Cancer Protocol Review Committee (CPRC)

Charter

Version 1

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Masonic Cancer Center

University of Minnesota

Comprehensive Cancer Center designated by the National Cancer Institute

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, feasible, and impactful research studies which 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 Mark Kirstein, PharmD and Brenda Weigel, MD, MSc. 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.

Committee Chairs

Mark Kirstein, PharmD
Associate Professor
College of Pharmacy and Masonic Cancer Center

Brenda Weigel, MD, MSc
Professor of Medicine
Division of Pediatric Hematology and Oncology

CPRC Review Oversight

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

The CPRC determination of clinical research is exclusive from an IRBs definition. Some 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.

2. The CPRC **does not** review:
    a. Single subject or compassionate use studies
    b. Specimen banking studies
    c. Retrospective chart or retrospective data review studies
    d. Patient populations outside the University of Minnesota
    e. Non-cancer research studies
        i. These protocols can be reviewed by the CPRC if the study will be managed by the Clinical Trials Office.

Committee Composition

The CPRC is composed of members with scientific expertise in medical oncology, hematology, blood and marrow transplant, pediatrics, epidemiology, pharmacology, 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.

Initial Review Process & Policies

Schedule

The CPRC meets twice monthly, on the first and third Tuesday. Submission deadlines are 14 calendar days prior to the scheduled meeting.

1. All protocols not applicable for Administrative, Cede, or Exempt review are placed on the CPRC meeting agenda and receive full scientific review.
2. Protocol reviews result in one of six determinations: approval, approval with major stipulations, approval with minor stipulations, deferral, disapproval, or study may proceed.

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 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. 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.

a. Review Process:
    a. Applications reviewed by the Committee Manager.
    b. Acknowledgment letters expected within 5 business days from submission.*

4. **Exempt Review**
    a. Study types:
        i. Those which 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.

**These trials are subject to feasibility review concurrently with the CPRC review. Letters can be delayed depending on feasibility reviewer turnaround time.*

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
- 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)
- 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

- 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

- 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)

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**
    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 end points, 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 study 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 study protocol as written does not warrant activation due to insurmountable concerns with scientific validity/merit and will require a re-design of the protocol.
        i. Examples include:
            1. Fatal design flaw--scientific methodology is fundamentally flawed; revision of the current proposal would not allow the flaws to be overcome.
            2. The hypothesis/objectives cannot be reached with the current study design.

3. The background does not adequately support the research plan.

b. The investigator is allowed one appeal to this decision with a revised protocol which 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. The PI should provide a tracked changes copy of the amended protocol, a summary of changes and either an IRB Change in Protocol Form or a CPRC Amendment Application which include a checklist for determining if the change affects the study's scientific objectives or study design, a brief summary of the change, and the rationale for the change.

1. **Full Committee Review**
   Amendments involving change in scientific objectives or study design will receive full committee review. (This excludes NIH peer reviewed studies, which fall into the Acknowledgement category below.) The IRB will not accept the submission until CPRC approval has been granted. Once approval is granted the CPRC Manager will submit a CPRC amendment approval letter to the PI, project manager, and regulatory specialist.

2. **Administrative Review**
   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. Again, this excludes NIH peer reviewed studies, which fall into the Acknowledgement category below. Once approval is granted the CPRC Manager will submit a CPRC amendment approval letter to the PI, project manager, and regulatory specialist.

3. **Acknowledgement**
   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.

4. **Discontinuation of Amendment Reviews**
   Once a study is closed to accrual, the CPRC will not review any further amendments to the protocol unless the changes affects patients currently on study or in follow up at the University of Minnesota.

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. Annual review for interventional and ancillary/correlative CPRC approved studies will begin one year after the initial CPRC approval date. Review periods are 12 months and begin one year from the date of the last review. Observational studies are exempt from annual reviews.

1. **Justification Requests**
    a. Upon annual review, justification requests will be sent for studies:
        i. Accruing less than 50% of the annual accrual goal
        ii. Not open within 1 year of CPRC initial approval
        iii. Whose continued scientific merit is in question
    b. If sufficient justification is provided, the study will be approved to continue for another year.

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

3. **Continuing Review Exemptions**
    Observational studies and those which do not meet requirements for initial review are completely exempt from the CPRC continuing review process and will not be evaluated on an annual basis.

4. **Closure Process**
    a. The CPRC may recommend closing of protocols to accrual if the circumstances below apply:
        i. New scientific findings have obviated the need to continue the study
        ii. Research conduct is of such poor quality that the integrity of the data is questionable
        iii. Subject accrual is significantly below expectations
    b. A recommendation of closure will be relayed to PI, research staff, and MCC leadership.

5. **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.

Interaction with 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.

- The CPRC is responsible for scientific review and prioritization with competing trials.
- 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.
- IRB reviews consent forms and other materials provided to subjects as these are not reviewed by CPRC.