols, impact on subject availability, MCC research priorities and resources, and endorsement by the interdisciplinary site-specific cancer care (ISC) team when applicable.
3. Data and Safety Monitoring Plan (DSMP): (if applicable) The committee reviews the data and safety monitoring plan for the protocol and verifies that the proposed plan is commensurate with the level of risk and correlates with the monitoring guidelines described in the University of Minnesota Masonic Cancer Center Data and Safety Monitoring Plan.

Discussion points to be included in the review:

- Acceptable title
- Justification for conducting the study and results of similar studies or pilot data
- Protocol phase description alignment with study design and research objectives
- Federal oversight (IND, IDE, ITP), if applicable
- Purpose of study and brief outline of proposed research to be evaluated
- Treatment or study plan (doses, schedules, dose adjustments, duration of therapy, design and conduct of study)
- Specific inclusion/exclusion requirements, which must be met.
- Adverse event reporting (compliance with FDA regulations, CTEP guidelines for toxicity reporting, Clinical Trials Office SOPs)
- Intervention information (description, formulae, known toxicities, means of supply, methods of storage, methods of procurement)
- Outcomes adequately described
- Data elements are complete, supportive of hypothesis/objectives, and support the analysis plan
- Statistical section (description of endpoints, method of analysis, justification of proposed accrual Schema and road map-diagram, algorithm or visual representation describing the proposed research plan (local, interventional studies only)
- Data and safety monitoring plan (SAE/AE reporting requirements, stopping rules for accrual suspension and study termination, entity monitoring patient safety and frequency of monitoring
- Total expected accrual
- Duration of accrual
- Associated risks with the trial
- Concerns regarding scientific merit
- Study type (observational with monitoring, non-treatment interventional, other, etc.)
- Risk level (high, moderate, low, minimal and not applicable)
- Citations for validity of patient-reported outcome instruments (see http://www.nihpromis.org/default)

Initial Review Decisions

Following CPRC discussion, the Committee votes to on the review determination for the protocol. The decision is indicated on the Chair Decision form and is signed by the Chair or committee member designee.

1. **Approved**
    a. The protocol meets all criteria for scientific merit, prioritization with no changes required. Can proceed with IRB review.

2. **Approved with Minor Stipulations**
    a. The protocol has minor areas the PI must address to satisfy full approval but the study may move to IRB review, e.g. minor clarifications in background data, spelling/grammar/typo corrections, clarification of non-treatment related components of protocol.
    b. The response to stipulations will be reviewed by all original reviewers. If the reviewers accept the response, final initial approval will be granted by the CPRC Chair. If the reviewers do not accept the response, additional stipulations will be sent to the PI.

3. **Approved with Major Stipulations** *(Investigator-Initiated and University Consortium Trials only)*
    a. The protocol has major areas the PI must address to satisfy full approval and is likely to require revision, e.g. questions about stopping rules, study endpoints, treatment delivery, etc. These must be resolved to no more than minor stipulations from the CPRC prior to IRB review.
    b. The response to stipulations will be reviewed by all original reviewers. If the reviewers accept the response, final initial approval will be granted by the CPRC Chair. If the reviewers do not accept the response, additional stipulations will be sent to the PI.

4. **Deferred**
    a. The protocol requires significant changes, which solicits full committee review of the response and revised protocol prior to IRB review.
    b. Examples include:
        i. Inadequate stopping rules
        ii. Trial design questions that would limit ability to answer study objectives.
        iii. Issues can be addressed within the current proposal.
        iv. Major components missing from the protocol.

5. **Disapproved**
    a. The protocol as written does not warrant activation due to insurmountable concerns with scientific validity/merit and will require a re-design of the protocol.
    b. Examples include:
        i. Fatal design flaw--scientific methodology is fundamentally flawed; revision of the current proposal would not allow the flaws to be overcome.
        ii. The hypothesis/objectives cannot be reached with the current study design.
        iii. The background does not adequately support the research plan.
    c. The investigator is allowed one appeal to this decision with a revised protocol that addresses committee concerns.

6. **Study May Proceed**
    a. The trial appears to meet criteria for IRB Exemption and may proceed with activation. Comments are provided to guide the investigator, but do not need to be resolved with the committee.

Ongoing Post-Approval Review

Protocol Amendments

Amended protocols must receive CPRC approval or acknowledgement regardless of the extent of the revisions. The PI should provide a tracked changes copy of the amended protocol, a summary of changes and a completed CPRC Amendment Application which includes documentation of whether the change affects the study's scientific objectives, study design or statistical analysis plan, a brief summary of the change(s), and the rationale for the change(s).

1. **Full Committee Review**
    a. Amendments involving change in scientific objectives, study design or study statistical analysis plan will receive full committee review.
    b. This excludes protocols approved via the Cancer Therapy Evaluation Program (CTEP) under the NCI or multi-site investigator initiated trials (IITs) where the initial CPRC review was ceded to the sponsoring institution--an NCI Comprehensive Cancer Center), which fall into the Acknowledgement category listed below.
    c. The IRB will not advance a submitted amendment for review until CPRC approval has been granted.
    d. Once approval is granted the CPRC Manager will distribute a CPRC amendment approval letter to the PI, project manager, regulatory specialist and protocol writer (if personnel are listed as active in these roles in the Staff section of OnCore).

2. **Administrative Review**
    a. Amendments that do not involve change in scientific objectives or study design can be simultaneously submitted to the IRB and the CPRC and will be administratively reviewed by the Chair or committee member designee.
    b. This excludes protocols approved via the Cancer Therapy Evaluation Program (CTEP) under the NCI or multi-site investigator initiated trials (IITs) where the initial CPRC review was ceded to the sponsoring institution--an NCI Comprehensive Cancer Center), which fall into the Acknowledgement category listed below.
    c. Once approval is granted the CPRC Manager will distribute a CPRC amendment approval letter to the PI, project manager, regulatory specialist and protocol writer (if personnel are listed as active in these roles in the Staff section of OnCore).

3. **Acknowledgement**
    a. Amendments for protocols that had an initial Cede Review will be sent an acknowledgment letter by the CPRC manager and do not need administrative or full committee review.

Continuing Reviews

The purpose of CPRC continuing review is to ensure studies are meeting their stated accrual goals and to evaluate for ongoing scientific merit.

Continuing review for interventional and ancillary/correlative CPRC approved studies will begin six months after the study opens to accrual. Observational studies are exempt from annual reviews.

Continuing review approval notices will not be sent to studies meeting the accrual and scientific merit requirements outlined below.

1. **Continuing Review Criteria**
    a. Upon bi-annual review, justification requests will be sent for studies with:
        i. Zero accruals after 6 months of initially opening to accrual.
        ii. <50% of the annual accrual goal after being open to accrual for >6 months.
        iii. Continued scientific merit in question.
    b. If sufficient justification is provided, the study will have 6 months to increase accrual.
    c. Studies that do not meet the above outlined thresholds after subsequent review in 6 months will be permanently closed.

2. **Low Accrual Review Exemptions**
    a. Protocols that address rare tumors or molecular phenotypes may be exempt from accrual expectations, but are still eligible for annual scientific merit review.

3. **Continuing Review Exemptions**
    a. Observational studies and those that do not meet requirements for initial review are completely exempt from the CPRC continuing review process and will not be evaluated for continuing review. This includes non-cancer protocols.
    b. Protocols categorized as "Not Applicable" for inclusion in NCI Data Table 4 are exempt from CPRC continuing review.
        i. This categorization is noted in OnCore's PC Console, Main screen, Details tab in the "Protocol Details" section.

4. **Discontinuation of Continuing Reviews**
    a. Once a study is closed to accrual, CPRC continuing reviews are discontinued. Notification or a final report will not be sent out to the investigator.

Recording Study Enrollment

1. **Individual participant information, including race, ethnicity, and gender, needs to be entered in real time as participants are accrued in either OnCore or REDCap** for NCI required CTRP reporting and MCC Leadership metrics.
    a. This is separate from the CTSI/Medical School requirement to enter summary accrual data in OnCore. If teams are only entering summary accrual data in OnCore, they must also be entering individual accrual data in REDCap in real time.

2. **Protocols using REDCap for individual participant registrations**:
    a. Teams must use the UMN MCC REDCap Subject Registration Template in the UMN REDCap Shared Library and follow the guidelines outlined in the MCC REDCap Subject Registration Code Book when setting up their data fields in REDCap.
        i. Template instructions and the codebook can be found on the CPRC website. You are required to add Vidhya Ramesh (rames007@umn.edu) from MCC OMIS to the project within REDCap in order to generate accurate data for NIH reporting requirements.
        ii. Teams choosing to use REDCap are encouraged to utilize the Masonic Cancer Center Data Solutions Group to assist with template development (contact: dsg1@umn.edu).

Differentiation from the Institutional Review Board

The CPRC and the IRB operate independently. The CPRC reviews all cancer-related research prior to IRB review. Protocols must be approved by both the CPRC and the IRB prior to activation.

The responsibilities of the IRB and the CPRC can be distinguished as follows.

1. The CPRC is responsible for scientific review and prioritization with competing trials.
2. IRB conducts risk/benefit assessment of the protocol. The CPRC may discuss risk/benefit issues, but ordinarily these do not form the basis of CPRC decisions.
3. IRB reviews consent forms and other materials provided to subjects as these are not reviewed by CPRC.