

Yale Cancer Center Protocol Review Committee Charter

Version 1.1

TABLE OF CONTENTS

1.0	Definitions	4
2.0	Mission	5
3.0	Authority	5
4.0	Membership	6
4.1	Protocol Review Committee	6
4.1.1	Chair	6
4.1.2	Vice Chair	6
4.1.3	Voting Members.....	6
4.1.4	Ad Hoc Members.....	7
4.2	Protocol Life Cycle Subcommittee	7
4.2.1	Chair	7
4.2.2	Voting Members.....	7
5.0	Responsibilities	7
5.1	Protocol Review Committee	7
5.1.1	Membership.....	7
5.1.2	Principal Investigator and Research Team.....	8
5.1.3	Office of Quality Assurance and Training.....	8
5.2	Protocol Life Cycle Subcommittee	8
5.2.1	Membership.....	8
5.2.2	Principal Investigator and Research Team.....	9
5.2.3	Office of Quality Assurance and Training.....	9
6.0	Procedures	9
6.1	Protocol Review Committee Initial Submissions	9
6.1.1	Review Criteria	9
6.1.2	Submissions for Full Committee Review.....	10
6.1.3	Submissions for Expedited Review	12
6.1.4	Submissions for Administrative Review.....	12
6.2	Protocol Review Committee Amendment Reviews.....	13
6.2.1	Review Criteria	13
6.2.2	Submission Requirements.....	13
6.2.3	Submission Review.....	13
6.2.4	Review Outcome	13
6.3	Protocol Review Committee Meeting.....	13

6.3.1	Schedule.....	13
6.3.2	Quorum.....	14
6.3.3	Attendance and Conflict of Interest.....	14
6.3.4	Meeting Conduct.....	14
6.3.5	Minutes.....	14
6.4	Protocol Life Cycle Subcommittee.....	14
6.4.1	Review Criteria.....	14
6.4.2	Submissions.....	14
6.4.3	Meetings.....	15
6.4.4	Minutes.....	15
7.0	Escalation.....	15
7.1	Protocol Review Committee.....	15
7.1.1	Clinical Research Oversight Committee.....	15
7.2	Protocol Life Cycle Subcommittee.....	16
7.2.1	7.2.2 Clinical Research Oversight Committee.....	16
8.0	Appendices.....	16
	Appendix A: Risk Assessment Score Sheet.....	17
	Appendix B: YCC Accrual Monitoring Policy.....	18
	Appendix C: YCC Scientific Progress Policy.....	2
	Appendix D: Protocol Review Committee Review Requirements by Protocol Type.....	2

Yale Cancer Center Protocol Review Committee (PRC) Charter

1.0 DEFINITIONS

Ancillary clinical trials: Studies that are stimulated by, but are not a required part of, a main clinical trial/study, and that utilize patient or other resources of the main trial/study to generate information relevant to it. Ancillary studies must be linked to an active clinical research study and should include only patients accrued to that clinical research study.

Behavioral clinical trials: Studies among cancer patients and healthy populations that involve no intervention or alteration in the status of the participants, e.g. surveillance, risk assessment, outcome, environmental, and behavioral studies.

Clinical Research Oversight Committee (CROC): An oversight body of the Yale Cancer Center comprised of senior leadership from the Yale Cancer Center and Smilow Cancer Hospital.

Correlative clinical trials: Laboratory-based studies using specimens to assess cancer risk, clinical outcomes, response to therapies, etc.

Disease Aligned Research Team (DART): Promote translational research at Smilow Cancer Hospital through scientific discovery, testing new discoveries in the clinics and, ultimately, turning new innovations into viable disease-specific therapeutics.

Externally Peer Reviewed: R01s, SPORes, U01s, U10s, P01s, CTEP or any other clinical research study funding mechanism supported by the National Institutes of Health (NIH) or organizations on the list of Organizations with Peer Review Funding Systems provided by the NIH

Interventional clinical trials: Individuals are assigned prospectively by an investigator based on a protocol to receive specific interventions. The participants may receive diagnostic, treatment, behavioral, or other types of interventions. The assignment of the intervention may or may not be random. The participants are followed and biomedical and/or health outcomes are assessed.

Investigator-initiated clinical trials: Also referred to as institutional clinical trials. In-house clinical research studies authored or co-authored by Cancer Center investigators and undergoing scientific peer review solely by the Protocol Review and Monitoring System of the Cancer Center. The Cancer Center investigator has primary responsibility for conceptualizing, designing, and implementing the clinical research study and reporting results. It is acceptable for industry and other entities to provide support (e.g., drug, device, other funding), but the trial should clearly be the intellectual product of the center investigator. This category may also include:

- Institutional studies authored and implemented by investigators at another Center in which your Center is participating
- Multi-Institutional studies authored and implemented by investigators at your Center (Note: National and externally peer-reviewed studies should be listed with those categories, not as Institutional studies)

Observational clinical trials: Studies that focus on cancer patients and healthy populations and involve no prospective intervention or alteration in the status of the participants. Biomedical and/or health outcome(s) are assessed in pre-defined groups of participants. The participants in the study may receive diagnostic, therapeutic, or other interventions, but the investigator of the observational study is not responsible for assigning specific interventions to the participants of the study.

Office of Quality Assurance and Training (OQAT): Office responsible for providing administrative support to the Yale Cancer Center review committees.

OnCore: Yale University School of Medicine's Clinical Trials Management System

Primary Completion Date: The date on which the last participant in a clinical study was examined or received an intervention to collect final data for the primary outcome measure. Whether the clinical study ended according to the protocol or was terminated does not affect this date. For clinical studies with more than one primary outcome measure with different completion dates, this term refers to the date on which data collection is completed for all the primary outcome measures.

Therapeutic clinical trials: Protocol designed to evaluate one or more interventions for treating a disease, syndrome, or condition.

Trials of Rare Diseases: Per the National Cancer Institute, incidence rate ≤ 6 newly diagnosed persons out of a population of 100,000 persons per year ($\leq 6/100,000$ per year). Using definition or cut-off, virtually all pediatric cancer types would be considered "rare cancers."

2.0 MISSION

The mission of the Yale Cancer Center (YCC) Protocol Review Committee (PRC) is to provide ongoing review of scientific merit, priorities and progress of YCC clinical research trials. The Yale Cancer Center (YCC) established the Protocol Review and Monitoring System (PRMS) in 1993 to be the internal review and monitoring system for all cancer clinical trials conducted at YCC. The PRMS evaluates the scientific merit and priority of all cancer-related clinical trials at YCC, and serves as the primary scientific review system for all cancer-related protocols prior to approval by the Yale University Institutional Review Board (IRB, locally known as Human Investigation Committee (HIC)) or Yale University Human Research Protection Program (HRPP) for those studies using an external IRB as the IRB of record.

There are two major components of the PRMS that provide for clinical research review and oversight: The Protocol Review Committee (PRC) and the Protocol Life Cycle Subcommittee (PLCS), a subcommittee for review of protocol-specific accrual and scientific progress. These two components function to approve and provide oversight to protocols submitted by each of the Disease Aligned Research Teams (DART), which serve as the first level to review proposed protocols and select them according to their scientific merit and strategic portfolio fit. When combined, the DART protocol review and committee review processes synergistically ensure that all proposed clinical trials receive high-quality peer review and monitoring, remain consistent with YCC clinical research priorities, and progress in a timely fashion.

3.0 AUTHORITY

The National Cancer Institute (NCI) Cancer Center Support Grant (CCSG) Guidelines call for a mechanism for assuring adequate internal oversight of the scientific aspects of all the cancer clinical trials within the Comprehensive Cancer Center. The Protocol Review and Monitoring System (PRMS) has ultimate authority for assessing scientific merit, research priority, and scientific progress of cancer clinical trials. The PRMS

has the authority to approve protocols that meet the scientific merit and scientific priorities of the center and to terminate protocols that do not demonstrate accrual and/ or scientific progress.

4.0 MEMBERSHIP

4.1 Protocol Review Committee

The PRC is comprised of voting and ad hoc members. The YCC Director appoints all members of the PRC and the PRC Chair(s). There will be a minimum of fourteen voting members of the PRC. Membership includes a broad range of representation from the YCC investigational community and includes investigators who are engaged daily in clinical research activities, protocol oversight, design and conduct. For studies requiring special expertise, the PRC Chair may request the YCC Director appoint ad hoc members to provide advice on protocols, including in the areas of behavioral studies and basic science. A list of current PRC members is maintained by the Office of Quality Assurance and Training (OQAT). Refer to *YCC Research Oversight Committees Membership Guidelines* for more information regarding recruitment, appointment and terms, evaluation of membership, Ad Hoc members and mentoring.

4.1.1 Chair

The PRC is chaired by a senior cancer center member and is appointed by the YCC Director. The Chair has ultimate responsibility to the YCC Director for meeting CCSG PRMS guidelines, including attendance at least 80% of meetings. The Chair duties include, but are not limited to:

- following up on committee actions.
- ensuring timely execution of correspondence.
- consulting on reviewer assignment.
- completing expedited scientific reviews.
- communicating with Principal Investigators (PIs) regarding PRC actions, when necessary.
- reviewing meeting agendas.
- reviewing and approving meeting minutes.
- evaluating member attendance and performance.
- mentoring primary and alternate voting members of the PRC.
- mentoring and assigning responsibilities to Vice Chair.
- evaluating committee composition.

4.1.2 Vice-Chair

The Vice-Chair is appointed by the YCC Director following recommendation from the Chair. The Vice-Chair plays a pivotal role in assuring timely and consistent quality reviews. Vice-Chair duties include, but are not limited to: completing expedited scientific reviews and mentoring primary and alternate voting members of the PRC as assigned by the Chair. The Vice-Chair chairs in the absence of the Chair.

4.1.3 Voting Members

Voting members are appointed by the YCC Director. The voting members of the PRC will represent the following disciplines:

- Clinical
- Population-Based Science
- Radiation
- Surgery
- Biostatistics
- Basic Laboratory*
- Prevention*

- Cancer Control*

Senior voting members of the PRC may be assigned as mentors to new committee members. Senior voting members of the PRC may be assigned to perform expedited reviews at the discretion of the Chair.

4.1.4 Ad Hoc Members*

Ad Hoc members are appointed by the YCC Director or Chair. Ad hoc members may be called upon to review studies when specific expertise in basic science, population-based science and/ or cancer prevention and control is required. When an ad hoc member is called upon to review a study, they will serve as a voting member of the PRC for their ad hoc review.

4.2 Protocol Life Cycle Subcommittee

The PLCS is comprised of a minimum of three voting members of the PRC, appointed by the YCC Director.

4.2.1 Chair

The PLCS is chaired by a senior member of the PRC and is appointed by the YCC Director. The Chair is responsible for attending at least 80% of meetings. The Chair duties include, but are not limited to:

- following up on committee actions.
- ensuring timely execution of correspondence.
- completing expedited accrual monitoring and/or scientific progress reviews.
- communicating with PIs regarding PLCS actions, when necessary.
- reviewing meeting agendas.
- evaluating member attendance and performance.
- mentoring members of the PLCS.
- evaluating committee composition.

4.2.2 Voting Members

Voting members are appointed by the YCC Director. All members of the PLCS serve as voting members. Senior members of the PLCS may be assigned as mentors to new committee members.

5.0 RESPONSIBILITIES

5.1 Protocol Review Committee

5.1.1 Membership

New members undergo orientation and training with the PRC Regulatory Analyst and/ or the Assistant Director of OQAT to review PRC procedures, meeting format, and scientific review instructions.

At least bi-annually and whenever membership changes, the YCC Director and Clinical Research Oversight Committee (CROC) will perform an assessment of the membership composition. The assessment considers areas of expertise and committee needs in addition to ongoing members' rates of attendance, participation in meetings, and quality and quantity of reviews performed.

Members must attend 75% of the meetings held in a calendar year. Members will be provided with an annual assessment of their attendance compared to expectations defined within the committee charter and the quality and quantity of reviews performed. Decisions regarding recruitment will be made to ensure that membership has the diverse expertise and knowledge required for appropriate review of the research within the scope of the PRC.

5.1.2 Principal Investigator and Research Team

The PI, in collaboration with the Research Team, is responsible for submitting all required documents for PRC review via the electronic Protocol Review and Monitoring System of Yale School of Medicine’s Clinical Trials Management System (OnCore). The PI is expected to respond to inquiries from the assigned scientific reviewer in a timely fashion and before the scheduled review, whenever feasible. The PI, in collaboration with the research staff, is required to respond to any required changes that the PRC may request for the submission post-PRC review. The PI, in collaboration with the research staff, is encouraged to respond to any recommended changes that the PRC may provide.

5.1.3 Office of Quality Assurance and Training

OQAT staff administratively coordinates the PRC meeting. This includes but is not limited to:

- Intake of PRC submission and notification of PI and relevant members of the research team of PRC decisions.
- Assigning reviewers.
- Preparing the agenda and meeting materials.
- Sending meeting materials to the PRC members at least one week in advance of the meeting.
- Preparing the meeting room including audio-visual equipment.
- Tracking attendance.
- Preparing PRC meeting minutes.
- Obtaining approval from Chair of PRC meeting minutes.
- Communicating PRC decisions to the PI in writing within one week of the meeting.
- Maintaining PRC activity tracking in OnCore.

A quality assurance risk assessment is completed by the OQAT on all trials reviewed by the PRC regardless of review type to assess regulatory and compliance risk for the institution. The PRC reviewer will be provided the risk assessment score sheet [Appendix A] completed by OQAT. The risk assessment total score guides the timing of the initial OQAT audit, however the PRC may adjust the audit schedule based on their review. The standard audit schedule is as follows:

Risk Assessment Score	Initial Audit
> 10	100% of the first 2 subjects accrued, regulatory, pharmacy for investigational products
7- 10	Consent & eligibility for first 2 subjects, regulatory
< 7	Random (1 trial per month; rotate Pediatric Department Sections): Consent & eligibility for 2 subjects, regulatory

5.2 Protocol Life Cycle Subcommittee

5.2.1 Membership

New members undergo orientation and training with PLCS Regulatory Analyst and/ or the Assistant Director of OQAT to review PLCS procedures, meeting format, and scientific progress and accrual monitoring review instructions.

At least bi-annually and whenever membership changes, the YCC Director and Clinical Research Oversight Committee (CROC) will perform an assessment of the membership composition. The assessment considers areas of expertise and committee needs in addition to ongoing member’s rate of attendance, participation in meetings, quality of reviews performed and quantity of reviews

performed. Members must attend 75% of the meetings held in a calendar year. Members will be provided with an annual assessment of their attendance compared to expectations defined within the committee charter and the quality and quantity of reviews performed. Decisions regarding recruitment will be made to ensure that membership has the expertise and knowledge required for appropriate review of the research within the scope of the research oversight committee.

5.2.2 Principal Investigator and Research Team

The PI, in collaboration with the Research Team, is responsible for submitting all required documents for scientific progress review. The PI, in collaboration with the research team, is responsible for maintaining up-to-date accrual information, enrollment status and primary completion dates in OnCore. The PI, in collaboration with the research staff, is required to respond to PLCS correspondence.

All responsibilities of the PI and Research Team are outlined in further detail in the YCC Accrual Monitoring Policy [Appendix B] and the Scientific Progress Policy [Appendix C].

5.2.3 Office of Quality Assurance and Training

OQAT staff administratively coordinates the PLCS meeting. This includes but is not limited to:

- Intake of PLCS submissions from DARTs.
- Preparing the agenda and meeting materials.
- Generating the accrual monitoring report from OnCore.
- Sending meeting materials to the PLCS members at least one week in advance of the meeting.
- Preparing the meeting room including audio-visual equipment.
- Tracking attendance.
- Preparing the PLCS meeting minutes.
- Communicating the committee decisions to the investigator in writing within one week of the meeting and on a rolling basis.
- Maintaining PLCS activity tracking in OnCore.

6.0 PROCEDURES

6.1 Protocol Review Committee Initial Submissions

6.1.1 Review Criteria

Interventional studies and ancillary or correlative studies that are institutionally or industry-sponsored undergo full board review at a convened PRC meeting. Interventional, ancillary or correlative studies that are nationally-sponsored or externally peer-reviewed, including those studies received from a site with an acceptable or provisionally acceptable PRMS, undergo expedited review. The PRC will receive a report of expedited review determinations. The reviewer may refer a study for full board review. Non-therapeutic non-interventional studies, such as quality of life studies and observational studies are administratively reviewed by the OQAT research oversight committee staff. The PRC will receive a report of administrative review determinations. Non-clinical non-hypothesis driven research, such as retrospective chart review, biorepository, tissue bank and single patient investigational new drug applications, is exempt from PRC review. See Appendix D: Protocol Review Committee Review Requirements by Protocol Type.

The PRC Regulatory Analyst triages a trial for PRC review. If the review type is not clear, the Chair is consulted.

6.1.2 Submissions for Full Committee Review

6.1.2.1 Review Criteria

All interventional studies and ancillary or correlative studies that are institutionally or industry-sponsored undergo full committee review by a quorum of the PRC at a convened meeting. See Section 6.1.3 for Multicenter externally-peer reviewed trials, including investigator-initiated trials from other Cancer Centers.

6.1.2.2 Submission Requirements

All submissions for full committee review must include the following:

- Submission via OnCore’s electronic Protocol Review and Monitoring System
- Protocol
- Investigator’s Brochure(s) (as applicable)
- DART Protocol Review Form

6.1.2.3 DART Protocol Review

DARTs meet on a regular basis to review their current clinical trials portfolio and accrual. The DART Leader reviews each application for protocol submission and must approve submission of the protocol to PRC. This review and approval is documented by signing the *DART Protocol Review Form*. Electronic signatures are acceptable. The signature by the DART Leader on this form represents a commitment to provide the necessary resources to conduct the trial, or ensure that the trial can be conducted using the resources available to each disease team within a reasonable timeframe.

The *DART Protocol Review Form* requires the PI to state the accrual targets at Yale, scope of participation, accrual considerations, importance of the study to YCC, how the study fits within the DART portfolio, and the role of Yale investigators and/ or scientists in the trial. When eligibility criteria overlap such that a proposed study competes with an open study for the same patients, the DART Leader must include a sound justification to open the newly proposed study. This justification must include whether patient characteristics will guide which study is prioritized, or the order in which competing studies will be considered when a potentially eligible subject is being evaluated, as well as the expected closure date of each competing trial and the enrollment to date on each competing trial.

PRC submission will occur after DART protocol review is complete.

6.1.2.4 PRC Review

The PRC reviews each submitted study to ensure scientific merit, appropriate prioritization, and lack of competition with existing protocols in the DART portfolio or within another DART focusing on the same patient population. The PRC review encompasses an assessment of the scientific rationale and merit, protocol design, safety parameters, biostatistical analysis of the protocol, and review of the investigator’s brochure (IB), if appropriate. Protocols are scored for scientific priority. The PRC has final authority to determine scientific priority.

6.1.2.5 Criteria for Scoring Scientific Priority

Category	Points Awarded
Clinical Significance	0, 1, 2, or 3

Patient Availability	0, 1, 2, or 3
Scientific Merit and Novelty	0, 1, 2, or 3
Peer reviewed Funding	0 or 3 pts
Yale Science Related	0 or 2 pts
Investigator Initiated	0 or 2 pts
Role of the Yale Investigator in Trial	0 or 2 pts
Availability of funding other than peer reviewed	0, 1, or 2

Overall Priority Score Scale	Priority Score
13 Points or greater (maximum = 20)	1
9 – 12 Points	2
6 – 8 Points	3

6.1.2.6 Voting

The possible PRC outcomes are:

- **Approved:** The committee has determined that the protocol has met all criteria for scientific merit and feasibility.
- **Approved with Recommendations:** The committee has determined that the protocol meets criteria for scientific merit and feasibility, but may require clarifications or minor changes that do not affect committee approval.
- **Approved Requiring Response:** The committee has determined that the protocol requires further clarifications or changes that may affect the assessment of scientific merit or feasibility. The PI will be requested to address recommendations and/or provide a detailed explanation for each concern.
- **Disapproval:** The committee has determined that the protocol lacks strong enough evidence of scientific merit and feasibility. This may include protocols with biostatistical calculations that are considered insufficient; trials which are of lower priority than competing trials currently accruing; or those which do not address an important question in clinical cancer medicine. The PI must address all issues and submit the revised protocol for another full-committee review if activation of the study will proceed.
- **Tabled:** The committee cannot review the protocol at a scheduled meeting due to time constraints, reviewer unavailability or other unforeseen circumstances. Tabled submissions will be re-scheduled for review at the first available meeting.
- **Withdrawn:** A protocol can be withdrawn by the PI at any point in the review process. PRC can also withdraw a protocol if it finds it is not well suited or appropriate as

designed.

The PRC actions on review are: approval, approval with recommendations, approval pending a required response, tabled, or disapproval. A letter is provided to the PI which states the decision. Studies approved pending a required response receive an additional letter once the required response is affirmed, and the study is then either approved or disapproved.

If a tied vote occurs, the study is considered disapproved. A disapproval letter will be issued to the PI.

6.1.3 Submissions for Expedited Review

6.1.3.1 Review Criteria

Interventional and ancillary or correlative studies that are nationally-sponsored or externally peer-reviewed by a site with an acceptable or provisionally acceptable PRMS undergo an expedited review by the PRC Chair, Vice-Chair, or designee.

6.1.3.2 Submission Requirements

All submissions must include the following:

- Initial Submission via OnCore's electronic Protocol Review and Monitoring System
- Protocol
- Investigator's Brochure(s) (as applicable)
- DART Protocol Review Form

6.1.3.3 PRC Expedited Review

Submissions are reviewed by the Chair, Vice-Chair, or designee to ensure scientific merit, appropriate prioritization, adequate resources, and lack of competition with existing protocols in the DART portfolio or within another DART focusing on the same patient population. Completed expedited reviews and their outcome are listed on the PRC meeting agenda for notification to PRC membership.

6.1.3.4 Review Outcome

Refer to section 6.1.2.6 Voting for possible review outcomes. At the discretion of the reviewer, the submission may be referred to the PRC for full committee review at a convened meeting.

6.1.4 Submissions for Administrative Review

6.1.4.1 Review Criteria

Non-therapeutic non-interventional studies, such as quality of life studies, and observational studies are administratively reviewed and acknowledged by the PRC Regulatory Analyst.

6.1.4.2 Submission Requirements

All submissions must include the following:

- Initial Submission via OnCore's electronic Protocol Review and Monitoring System
- Protocol or equivalent
- DART Protocol Review Form

6.1.4.3 Submission Review

Submissions are reviewed administratively by the PRC Regulatory Analyst. Completed administrative reviews and their outcome are listed on the PRC meeting agenda for notification to PRC membership.

6.1.4.4 Review Outcome

Administratively reviewed studies are acknowledged. The administrative reviewer may consult the Chair and/ or Vice-Chair if significant concerns arise during review of the submission. The Chair and/ or Vice-Chair may elect to perform an expedited review of the submission or refer the submission for full committee review at a convened PRC meeting.

6.2 Protocol Review Committee Amendment Reviews

6.2.1 Review Criteria

Substantial changes to protocols including changes to the drug compound, dosing, or schedule; significant eligibility changes; methods of response evaluation; study objectives (primary and secondary); and the statistics or statistical analysis plan must be approved by the PRC prior to submission to the IRB.

6.2.2 Submission Requirements

All submissions must include the following:

- Submission via OnCore's electronic Protocol Review Submission system
- Protocol (tracked version, if available)
- Protocol (clean version)
- Investigator's Brochure (only if accompanying an amendment to the protocol)
- Summary of Changes document for protocol
- Summary of Changes document for the Investigator's Brochure (if available)
- Sponsor correspondence (if amendment is initiated by an external sponsor)
- Updated DART Review Form signed (or email acknowledged) by DART Leader*

**Required for Full Board review only*

6.2.3 Submission Review

Significant Amendment changes to the drug (compound) and eligibility, such as additional disease areas or updates reflecting a change in SOC) are reviewed by the full PRC. Other significant amendments undergo expedited review by the Chair, Vice-Chair, or designee to assess if the revisions impact the scientific merit of the study. The expedited reviewer assesses any change in prioritization within the DART portfolio. The expedited reviewer may require a change to the DSMP based on the amendment, which would be communicated to the PI and research team via PRC decision letter. At the discretion of the expedited reviewer, an amendment may be referred for full committee review at a convened PRC meeting.

6.2.4 Review Outcome

Refer to section 6.1.2.6 Voting for possible review outcomes.

6.3 Protocol Review Committee Meeting

6.3.1 Schedule

The Protocol Review Committee typically meets two times per month. Meetings are subject to rescheduling if quorum cannot be met or at the discretion of the Chair. The meeting schedule and corresponding submission deadlines can be found [on the PRC website](#).

6.3.2 Quorum

Quorum for this committee is achieved with votes from at least seven voting members which must include a minimum of one biostatistician and three medical oncologists or hematologists.

6.3.3 Attendance and Conflict of Interest

Members sign in at each committee meeting and declare in writing any protocol on the agenda item(s) which may present a conflict of interest (COI) for them. All committee members who have a COI recuse themselves from the closed protocol discussion and vote.

6.3.4 Meeting Conduct

The Chair, Vice Chair or Chair designee, a member identified as needed in times of Chair/Vice Chair recusal or absences, will begin the meeting when quorum is met. Primary reviewers present a detailed evaluation of each protocol they are assigned to review. Reviewers critique against the criteria that protocols be well focused, hypothesis-driven and based on sound scientific rationale. The risk assessment, data and safety monitoring plan and accrual considerations (if the study includes a rare disease or rare molecular subtype) are discussed. Members with a COI are asked to leave the room or telephone line so a closed discussion may occur. The discussion culminates in a vote. In addition to voting, committee members score each study using the criteria for scoring scientific priority outlined in Section 6.1.2.5. Following the meeting, the PRC Regulatory Analyst assigns an overall priority score of 1-3, with 1 being top priority, from the average of the individual scores provided by the committee members.

6.3.5 Minutes

OQAT staff attends PRC meetings to record minutes, which includes a detailed summary of the meeting discussion and all recommendations and required responses from the PI. Minutes are provided to the PRC Meeting Chair for review and approval post-meeting. Chair approved minutes are circulated to committee members at a subsequent meeting for final approval.

6.4 Protocol Life Cycle Subcommittee

6.4.1 Review Criteria

All interventional cancer clinical trials reviewed by the Protocol Review Committee that are open to accrual are reviewed by the PLCS.

6.4.2 Submissions

6.4.2.1 Scientific Progress Reviews

Protocols that are open to enrollment are reviewed for continuing validity of the scientific question as well as the anticipated timeframe for completion. The PLCS will evaluate the scientific progress of all interventional trials that are open to enrollment or temporarily suspended to enrollment with intention to re-open to accrual at the time of continuing review with the IRB of record. Trials that are no longer scientifically relevant or that will not meet their scientific objective(s) will be recommended to the PRC for closure to further accrual. Refer to Appendix C: *YCC Scientific Progress Policy* for more information.

6.4.2.2 Accrual Monitoring Reviews

The PLCS functions under accrual monitoring guidelines originally adopted in March 2017 requiring warning letters and closure recommendations to PRC using the milestones as described in the *YCC Accrual Monitoring Policy*. Refer to Appendix B: *YCC Accrual Monitoring Policy* for more information.

6.4.3 Meetings

6.4.3.1 Schedule

The Protocol Life Cycle Subcommittee typically meets every other month. Meetings are subject to rescheduling at the discretion of the Chair. The meeting schedule and corresponding submission deadlines can be found [on the PLCS website](#).

6.4.3.2 Quorum

Quorum for this committee is achieved with attendance at least half of the membership.

6.4.3.3 Attendance and Conflict of Interest

Members sign in at each committee meeting and declare in writing any protocol on the agenda for which they have a COI. All committee members who have a COI recuse themselves for the protocol scientific progress discussion and vote.

6.4.3.4 Meeting Conduct

The Chair (or designee for Meeting Chair) will begin the meeting when quorum is met. Scientific progress reviews are presented to the committee. An open discussion will occur and culminate with a vote. The YCC Accrual Monitoring Report is reviewed by the committee using the aforementioned criteria.

6.4.3.5 Voting

Scientific progress reviews may require a vote by the PLCS if brought to a convened meeting for discussion. Accrual monitoring is discussed openly and consensus reached on the outcome.

The possible PLCS outcomes for accrual monitoring are:

- Recommended for Closure to PRC
- Approved to Continue
- Request for Additional Information

If a tied vote occurs, the study will be recommended for closure to PRC.

The PI is notified by an action notice within approximately 1-3 working days of the committee's decision.

6.4.4 Minutes

The OQAT staff attends all PLCS meetings to take minutes, which includes a detailed summary of meeting discussion and all requests for more information from the PI. Minutes are provided to the PLCS Chair for review and approval post-meeting. Chair approved minutes are circulated to committee members at a subsequent meeting for final approval.

7.0 ESCALATION

7.1 Protocol Review Committee

7.1.1 Clinical Research Oversight Committee

The Clinical Research Oversight Committee (CROC) may be consulted for issues that cannot be resolved by the PRC. Requests for escalation may be made to the Chair, Vice Chair and/ or OQAT staff or to CROC directly. Non-PRC members may also consult CROC for issues related to PRC. Recommendations from

CROC will be reviewed and resolved by the PRC Chair. The PRC chair may consult other members of the committee regarding recommendations at their discretion.

7.2 Protocol Life Cycle Subcommittee

7.2.1 7.2.2 Clinical Research Oversight Committee

The Clinical Research Oversight Committee (CROC) may be consulted for issues that cannot be resolved by the PLCS. Requests for escalation may be made to the Chair and/ or OQAT staff or to CROC directly. Non-PLCS members may also consult CROC for issues related to PLCS. Recommendations from CROC will be reviewed and resolved by the PLCS Chair. The PLCS chair may consult the PRC Chair and other members of the committee regarding recommendations at their discretion.

8.0 APPENDICES

Appendix A: Risk Assessment Score Sheet



Office of QA and Training
2 Church Street
South
Suite 112
New Haven, CT
06519

Protocol Risk Assessment Score Sheet			
IRB#	Primary Investigator:	Dept/Div:	
Risk Factors		Score	Comments
Phase (Select 1 from the group below)			
Phase I	(worth 5 points; add 2 pts if First in Human)		
Phase II	(worth 4 points; add 1 pt for Stopping Rules)		
Phase III	(worth 3 points)		
Phase IV/Expanded Access	(worth 1 point)		
Non-therapeutic	(worth 0 points)		
Phase 0/Feasibility/Pilot/behavioral intervention/ Diagnostic	(worth 3 points)		
Phase Total Points			
Sponsor (Select 1 from the group below)			
Investigator Sponsor (Investigator Initiated Trial (IIT) with an FDA Investigational New Drug (IND) or Investigational Device Exemption (IDE))	(worth 5 points)		
IIT — no IND or IDE	(worth 4 points)		
Government (NIH, NCI, etc.)	(worth 3 points; add 1 pt if no sponsor monitoring)		
Industry	(worth 2 points)		
Subtotal			
Modality			
Number of treatment modalities	(worth 1 point for each modality >1)		
Subtotal			
Agent or Intervention Risk Factors (Select 1 or more from the group below)			
Not Applicable	(worth 0 points)		
>1 invasive procedure	(worth 3 points)		
Device	(worth 3 points)		
Bone Marrow Transplant/Peripheral Blood Stem Cell Transplant/ Gene Therapy/ Gene Transfer studies/ Cellular Manipulation	(worth 4 points)		
Radio-labeled research studies	(worth 4 points)		
Agent developed with Yale input	(worth 4 points)		
Subtotal			
Biospecimens (Select if applicable)			
Not Applicable	(worth 0 points)		
Research Tissue or Blood Samples (Trial with correlative component/ Pharmacokinetics/Pharmacodynamics/ Immunogenicity studies)	(worth 3 points)		
Subtotal			
Expected Accrual Rate (Select if applicable)			
Not Applicable	(worth 0 points)		
Trial to be completed in < 12 months	(worth 4 points)		
High accruing	(worth 3 points)		
Subtotal			
Multi Center — Yale as Lead (Select 1 or more from the group below)			
Not Applicable	(worth 0 points)		
1-3 additional sites	(worth 2 points)		
> 3 sites	(worth 5 points)		
1 or more international sites	(worth 3 points)		
Smilow Hospital Care Centers (SHCC) — off main campus	(worth 2 points)		
Yale-New Haven Hospital (YNHH) affiliates	(worth 2 points)		
Subtotal			
Populations (Select 1 or more from the group below)			
Not Applicable	(worth 0 points)		
Children (teens of child bearing potential code once)	(worth 3 points)		
Prisoners	(worth 3 points)		
Women of child bearing potential (w/ treatment/risks)	(worth 3 points)		
Decisionally impaired	(worth 3 points)		
Culturally sensitive and/or Certificate of Confidentiality	(worth 3 points)		
Subtotal			
Special Circumstances (Select if applicable)			
Not Applicable	(worth 0 points)		
Yale Institutional Review Board (IRB) is not IRB of record	(worth 3 points)		
First trial for this Principal Investigator	(worth 1 point)		
Subtotal			
Total Score			
Quality Assurance Team Reviewer:			Date:
Score >10 = High Risk, 100% audit of first 2 subjects. Depending upon audit findings, committee determines next steps.			
Score 7-10 = Moderate Risk, Regulatory, Eligibility & Consent audit for first 2 subjects. Depending upon audit findings committee determines next steps.			
Score < 7 = Low Risk, Random Selection, Regulatory, Eligibility & Consent review for randomly selected subjects, rotating through departments. Depending upon audit findings committee determines next steps.			

YCCI Office of Quality Assurance and Training Form Version 5, Date: March 27, 2017.

Appendix B: YCC Accrual Monitoring Policy

**Yale Cancer Center
Accrual Monitoring Policy**

Contents

1. INTRODUCTION	3
1.1 Background	3
1.2 Definitions	3
2. ACCRUAL MONITORING POLICY.....	3
2.1 Accrual Monitoring Rules for Non-Rare Trials	3
2.1.1 Accrual Monitoring Table.....	3
2.1.2 Calculation of Percentage of Target Accrual Rate	4
2.1.3 Trials That Have Not Reached Accrual Goal Prior to Anticipated Primary Completion Date.....	5
2.1.4 Trials Meeting Target Accrual Rate, but with Zero Accrual in the Past Six Months.....	5
2.2 Guidance for Trials of Rare Diseases and Rare Molecular Subtypes.....	5
2.3 Accrual Monitoring Procedures	5
2.3.1 Identifying Trials of Rare Diseases and Rare Molecular Subtypes	5
2.3.2 Principal Investigator’s Role in Maintaining OnCore Study Record	5
2.4 Accrual Monitoring Process	6
2.4.1 Reassessment of Closure Recommendation.....	6
2.4.2 PRC Ratification of PLCS Closure Recommendations.....	6
2.5 Closure of a Clinical Trial	7
2.6 Appeal Process	7

1. INTRODUCTION

1.1 Background

The National Cancer Institute (NCI) Cancer Center Support Grant (CCSG) guidelines call for a mechanism for assuring adequate internal oversight of the scientific aspects of all the cancer clinical trials in the institution. The focus of the Protocol Review and Monitoring System (PRMS) is scientific merit, prioritization, and progress of cancer clinical trials. The PRMS has the authority to open protocols that meet the scientific merit and scientific priorities of the center and to close protocols that do not demonstrate scientific progress. The Protocol Life Cycle Subcommittee (PLCS) of the Protocol Review Committee (PRC), a component of Yale Cancer Center's PRMS, is responsible for monitoring the accrual and scientific progress of all active, interventional, cancer clinical trials. This is facilitated through review of scientific progress and a report of accrual for all open to accrual cancer clinical trials.

1.2 Definitions

Clinical Research Oversight Committee (CROC): An oversight body of the Yale Cancer Center comprised of senior leadership from the Yale Cancer Center and Smilow Cancer Hospital.

Office of Quality Assurance and Training: Office responsible for providing administrative support to the Yale Cancer Center review committees.

OnCore: Yale University School of Medicine's Clinical Trials Management System

Trials of Rare Diseases: Per the NCI, Incidence rate ≤ 6 newly diagnosed persons out of a population of 100,000 persons per year ($\leq 6/100,000$ per year). Using definition or cut-off, virtually all pediatric cancer types would be considered "rare cancers."

IREs IRB: Yale University's electronic submission and review system for human subjects' research studies.

2. ACCRUAL MONITORING POLICY

2.1 Accrual Monitoring Rules for Non-Rare Trials

2.1.1 Accrual Monitoring Table

The following accrual monitoring rules will be applied for all interventional cancer clinical trials that are open to enrollment, except for trials of rare diseases or rare molecular sub-types. Trials with dose escalation and dose expansion phases will be evaluated according to the criteria provided below and will follow the *Protocol Life Cycle Subcommittee OnCore Instructions for Dose Escalation/ Dose Expansion Studies* for dose escalation accrual targets to be accurately monitored.

Assessment Time	Percentage of Target Accrual Rate	Action
3 months	0%	Warning
6 months	0%	Closure
9 months	< 30%	Warning
12 months	< 30%	Closure
15 months	< 40%	Warning
18 months	< 40%	Closure
21 months	< 50%	Warning
24 months	< 50%	Closure

After 24 months open, trials are evaluated for closure every 6 months with warning notices issued 3 months prior if not meeting $\geq 50\%$ of target accrual.

2.1.2 Calculation of Percentage of Target Accrual Rate

$$\frac{\text{Actual Accrual}}{\text{Current \# of days open}} \div \frac{\text{Target Accrual Goal}}{\text{Expected Duration (days)}}$$

Example: A trial has an expected accrual duration of 365 days with an expected accrual of 8 study participants. At the time of review, the trial has been open 377 days with 2 accruals to date. Since the trial has been open for more than 12 months with only 24% of the target accrual rate reached, the trial will be issued a closure notice.

$$\frac{2}{377} \div \frac{8}{365} = .2420 \text{ or } 24\%$$

2.1.3 Trials That Have Not Reached Accrual Goal Prior to Anticipated Primary Completion Date
Applicable to all interventional trials unless they are national or international cooperative group or industry studies which have not reached their overall accrual goals.

On the anticipated primary completion date, if trial has not reached total accrual goal, a warning notice is issued.

Six (6) months past the anticipated primary completion date, if trial has not reached total accrual goal, a recommendation for closure is provided by the PLCS to the PRC.

The PRC will vote on and ratify all PLCS closure recommendations. The PLCS will also receive a report of PRC accrual monitoring decisions.

2.1.4 Trials Meeting Target Accrual Rate, but with Zero Accrual in the Past Six Months

PLCS will review trials with zero accrual in the past six months. A response may be requested from the Principal Investigator (PI) regarding accrual plans and continued interest in enrolling to the trial. PLCS may recommend closure of these trials.

2.2 Guidance for Trials of Rare Diseases and Rare Molecular Subtypes

The PLCS will review accrual targets and screening efforts for trials of rare diseases and rare molecular subtypes during scientific progress reviews. Refer to Yale Cancer Center's Scientific Progress Policy for more information. The PLCS will review screening activity for the prior 12 months for consideration.

2.3 Accrual Monitoring Procedures

2.3.1 Identifying Trials of Rare Diseases and Rare Molecular Subtypes

The PI and research team will be responsible for identifying trials of rare diseases including rare molecular subtypes and uncommon clinical subsets of more common cancers on the *DART Protocol Review Form* (PRC submission requirement). The rare determination will be discussed and verified during PRC review. After verification at PRC review, the rare categorization will be captured in Yale School of Medicine's Clinical Trials Management System, OnCore.

2.3.2 Principal Investigator's Role in Maintaining OnCore Study Record

The PI and research team are expected to maintain the study record in OnCore including any change in accrual goals as reported to the IRB of record, change in anticipated primary completion date, and updating the status to "suspended" during any periods when the study temporarily cannot enroll new participants (study placed on hold by sponsor due to drug shortages, statistical analysis, etc.), in order to accurately assess accrual and scientific progress.

2.4 Accrual Monitoring Process

The Office of Quality Assurance and Training will be responsible for generating an accrual monitoring report from OnCore for PLCS review. Warning notices are issued as the criteria in Section 2.1.1 are met. A report of warning notices distributed will be provided to the PLCS via meeting agenda. Those trials that meet the criteria for closure recommendation, as outlined in Section 2.1.1, will be added to the PLCS meeting agenda for discussion. Trials of rare diseases and rare molecular subtypes will not be included the accrual monitoring report.

The PLCS will discuss and decide if a trial will be recommended for closure to the PRC. If consensus is reached by the PLCS, the PI will be notified and the trial will be scheduled for discussion at an upcoming PRC meeting.

The Office of Quality Assurance and Training will be responsible for issuing the “Accrual Monitoring Warning” or “Closure Recommendation Notice” on behalf of the PLCS. The correspondence will be addressed to the PI with copy to the DART Leader, Assistant Director of Clinical Trials Operations in Clinical Research, Assistant Director of Clinical Trials Operations in Regulatory Affairs, Clinical Trial Team Manager (CTTM), and Regulatory Assistant.

2.4.1 Reassessment of Closure Recommendation

Upon receipt of a “Closure Recommendation Notice” from the PLCS, if the PI would like to have the closure recommendation reassessed by the PLCS, the Office of Quality Assurance and Training must be notified by the PI in writing within 5 business days. The PI will need to explain barriers to enrollments, provide a plan for increasing accrual and a justification for keeping the trial open.

If a request to reassess a closure recommendation is received within 5 business days, the PLCS Chair will review the request and determine if the PI needs to attend the PRC meeting, either in person or remotely, to discuss the trial or if the PRC’s review of the PI’s request is sufficient.

2.4.2 PRC Ratification of PLCS Closure Recommendations

The PRC will vote on and ratify all PLCS closure recommendations. The PLCS will also receive a report of PRC accrual monitoring decisions.

The Office of Quality Assurance and Training will be responsible for issuing the accrual monitoring decision letters on behalf of the PRC. The correspondence will be addressed to the PI with copy to the DART Leader, Assistant Director of Clinical Trials Operations in Clinical Research, Assistant Director in Clinical Trials Operations in Regulatory Affairs, CTTM, and Regulatory Assistant.

2.5 Closure of a Clinical Trial

The PI and research team are responsible for updating the OnCore status as well as submitting the necessary paperwork to the study sponsor and the IRB of Record according to their policies and procedures. The Office of Quality Assurance and Training will monitor OnCore and IRES IRB to ensure that the status of the trial is updated accordingly. If a trial has not accrued study participants and the study sponsor agrees, paperwork will be submitted for IRB study closure and the OnCore status will be updated accordingly. If a trial has participants on treatment or in follow-up, the trial will be closed to further enrollment. The Office of Quality Assurance and Training will monitor the trial until it is completely closed with the IRB of record.

The PI and research team will take all necessary actions to comply with closure notices within 5 business days of receipt of the closure notice.

2.6 Appeal Process

The PI may request reassessment of the PLCS closure recommendations within 5 business days, as outlined in 2.3.4 above, and request appeal of PRC closure decisions to the PRC within 5 business days. The PI will explain barriers to enrollments, provide a plan for increasing accrual and a justification for keeping the trial open.

Reassessment and appeal requests regarding decisions from PLCS and PRC may be submitted to the Clinical Research Oversight Committee (CROC) for initial review and discussion.

During the appeal process, no new study participants may be accrued. The study status will be changed to “Suspended” in OnCore.

The CROC review and recommendation on the appeal will be submitted to the PRC for their decision on the appeal.

The PRC has final and absolute authority on all appeals related to the PRMS. The PRC has the authority to close any study.



Appendix C: YCC Scientific Progress Policy

**Yale Cancer Center
Scientific Progress Policy**

Contents

1.	INTRODUCTION.....	3
1.1	BACKGROUND	3
1.2	DEFINITIONS.....	3
2.	SCIENTIFIC PROGRESS POLICY AND PROCEDURE.....	3
2.1	POLICY	3
2.2	PROCEDURE	3
2.3	DETERMINATIONS.....	4
2.3.1	EXPEDITED REVIEW	4
2.3.2	FULL BOARD REVIEW	5
2.4	CORRESPONDENCE REGARDING DETERMINATIONS	5
2.5	REASSESSMENT OF CLOSURE RECOMMENDATION.....	5
2.6	PRC REVIEW OF SCIENTIFIC PROGRESS CLOSURE RECOMMENDATIONS	5
2.7	CLOSURE OF A CLINICAL TRIAL.....	6
2.8	APPEAL PROCESS.....	6

1. INTRODUCTION

1.1 BACKGROUND

The National Cancer Institute (NCI) Cancer Center Support Grant (CCSG) Guidelines call for a mechanism for assuring adequate internal oversight of the scientific aspects of all the cancer clinical trials in the institution. The focus of the Protocol Review and Monitoring System (PRMS) is scientific merit, prioritization, and progress of cancer clinical trials. The PRMS has the authority to open protocols that meet the scientific merit and scientific priorities of the center and to close protocols that do not demonstrate scientific progress.

The Protocol Life Cycle Subcommittee (PLCS) of the Protocol Review Committee (PRC), a component of Yale's PRMS, is responsible for monitoring the accrual and scientific progress of all active interventional cancer clinical trials. This is facilitated through review of scientific progress and a report of accrual for all open to accrual clinical trials.

1.2 DEFINITIONS

Clinical Research Oversight Committee (CROC): An oversight body of the Yale Cancer Center comprised of senior leadership from the Yale Cancer Center and Smilow Cancer Hospital.

Office of Quality Assurance and Training (OQAT): Office responsible for providing administrative support to the Yale Cancer Center review committees.

OnCore: Yale University School of Medicine's Clinical Trials Management System

ePRMS: ePRMS is a paperless committee management system within OnCore. It is designed to assist the workflow of the PRMS.

2. SCIENTIFIC PROGRESS POLICY AND PROCEDURE

2.1 POLICY

The PLCS will evaluate the scientific progress of all interventional trials that are open to accrual or temporarily suspended to enrollment with intention to re-open to accrual at the time of continuing review with the Institutional Review Board (IRB) of record. Trials that are no longer scientifically relevant or that will not meet their scientific objective(s) will be recommended to the PRC for closure to further accrual.

2.2 PROCEDURE

Approximately 2 months prior to the IRB expiration date, the Office of Quality Assurance and Training (OQAT) research oversight committee staff will request the scientific progress report from the Principal Investigator, including the Clinical Trial Team Manager (CTTM) and

Regulatory Assistant on the correspondence. Reports of scientific progress will be due within 10 business days of the OQAT request. The report will include completion of the *Scientific Progress Report* form (See Appendix A) and any supporting documentation.

The ePRMS Submission Console of Yale School of Medicine's Clinical Trials Management System, OnCore, will be utilized for submission of scientific progress reports. Scientific progress reports will be submitted as Continuation Reviews within ePRMS.

The following documentation will be attached in ePRMS:

- Scientific Progress Report form
- Supporting documentation, such as:
 - Progress Reports from the Sponsor
 - Study Newsletters or Updates
 - Email correspondence from the Sponsor
 - Publications, manuscripts, etc.

Scientific progress reports will be assigned to a PLCS member for expedited review. The reviewing PLCS member will make a determination as outlined in Section 2.3 below. At the discretion of the PLCS reviewing member, the scientific progress report may be referred for review at a convened PLCS meeting.

If the reviewing PLCS member requires additional information to complete their review, the member may request the information from the Disease Aligned Research Team (DART) Leader or PI. This request may include but is not limited to:

- Further details on DART priorities and where the trial aligns.
- Written justification for why the trial should remain open.
- Attendance at a convened PLCS meeting.

Reviews of scientific progress should be completed by the PLCS member prior to the IRB expiration date. The PLCS will receive a report of expedited review determinations.

2.3 DETERMINATIONS

2.3.1 EXPEDITED REVIEW

Following expedited review, the following determinations may be made:

- No further action is required and plan to review at the time of the next continuing review.
- Request that the status of the trial be re-evaluated prior to the next continuing review. The timeframe for re-review will be determined by the PLCS reviewing member.
- Request full board review.

- Recommend the study for closure to the PRC.

2.3.2 FULL BOARD REVIEW

Following full board review, the following determinations may be made:

- The PLCS may determine that no further action is required and plan to review at the time of the next continuing review, as applicable.
- The PLCS may request that the status of the trial be re-evaluated prior to the next continuing review. The timeframe for re-review will be determined by the PLCS.
- The PLCS will vote to decide if a trial will be recommended for closure to the PRC. If a majority vote is reached by the PLCS, the PI will be notified and the closure recommendation will be scheduled for review at an upcoming PRC meeting. If a tied vote occurs, the study will be recommended for closure to the PRC.

2.4 CORRESPONDENCE REGARDING DETERMINATIONS

The OQAT staff will be responsible for issuing the “No Action Required Notice”, “Re-evaluation Prior to Next Continuing Review Notice” or “Closure Recommendation Notice” on behalf of the PLCS. The correspondence will be addressed to the PI with a copy to the DART Leader, Assistant Director of Clinical Trials Operations in Clinical Research, Assistant Director of Clinical Trials Operations in Regulatory Affairs, CTTM, and Regulatory Assistant.

2.5 REASSESSMENT OF CLOSURE RECOMMENDATION

Upon receipt of a “Closure Recommendation Notice” from the PLCS, if the PI would like to have the closure recommendation reassessed by the PLCS, the Office of Quality Assurance and Training must be notified by the PI in writing within 5 business days. The PI will need to offer a justification for keeping the trial open.

If a request to reassess a closure recommendation is received within 5 business days, the PLCS Chair will review the request and determine if the PI needs to attend the PRC meeting, either in person or remotely, to discuss the trial or if the PRC’s review of the PI’s request is sufficient.

2.6 PRC REVIEW OF SCIENTIFIC PROGRESS CLOSURE RECOMMENDATIONS

Any trial recommended for closure due to lack of scientific progress will be placed on an upcoming PRC meeting agenda for discussion. The PRC will vote on and ratify all PLCS closure recommendations. The PLCS will receive a report of PRC decisions.

The Office of Quality Assurance and Training will be responsible for issuing the scientific progress decision letters on behalf of the PRC. The correspondence will be addressed to the PI with a copy to the DART Leader, Assistant Director of Clinical Trials Operations in Clinical Research, Assistant Director in Clinical Trials Operations in Regulatory Affairs, CTTM, and Regulatory Assistant.

2.7 CLOSURE OF A CLINICAL TRIAL

The PI and research team are responsible for updating the OnCore status as well as submitting the necessary paperwork to the study sponsor and the IRB of Record according to their policies and procedures. The Office of Quality Assurance and Training will monitor OnCore and IRES IRB to ensure that the status of the trial is updated accordingly. If a trial has not accrued study participants and the study sponsor agrees, paperwork will be submitted for IRB study closure and the OnCore status will be updated accordingly. If a trial has participants on treatment or in follow-up, the trial will be closed to further enrollment. The Office of Quality Assurance and Training will monitor the trial until it is permanently closed with the IRB of record.

The PI and research team will take all necessary actions to comply with closure notices within 5 business days of receipt of the closure notice.

2.8 APPEAL PROCESS

The DART Leader or PI may request appeal of PRC closure decisions to the PRC within 5 business days of receipt of the closure letter. The DART Leader or PI will offer justification for keeping the trial open.

Reassessment and appeal requests regarding decisions from PLCS and PRC may be submitted to the Clinical Research Oversight Committee (CROC) for initial review and discussion. The CROC review and recommendation on the appeal will be submitted to the PRC for their decision on the appeal.

During the appeal process, no new study participants may be accrued. The study status will be changed to “Suspended” in OnCore.

The PRC has final and absolute authority on all appeals related to the PRMS. The PRC has the authority to close any study.

Appendix D: Protocol Review Committee Review Requirements by Protocol Type

Protocol Review Committee
Review Requirements by Protocol Type

Protocol Type	Sponsor Type	Review Required	Review Type	Scientific Review	Biostatistician Review
Therapeutic Interventional	National	Yes	Expedited ¹	1 Reviewer	N/A
	Externally Peer-Reviewed	Yes	Expedited ¹	1 Reviewer	N/A
	Institutional	Yes	Full Board	2 Reviewers	1 Reviewer
	Industry	Yes	Full Board	1 Reviewer	N/A
Non-therapeutic Interventional, i.e., diagnostic, staging, behavioral, etc.	National	Yes	Expedited ¹	1 Reviewer	N/A
	Externally Peer-Reviewed	Yes	Expedited ¹	1 Reviewer	N/A
	Institutional	Yes	Full Board	2 Reviewers	1 Reviewer
	Industry	Yes	Full Board	1 Reviewer	N/A
Non-therapeutic Non-Interventional, i.e., Quality of Life Studies, etc.	National	Yes	Administrative ²	N/A	N/A
	Externally Peer-Reviewed	Yes	Administrative ²	N/A	N/A
	Institutional	Yes	Administrative ²	N/A	N/A
	Industry	Yes	Administrative ²	N/A	N/A
Ancillary or Correlative, i.e., specimen/ data collection³	National	Yes	Expedited ¹	1 Reviewer	N/A
	Externally Peer-Reviewed	Yes	Expedited ¹	1 Reviewer	N/A
	Institutional	Yes	Full Board	1 Reviewer	N/A
	Industry	Yes	Full Board	1 Reviewer	N/A
Observational including cancer patients and healthy populations	National	Yes	Administrative ²	N/A	N/A
	Externally Peer-Reviewed	Yes	Administrative ²	N/A	N/A
	Institutional	Yes	Administrative ²	N/A	N/A
	Industry	Yes	Administrative ²	N/A	N/A
Exempt from Review: Any Non-hypothesis driven research³			Retrospective chart review, biorepository, tissue bank, Single Patient IND		

¹ Expedited Review: Submissions are reviewed by the chair, vice-chair, or designee for prioritization. The risk assessment is conducted by the Office of Quality Assurance and Training and the data and safety monitoring plan is reviewed and approved by the reviewer at time of review. Approved submissions are listed on the Protocol Review Committee (PRC) meeting agenda for notification to PRC membership.

² Administrative Review: Submissions are reviewed administratively by the PRC Regulatory Analyst. The risk assessment is conducted by the Office of Quality Assurance and Training and the study is assigned a data and safety monitoring plan. Acknowledged submissions are listed on the PRC meeting agenda for notification to PRC membership.

³ Only studies that can be linked to individual participant data will be reported to the NCI.