Center for Cancer Research (CCR) Scientific Review (SR) Process

---

Step 1: Branch Concept Review

During the Branch Concept Review: All concepts (or Letter of Intent (LOIs)) will first be reviewed within each branch (i.e., formal or informal review as determined/operationalized by the branch) and approved by the Branch Chief (BC) to proceed. During this review, branches should consider:

- Feasibility of the study
- Fit of the study within the mission of the branch and CCR
- Study branch-level resources required (and any additional resources that are needed outside the branch)

The branch will coordinate and schedule these meetings. The CCR Protocol Support Office (PSO) Staff will not be involved in the conduct of these meetings in any way. No minutes need to be taken at these meetings; however, the signature of the Branch Chief on the iRIS submission form indicates that the concept has been discussed and approved at the branch level.

It is highly advisable that following branch approval, the Principal Investigator (PI) contact the Office of Sponsor and Regulatory Oversight (OSRO) to assist in the determination of whether an IND or IDE is required, and to discuss the regulatory pathways for the protocol.

Step 2: CCR Scientific Review

Standard Review Process:

Prior to the CCR Scientific Review:

Submission:

The following documents are required for submission of each protocol:

- Protocol or Letter of Intent (LOI) if protocol is being submitted to CTEP. If the protocol is written by a third party (i.e., pharma or cooperative group) the NCI-specific supplement must be included.
- Study Personnel Page (if not included on the Protocol Title Page)
- CCR Resource Form
- Principal Investigator (PI) CV
- Milestone Plan
- Genomic Data Sharing Sensitivity Determination Form
- Memo from the PI which briefly outlines:

- Why the study should be done at the NCI
- How the study fits with the overall interests and programmatic goals of his/her group
- In the case of multicenter studies, what the specific contribution of the NCI will be.

The PI will provide the protocol document to their assigned Protocol Support Office (PSO) Manager. The protocol will either be handled by the PSO Manager or by a PSO Writer for SRC submission (this decision will be made within the PSO Office). The PI should allow up to two (2) weeks for abbreviated, administrative review of the protocol document by PSO prior to SRC submission (i.e., for confirmation of correct template/formatting, consistency [e.g., objectives in introduction vs. statistics], and inclusion of key elements/sections).

The PSO Manager/Writer will work with the PI to complete the other required documents for SRC submission (e.g., milestone plan and planned enrollment form, etc.).

The Clinical Center PRIA submission in iRIS must also be completed by the PI and submitted by the PSO Manager/Writer via iRIS concurrently with the submission to SRC as per **Appendix 1: Protocol Resource Impact Assessment (PRIA) form submission requirements, approval process, and timeline**.

All protocols will be submitted via iRIS for CCR SRC review at least 10 days prior to the scheduled meeting; the protocol may be scheduled for the next available meeting in the case of a full docket and/or availability of the PI to attend the meeting and present the study. The PI, BC and the Accountable Investigator (if different from the PI) will need to sign off on the submission in iRIS. The CCR SRC must receive the full submission with BC signature of approval in order to schedule the study on the review docket.

Committee Invitees & Responsibilities:

- The Committee has a standing membership with ad hoc reviewers as required.
- The Committee will have rotating chairs. The Chair cannot preside over the Committee if he/she is the PI or an Associate Investigator (AI) on a protocol being presented.
- Two (2) members will be assigned by the Committee Chair as reviewers. Neither reviewers may be the PI or an AI on the protocol. Reviewers may be selected from external organizations, if required. All assigned reviewers are required to provide comments in writing to the PSO at least one (1) day prior to the meeting and should make every effort to attend the meeting. The reviewer comments will be compiled and sent to the Chair no later than the morning of the meeting.
- The protocol and resource form will also be distributed to CC Pharmacy, CC Department of Transfusion Medicine (DTM), Pathology, Office of Research Nursing (ORN), Data Management and monitoring, Pharmacokinetics, Genomic Data Sharing/Sensitivity, Technology Transfer, Radiation, CCR Office of Information Technology, Molecular Imaging, Office of Sponsor and Regulatory Oversight (OSRO), and Protocol Support Office (PSO) to review for department impact no later than seven (7) days prior to the

review meeting. Each department should submit their comments in writing (via email) to the PSO at least one (1) day prior to the meeting. These comments will be collated and reviewed by the Office of the Clinical Director (OCD) of the CCR.

- The protocols that are scheduled for each review will be sent via email to the CCR protocol listserv so that all investigators can be made aware of new protocols in the CCR. Any investigator is welcome to send comments about protocols being reviewed to the PSO who will include the comments for the Chair's consideration.

Scheduling:

The Committee will meet approximately every 2 weeks.

During the CCR Scientific Review:

PSO will administer the CCR Scientific Review meeting including scheduling, taking minutes and attendance, and coordinating efforts. **The PI must be available for the review of the protocol**.

Structure of the meeting:

- The assigned reviewers will present their comments to the members and discuss.
- Reviewers should comment on: research strategy, feasibility, clinical strategy and impact.
- The main criteria on the basis of which the review will be conducted are:
    - **Adequacy of Background and Preliminary Data** (e.g., adequacy of preclinical and clinical data supporting prioritization of the proposed question of therapy; adequacy of clinical data supporting the ability to administer therapy as proposed)
    - **Importance of the Proposed Study in Advancing the Investigator's Research Program** (i.e., does this build on existing research? Is the research unique to the program? Will the results open new directions for the investigator and the field?)
    - **Strength of Study Design, Including Statistical Design/Correlative Science, etc.** (e.g., appropriate primary and secondary endpoints to address the hypotheses, adequate sample size to meet study objectives, optimal use of resources, appropriate patient selection, and safeguards in place for patient protection.) The committee should weigh in on the completeness of the design (i.e., whether the protocol design will support achieving the objectives, whether the protocol describes all necessary activities and decision points without the need for amendments, etc.).
    - **Study Feasibility** (e.g., likelihood of achieving the stated accrual rates and proposed study duration and of collecting and testing tissues as specified)

    - **Importance of the Research Question in Contributing the Overall Management of the Disease** (In view of the current treatment approaches for the disease, is the study likely to make a meaningful contribution to patient care?)
- The PI will be available to answer questions from the Committee.
- The Committee will vote by secret ballot at the meeting; outcome decisions will be made by majority vote.
- If a Committee member is listed as the PI or has a significant Conflict of Interest on a study being reviewed (e.g., is listed as an AI), that person will not participate in the vote.
- The Chair will participate in the vote.
- Possible voting outcomes as per the ballot are:
    - Approved
    - Approved with recommendations
    - Returned with stipulations back to the chair
    - Deferred with stipulations back to the full Committee
    - Disapproved
- The ballot includes a score based on scientific merit between 1 (lowest) – 10 (highest). (NOTE: This applies only for new protocols, not to amendments.)
- Stipulations and recommendations MUST be responded to in iRIS within the deadline (1 month from the date of PI receipt of the outcome letter). An extension can be requested in case more time is needed.
- The Chair has final say on the outcome; s/he can resolve a deadlock and revise the outcome accordingly.
- The final vote outcome along with the average score will be calculated and sent to the committee the next working day.

After the CCR Scientific Review:

- Meeting minutes, voting outcome, reviewer comments, and attendee comments are sent to the Chair and Clinical Director for review and approval.
- Approved meeting minutes, voting outcome, comments, and the Chair's summary are entered into iRIS and sent to the respective PI and BC.
- The OCD designee will review resources and will sign off in iRIS prior to the outcome letter being distributed.
- The approved minutes will be complied with the scientific review package and be forwarded to the Clinical Center (CC) Scientific Review Coordinator for approval by the CC Scientific Review Officer.

- Once final approval is obtained, the complete scientific review package will be returned to the PI by the SRC coordinator via iRIS.

Expedited Review Procedure:

Some protocols may bypass review at a convened CCR scientific review meeting and may be reviewed via email by the Committee. The Chair will initially determine if the study needs to be reviewed at the convened Committee meeting based on the criteria below. The Committee members will indicate (e.g., via email) if they agree with the protocol moving forward as written or if they think the protocol needs to be reviewed at a convened Committee meeting. These protocols will still require resource review by the OCD.

Examples of protocols that may qualify for expedited review include:

- Cooperative groups studies where CCR is a participating site
- U01 grant protocols where CCR is a participating site
- Long-term follow-up/data collection protocols from patients enrolled on other trials
- Data and specimen analysis protocols
- Retrospective chart review protocols

CTEP Dual Review:

CTEP Letters of Intent (LOIs) should be reviewed at the CCR scientific review meeting **prior** to submission to CTEP as an LOI, to include all of the documentation outlined above in step 2. Resource review by the OCD of these protocols will occur at this stage as well. Approved LOIs will be submitted to CTEP by the SRC Coordinator after the CCR review has been completed. Reviewers as designated at the scientific review will join the call for review with CTEP Protocol Review Committee, for both the CTEP LOI review and the CTEP protocol review.

Protocols that are being reviewed as part of the dual review process still require review and approval by the CC Scientific Review Officer.

Step 3: Amendments

The CCR Scientific Review Committee will also review amendments that meet any of the following criteria:

1. A change in protocol primary objectives.
2. Adding any new study agent (including significant change in manufacturing which may change the risk/benefit ratio).
3. Change in trial design of significant consequence. For example, adding arms or removing arms to randomized phase II trial.
4. Adding more than 20% additional patients to the currently approved ceiling. (Note: In protocols with 2-part registration, this calculation excludes additional patients added to the ceiling for allowance of screen failures.)

For amendments that require CCR review:

- Amendment will be submitted to the Committee via iRIS and will include a tracked protocol, consent (as applicable), and cover memo.
- The BC signature will be required on all amendment submissions, which indicates that this amendment has been approved at the branch level.
- Protocols that go through CTEP review must be also submitted in iRIS for resource review if the amendment meets the above criteria.
- The protocol and resource form will also be distributed for department resource review similar to all new protocols.
- Reviewers will be assigned as determined by the Chair.
- If a PI wishes to expand his/her protocol to other sites, this does not need to go through SR but must be discussed with and approved by the Office of the Clinical Director (OCD) prior to submitting amendment to the IRB; OCD will facilitate NIH IRBO review of single IRB review requirement, if applicable.

Step 4: Quadrennial Protocol Review

[PENDING]

APPENDIX

Appendix 1: Protocol Resource Impact Assessment (PRIA) form submission requirements, approval process, and timeline

1. The following items are required to submit the PRIA form in iRIS:
    - Completed PRIA form
    - Protocol (same document being submitted to Scientific Review)
2. The form should be sent concurrently with the submission to Scientific Review and requires PI signoff in iRIS.
3. The Clinical Center PRIA approval is sent via iRIS to the protocol PI and study contacts.
4. OPS can verify that the PRIA process has been completed by accessing the Clinical Center's central file which houses all the PRIA approvals. If a PRIA form has not been submitted to the Clinical Center, OPS will email the PI to request the PRIA form be submitted.
5. The PRIA approval does not need to be retained as part of the official regulatory binder.