The Clinical Scientific Review Committee (SRC) at The Medical College of Wisconsin Cancer Center plays a vital role in protocol review and monitoring to ensure that clinical trials are scientifically sound and that approved trials maintain patient accrual goals and scientific progress.

The SRC operates in collaboration with the Clinical Trials Office (CTO) while maintaining separate responsibilities and reporting. The SRC meets to review all proposed interventional cancer-related protocols conducted by the Cancer center. All cancer-related research is required to have prior SRC approval before the protocol can be submitted to one of the MCW Institutional Review Boards (IRB).

QA audits are performed by the Clinical Trials Office. Monitoring for accrual is performed by the SRC. Serious adverse events (SAEs) are reported by CTO staff to the Cancer IRB, and the routine monitoring of SAEs is performed by the Data Safety and Monitoring Committee.

MISSION
The mission of the CCSRC is to evaluate the scientific validity of all proposed MCWCC clinical trials and monitoring the scientific progress and accrual status of open trials.

The specific aims of the SRC are:
1. To establish and maintain a review committee of sufficient size and breadth of expertise to conduct a critical and fair scientific review of institutional cancer-related research involving human subjects;
2. To conduct a thorough scientific review of all non-peer-reviewed, cancer-related clinical protocols conducted at the MCWCC based on specific, pre-determined review criteria;
3. To oversee and facilitate the prioritization of competing protocols by disease Faculty disease site-specific Research Committees (FRCs), thus ensuring optimal use of the cancer center’s clinical resources for the achievement of its scientific goals;
4. To establish clear criteria for determining whether ongoing clinical trials are making sufficient scientific progress, including the attainment of adequate patient accrual rates; and
5. To monitor all cancer-related research protocols based on the criteria established by the CSRC and to terminate protocols that do not meet these expectations.

The specific functions of the SRC are to:

- Review the scientific merit of cancer-related research involving human subjects at the MCWCC
- Foster the development of innovative, collaborative, and scientifically-sound studies that focus on the prevention, detection, diagnosis, and treatment of cancer as well as long-term follow-up and care
- Review the proposed utilization of MCWCC resources including, but not limited to, personal, human responses, patient entry, tissue, blood and data
- Assist MCWCC investigators in the development of scientifically- and clinically-sound research through well-written and well-conducted clinical trials
- Provide a standard format for review of scientific feasibility and merit

The SRC is complementary to the Institutional Review Board (IRB), but it does not duplicate or overlap the responsibilities of the IRB, which focuses primarily on the protection of human subjects. The MCW IRB will not approve any cancer-related study involving human subjects without first receiving notice of approval from the SRC.

**Committee Composition**

SRC members are appointed by the MCWCC Associate Director for Clinical research for three (3) year appointments. At least ten members will serve on the SRC with representative members from each of the following: Pediatric Hematology/Oncology, Adult Hematology/Oncology, Nursing, Obstetrics and Gynecology, Radiation Oncology, Surgery, Pharmacy and Statistics. Members are invited to participate based on disciplinary expertise as well as expertise in the design, conduct and analysis of specific trials. Ad hoc members may be appointed to the SRC based on the areas of research and expertise needed for specific protocol review. A statistician and the CTO Administrative Director will also be standing members of the SRC. The CTO will provide administrative support for the SRC. The SRC chair is appointed by the SCC Director for a three (3) year appointment. The responsibilities of the Chair include the following: conducting bi-monthly SRC meetings; corresponding with PIs with regard to initial review and committee actions; assigning reviews to SRC members; maintaining the integrity, quality, and records of the SRC; and reporting SRC activities to the MCWCC leadership. The Co-Chair performs the responsibilities of the Chair in the absence of, or as delegated by, the latter. A meeting quorum requires the presence of 50% of voting members. Each SRC member will have one vote. On issues where an SRC member is a PI, Co-PI, or sub-PI, the SRC member is permitted to discuss, but not vote. The SRC meets on the first and third Monday of every month from 5:00pm-6:00pm in Clinical Cancer Center Conference Room N.

The SRC will be supported by a CTO Coordinator whose responsibilities include: maintaining a database and tracking sheet of protocols reviewed by the SRC; maintaining files on all active protocols reviewed by the SRC; assisting PIs in preparing submissions to the SRC to assure that all documentation is complete; maintaining records concerning appointment and term of SRC
members; documenting meetings through generating and distributing meeting minutes; providing other administrative support as required by the SRC Chair or committee.

**SRC Review Process**
New protocols submitted to the SRC are first reviewed by the CTO administrative staff to assure that all required components of a research protocol are included. They are then forwarded to the appropriate Faculty Research Disease Site Committee for review and approval. Protocols are then reviewed by the SRC. The SRC Chair assigns committee members to review protocols based upon member expertise. Any SRC member serving as a PI of a protocol coming before the committee for scientific review will not be allowed to serve as a reviewer for that protocol. The Coordinator will send the protocol and the SRC Reviewer’s Form (Appendix A) to the reviewers at least one week before the SRC meeting. The assigned statistician and pharmacy representative will also receive the protocol for review to ensure that statistical considerations are appropriate and valid, and that potentially adverse drug interactions are appreciated and acknowledged.

**Levels of SRC Review**
There are two levels of SRC review: Full Review and Expedited Review. The SRC Chair determines the level of review according to the type of trial.

**Full Review:** For Full Review, the SRC Chair identifies a primary reviewer, a secondary reviewer (if required), and a statistician (if required). The entire protocol or amendment is made available for review, and the assigned reviewer is required to comment on specific items regarding the scientific merit of the study and submit their remarks on the SRC Reviewer’s Form. The SRC can take one of the actions defined below. Protocols that require Full Review include:

- **Investigator-Initiated Protocols (Phase I-III):** Requires a primary and secondary reviewer, a statistical reviewer, and must receive a majority vote by the SRC for approval.
- **Industry-Sponsored Protocols (Phase I-III):** Requires a primary reviewer, a statistical reviewer, and must receive a majority vote by the SRC for approval.

**Expedited Review:** Studies or amendments subject to Expedited Review are reviewed by the SRC Chair, who is responsible for approval or disapproval. The outcomes of Expedited Reviews are reported to the full committee at the next scheduled meeting. Protocols that require only Expedited Review include:

- **National Cooperative Group / CTEP Protocols:** These protocols must demonstrate evidence of external peer-review at the CTEP or National Cooperative Group level. The Chair has the discretion to approve through Expedited Review. These protocols may be submitted and will be reviewed on a rolling basis. The Expedited Review will be done in an effort not to delay the process of subsequent IRB review and approval. These protocols may undergo Full Review if directed by the Chair. National cooperative group and industry protocols can be submitted simultaneously to the SRC and the IRB.
Committee Actions

For protocols requiring Full Review, a summary will be presented by the assigned primary review. Comments and recommendations will be made by the primary reviewer and, where applicable, the secondary reviewer. Statistical considerations will be addressed by the assigned statistician. Pharmaceutical issues and potential adverse drug interactions will be addressed by the assigned pharmacy representative. All therapeutic protocols will be reviewed by at least one physician member of the SRC. Recommendations relative to protocol approval by the SRC will be based upon the criteria listed below:

- **Accepted for submission to the IRB:** the protocol is scientifically-sound and acceptable as written and may be forwarded to the IRB without modifications.
- **Accepted with Minor Revisions:** 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.
- **Approval with Major Revisions:** The study is scientifically-sound and acceptable if the PI can make modifications to the protocol and/or provide clarifications as requested by the SRC. The protocols must return to the SRC for review and approval before IRB submission.
- **Tabled:** The protocol was not reviewed and must return to the SRC for Full review and approval before IRB submission.
- **Disapproved:** The study is not scientifically-sound, not ethical, and not acceptable as written, or not within the mission of the MCWCC.

The actions of SRC will be recorded in the form of minutes and will be distributed to all SRC members at the following SRC meeting. The recommendations of the SRC will be forwarded by the Chair via email to the protocol PI within seven (7) days of the SRC meeting. The PI must submit a copy of any revised protocol directly to the SRC at least one (1) week before the next scheduled meeting targeted for re-review. Review will occur as outlined above. All substantive changes to investigator-initiated and industry sponsored protocols must be reviewed and approved by the SRC before approval by the IRB. Major protocol changes (e.g. modifications in drug dosage or delivery, change in methods, procedure or study design, changes in exclusion or inclusion criteria, addition / reduction of subject accrual goals, etc.) will be held for the next SRC meeting and must receive Full Review. Minor protocol changes will receive Expedited Review. All requests for protocol changes should be submitted to the SRC Chair by the PI. 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 SRC approval. A PI may petition the SRC for an Expedited Review of a major change in protocol. The PI must contact the SRC Chair and demonstrate that delaying implementation of the protocol change until the next scheduled SRC meeting would seriously impede the research project. The SRC Chair may decide to grant approval of the change pending Full Review or may convene three (3) or more SRC members to perform an ad hoc Expedited Review.
FAQs

Q: Does an IRB Exempt protocol need SRC review?
A: Yes

Q: Does the protocol go to the SRC for review prior to being sent to the IRB?
A: yes

Q: Does the PI have to present at a SRC meeting?
A: No

Q: How long does the PI have to respond to a deferral or stipulations?
A: 60 days

Q: What is included in an Amendment Submission?
A: Summary of Changes, marked-up version, new protocol

Q: How long does the PI have to respond to a warning letter?
A: 2 weeks

Q: Do I need to have funding confirmed before I submit my trial to the CSRC?
A: No, however, it is encouraged. The CTO Office provides assistance in developing and negotiating budgets as well as contracts.

Q: Can accrual goals be modified?
A: Yes