SCIENTIFIC REVIEW COMMITTEE (SRC) CHARTER

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1.0 PURPOSE

The purpose of the Robert H. Lurie Comprehensive Cancer Center (RHLCCC) Scientific Review Committee (SRC) is to evaluate all new and ongoing clinical trials for scientific merit, institutional priority, and ongoing progress, including review of accrual for all clinical trials. The SRC is an independent committee within the Lurie Cancer Center's (LCC) Protocol Review and Monitoring System (PRMS).

2.0 MEMBERSHIP

The LCC's Deputy Director appoints committee members in consultation with the SRC Chairs. Committee membership is as follows:

2.1 Leadership

The SRC includes one (1) Chair and two (2) Co-chairs.

2.2 Members

Membership consists of two (2) panels of 8-15 core voting members, as well as rotating departmental and *ad hoc* members assigned to specific studies as needed. Each panel includes multidisciplinary representation from Northwestern Medicine's medical oncology, radiation oncology, surgical oncology, pediatric oncology, medical social sciences, biostatistics, pharmacy, pathology, and data quality assurance groups. *Ad hoc* reviewers may be used for either full-panel or designated review purposes as needed. *Ad hoc* reviewers will vote only on protocols they review.

2.3 Non-voting Members

Each panel has an administrative PRMS coordinator. Other non-voting members representing clinical research interests may attend meetings but are not considered voting members. In conjunction with the Division of Hematology/Oncology and other clinical departments or units, second- and third-year fellows are also assigned as rotating secondary reviewers for each panel meeting; fellows are also considered non-voting.

2.4 Appointment Term

Members are appointed for two-year renewable terms. The Deputy Director and the committee Chairs review membership and meeting attendance at least annually.

3.0 AUTHORITY AND RESPONSIBILITY

3.1 Scientific Merit

The SRC is primarily focused on the scientific design and importance of new studies. Review focuses on the:

- Background and rationale

- Objectives and endpoints
- Adequacy of the study design to meet primary objective
- Statistical plan
- Feasibility/Ability to complete the trial as proposed, and
- Adequacy of data and safety monitoring plan of the protocol

Each protocol receives an overall review score based on the combined consensus of the assigned reviewers and all other voting panel members present (for full-panel reviews). Review scores include:

Approved (1)	Comments or suggestions may be made, but no formal response is necessary.
Modifications required (2a)	Response and/or revisions are required prior to approval, administrative confirmation of response/revisions is required.
Modifications required (2b)	Response and/or revisions must be confirmed by individual reviewer(s).
Held for re-review (3)	Substantial revisions to the protocol are required and it must be re-reviewed by the same panel.
Disapproved (4)	There are fundamental design flaws or feasibility issues and/or the study does not align with LCC priorities.

Please refer to Section 4.4 for more detail regarding review types and outcomes.

3.2 Institutional Priority

Priority is initially set by the Disease Team (DT) within the context of their trial portfolio and is communicated to SRC upon protocol submission. The SRC has final authority to confirm priority. In addition to the review score, the SRC provides a merit score (refer to Section 3.2.1) for each protocol upon initial approval. The SRC merit score [which follows the National Institutes of Health (NIH) Center for Scientific Review (CSR) Merit descriptors] is considered if the study is submitted for additional funding through the Lurie Clinical/Translational Resource Allocation Committee (LCTRAC) mechanism.

3.2.1 Merit Scores

1. **Exceptional**: Exceptionally strong with essentially no weaknesses
2. **Outstanding**: Extremely strong with negligible weaknesses
3. **Excellent**: Very strong with only some minor weaknesses
4. **Very Good**: Strong but with numerous minor weaknesses
5. **Good**: Strong but with at least one moderate weakness
6. **Satisfactory**: Some strengths but also some moderate weaknesses
7. **Fair**: Some strengths but with at least one major weakness

8. **Marginal**: A few strengths and a few major weaknesses
9. **Poor**: Very few strengths and numerous major weaknesses

3.3 On-going Progress

On-going progress review is performed by the SRC Sub-Committee for Comprehensive DT Progress Review. This sub-committee meets quarterly to review each DT portfolio in full at least annually, and to make recommendations which are communicated back to the DT leaders and full SRC panel(s) as needed. The SRC considers multiple factors when reviewing a portfolio for progress. These may include annual and overall accrual rate(s) as compared to projected rate(s) at study submission, existence of competing studies, slot-based enrollment, and/or rare disease designation. The committee has sole authority to close studies not meeting minimum accrual requirements.

Possible review outcome recommendations may include:

Under monitoring	Study is not meeting one or more benchmarks for accrual progress.
Risk of closure	Study has consistently not met accrual benchmarks and may have received one or more “Under Monitoring” outcomes with no significant improvement. A corrective action plan will usually be required and re-review within six (6) months is often recommended.
Closure	Study has previously received a “Risk of Closure” outcome and continues to not meet accrual benchmarks.

4.0 PROCEDURES AND ADMINISTRATION

4.1 Meetings

4.1.1 Panel Meetings

Each panel meets once a month at regularly scheduled times. Additional meetings may be called with agreement of the Chairs as needed. Each meeting will be attended by at least one (1) chair or Co-chair. The meeting agenda may include new protocols for full-panel review, protocol revisions requiring full-panel review, and any other relevant business.

4.1.2 SRC Leadership Team Meetings

The SRC leadership team – consisting of the SRC Chair and Co-chairs, as well as SRC administrative coordinators – meets weekly to review administrative updates or other outstanding issues. Occasionally, actions may be taken, or determinations may be made outside of panel or sub-committee meetings, in which case these are documented in the weekly leadership team minutes.

4.1.3 SRC Sub-Committee Meetings

The SRC Sub-Committee for Comprehensive DT Progress Review meets quarterly to review full DT portfolios. Each DT is reviewed in full at least annually, with individual studies occasionally assigned for an interim re-review as needed. The sub-committee consists of the SRC Chair and Co-chairs, the Deputy Director of the LCC, the Clinical Trials Office (CTO) medical director and other CTO leadership, and a subset of voting members representing various oncology specialties. Administrative support for the meetings is provided by the PRMS coordinators.

4.2 Committee Support

The LCC employs three to four (3-4) staff members who provide administrative support to the PRMS (SRC and DTs). The PRMS team is responsible for:

- Assigning panel and designated reviewers, and distributing review packets
- Creating meeting agendas, materials, and minutes
- Generating SRC review outcome letters and processing responses
- Facilitating communications between the SRC and DTs, as well as with other components of the LCC Research Oversight System (ROS)
- Tracking on-going accruals for all active studies subject to progress review

4.3 Quorum

Quorum for full-panel meetings is defined as seven (7) core voting members, including at least one (1) biostatistician and one (1) Chair or Co-chair. An *ad hoc* primary reviewer may count towards quorum if in attendance. If quorum is not met for a panel meeting, studies for review may still be presented; essential review documents will then be routed for electronic review to the rest of the panel to submit scores. If needed, the review outcome may be finalized in the next SRC leadership meeting.

4.4 Levels of SRC Review

All cancer-relevant research protocols must be submitted to the LCC for tracking and reporting purposes. The study source (D/E/I/N) and clinical research category [as defined in the Cancer Center Support Grant (CCSG) Data Guide] helps determine what level of review is required. The table below summarizes the review types required for different types of protocols:

Clinical Research Category	Study Source	Review Required	Level of Review
Interventional	D (industry)	Y	Full panel review
	E (external peer review)*	Y	Designated review
	I (institutional) – LCC is lead site	Y	Full panel review
	I (institutional) – other NCI center is lead site	Y	Designated review
	N (national)	Y	Designated review
Ancillary/correlative	D (industry)	Y	Designated review
	E (external peer review)	Y	Designated review
	I (institutional) – LCC is lead site	Y	Designated review
	I (institutional) – other NCI center is lead site	Y	Designated review
	N (national)	Y	Designated review
Observational	D (industry)	Y	Designated review
	E (external peer review)	Y	Designated review
	I (institutional) – LCC is lead site	Y	Designated review
	I (institutional) – other NCI center is lead site	Y	Designated review
	N (national)	Y	Designated review
Non-hypothesis driven research (e.g., biorepositories, registries, retrospective chart reviews, single-patient IND)	All	Y – entry and tracking only	Administrative processing
Expanded access – multi-patient	All	Y	Designated review (if research endpoints) or administrative processing (if only objective is to provide access to drug/biologic)

*Please note that grant-funded LCC IIT's may be required to go full panel re-review

4.4.1 **Full Panel Review**

Full panel review is required for all interventional protocols that have not

been previously reviewed and approved by a National Cancer Institute (NCI)-approved peer-review agency. Examples include LCC investigator-initiated trials (IITs) and industry-sponsored trials. Full panel review includes, at a minimum, one (1) primary reviewer (an MD or PhD, depending on the aims of the trial), a biostatistician, and *ad hoc* reviewers from the pharmacy, Pathology Core Facility, and/or Quality Assurance teams as applicable.

NOTE: Interventional protocols generated from federal grants and SPORE trials are not exempt from this process. They do require full panel review in order to assign the level of monitoring required under the Lurie Cancer Center DSMP. Furthermore, the clinical trial protocol (which contains additional relevant details) is not included in the grant submission, and therefore a thorough review is needed.

4.4.2 Designated Review

Designated review is utilized for all observational and ancillary/correlative protocols, as well as for interventional protocols where NCI-approved peer-review has already been obtained [such as National Clinical Trials Network (NCTN)/Experimental Therapeutics Clinical Trials Network (ECTCN) protocols]. Designated review is typically performed by the SRC Chair, Co-chair, or another assigned reviewer, and primarily consists of a high-level check of the study's scientific merit as defined above. The reviewer may refer a protocol for full panel review if they feel it is appropriate.

NOTE: Institutional trials for which the lead site provides documentation of SRC review in good-standing may also qualify for designated review.

4.4.3 Administrative Processing

Protocols which are non-hypothesis driven do not undergo review by SRC. However, these are still tracked by the Cancer Center for reporting purposes and should still be submitted the same way for entry into the Clinical Trial Monitoring System (CTMS) – NOTIS.

4.5 Review of Protocol Revisions

The SRC reviews all protocol revisions submitted following initial approval. Revisions generally follow the same review path as the initial review. Revisions that affect eligibility, sample size, treatment design, endpoints, statistical plans, or that impact patient safety are reviewed in a full panel meeting; these may be assigned to a reviewer on the panel or may be reviewed in summary by the full panel during the meeting or via email. All other revisions are typically reviewed by designated review, except for those which are purely administrative or editorial in nature and may be simply acknowledged by the PRMS team.