IRP Scientific Review Process of Human Subjects Research

Submission Requirements for Initial Scientific Review

Note: The Scientific Review policy does not apply to Single Patient Expanded Access protocols, whether emergency or non-emergency, and therefore do not require submission in PROTECT nor the review and concurrence of the Chief Scientific Officer.

PI Requirements

Scientific Review Form (required elements that are not addressed in the protocol. Form located in PROTECT.)

- Are you requesting a waiver of scientific review? y/n. If yes, provide justification for why this protocol qualifies for a waiver.
- Study type: Interventional/Observational/Expanded Access
- Milestone Plan.
- Common Data Elements (CDE) Applicability.
- Disease Community Partnership.
- Investigator Qualifications.

Attachments to SR submission form:

- Protocol--The full protocol is required. If the protocol is written by a third party (i.e., pharma or cooperative group) an addendum with the NIH description of the protocol should be included.
- Consent documents are optional (only if required by IC committee)
- Planned Enrollment table must be completed on a fillable PDF
- Data Management and Sharing Plan
- Any additional IC specific required attachments

Signatures obtained in PROTECT as an ancillary review before the action is submitted for scientific review by the committee:

- Principal Investigator
- Accountable Investigator (when applicable)
- Lab/Branch Chief or CC Department Chief

Committee Review Requirements

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.

Membership requirement:

- 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.

When the Chair of the Scientific Review Committee is the PI, the Deputy Chair of the Committee, Clinical Director, Scientific Director, a 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.

The PI or designee must be available to discuss the protocol and/or answer questions during the committee review.

Each committee will have the same outcome letter template to be used in PROTECT. The committee will vote and possible outcomes for each review are:

- Approved
- Approved with recommendations/stipulations
- Disapproved
- Waiver approved

**Overall Protocol Assessment Rating:** In each committee, members should rank the overall scientific merit of the protocol on a scale of 1-10, 10 being the highest score. This should be obtained by anonymous/secret ballot and tallied with an average overall score by the SR coordinator. This numerical score should be entered into PROTECT in the “submit committee review” activity.

Outcome letter will reflect the minutes of the meeting. This letter should be generated before the action is sent for further review/signatures.

- Attendance record (this should specify the number of members present, if quorum was met/maintained, and note the number (if any) extramural members in attendance
- The outcome (approved, etc.).
- Summary of the discussion/review
- Specific line items/headers to address the committee’s discussion of the following topics:
  - Milestone Plan.
  - Data management and sharing plan.
  - Note that committee discussion about the adequacy of the DMSP must be reflected in the outcome letter.
  - Common Data Elements (CDE) Applicability.
  - Disease Community Partnership.
  - Investigator Qualifications.
  - Planned enrollment
- Any stipulations/recommendations to be addressed by the PI

If the committee has any stipulations or recommendations, these must be entered into PROTECT under the “submit committee review” activity and sent in the outcome letter to the PI. The PI can download this document and respond to each stipulation/recommendation and attach that document along with returning the modified protocol (if needed). Responses should then be reviewed by the Scientific Review Committee Chair/Clinical Director or Institute designee who will decide if re-review by the full committee is necessary.

Scientific Director or Clinical Director approval must be obtained in PROTECT as an Ancillary Review after the Committee has completed final review (to provide final approval). The SD or CD may function as Chair of the review committee. These signatures must be obtained prior to the action being sent to Chief Scientific Officer for review and approval.
Chief Scientific Officer, CC is then assigned to review the scientific review as an Ancillary Review to approve in the system.

Final approval letter should be sent to the study team after Chief Scientific Officer, CC has signed off. This will complete the review in PROTECT.

**Expedited Scientific Review**
Conducted at the discretion of the Chair, Scientific Review Committee, IC Scientific Director 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.

The action will be assigned to the Chair of the Scientific Review committee as a designated reviewer for review and approval in PROTECT.

The outcome letter documenting the expedited review must be generated in the system and must include the justification for why this protocol qualified.

Scientific Director or Clinical Director approval must be obtained in PROTECT as an Ancillary Review after the Chair has approved the protocol. The SD or CD may function as Chair of the review committee. This signature must be obtained prior to the action being sent to Chief Scientific Officer for review and approval.

Chief Scientific Officer, CC is then assigned to review the scientific review as an Ancillary Review to approve in the system.

Final approval letter should be sent to the study team after Chief Scientific Officer, CC has signed off. This will complete the review in PROTECT.

**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 types of protocols may be waived:
- Retrospective analysis protocol (secondary analysis).
- Data collection/repository protocols (prospectively collecting data/samples).
- Screening protocols.
- Tissue collection/procurement protocols.
- Expanded access protocols

The action will be assigned to the Chair of the Scientific Review committee for review and approval of the waiver in PROTECT.
The outcome letter documenting the waiver must be generated in the system and must include the justification for why this protocol qualified.

Scientific Director or Clinical Director approval must be obtained in PROTECT as an Ancillary Review after the Chair has approved the protocol prior to the action being sent to Chief Scientific Officer for review and approval.

Chief Scientific Officer, CC is then assigned to review the scientific review as an ancillary review to approve in the system.

Final approval letter should be sent to the study team after Chief Scientific Officer, CC has signed off. This will complete the review in PROTECT.

**Annual Merit Review of Protocols --this is done at the IC/branch level and does not require review/signature by the Chief Scientific Officer**

All protocols will undergo annual scientific review, except for protocols that are complete and conducting data analysis only or protocols that exclusively conduct secondary analysis. PROTECT will send a reminder to the investigator when the annual review is due at 90, 60 and 30 days before the due date.

The Cumulative Inclusion Enrollment Report (CIER) must be attached to the annual review that is completed in PROTECT, along with the Participant Age Data for protocol initiated on or after January 25, 2019. This is required to be in compliance with the NIH Inclusion Across the Lifespan Policy. For protocols conducted at the NIHCC, the data can be generated using BTRIS. Note: that a CIER and Participant Age Data is not required for a protocol with an accrual status of ‘Completed Study’ unless this is the first annual review with the status of “Completed Study”.

The action will be assigned to either the Committee for review or the Chair (or delegate) of the Scientific Review committee (as per IC SOP) for review and approval in PROTECT. This review confirms the continued scientific relevance, satisfactory accrual, and absence of patient safety concerns.

The outcome letter documenting the annual review must be generated in the system.

With the approval of the Clinical Director, final approval of annual merit reviews may be delegated 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. This approval must be obtained in PROTECT as an ancillary review after the Chair or Committee has approved the protocol.

Final approval letter should be sent to the study team after IC approver has completed his/her review. This will complete the review in PROTECT.

**Modification Reviews**
Modifications to the protocol 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 or change in study type).
- Increase in the projected number of participants.

Modifications requiring Scientific Review must be submitted via PROTECT and include:

- Signatures as above with the IR using the Ancillary Review functionality
- Scientific Review Form for a modification.
- Protocol and Consent (tracked change versions may be required per IC SOP).

**Committee Review:**

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.

Membership requirement:

- 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.

When the Chair of the Scientific Review Committee is the PI, the Deputy Chair of the Committee, Clinical Director, Scientific Director, a 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.

The PI or designee must be available to discuss the protocol and/or answer questions during the committee review.

Each committee will have the same outcome letter template to be used in PROTECT. The committee will vote and possible outcomes for each review are:

- Approved
- Approved with stipulations
- Approved with recommendations
- Disapproved

Outcome letter will reflect the minutes of the meeting.

- Attendance record (this should specify the number of members present, if quorum was met/maintained, and note the number (if any) extramural members in attendance
- The outcome (approved, etc.).
- Summary of the discussion/review
- Any stipulations/recommendations to be addressed by the PI

If the committee has any stipulations or recommendations, these must be entered into PROTECT under the “submit committee review” activity and sent in the outcome letter to the PI. The PI can download
this document and respond to each stipulation/recommendation and attach that document along with returning the modified protocol (if needed). Responses should then be reviewed by the Scientific Review Committee Chair/Clinical Director or Institute designee who will decide if re-review by the full committee is necessary.

Scientific Director or Clinical Director approval must be obtained in PROTECT as an Ancillary Review after the Committee has completed final review (final approval) prior to the action being sent to Chief Scientific Officer for review and approval.

Chief Scientific Officer, CC is then assigned to review the scientific review as an Ancillary Review to approve in the system.

Final approval letter should be sent to the team after Chief Scientific Officer, CC has signed off. This will complete the review in PROTECT.

**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 initial approval date in the system. PROTECT will send a reminder to the investigator when the quad review is due at 90, 60 and 30 days prior to the due date.

All protocols will undergo quadrennial merit review except for protocols that have completed recruitment/follow-up and are now conducting data analysis only or protocols exclusively performing secondary data analysis. However, the Institute may conduct a review when and if they believe it is appropriate.

Quadrennial Merit Review must be submitted via PROTECT and include:

- Scientific Review Form for a Quadrennial Review
- Protocol/Consents (currently approved version is available in the Documents tab in PROTECT)
- Other relevant documentation as required by the Institute

Signatures obtained are the same as the IR using the Ancillary Review functionality.

**Committee Review:**
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.

Membership requirement:

- 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.

When the Chair of the Scientific Review Committee is the PI, the Deputy Chair of the Committee, Clinical Director, Scientific Director, a 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.
The PI or designee must be available to discuss the protocol and/or answer questions during the committee review.

Each Committee will have the same outcome letter template to be used in PROTECT. The Committee will vote and possible outcomes for each review are:

- Approved
- Approved with stipulations
- Approved with recommendations
- Disapproved

Outcome letter will reflect the minutes of the meeting.

- Attendance record (this should specify the number of members present, if quorum was met/maintained, and note the number (if any) extramural members in attendance
- The outcome (approved, etc.).
- Summary of the discussion/review
- Any stipulations/recommendations to be addressed by the PI

If the committee has any stipulations or recommendations, these must be entered into PROTECT under the “submit committee review” activity and sent in the outcome letter to the PI. The PI can download this document and respond to each stipulation/recommendation and attach that document along with returning the modified protocol (if needed). Responses should then be reviewed by the Scientific Review Committee Chair/Clinical Director or Institute designee who will decide if re-review by the full committee is necessary.

Scientific Director or Clinical Director approval must be obtained in PROTECT as an Ancillary Review after the Committee has completed final review (final approval) prior to the action being sent to Chief Scientific Officer for review and approval.

Chief Scientific Officer, CC is then assigned to review the scientific review as an Ancillary Review to approve in the system.

Final approval letter should be sent to the team after Chief Scientific Officer, CC has signed off. This will complete the review in PROTECT.