Scientific Review Standard Operating Procedures rev. 04-06-20

NIH Policy for Scientific Review of Clinical Protocols Utilizing the NIH Intramural Program

*https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/review_science/policy-scientific_review_clinical_protocols.pdf

Submission Requirements for Initial Scientific Review

1. Protocol/Consents –The full protocol is required. If the protocol is written by a third party (i.e., pharma or cooperative group) an appendix/supplement with the NIH description of the protocol should be included.
2. Scientific Review Form (required elements addressed in policy) completed in iRIS
    - Initial Protocol Review
    - Enrollment.
    - Clinical Monitoring Plan.
    - Data and Safety Monitoring Plan.
    - Data Access and Sharing Plan.
    - Milestone Plan.
    - Common Data Elements (CDE) Applicability.
    - Clinical Protocol Schedule of Events/Study Calendar.
    - Statistical Analysis Plan.
    - Disease Community Engagement and Study Design.
    - Investigator Qualifications.
    - Overall Protocol Assessment Rating.
3. Institute Scientific Review (uploaded into NIH iRIS)
    - Recommendations or Stipulations.
    - Responses to Recommendations or Stipulations.
4. Signatures (signed in NIH iRIS)
    - Principal Investigator.
    - Accountable Investigator (when applicable).
    - Lab/Branch Chief or CC Department Chief.
    - Chair, Scientific Review Committee (this may be the Clinical Director or Scientific Director).
    - Institute or Center leadership (i.e., Scientific Director and/or Clinical Director.
5. Other relevant documentation as required by the Institute (See Institute specific policy)

Note: The Scientific Review policy does not apply to Single Patient Expanded Access protocols, whether emergency or non-emergency, and therefore do not require the review and concurrence of the Chief Scientific Officer.

Conduct of Scientific Review

Concept review is not required to be submitted, however, the outcome of the review will be recorded in the iRIS. The Institute Review may be conducted by an internal Institute/Center convened formal committee overseen by the Scientific Review Committee Chair or a review overseen by the Scientific Review Chair using written input from independent/outside reviewers.

A. Convened formal committee review by Internal Institute/Center Review:
   - Minutes
   - Attendance recorded
     - at least two additional reviewers from the IRP must be from outside the lab/branch or CC department, in addition to a statistician;
     - the presiding chair will be a voting member;
     - NIH reviewers from outside the IC of the Principal Investigator or from the extramural community are welcome.
   - Summary of the discussion/review.
   - Indication that the number of tests requested for research subjects (e.g., laboratory studies, radiology tests [CT scans, PET scans], etc.) to answer the research question is appropriate.
   - Identification of the outcome (recommendations or stipulations).
   - Overall protocol rating score as defined in the policy appendix. *
   - The PI or designee must be available to discuss the protocol and/or answer questions.

B. Independent/Outside Reviewers providing written reviews:

   The Chair of the Scientific Review Committee or Clinical Director selects reviewers:
   - Affiliation of reviewers identified.
   - External reviewers (reviewers not affiliated with the NIH) must complete the appropriate clearance of conflict of interest, Short Certification Form, [https://ocr.od.nih.gov/pdfs/NIH-Conflict-of-Interest-Form-Review-Protocols.pdf]
   - Summary of the written reviews added to iRIS form.
   - Indication that the number of tests requested for research subjects (e.g., laboratory studies, radiology tests [CT scans, PET scans], etc.) to answer the research question is appropriate.
   - Identification of the outcome (recommendations or stipulations).
   - Overall protocol rating score as defined in policy appendix. *

*NOTE: The overall protocol rating, as defined by the policy, is that of the protocol submitted to the Chair, Scientific Review Committee. Depending on IC process (word or numerical rating score) the protocol scientific review score should be communicated

back to the PI by either the chair of the Scientific Review Committee or institute Clinical Director or Scientific Director.

When the Chair of the Scientific Review Committee is the PI, the Deputy Chair of the Committee, Clinical Director, Scientific Director or designee should oversee the review as appropriate. When the Clinical Director or Scientific Director is the PI, the Scientific Review should include review by a committee comprised of membership outside their supervisory structure within the IC or by another IC.

Recommendations or stipulations should be addressed by the PI and the PI responses reviewed by the Scientific Review Committee Chair/Clinical Director or Institute designee who will decide if re-review by the full committee is necessary.

Expedited Scientific Review

Conducted by the Chair, Scientific Review Committee or IC Clinical Director. The following protocols may receive expedited review.

- Phase II/III, multi-center protocols which have previously undergone a written scientific review elsewhere that the Institute validates as acceptable;
- For other studies, an appeal to the Committee Chair or Clinical Director may be made for consideration of expedited review.

Waived from Scientific Review

The PI should provide the justification to waive scientific review in the Scientific Review form. A protocol may be waived at the time of initial and quadrennial review and if approved by the Scientific Review Committee Chair, with concurrence by the Clinical Director or Scientific Director, forwarded to the Chief Scientific Officer, NIH Clinical Center, for concurrence. The following protocols may be waived:

- Retrospective analysis protocol (secondary analysis).
- Data analysis/repository protocols (prospectively collecting samples).
- Screening or Training protocols.
- Tissue collection/procurement protocols.

Annual Merit Review of Protocols

With the approval of the Clinical Director, annual merit reviews may be delegated at the time of continuing review to the IC Lab/Branch Chief or CC Department Chief where the clinical study is being performed. If the PI of the study is an IC Branch/Lab Chief or a CC Department Chief, the Clinical Director or his/her designee will perform the annual merit review. The signature of the person overseeing the review attests by electronically signing in iRIS, to continued scientific relevance, satisfactory accrual, and absence of patient safety concerns. All protocols will

undergo annual scientific review, except for protocols that are complete and conducting data analysis only.

Amendment Reviews

Amendments require review if, in the opinion of the Clinical Director or designee, changes to the protocol affect the level of risk, scientific question, or statistical analysis of the protocol. Examples include:

- Change in the protocol primary objectives.
- Addition of a new study agent.
- Change in trial design of significant consequence (e.g., adding arms or removing arms to a randomized phase II trial).
- Increase in the projected number of participants by 15% or greater or as designated Institute policy.

Amendments requiring Scientific Review must be submitted via iRIS and include:

- Signatures of the Principal Investigator, Lab/Branch Chief or CC Department Chief, Accountable Investigator, Chair Scientific Review Committee, and Institute or Center leadership (i.e., Scientific Director and/or Clinical Director.
- Scientific Review Form for an Amendment.
- Protocol and Consent (tracked change versions).
- Updated PRIA, if changing the research.

Quadrennial Merit Review

Active protocols require "deep dive" Scientific Review every 4 years; the anniversary date for the Quadrennial Merit Review is based on the IRB approval date. Quadrennial merit reviews will follow Initial Scientific Review guidance.

All protocols will undergo quadrennial merit review except for protocols that have completed recruitment/follow-up and are now conducting data analysis only.

Quadrennial Merit Review must be submitted via iRIS and include:

- Protocol/Consents
- Scientific Review Form for a Quadrennial Review
- Institute Scientific Review
- Signatures
- Other relevant documentation as required by the Institute