Medical College of Wisconsin Cancer Center

Scientific Review Committee (SRC) Charter

Version Date
05/03/2025

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List of Abbreviations

BMT CTN	Blood & Marrow Transplant Clinical Trials Network
CAP	Corrective action plan
CCSG	Cancer Center Support Grant
CTO	Clinical Trials Office
CREC	Clinical Research Executive Committee
DSMC	Data and Safety Monitoring Committee
FC	Feasibility Committee
iDOT	Integrated Disease-Oriented Team
IIT	Investigator-initiated trial
IND	Investigational New Drug
IRB	Institutional Review Board
MCWCC	Medical College of Wisconsin Cancer Center
NCI	National Cancer Institute
NCTN	National Clinical Trials Network
PI	Principal investigator
PRMS	Protocol Review and Monitoring System
SRC	Scientific Review Committee

1.0 Protocol Review and Monitoring System Overview

The Protocol Review and Monitoring System (PRMS) at the Medical College of Wisconsin Cancer Center (MCWCC) comprises of two stages: the integrated Disease-Oriented Teams (iDOTs, stage 1) and the Scientific Review Committee (SRC, stage 2). These committees foster the development and implementation of innovative, collaborative, and scientifically-sound studies that focus on prevention, detection, diagnosis, and treatment of cancer, as well as long-term follow-up and care.

The protocol review and activation process is shown schematically in **Appendix A**. The first stage of protocol review occurs within the 16 disease- or discipline-specific iDOTs. Each meets monthly to exchange ideas and evaluate their research portfolio (active and pending trials). iDOTs discuss the feasibility and merit of new concepts and protocols proposed by members, as well as protocol prioritization. An important function of the iDOTs is to provide mentorship to members with clinical research ideas so that these concepts can be developed into high quality, fundable protocols. iDOT members also review accrual to active trials and consider the closure of low accruing trials to free up resources for potentially more successful studies. The Adult and Pediatric Feasibility Committees (FCs) provide additional input to the iDOTs by determining if adequate financial and staff resources are available for trial conduct and for prioritizing trials across iDOTs.

The second stage of review is done by the SRC, which is composed of oncologists from a range of disease groups and modalities, biostatisticians and a community representative. The SRC meets twice per month and reviews all proposed clinical cancer-related protocols. In addition to reviewing new protocols, the SRC monitors the scientific progress of active protocols. The SRC is empowered to close trials to further accrual if the scientific objectives of the trial are no longer relevant, or if the rate of MCWCC accrual to the study is too low to justify keeping it open.

The iDOTs and SRC operate in collaboration with and are supported by the Clinical Trials Office (CTO) and maintain separate responsibilities and reporting. The PRMS review process is complementary to and independent of Institutional Review Board (IRB) review and oversight. For cancer-related protocols, SRC approval is required before a protocol can by reviewed by the IRB, and both the PRMS and IRB must approve a protocol before it can be activated. The IRB focuses on the ethical and regulatory requirements for the conduct of research involving human subjects, paying particular attention to subject safety, while the SRC primarily reviews scientific quality and merit.

Policies for the iDOTs, FCs, SRC and Data and Safety Monitoring Committee (DSMC) are provided by the MCWCC Clinical Research Executive Committee (CREC), which meets quarterly and ad hoc for urgent matters. The committee oversees and directs clinical research at the MCWCC and its affiliates. CREC establishes clinical research priorities, reviews general accrual and resource allocation issues and facilitates integration of research into the multidisciplinary clinics. CREC is chaired by the Associate Director of Clinical Research who has direct responsibility for overseeing the activities of the iDOTs and FCs. Oversight of the SRC and DSMC is provided by the Deputy Director, to avoid conflicts of interest.

2.0 Scientific Review Committee

The MCWCC SRC ensures that MCWCC clinical trials are scientifically sound and that approved trials maintain patient accrual goals and scientific progress. Specific functions of the SRC include:

- Maintaining a committee of sufficient size and breadth of expertise to conduct critical and fair scientific reviews of cancer-related research involving human subjects
- Conducting thorough scientific review of all non-peer-reviewed, cancer-related clinical protocols using a standard format based on specific, pre-determined review criteria
- Providing feedback to MCWCC investigators to enhance the development of scientifically and clinically sound research through well-written protocols
- Reviewing how each new protocol complements the overall trial portfolio of MCWCC

- Establishing clear criteria for determining whether ongoing clinical trials are making sufficient scientific progress, including the attainment of adequate patient accrual rates
- Monitoring accrual to all cancer-related research protocols, notifying investigators of underperforming studies, requesting corrective action plans, and terminating protocols that do not meet accrual thresholds

2.1 Committee Composition and Roles

SRC members are appointed by the MCWCC Deputy Director. At least 14 individuals serve on the SRC with members from each of the following Divisions, Departments and disciplines: Pediatric Hematology/Oncology, Adult Hematology/Oncology, Gynecologic Oncology, Radiation Oncology, Surgical Oncology, Population Science, Basic Science, Biostatistics, and an external community representative. Members are invited to participate based on subject matter expertise, as well as proficiency in the design, conduct and analysis of clinical trials. SRC members cannot also serve as DSMC members (membership of the two committees cannot overlap). Ad hoc members may be appointed to the SRC based on areas of research and expertise needed for specific protocol review. The SRC Chair is appointed by the MCWCC Deputy Director in consultation with the Cancer Center Director. The responsibilities of the Chair include the following: conducting bi-weekly SRC meetings, maintaining the integrity and quality of the SRC, assigning protocols to SRC members for review, monitoring accrual and identifying low-accruing trials, communicating committee actions to principal investigators (PIs), and reporting SRC activities to the MCWCC leadership. The Co-Chair performs the responsibilities of the Chair when delegated. SRC members are appointed to three-year, renewable terms. The Deputy Director meets with the SRC Chair and co-Chair and the PRMS manager quarterly to review activities and address issues.

The SRC is supported by PRMS Coordinators, who are CTO staff members. The coordinators are responsible for maintaining SRC records: a log of appointment and term length of SRC members, the database of protocols reviewed by the SRC, files pertaining to reviewed protocols (agendas, attendance sheets, protocols, reviews, letters to PIs, etc.), and meeting minutes. The coordinators also assist PIs in preparing submissions to the SRC, ensuring all documentation is complete. A coordinator is responsible for running accrual reports and providing a summary of low-accruing studies to the SRC Chair for review and potential closure. Lastly, staff provide any other administrative support as required by the SRC Chair or committee.

SRC Ad Hoc Reviewers

The SRC may utilize ad hoc reviewers when additional, specialized expertise is needed to adequately review a protocol, especially an investigator-initiated trial. For example, external expert reviewers were utilized when the first MCWCC cellular therapy protocols were reviewed by SRC. In the event that an ad hoc reviewer is contacted, the reviewer provides a written evaluation of the protocol and attends the full SRC meeting if possible. The disposition of the protocol is voted on by the full committee.

2.2 New Protocol Submission to the SRC

The SRC reviews prospective, hypothesis-driven, cancer-related studies. After a protocol is reviewed and approved by an iDOT and FC, it is submitted to the SRC for review. Every protocol submission is accompanied by a completed New Trial Submission Form (**Appendix B**) and Prioritization Scoresheet (the latter only for interventional trials managed by the CTO). The New Trial Submission Form helps the SRC categorize studies for review and provides SRC reviewers with basic information about a trial such as the target accrual, the proposed timeline, and the existence of competing protocols, etc. Studies involving INDs must also provide an Investigator's Brochure for the SRC's reference. For industry trials, the sponsor must select MCW as a participating site before the protocol is submitted to the SRC.

Investigator-initiated trials (IITs) must meet additional requirements before they can be accepted for SRC review. As of April 2025, all IITs must first undergo review by the IIT Steering Committee (concurrent with iDOT review) before being submitted to the SRC, to ensure that quality protocols are entering the study activation pipeline. Also, IITs requiring FDA approval must complete FDA review before being submitted to the SRC.

2.3 SRC Protocol Review Process

2.3.1 Levels of Protocol Review

There are two levels of SRC review: Full Committee Review and Expedited Review. The SRC Chair determines the level of review according to the type of trial (**Table 1**).

Table 1. Levels of SRC review for new cancer-related protocols

Review Type	Study Type
Full Committee Review	• Interventional studies (treatment, non-treatment) ▪ Investigator-initiated – primary and secondary reviewer ▪ Investigator-initiated from another center – primary reviewer ▪ Industry-initiated – primary reviewer ▪ Consortium – primary reviewer • Non-interventional investigator-initiated studies – epidemiological or observational studies involving cancer patients or healthy subjects with a cancer focus (*e.g.*, population science, surveillance, risk assessment, behavioral) – primary and secondary reviewer • Correlative or ancillary investigator-initiated studies – primary reviewer ▪ Imaging, diagnostic ▪ Prospective studies of tissues, body fluids with a scientific hypothesis ▪ Prospective molecular or genetic epidemiology studies that evaluate aspects of patient care but do not answer questions about impacts of particular interventions and do not use information from tests to alter treatment for study subjects
Expedited Review	• National Clinical Trials Network (NCTN), Blood & Marrow Transplant Clinical Trials Network (BMT CTN), and protocols approved by the NCI's Cancer Therapy Evaluation Program or the Cancer Control Protocol Review Committee (these are not reviewed for scientific merit but rather for prioritization and portfolio fit only) • Multisite institutional trials already reviewed and approved by an institution with a fully acceptable PRMS (not conditionally acceptable or unacceptable) • External noninterventional studies • Noninterventional survey/questionnaire IITs
Exempt from Review	• Emergency Use, Expanded Access, Treatment Use • Medical chart reviews, retrospectives • Registries, Tissue Bank studies with no scientific hypothesis • FDA-required long-term follow-up protocols for patients who received cell/gene therapy • Population-based studies using cancer patients and healthy subjects where focus of study is not cancer-related

Full Committee Review: The SRC Chair assigns committee members to review protocols based upon member expertise. Any SRC member serving as a PI, co-PI, or sub-investigator of a protocol coming before the committee for scientific review is considered to have a conflict of interest and is not allowed to serve as a reviewer for that protocol. The Coordinator sends the protocol, the appropriate SRC Reviewer Form, and

any other supporting documentation (Investigator's Brochures, PI responses to comments, etc.) to the reviewers approximately one week before the SRC meeting. All therapeutic protocols are reviewed by at least one physician member of the SRC and a biostatistician; IITs are reviewed by two physicians and a biostatistician. At the meeting, the primary reviewer summarizes the protocol for the committee. Then, the primary and secondary (where applicable, See Table 2) reviewers present their comments and recommendations, which are discussed by the full committee. Statistical considerations are addressed by the biostatistician, and other members are given the opportunity to comment or ask questions. The assigned reviewers are required to complete and submit the appropriate SRC Reviewer Form. In the event a protocol is "Deferred" or "Disapproved" by the SRC, the PI is welcome to attend a subsequent meeting to answer questions about his or her protocol. The PI may give a 5-minute synopsis of the trial and answer the committee's questions, but they are not present for further discussion or for the vote.

The SRC normally meets on the first and third Monday of every month. If the volume of submissions is high, then the SRC may schedule a third meeting. A meeting quorum requires the presence of 50%+1 of voting members. Each SRC member has one vote, including the chair. On protocols where an SRC member is a PI or Co-PI, the member cannot be present for the vote. Sub-investigators may be present but must recuse themselves from discussion and voting.

Expedited Review: Studies qualifying for Expedited Review are reviewed by the SRC Chair or co-Chair. At their discretion, the chairs can approve studies, request clarifications, or send the study to full committee for review. The outcomes of Expedited Reviews are reported to the full committee at the next scheduled meeting. These protocols are submitted and reviewed on a rolling basis, to avoid delaying the process of subsequent IRB review and approval.

2.3.2 Amendment reviews

All substantive changes to MCW investigator-initiated and externally sponsored protocols must be reviewed and approved by the SRC (**Table 2**). NCTN and BMT CTN amendments are exempt as their science receives sufficient external peer review; FDA-required long-term follow-up protocols for patients receiving cell/gene therapy are also exempt. PIs submit the following to the SRC: a summary of changes with justifications, the revised protocol with changes tracked, and the revised protocol clean.

Table 2. Amendment types reviewed by the SRC and exempted from review

Review Type	Amendment Types
SRC Review	Scientific changes, including but not limited to: • Inclusion or exclusion criteria • Drug dosage or delivery, treatment, schedule • Objectives or endpoints • Study design, methods, response criteria • Biostatistics, sample size (accrual goal) • Change in stopping rules • Sample collection (e.g., additional time points, sample types) • Change from institutional single-center study to multi-center study where MCW is coordinating center
Exempt from Review	Administrative changes, including but not limited to: • Personnel • Consent form • Investigator's Brochure • Recruitment material • Non-scientific changes to protocol • Clarifications to AE reporting, etc.

The level of SRC review is at the Chair's discretion. Minor changes may be given an Expedited Review by the Chair, while more substantial changes will receive Full Review. When a change is related to the protection of

research subjects, the IRB is obligated to review the request immediately. In this event, IRB approval will not require prior SRC approval.

2.3.3 Protocol Review Criteria

The SRC is responsible for reviewing the scientific merit of protocols and determining whether the research question and study design are scientifically sound and feasible. Additionally, the SRC reviews the clarity and thoroughness of the protocol document. Specifically, the SRC evaluates the following:

- Background information – Relevant literature is summarized, citations are included, and a clear rationale for the study is presented.
- Study objectives – The objectives are clear, appropriate, and feasible.
- Study design – The design is appropriate for accomplishing the objectives.
- Patient registration – Procedures for registering subjects are included, as is the contact information for the person to whom questions about eligibility and treatment should be directed.
- Eligibility criteria – Criteria are clear, thorough, and include laboratory parameters.
- Treatment plan – Dosage, duration, and follow-up are specified, as are subject withdrawal criteria.
- Study calendar – A schedule of labs and procedures is provided.
- Toxicities – The toxicity criteria are clearly stated and the grading system is identified.
- Pharmacy considerations – Drug procurement, storage, administration, dosage, and interactions etc. are provided.
- Endpoints – The endpoints are clear and appropriate.
- Statistical considerations – The proposed statistical tests are appropriate for answering the study question, the sample size will provide sufficient statistical power, appropriate stopping rules are included.
- Data and safety monitoring – According to the MCWCC Data and Safety Monitoring Plan, all interventional protocols must have an appropriate data and safety monitoring plan specified. Also, protocols should have a risk-based quality assurance review plan specified.

The community representative assesses protocols for their acceptability and accessibility to patients in the catchment and the potential burden of protocol required assessments for patients.

These and other criteria are detailed in the SRC Reviewer forms (**Appendix C-F**).

2.3.4 Committee Actions

After reviewing a protocol, the SRC recommends one of the following actions:

- *Approved:* The protocol is scientifically sound and acceptable as written and may be forwarded to the IRB without modifications.
- *Approved with Clarifications:* The protocol is scientifically sound and acceptable pending PI clarification of specific points. The PI must submit a copy of any protocol revisions to the Chair for expedited review and approval.
- *Deferred:* The study requires significant revisions to satisfy review criteria. The PI must submit a revised protocol and a written response to the SRC's concerns. The protocol will then receive an SRC re-review at a full committee meeting.
- *Disapproved:* The study is not scientifically sound, not ethical, not acceptable as written, and/or is not within the mission of the MCWCC. The PI can resubmit the protocol as a new study if substantive changes that address the SRC's concerns are made.

The actions of the SRC are recorded in committee minutes and in the Clinical Trial Management System. For approved protocols, the Chair sends a letter notifying the PI, iDOT Chair, and research manager (if applicable) of the approval, the study's categorization for accrual monitoring (rare or not rare), its expected annual accrual goal, and its assigned risk category (for interventional investigator-initiated trials only). For committee decisions

requiring a response from the PI, the Chair sends a letter to the PI within seven days of the SRC meeting. PIs of protocols that were “Approved with Modifications” are expected to respond to SRC comments within 30 days. These responses are given an Expedited Review by the SRC Chair and usually the assigned reviewers. PIs of “Deferred” protocols are expected to respond to SRC comments within 60 days. PI responses to “Deferred” are re-assigned to the original reviewers whenever possible and placed on the next available meeting agenda. They go before the full committee and are evaluated with the same possible outcomes as above.

3.0 SRC Monitoring of Ongoing Protocols

Per the National Cancer Institute’s Cancer Center Support Grant guidelines, the SRC is responsible for monitoring the progress of trials open to accrual. Protocols are reviewed by the SRC for continued scientific relevance, progress towards completion of scientific objectives, and accrual, including accrual of underserved populations such as women, minorities, children, and the elderly.

3.1 Annual Review for Scientific Relevance

On an annual basis, the SRC reviews the entire MCWCC trial portfolio for ongoing scientific relevance. For each iDOT, the SRC generates a list of trials that are currently open or suspended, including the protocol’s title, PI, and accrual history. The lists are sent out to the iDOTs, which then add the review as an item on their next meeting agenda. For each protocol, iDOTs are asked to confirm whether any change in standard of care, other progress in the field, or new safety information has arisen in the previous 12 months that impacts the scientific relevance or value of the trial. If there has been a change, the iDOT is asked to describe it. Once the iDOT has reviewed and responded, the iDOT Chair or Vice Chair must sign off on the report, confirming its accuracy to the best of their knowledge. The SRC Chair or Co-Chair reviews the reports to determine whether any action (including further discussion with the iDOT or potential trial closure) needs to be taken.

3.2 Accrual of Populations in the Catchment Area

The PRMS is responsible for monitoring accrual demographics to ensure that trial participants are being enrolled in proportion to their frequency in the Catchment Area. On a quarterly basis, the SRC Coordinator generates interventional treatment accrual reports for each iDOT, summarizing the iDOT’s accrual by race, ethnicity, gender, and age (older adult and pediatric). The reports include data from the previous year to help iDOTs understand trends. For comparison purposes, the reports also include new patient demographics from recent tumor registry data, as an approximation of the demographics of the hospital’s cancer patient population.

Each quarter, the underserved accrual reports are sent to the iDOTs, and iDOTs are required to discuss their reports at their next available iDOT meeting. Accrual reports are also reviewed by the CREC and MCWCC leadership.

3.3 Monitoring Low-Accruing Trials

Low-accruing trials may fail to reach enrollment levels necessary for properly evaluating the hypotheses being tested, or the cost of maintaining them may outweigh the benefit of keeping them open. The SRC is empowered to identify low-accruing trials and initiate their closure. The SRC Coordinator generates monthly reports in OnCore, identifies protocols due for review, and reports these to the SRC Chair. The iDOTs also monitor study accrual and may initiate study closure or amendment.

Below is a summary of the SRC’s policy. Please see **Appendix G** for a full description.

Review Criteria

The SRC is required to monitor accrual to Cancer Center clinical trials. Trials that do not meet the expected minimum annual enrollment per this policy (**Table 3**) will be notified and given the opportunity to take corrective action. If enrollment does not improve, then they will be closed to further accrual.

Table 3. Accrual Monitoring Guidelines

<table>
<tr><th>Trial type</th><th>Industry, external institutional (external investigator-initiated, consortium)</th><th>National (NCTN, BMT CTN)</th><th>Investigator-initiated</th><th>Rare disease</th></tr>
<tr><td>Expected annual enrollment</td><td>At least 40% of projected, or minimum of 2 (whichever is greater)</td><td>At least 40% of projected, or minimum of 1 (whichever is greater)</td><td>At least 40% of projected</td><td rowspan="5">Initial review at 2 years, then reviewed annually for overall activity

Zero accrual at 2 years: Review screening history and ongoing scientific relevance with iDOT</td></tr>
<tr><td>6 Months</td><td colspan="3">Minimum accrual met: Reviewed again at 12 months
Zero or low accrual: Warning issued, corrective action plan (CAP) requested; reviewed again at 9 months</td></tr>
<tr><td>9 Months</td><td colspan="3">Minimum accrual met: Reviewed again at 12 months
Zero or low accrual: Warning reminder issued, listed for potential closure at 12 months if no improvement</td></tr>
<tr><td>12 Months</td><td colspan="3">Minimum accrual met: Approved for 1 year
Low accrual: Reviewed by SRC for potential closure
Zero accrual: Closed to accrual</td></tr>
<tr><td>Years 2+</td><td colspan="3">Reviewed annually after initial 12 months open
Minimum accrual met: Approved for 1 year
Low accrual: Warning issued, corrective action plan (CAP) requested, re-reviewed in 6 months</td></tr>
</table>

Rare diseases, as a group, are an MCWCC priority cancer. Trials involving rare diseases are expected to have slow accrual, thus they are treated more leniently. The MCWCC uses an annual incidence of <6/100,000 people in the United States as a guideline for defining cancers as rare. Studies of rare molecular subtypes of common cancers are also rare if they are distinct subgroups that receive specific, targeted therapy. All pediatric trials are considered rare. Lastly, uncommon clinical situations of more common cancers are considered rare.

Trials may also be closed for lack of scientific merit, changing clinical practice patterns, loss of a key investigator, or for other reasons that would compromise the successful completion of trial objectives as determined by the SRC.

Appeals Process

When the SRC determines that a trial should be closed to accrual, the iDOT Chair and PI are by email. The trial's research manager, primary clinical coordinator, and regulatory coordinator also notified. If the iDOT Chair and PI feel that there are significant extenuating circumstances, they may appeal to the SRC for reconsideration. The SRC Chair makes the final determination regarding closure.

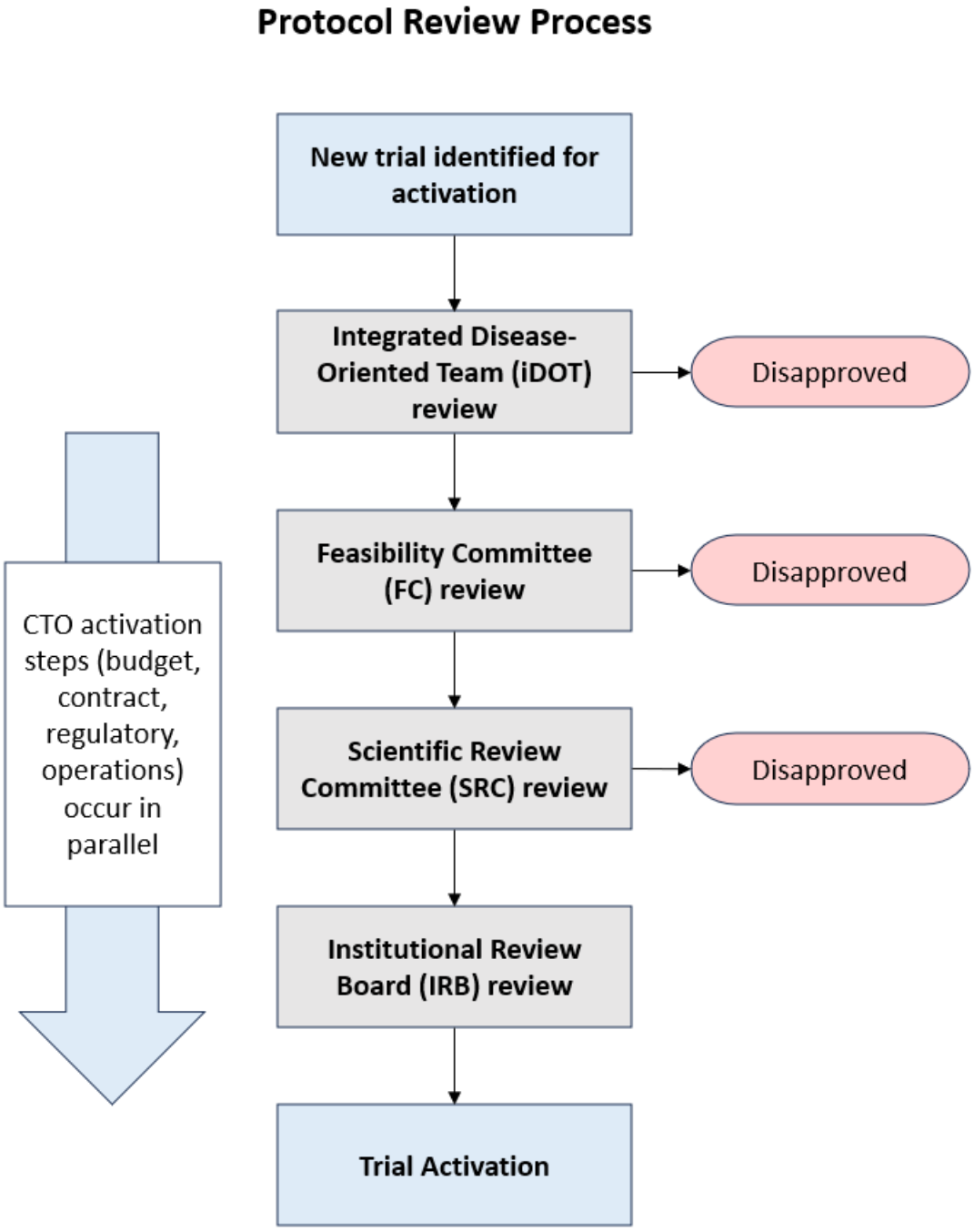
3.4 Studies Active Under 2017 Policy

Studies opened or already active under the 2017 accrual monitoring policy were grandfathered and continue to be monitored under that policy.

Under the 2017 policy:

- Studies were first monitored 12 months after opening and annually thereafter. Corrective action plans are requested from underperforming studies, and studies are granted 6 months to improve accrual.
- Rare disease studies are exempt from review.
- Non-rare studies have minimum annual accrual thresholds per below:
    - National trials (NCTN, BMT CTN) – at least 1 per year
    - Industry trials – at least 2 per year
    - External institutional trials – at least 2 per year
    - MCW IITs – at least 33% of projected annual accrual goal

Appendix A. Protocol Activation Process



Appendix B. New Trial Submission Form

Principal Investigator:	
Full Protocol Title:	
Patient-friendly Title:	
Planned study site(s):	☐Froedtert ☐CW ☐FMF ☐FWB ☐Drexel ☐Moorland ☐Community
Study Overview	
Type of Study	☐ MCW Investigator-Initiated ☐ NCTN/CTN ☐ External Institutional ☐ Industry/Pharmaceutical ☐ Consortium ☐ Other _____
	☐ Drug ☐Device ☐Radiation ☐Surgical ☐Behavioral/Education Intervention ☐Observational ☐ Other _____
	Scope of trial: ☐ Local (MCW/community) ☐ National/Multisite
	☐ Treatment ☐ Diagnostic ☐ Epidemiologic/Observational ☐ Supportive Care ☐ Device Feasibility ☐ Ancillary ☐ Screening ☐ Health Services Research ☐ Correlative ☐ Prevention ☐ Basic Science ☐ Other _____
Phase of Study	☐ I ☐ I/II ☐ II ☐ II/III ☐ III ☐ III/IV ☐ IV ☐ N/A ☐ Early Phase I ☐ Other _____ Pilot Study? ☐ Yes ☐ No
Authorship	Is authorship likely? ☐Yes ☐No If yes: ☐First/last author ☐Middle author Comments:
Accrual	
Local accrual goal	Projected annual accrual _____ Overall accrual duration (months) _____ Overall local accrual goal _____ How many patients with this specific disease are seen at our institution per year (include source of data for expected enrollment, e.g. tumor registry, EPIC, CDW, etc.)?
National accrual goal	Overall target accrual goal: Date accrual opened nationally: Current overall enrollment: Expected closing date:
Rare disease	☐ Check box if annual incidence is <6 newly diagnosed persons per 100,000 persons in U.S. (rare cancer, rare molecular subtype of common cancer, or unusual clinical situation)
Competing Trials	
Will this study compete with any currently accruing or pending trials? ☐ Yes ☐ No If yes, indicate which trial(s) and describe prioritization plan for enrollment:	

Funding Source

☐ NCTN/CTN ☐ Pharmaceutical ☐ MCW Cancer Center ☐ There is no funding for this study.
☐ Consortium ☐ Department ☐ Other_____ ☐ Additional funding is needed.
☐ NCI CTEP ☐ External Institutional
Is the budget negotiable? ☐Yes ☐No Comments:

For Investigator-Initiated Trials:
Funding Source: _____ Funding Proposal #:_____
Has funding been approved? ☐Yes ☐No Amount of award/approved funding: $_____

Study Complexity

No. of Arms ☐ 1 ☐ 2 ☐ 3 ☐ ≥4	**Eligibility Review** ☐ Basic ☐ Complex/multi-step	**Registration/Randomization** ☐ One step ☐ Multiple steps	**Frequency of Study Tasks** ☐ Daily ☐ Weekly ☐ Every 21-30 days or more

Department/Team Impact	☐ One or two departments involved – Standard clinical research team ☐ Three or more departments involved – Complex coordination needed ☐ Inpatient Care Required
Radiology	Is there an imaging requirement in the protocol? ☐Yes ☐No
	If Yes- The requirements are: ☐ standard ☐ study-specific For IITs, has a radiologist been identified as a collaborator? ☐Yes ☐No
Ancillary Studies	☐ Banking ☐ QoL ☐ PK samples ☐ Other
Data Collection on Treatment	☐ Basic – No AE reporting, batching of data ☐ Standard – AE reporting and data collection ☐ Complex – Real time data submission, review of source documents for endpoints, etc.
Follow-up Requirements	☐ Annual or minimal follow-up ☐ At each time point of clinical activity ☐ Complex multiple clinical points
Special Requirements	☐ IND application ☐ Clinicaltrials.gov ☐ Coordinating center for multi-site study ☐ Other
Beacon Build needed?	☐Yes ☐No

Additional Comments

Integrated Disease-Oriented Team approval to send to SRC:

iDOT Chair Signature Date

Appendix C. SRC Reviewer Form for Treatment Interventional Investigator-Initiated Protocols

Medical College of Wisconsin Cancer Center
Scientific Review Committee (SRC)

Treatment Interventional Investigator-Initiated Reviewer Form

All reviewers are expected to attend the SRC meeting. SRC meetings are held on the 1st and 3rd Monday of each month at 5 PM. Please e-mail the SRC Coordinator regarding any questions or issues about your review of this protocol (SRC_MCWCC@mcw.edu). If you are unable to attend, please email your review to SRC_MCWCC@mcw.edu by 4 PM, the day of the meeting.

Protocol Title: _____
Principal Investigator:_____
Sponsor: _____
Funding Source: _____
Reviewer: _____ Meeting Date: _____

OVERALL EVALUATION OF PROTOCOL - ACTION RECOMMENDED:

_____ ***Approved***: The protocol is scientifically sound and acceptable as written and may be forwarded to the IRB without modifications.

_____ ***Approved with Clarifications:*** The protocol is scientifically sound and acceptable pending clarification on the part of the PI of specific points. The PI must submit a copy of any protocol revisions to the Chair for Expedited Review and approval.

_____ ***Deferred:*** The protocol requires significant revisions in order to satisfy review criteria. The PI must submit a revised protocol and written response to the SRC's concerns for re-review at a full committee meeting.

_____ ***Disapproved:*** The study is not scientifically sound, not ethical, not acceptable as written, and/or is not within the mission of the MCW Cancer Center.

Please make your assessment of each section by marking all items that are satisfactory with a "**Y**". If something is missing or needs revision, please mark with an "**N**". Mark any items that do not apply to this particular protocol with "**N/A**". Do not hesitate to add notes, comments, evaluations, etc., as you feel necessary in the "**Comments**" field following each section.

Accrual Monitoring

_____ Should this study be classified as rare disease for accrual monitoring? (incidence <6 per 100,000 people in US: rare cancer, rare molecular subtype of common cancer, unusual clinical situation)

Overall study accrual goal: _____
Predicted duration of accrual (in years): _____
Predicted annual accrual goal: _____

Comments:

Study's Position in MCWCC's Trial Portfolio

_____ How well does this trial complement MCWCC's existing trial portfolio? I.e., are there competing trials? If so, does the iDOT have a reasonable plan for triaging accrual?

Comments:

I. Title Page and Table of Contents

_____ The protocol date and/or version number is included.

_____ The Sponsor is appropriately identified as the originating institution; information for any funding Sponsors (if applicable) is also included.

_____ The title accurately represents or includes ***all*** aspects of the protocol.

_____ The Principal Investigator (PI) is identified by name, address, phone number and email.

_____ Each affiliate that may participate is identified with local PIs and their address, phone #, and email.

_____ The Sub-Investigators or Chairs for each modality (e.g. radiation, surgery, laboratory) are identified.

_____ The Statistician is identified.

_____ A table of contents is present and each section is correctly identified and numbered.

_____ A description of the type/design of trial to be conducted is clear (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures, and stages is given.

_____ Page footers have all of the following: page numbers, protocol number or short title, version and date.

Comments:

II. Introduction (Background and Rationale)

_____ The name and description of the investigational product(s) are included (if applicable).

_____ A summary of findings from nonclinical and clinical studies relevant to the trial.

_____ A summary of the known and potential risks and benefits, if any, to human subjects is included.

_____ A description and justification for the route of administration, dosage, regimen, and treatment period(s).

_____ There is a description of the population that is to be studied.

_____ References to relevant literature and data that provide background for the trial are included.

_____ Sufficient background is given to understand the reason(s) for conducting this study.

Comments:

III. Objectives (Primary and secondary endpoints of the study, listed and numbered individually)

_____ The objectives are stated clearly.

_____ The study design is appropriate to answer questions posed by these objectives.

Comments:

IV. Eligibility Criteria

_____ Subject inclusion and exclusion criteria are listed separately.

_____ The disease type/site required is described.

_____ The extent or stage of disease required is described.

_____ Information about whether the disease must be measurable or evaluable with a pertinent definition.

_____ A description of all pathology that is required is included (e.g., what type of biopsy is required? Is the initial biopsy sufficient proof of recurrent or metastatic disease or does the biopsy have to be obtained more recently?). The protocol states whether or not a verbal confirmation of the pathology report is sufficient or specifies if a separate review of pathology materials is required.

_____ If pathology materials are required, it is clear where these are to be sent.

_____ A description of the prior therapies permitted and/or not allowed is included.

_____ A description of the performance status criteria used in the study is included.

_____ A statement regarding the concomitant medications that are permitted or prohibited is included.

_____ A statement regarding a “wash-out” (if applicable) period for any medications is included.

_____ A statement regarding the concurrent diseases that are permitted or prohibited is included.

_____ Any requirements regarding the allowance of concurrent and prior malignancies are included.

_____ Required laboratory parameters, scans, and tests are included.

_____ The study is age range appropriate (e.g. ≥ 18 years). If minors are permitted, please make note of this (a minor consent and parental assent form will be required).

_____ A statement that pregnant or lactating subjects are ineligible (if applicable) is included.

_____ A statement advising women of childbearing potential and sexually active males and females to use effective contraception while on study is included (if applicable).

_____ A statement that the patient must have signed informed consent ***prior to registration on study is included.***

Comments:

V. Patient Registration

_____ Registration procedures are clear. The data needed to register study patients is provided, including whom to call and phone number(s) if there are questions regarding eligibility, eligibility forms, or registration procedures.

_____ If this is a multi-center trial, the protocol specifies whether patients will be registered locally or through a central office.

_____ Randomization procedures are described and are adequate.

Comments:

VI. Treatment Plan

_____ The treatment(s) to be administered is specified, including the name(s) of all the product(s), the dose(s), the dosing schedule(s) (over ___ minutes or hours; 3X per day at mealtime, etc.), and the route/mode(s) of administration (e.g. IV bolus, IV infusion, oral). The treatment periods (e.g. q 3 weeks, daily for 28 days, etc.) for subjects for each investigational treatment/group are specified.

_____ The total duration of treatment is specified, including the follow-up period(s) for subjects for each investigational treatment/ group (e.g. for a maximum of cycles, until progression, other specified time).

_____ If the study does require patients to be followed after active study treatment is over, the protocol states for how long patients will be followed (e.g. until disease recurrence, until disease progression, until death). NOTE: Any long-term follow-up should also be specified in the consent template.

_____ Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial are specified.

_____ Procedures for monitoring subject compliance and/or side effects (e.g. patient diaries, special patient instructions regarding self-injections, etc) are included, if appropriate.

_____ The schema completely and accurately reflects the treatment plan.

Comments:

VII. Assessment of Safety, Dose Modifications, and Dose Delays

_____ DSMC-specific data and safety monitoring plan included.

_____ Ensure AE reporting is consistent with DSMC charter. (All grade 3-5 AEs reported; Unexpected grade 3 and all grade 4 & 5must be submitted within 5 days.)

_____ The methods and timing for assessing, recording, and analyzing safety parameters are included.

_____ The type and duration of the follow-up of subjects after adverse events is specified.

_____ Criteria for grading toxicities and criteria for dose modifications are specified (e.g. CTCAE v4.0)

_____ Instructions are included for dose modifications of *each* study drug.

_____ Instructions are included for *each* modality (chemo, radiation).

_____ Definitions for Dose Limiting Toxicity (DLT) and/or Maximum Tolerated Dose (MTD) are provided, clear, and adequate (if applicable). If no, specify what needs to be changed in the comments section.

Comments:

VIII. Subject Withdrawal Criteria

_____ Subject withdrawal criteria are included. (i.e., terminating investigational product treatment/trial treatment). There are procedures that specify:

_____ (a) When and how to withdraw subjects from investigational treatment.

_____ (b) Data collection procedures for withdrawn subjects.

_____ (c) Whether and how subjects are to be replaced.

_____ (d) The follow-up for subjects withdrawn from investigational product treatment/ trial treatment.

Comments:

IX. Endpoint Assessment

_____ Methods and timing for assessing, recording, and analyzing study endpoints are included.

_____ If this section includes information regarding the "adequate course" of therapy that a subject must receive to be considered evaluable for response, the information provided matches what is specified in the statistical section.

_____ Criteria is provided for assessing response for the following categories, depending on what is permitted in the protocol:

- ____ - bidimensionally measurable disease
- ____ - unidimensional disease
- ____ - nonmeasurable evaluable disease
- ____ - leukemia/lymphoma

_____ The definitions of what constitutes a complete response, a partial response, stable disease, minimum residual disease (MRD) (if applicable) and progressive disease are defined.

Comments:

X. Study Parameters (Table format required)

All required lab tests, scans and measurements, ancillary labs, etc. should be included in chart format so that the intervals at which they are required are clear.

_____ Labs and procedures required to determine a patient's eligibility are listed in the table. Please list any labs/procedures that do not "match up" with those described in the eligibility section.

_____ Labs and procedures to be conducted when the subject is actively being treated are listed in the table. Please list labs/procedures that should be added or that do not "match up" with those described in the study procedures and response assessment sections.

_____ Unnecessary tests are included. Consider removing the following: _____.

_____ The study parameter table clearly outlines how often all labs and procedures are to be done. The specified intervals are reasonable.

_____ The time limit for pre-study labs is defined (how many days/weeks a lab can be conducted prior to on study).

Comments:

XI. Drug Formulation and Procurement

The following is provided for ***each*** study drug:

_____ Other names, if any, for the drug(s) are specified.

_____ The classification of each drug are included (type of agent).

_____ The mode of action is included.

_____ The procedures for drug(s) storage and stability are included.

_____ The specific dosing for this study is included.

_____ The procedures for drug preparation are included (diluents to be used, etc).

_____ The study-specific route of administration is included.

_____ Incompatibilities with all drug(s) are included.

_____ The source of drug (NCI, pharmaceutical company, commercially available) is included.

_____ The side effects for each drug are included.

_____ The nursing implications are included.

_____ Contact information and procedures for ordering drug are provided and clear.

Comments:

XII. Risk level assignment for DSMC/Quality assurance monitoring

_____ What level of risk would you assign this protocol based on the following guidelines? (can use discretion based on trial's specific characteristics):
Low Risk: Non-treatment trials (e.g., nutritional or behavioral interventional)
Intermediate Risk: Treatment phase II ; no local IND, IDE
High Risk: Phase I; IND, IDE
Special Status: cellular/gene therapy, first-in-human

Comments:

XIII. Statistical Considerations

_____ Descriptions of the statistical methods to be employed, including timing of any planned interim analysis(es) are included.

_____ A description of the measures taken to minimize/avoid bias (e.g. randomization, blinding) is included.

_____ The number of subjects planned to be enrolled is specified. In multicenter trials, the number of enrolled subjects projected for each trial site is specified.

_____ The reasons for the choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification are included.

_____ The level of significance to be used is specified.

_____ The criteria for the termination of the trial due to safety concerns (stopping rules) are specified.

_____ The procedures for accounting for missing, unused, and spurious data are specified.

_____ The procedures for reporting any deviation(s) from the original statistical plan are described and justified in the protocol and/or in the final report, as appropriate.

_____ The "adequate course" of therapy that a subject must receive to be considered evaluable for study endpoints is included. If this information is provided in any other section of the protocol, it matches what is included in the statistical section.

_____ The selection of subjects to be included in the analyses (e.g., all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects) is specified.

_____ Appropriate data points (including specific questions, responses and time points) have been identified to address the aims of the trial and facilitate case report form development.

Comments:

XIV. Laboratory and Correlative Requirements

_____ The methods for the sample collection, processing, and shipment described in the protocol are fully detailed, adequate and appropriate.

_____ The methods for sample analysis described in the protocol are fully detailed, adequate and appropriate.

_____ All involved personnel are identified and contact information is included.

Comments:

Additional Comments:

Appendix D. SRC Reviewer Form for Non-Treatment Investigator-Initiated Protocols

Medical College of Wisconsin
Scientific Review Committee (SRC)

Non-Treatment Investigator-Initiated Protocol Review Form

Return by email to SRC_MCWCC@mcw.edu

Protocol Title:	
Principal Investigator:	
Funding Source:	
Reviewer:	
Meeting Date:	

Items to assess	Yes	No	Don't Know	Comments
Protocol date or version number is present				
Principal Investigator is identified by name and contact information				
Co-investigators are identified with contact information				
Statistician is identified with contact information				
Funding source is identified				
Background (including relevant citations) supports the rationale for conducting study				
Objectives are clear and appropriate				
Inclusion/exclusion criteria are appropriate				

Accrual goal and duration of study are specified				
Patient registration procedures are clear and contact info for questions is included				
Study design is feasible and appropriate				
Is long-term follow-up required? Is it appropriate in length?				
Subject withdrawal criteria are included (subjects replaced?)				
Statistical analyses are appropriate				
Safety considerations, patient confidentiality are addressed				
If protocol is interventional, DSMC language is present				
Data management plan is included- where data will be captured (OnCore, RedCap, Excel)				
List of references is included				
How well does this trial complement MCWCC's existing trial portfolio? I.e., are there competing trials? If so, does the iDOT have a reasonable plan for triaging accrual?				
Classify as rare disease for accrual monitoring? (incidence <6 per 100,000 people in US: rare cancer, rare molecular subtype of common cancer, unusual clinical situation)				Overall accrual goal: Predicted duration of accrual (yrs): Predicted accrual per year:

Assignment of Risk Level For DSMC/Quality Assurance Review (guidance below but can use discretion based on trial's specific characteristics):

_____ Exempt (Noninterventional)

_____ Low (Non-treatment interventional; e.g., behavioral or nutritional interventions)

_____ Intermediate (Phase II treatment trial; no local IND)

_____ High (Phase I treatment trial; local IND)

_____ Special Status (Cell/gene therapy; first-in-human)

Any other comments (major issues or problems with study?):

OVERALL EVALUATION OF PROTOCOL - ACTION RECOMMENDED:

_____ ***Approved***: The protocol is scientifically sound and acceptable as written and may be forwarded to the IRB without modifications.

_____ ***Approved with Clarifications:*** The protocol is scientifically sound and acceptable pending clarification on the part of the PI of specific points. The PI must submit a copy of any protocol revisions to the Chair for Expedited Review and approval.

_____ ***Deferred:*** The protocol requires significant revisions in order to satisfy review criteria. The PI must submit a revised protocol and written response to the SRC's concerns for re-review at a full committee meeting.

_____ ***Disapproved:*** The study is not scientifically sound, not ethical, not acceptable as written, and/or is not within the mission of the MCW Cancer Center.

Appendix E. SRC Reviewer Form for Externally sponsored Protocols

Medical College of Wisconsin Cancer Center
Scientific Review Committee (SRC)

Externally Sponsored Protocol Review Form

Protocol #: _____
Protocol Title: _____
Local PI: _____
Responsible Sponsor: _____
Funding Source: _____
Reviewer (print): _____ Signature: _____
Date of Review: _____

Return by email to SRC_MCWCC@mcw.edu.

Please check Yes, No, or Don't Know for each category	Yes	No	Don't Know	Comments
Background supports the rationale for conducting study?				
Valid study objectives?				
Valid study design?				
Appropriate inclusion and exclusion criteria?				
Adequate response or outcome measures?				
Appropriate statistical methods?				
Is there an appropriate Data and Safety Monitoring Plan described with AE reporting, data management and oversight language? (e.g., DSMB for phase 3; medical monitor, calls with site PIs, or some type of safety committee or data monitoring committee for phase 1, 2)				

Is long-term follow-up required? Is length adequate to meet endpoints?				
How well does this trial complement MCWCC's existing trial portfolio? I.e., are there competing trials? If so, does the iDOT have a reasonable plan for triaging accrual?				
Classify as rare disease for accrual monitoring? (incidence <6 per 100,000 people in US: rare cancer, rare molecular subtype of common cancer, unusual clinical situation)				

Any major problems, concerns, or comments with regard to the proposed study?

OVERALL EVALUATION OF PROTOCOL - ACTION RECOMMENDED:

_____ ***Approved***: The protocol is scientifically sound and acceptable as written and may be forwarded to the IRB without modifications.

_____ ***Approved with Clarifications:*** The protocol is scientifically sound and acceptable pending clarification on the part of the PI of specific points. The PI must submit a copy of any protocol revisions to the Chair for Expedited Review and approval.

_____ ***Deferred:*** The protocol requires significant revisions in order to satisfy review criteria. The PI must submit a revised protocol and written response to the SRC's concerns for re-review at a full committee meeting.

_____ ***Disapproved:*** The study is not scientifically sound, not ethical, not acceptable as written, and/or is not within the mission of the MCW Cancer Center.

Appendix F. Community Representative Reviewer Form

Medical College of Wisconsin Cancer Center
Scientific Review Committee (SRC)

Community Representative IIT Protocol Review Form

Protocol #: _____
Protocol Title: _____
Local PI: _____
Funding Source: _____
Reviewer: _____
Date of Review: _____

Return by email to SRC_MCWCC@mcw.edu.

Please check Yes, No, or Don't Know for each category	Yes	No	Don't Know	Comments
Is this study asking a question that is important to patients				
Is this a study that a patient would be willing to participate in?				
Are all required procedures justified and safe for patients?				
Does the proposed intervention, study schedule or testing involve a significant burden to the patient/family?				
Do the criteria for inclusion and exclusion seem reasonable and necessary considering the intervention?				

OVERALL EVALUATION OF PROTOCOL - ACTION RECOMMENDED:

_____ ***Approved***: The protocol is scientifically sound and acceptable as written and may be forwarded to the IRB without modifications.

_____ ***Approved with Clarifications:*** The protocol is scientifically sound and acceptable pending clarification on the part of the PI of specific points. The PI must submit a copy of any protocol revisions to the Chair for Expedited Review and approval.

_____ ***Deferred:*** The protocol requires significant revisions in order to satisfy review criteria. The PI must submit a revised protocol and written response to the SRC's concerns for re-review at a full committee meeting.

_____ ***Disapproved:*** The study is not scientifically sound, not ethical, not acceptable as written, and/or is not within the mission of the MCW Cancer Center.

Appendix G. Monitoring of Ongoing Trials

1.0 Purpose/Background

The National Cancer Institute (NCI) requires cancer centers to monitor accrual to their open trials and close those making insufficient progress. Low-accruing trials (especially local trials) may fail to reach enrollment levels necessary for properly evaluating the hypotheses being tested, while national trials may accrue well overall but be a poor fit for a particular institution's patient population. Low-accruing trials require substantial support and resources to screen patients and maintain regulatory compliance, and they may prevent other, potentially more successful trials from opening due to concerns about limited resources and competition. In keeping with NCI Cancer Center Support Grant (CCSG) guidelines, the purpose of this document is to establish processes for monitoring accrual and closing underperforming trials. The Scientific Review Committee (SRC) will be the primary entity responsible for identifying low-accruing studies, warning integrated Disease-Oriented Team (iDOT) Chairs and principal investigators (PIs) about potential closure, and closing trials that fail to increase their rate of enrollment. However, the iDOTs are strongly encouraged to closely monitor accrual and proactively address underperforming studies in their portfolios. It should be noted that trials focusing on rare cancers are expected to have low accrual; thus, they are given special consideration.

2.0 Scope

This document applies to all prospective, hypothesis-driven, cancer-related clinical trials and studies (both interventional and noninterventional) open to accrual at the Medical College of Wisconsin Cancer Center (MCWCC).

3.0 Responsibilities

MCWCC Clinical Research Executive Committee: reviews and approves changes to this SRC accrual monitoring policy

SRC Chair, Committee: monitors accrual to open trials; determines when to issue warnings and closures; reviews corrective action plans and appeals; closes underperforming trials

SRC Coordinator: identifies trials due for review; provides SRC with accrual data; maintains SRC accrual monitoring records

iDOT Chairs and PIs: respond to SRC requests; provide corrective action plans

4.0 Definitions

Rare cancer trial: Trials involving rare diseases are expected to have slow accrual, and for this reason must be treated separately. The MCWCC defines a rare cancer as one with an incidence of ≤4 newly diagnosed persons out of a population of 100,000 persons per year (<6/100,000 per year). Studies of rare molecular subtypes of common cancers may also be considered if they are distinct subgroups that receive specific, targeted therapy. All pediatric trials are considered rare. Lastly, uncommon clinical subsets of more common cancers will also be considered rare.

5.0 Policy

The SRC is required to monitor accrual to Cancer Center clinical trials. Trials that do not meet the expected minimum annual enrollment per this policy (**Table 1**) will be notified and given the opportunity to take corrective action. If enrollment does not improve, then they will be closed to further accrual.

Table 1. Accrual Monitoring Guidelines

Trial type	Industry, external institutional (external investigator-initiated, consortium)	National (NCTN, BMT CTN)	Investigator-initiated	Rare disease
Expected annual enrollment	At least 40% of projected, or minimum of 2 (whichever is greater)	At least 40% of projected, or minimum of 1 (whichever is greater)	At least 40% of projected	Initial review at 2 years, then reviewed annually for overall activity *Zero accrual at 2 years:* Review screening history and ongoing scientific relevance with iDOT
6 Months	*Minimum accrual met:* Reviewed again at 12 months *Zero or low accrual:* Warning issued, corrective action plan (CAP) requested; reviewed again at 9 months			
9 Months	*Minimum accrual met:* Reviewed again at 12 months *Zero or low accrual:* Warning reminder issued, listed for potential closure at 12 months if no improvement			
12 Months	*Minimum accrual met:* Approved for 1 year *Low accrual:* Reviewed by SRC for potential closure *Zero accrual:* Closed to accrual			
Years 2+	Reviewed annually after initial 12 months open *Minimum accrual met:* Approved for 1 year *Low accrual:* Warning issued, corrective action plan (CAP) requested, re-reviewed in 6 months			

6.0 Procedures

6.1 Pre-activation

At initial review of a new study, the SRC will determine which of the Table 1 trial types is applicable.

6.2 Monitoring of open trials

Monthly, the SRC Coordinator provides the SRC Chair with a report listing studies due for SRC continuing review: studies that have been open 6, 9, or 12 months or are due for annual review. Temporary study suspensions are taken into account in the timing of reviews. Included on the report is the following: study title, PI, sponsor type, open/suspension dates, accrual goal, and accrual history.

Timeline and actions

If at 6 months the trial meets the minimum enrollment listed in Table 1, then it will not require a 9-month review and will be re-reviewed at 12 months. If at 6 months a trial's minimum accrual has not met 20% of the trial's annual accrual goal, the SRC will request a corrective action plan (CAP) from the iDOT Chair and trial PI. The iDOT Chair and PI must respond within 30 days or the trial may be closed to further accrual. If the CAP does not sufficiently address SRC concerns, the SRC may request further action or close the study to accrual.

If the CAP is acceptable, the study will be re-reviewed at 9 months. If at 9 months a trial's minimum accrual continues to fall below the target in Table 1, a warning will be issued noting that the trial will be listed for potential closure at 12 months.

If at 12 months the trial meets the minimum enrollment listed in Table 1, then it is approved for another year. At 12 months, trials with zero accrual will be closed, and low-accruing trials may be closed.

At 24 months and each subsequent year, trials meeting minimum enrollment listed in Table 1 will be approved for another year. Trials falling below the target in Table 1 will receive a CAP request from the SRC and will be reviewed for potential closure after 6 months.

Rare disease trials

Studies classified as rare disease are be held to the 40% accrual threshold. SRC initially reviews these trials two years from activation and then annually thereafter for overall activity. As a part of this review, the SRC considers the study's screening and consent history, continued scientific relevance, and dialogue with the PI and iDOT. Zero-accruing studies require discussion with the iDOT to determine the feasibility of identifying eligible patients at MCWCC. Following this review process the study may be subject to a request for a CAP or may receive a closure letter.

6.3 Trial closure

When the SRC determines that a trial should be closed to accrual, the iDOT Chair and PI are notified by email. The trial's research manager, primary clinical coordinator, and regulatory coordinator are also notified. If the iDOT Chair and PI feel that there are significant extenuating circumstances, they may appeal to the SRC for reconsideration and final determination.

Per NCI's current CCSG guidelines, the SRC "*should have final authority to close trials; no appeal should be allowed to any other person or entity*."