

Yale Cancer Center Protocol Review Committee Charter

Version 2.0

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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. Only studies that can be linked to individual patient or participant data should be reported.

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 Trials Advisory Committee (CTAC): An advisory body of the Yale Cancer Center chaired by the Associate Director for Clinical Research at YCC and comprised of senior leadership from different disciplines whose primary focus is clinical research. CTAC is charged with developing and overseeing the implementation of strategic plans to optimize the clinical research enterprise, providing broad oversight and policy direction, ensuring continuity and progress on key issues such as clinical trial accrual and time to activation. CTAC also provides critical advice and feedback on the operational directions and activities of the Clinical Trials Office, and reviews and approves the policies and procedures of the Protocol Review Committee and Data and Safety Monitoring Committee.

Correlative clinical trials: Laboratory-based studies using specimens to assess cancer risk, clinical outcomes, response to therapies, etc. Only studies that can be linked to individual patient or participant data should be reported.

Clinical Research Team (CRT): Disease and/or modality-specific study teams who promote translational research at Smilow Cancer Hospital and its network of affiliated care centers 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.

Industry-sponsored: Also referred to as industrial clinical trials. A pharmaceutical company controls the design and implementation of these clinical research studies.

Investigator-initiated clinical trials: Also referred to as institutional clinical trials. In-house clinical research studies authored or co-authored by Yale Cancer Center investigators and undergoing scientific peer review solely by the Protocol Review and Monitoring System of the Yale Cancer Center. The Yale 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)

National: NCI National Clinical Trials Network (NCTN) and other NIH-supported National Trial Networks

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.

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.

Treatment 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."

YCC Quality and Education Unit: Responsible for providing administrative support to the Yale Cancer Center research oversight committees.

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. YCC established the Protocol Review and Monitoring System (PRMS) in 1993 to be the internal review and monitoring system for all cancer and cancer-related clinical trials conducted at YCC. The PRC, YCC's second stage of

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 and cancer-related protocols prior to approval by the Institutional Review Board (IRB) of record. The PRC is also responsible for monitoring the accrual and scientific progress of all active, interventional cancer and cancer-related clinical trials.

The PRC functions to approve and provide oversight for protocols submitted by each of the Clinical Research Teams (CRT), which serves as the first stage for review of proposed protocols and select them according to their scientific merit and strategic portfolio fit. When combined, the CRT protocol review and PRC 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 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 cancer center and to terminate protocols that do not demonstrate accrual and/ or scientific progress.

4.0 MEMBERSHIP

The PRC is comprised of two panels with identical scope of reviews each with voting and non-voting members. There will be a minimum of ten voting members on each panel. A minimum of half plus one voting members must be present to satisfy quorum requirements for a meeting. Membership includes a broad range of representation from the YCC research community and consists largely of those who are engaged daily in clinical research activities including protocol oversight, design and conduct. For studies requiring special expertise, the YCC Director, at the Chair's request, may appoint ad hoc non-voting members to provide advice on protocols.

The YCC Director appoints all members of the PRC, the PRC Chair(s), and Vice Chair(s). Approximately bi-annually and whenever membership changes, the YCC Director 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.

A list of current PRC members is maintained by the YCC Quality and Education unit.

4.1.1 Chair(s)

Each PRC panel 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 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.
- consulting on reviewer assignments.
- completing scientific reviews, scientific progress reviews, accrual monitoring reviews, and closure reviews.
- communicating with Principal Investigators (PIs) regarding PRC actions, when necessary.
- reviewing meeting agendas.
- reviewing and acknowledging meeting minutes.
- evaluating member attendance and performance.
- mentoring voting members of the PRC.
- mentoring and assigning responsibilities to Vice Chair.
- evaluating committee composition.

4.1.2 Vice Chair(s)

Each 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 scientific reviews, scientific progress reviews, accrual monitoring reviews, and closure reviews.
- mentoring voting members of the PRC as assigned by the Chair.

The Vice Chair chairs meetings in the absence of the Chair and fulfills the duties of the chair, as outlined in 4.1.1, as applicable, for the assigned meeting. In the event the chair must recuse from a portion of the meeting, the Vice Chair will fulfill the duties of the chair for the recused protocol(s).

4.1.3 Voting Members

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

- Basic Laboratory
- Prevention
- Clinical
- Cancer Control
- Population-Based Science
- Radiation
- Surgery
- Biostatistics

The Chair may assign senior voting members of the PRC as mentors to new committee members. Voting members of the PRC are assigned to perform scientific reviews and closure reviews.

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 a therapeutic area or approach is needed. 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.

5.0 RESPONSIBILITIES

5.1.1 Committee Members

New members undergo orientation and training with the YCC Quality and Education unit to review PRC procedures, meeting format, and review instructions.

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 quantity of reviews performed. Decisions regarding committee member recruitment will ensure that membership has the diverse expertise and knowledge required for appropriate review of the research within the scope of the PRC.

The PRC is responsible for assessing the protocol-specific data and safety monitoring plan (DSMP) to confirm appropriate oversight and monitoring of the conduct of the clinical trial is planned to ensure the safety of study participants and the validity and integrity of the data. At the time of the initial review, the PRC reviews the protocol to determine if the DSMP is adequate for the risk level of the study, taking into account the phase of the study, the plan for external clinical monitoring, the utilization of an independent Data and Safety Monitoring Board (DSMB) or equivalent, as applicable, and other special circumstances that the committee feels may impact the safety of the study participants.

Studies without external data and safety monitoring or studies where the DSMP is not adequate will be scheduled for review by the Yale Data and Safety Monitoring Committee every six months. High risk studies, regardless of external data and safety monitoring, may be assigned for Yale DSMC reviews every six months or more frequently at the discretion of the PRC.

Refer to the DSMC Charter for more information.

5.1.2 Principal Investigator (PI)

The PI or their designee is responsible for submitting all required documents for PRC review via the electronic Protocol Review and Monitoring System (ePRMS) of Yale School of Medicine's Clinical Trials Management System (OnCore). The PI or their designee is expected to respond to inquiries from the Quality and Education unit and/ or assigned reviewer(s) in a timely fashion and before the scheduled review. The PI or their designee is required to respond to any required changes that the PRC may request for the submission post-PRC review.

5.1.3 Clinical Research Team (CRT)

As the first stage of YCC’s protocol review and monitoring process, proposed protocols are initially discussed by the CRT, including disease-oriented and modality CRTs (e.g., Phase 1 and Cell Therapy) who meet on a regular basis to review their current clinical trials portfolio and accrual. Each CRT is required to conduct an internal review to assess all newly proposed research for clinical significance, scientific merit and novelty, portfolio suitability, feasibility, and consistency with overall YCC goals. CRTs are required to utilize a protocol scoring rubric to prioritize trials for submission to PRC. Studies are reviewed during CRT meetings and scored by the CRT leader. A study’s total score will equate to a YCC Priority Score between 1 – 4, and will move along the approval pathway as follows:

Priority Score	Protocol Total Score	Next Steps
Priority 1	20-31	Protocol may proceed to PRC
Priority 2	11-19	Protocol requires clear written justification from CRT Leader to proceed
Priority 3	6-10	If CRT endorses, protocol must be approved by Associate Director, Clinical Research
Priority 4	0-5	Protocol does not move forward (as written) to PRC

The review and approval are documented by signing the CRT Protocol Review Form. Electronic signatures are acceptable. The signature by the CRT 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.

PRC initial submission will occur after CRT protocol review process is complete and the CRT Leader has approved this study for submission to PRC.

5.1.4 Yale Cancer Center Quality and Education Unit

YCC Quality and Education unit staff administratively coordinate the PRC meeting. This includes but is not limited to:

- Intaking PRC submission and triaging a trial for PRC review and consulting the chair if the review type is not clear.
- Assigning reviewers.
- Preparing the agenda and meeting materials.
- Sending meeting materials to the PRC members at least one week in advance of the meeting.
- Setting up virtual conferencing.
- Documenting attendance.
- Documenting member conflicts of interest due to inclusion on study team or other disclosed conflicts.
- Preparing PRC meeting minutes.
- Obtaining acknowledgement from Chair of PRC meeting minutes.

- Communicating PRC decisions to the PI and relevant members of the research team in writing within one week of Chair acknowledgement of the minutes.
- Maintaining PRC activity tracking in OnCore.

5.1.4.1 Quality Assurance Process

A quality assurance risk assessment (Appendix A: Risk Assessment Score Sheet) is completed by the Quality and Education Unit on all trials reviewed by the PRC regardless of review type to assess regulatory and compliance risk for the institution. The risk assessment total score guides the timing of the initial OQAM audit; however, the PRC may adjust the audit schedule based on their review. The YCCI Quality Assurance team conducts internal audits, in partnership with the Yale Human Subjects Protection Program (HRPP), using risk-based stratification methods. The internal audit includes review of regulatory records, case reviews and review of the investigational pharmacy. The PRC is provided the planned audit schedule based upon the risk assessment for initial full committee reviews.

The standard internal audit schedule is as follows:

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

6.0 DETERMINATIONS/PROCEDURES

The PRC may make the following determinations on any review:

- Approved: The committee has determined that the protocol has met all criteria for scientific merit and feasibility.
- 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. The committee will determine if the response is required to be reviewed at a full committee meeting or can be reviewed by a designee for final approval.
- Disapproved: 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. Note: If a tied vote occurs, the study is considered disapproved.

- Deferred: The committee cannot review the protocol at a scheduled meeting due to time constraints, reviewer unavailability or other unforeseen circumstances. Deferred submissions will be re-scheduled for review.

6.1 Initial Review Criteria

The PRC reviews each submitted study initially to ensure scientific merit, appropriate prioritization, and lack of competition with existing protocols in the CRT portfolio or within another CRT 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(s) (IB), package insert(s) and/ or Instructions for Use, if appropriate. The PRC reviews the CRT's assigned scores in each of the categories noted in *Section 5.1.3*. The committee may change the score in any of the categories as applicable.

If the change in score(s) does not impact the Priority Level (1, 2, 3), the protocol can be approved with the requested changes documented in the minutes and PI PRC Decision letter. The Quality and Education Unit will then follow-up directly with the corresponding Clinical Research Team (CRT) who will update REDCap accordingly.

If the change in score(s) does impact the Priority Level (level decreases to a 2, 3, or 4), the protocol can be approved with required response as additional justification and/or approval by the Associate Director of Clinical Research will be needed. These will be required to come back to full committee for review and final approval.

All submissions for initial review must include the following:

- Application via OnCore's electronic Protocol Review and Monitoring System
- Protocol
- Investigator's Brochure(s) (as applicable)
- CRT Review and corresponding CRT Protocol Review and Prioritization Form

6.1.1 Expedited

Interventional and ancillary or correlative studies that are nationally sponsored or external investigator-initiated trials from a site with an acceptable or provisionally acceptable PRMS undergo an expedited initial review performed by a member who conducts expedited reviews.

Submissions are reviewed by a member who conducts expedited reviews to ensure scientific merit, appropriate prioritization, adequate resources, and lack of competition with existing protocols in the CRT portfolio or within another CRT focusing on the same patient population. Completed expedited reviews and their outcome are listed on the PRC meeting

agenda for notification to PRC membership. At the discretion of the reviewer, the submission may be referred to the PRC for full committee review at a convened meeting.

6.1.2 Full Board

All interventional studies and ancillary or correlative studies that are institutionally or industry-sponsored undergo full committee initial review by a panel of the PRC at a convened meeting.

6.1.3 Administrative

Non-therapeutic non-interventional studies, such as quality of life studies, and observational studies are initially administratively reviewed and acknowledged by the Quality and Education Unit.

The Quality and Education Unit completes a Risk Assessment and conducts an initial submission administrative review. Completed administrative reviews and their outcome are listed on the PRC meeting agenda for notification to PRC membership. Administratively reviewed studies are acknowledged. The administrative reviewer may consult the Chair and/ or Vice-Chair if significant concerns arise during initial 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 Amendment 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 at a convened meeting or by an expedited PRC reviewer prior to submission to the IRB. The reviewer will assess any change in prioritization within the CRT portfolio and may require a change to the protocol specific DSMP based on the amendment, which would be communicated to the PI and research team via PRC decision letter.

All submissions must include the following:

- Application 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)
 - Amendment Cover Sheet
 - CRT Amendment Review Form signed (or email acknowledged) by CRT Leader and PI*
- *Required for Full Board amendment review only*

6.3 Accrual Review Criteria

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 or enrollment progress. The PRC 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 and temporarily suspended cancer clinical trials.

All interventional cancer clinical trials initially reviewed by the Protocol Review Committee that are open to accrual or temporarily suspended to enrollment are monitored for accrual. The PRC will review accrual targets and screening efforts for trials of rare diseases and rare molecular subtypes during scientific progress reviews. *Please see the accrual guidelines below:*

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

6.3.1 Submission Requirements

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 (for example if the study is placed on hold by sponsor due to drug shortages, statistical analysis, etc.), in order to accurately assess accrual.

The Quality and Education Unit will be responsible for generating an accrual monitoring report from OnCore for PRC review. Notices and warning letters are issued as the criteria are met. Those trials that meet the criteria for closure recommendation will receive a closure recommendation notice. Upon receipt of this notice, if the PI would like to have the closure recommendation reassessed, the Quality and Education Unit must be notified by the PI in writing within 10 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.

6.3.2 Procedure

A report of notices and warning letters distributed will be provided to the PRC at convened meetings. A report of closure recommendation notices distributed, and any received reassessment requests will be provided to the PRC at convened meeting for discussion and voting.

Following full committee review, the following determinations may be made for each protocol:

- Approved 3-month extension: The committee has determined that the submitted plan for increasing accrual and justification for keeping the trial open is adequate and will reassess the trial’s accrual status in 3 months.
- Approved 6-month extension: The committee has determined that the submitted plan for increasing accrual and justification for keeping the trial open is adequate and given the barriers to enrollment and/or complexity of the trial will reassess the trial’s accrual status in 6 months.
- PRC Closure: The committee has chosen to close the trial due to at least one of the following reasons: the trial is no longer of scientific relevance, the submitted plan for increasing accrual and/or justification for keeping the trial open is unsatisfactory, the barriers to enrollment are too prevalent, or due to other concerns submitted by the PI and/or sponsor.

The Quality and Education Unit will be responsible for issuing the accrual monitoring decision letters on behalf of the PRC.

6.4 Scientific Progress Review Criteria

The PRC reviews scientific progress for active open to accrual and temporarily suspended to enrollment interventional cancer and cancer-related clinical trials annually. Trials that are no longer scientifically relevant or that will not meet their scientific objective(s) may be closed to further accrual.

6.4.1 Submission Requirements

The Quality and Education Unit will provide the CRT with templated slides to be used during the presentation. The following information will be prepopulated:

- Summary of accrual
 - Last 30 days
 - Last 6 months
 - Last 12 months
 - Number of analytic cases
- Summary of trial status
 - Number of trials open to accrual
 - Number of trials suspended
 - Number of trials closed to accrual
- List of all CRT trials including the following for each:
 - Status
 - Status date
 - Rare designation
 - Yale Target Accrual
 - Yale Accrual to Date

6.4.2 Procedure

A PRC Chair/Vice Chair and two senior voting members will attend each CRT Meeting to assess the presentation of each team's portfolio. Following the meeting, a staff member from the CRT will provide the Quality and Education Unit with the completed slides and attendance sheet. The scientific progress review will be placed on the next available agenda of the corresponding PRC for discussion. The committee will vote on a final decision and the decision will be shared with the CRT Leader and the corresponding PIs.

Following full committee review, the following determinations may be made for each active protocol within the CRT portfolio:

- Approved
- Approved requiring response
- Recommend Closure
- Closure: 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 Quality and Education Unit 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 Quality and Education Unit 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.

The Quality and Education Unit will be responsible for issuing the scientific progress decision letters on behalf of the PRC. The correspondence will be entered in ePRMS.

6.5 Protocol Review Committee Panel Meeting

6.5.1 Schedule

Meetings are held approximately four times each 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.

6.5.2 Quorum

A minimum of half plus one voting members must be present to satisfy quorum requirements for a meeting. A protocol will be deferred by the Chair if the composition of the voting members does not include the required membership with the knowledge to provide a robust review of the protocol.

6.5.3 Attendance and Conflict of Interest

PRC members will be expected to follow the Yale University guidelines for disclosing conflicts of interest. Committee members who have a COI may be asked to recuse themselves from a protocol discussion and determination deliberations, as appropriate. All committee members who have a COI recuse themselves from the closed protocol discussion and vote.

6.5.4 Meeting Conduct

The Chair, Vice Chair or Chair designee, or 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. The discussion culminates in a vote. In addition to voting, committee members score each study using the criteria for scoring scientific priority.

6.5.5 Minutes

YCC Quality and Education Unit staff attends PRC meetings to record minutes, which includes a detailed summary of the meeting discussion and all required responses from the PI. Minutes are provided to the PRC Meeting Chair for acknowledgement.

7.0 ESCALATION

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, committee 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.

8.0 APPENDICES

8.1 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 Aneurysm 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)		
Smlow 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.			

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8.2 Appendix B: Protocol Review Committee Initial Review Requirements by Protocol Type

Protocol Type	Sponsor Type	Review Required	Review Type	Scientific Review	Biostatistical Review
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	1 Reviewer
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	1 Reviewer ⁴
	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, Expanded Access protocols		

¹ Submissions are reviewed by a Protocol Review Committee (PRC) member. The quality assurance risk assessment is conducted by the Office of Quality Assurance and Monitoring (OQAM) and the data and safety monitoring plan is reviewed and assigned by the scientific reviewer at time of review. A priority score is assigned by the scientific reviewer. Approved submissions are listed on the PRC meeting agenda for notification to PRC membership.

² Submissions are reviewed administratively by the YCC Quality and Education Unit. The quality assurance risk assessment is conducted by OQAM 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 Studies that can be linked to individual participant data will be reported to the NCI.

⁴ If protocol includes statistical plan. Not applicable if statistical plan is not required based upon the study design.

8.3 Appendix C: Protocol Review Committee Amendment Review Requirements by Protocol Type

Protocol Type	Sponsor Type	PRC Review Required before IRB Submission	Submit Concurrent with IRB Submission	Review Type
Interventional	National	No	No	Exempt from Review
	Externally Peer-Reviewed	No	No	Exempt from Review
	Institutional	Yes	No	Full or Expedited ¹
	Industry	No	Yes	Full or Expedited ¹
Non-Interventional, i.e., Quality of Life Studies, etc.	National	No	No	Exempt from Review
	Externally Peer-Reviewed	No	No	Exempt from Review
	Institutional	No	No	Exempt from Review
	Industry	No	No	Exempt from Review
Ancillary or Correlative, i.e., specimen/ data collection³	National	No	Yes	Exempt from Review
	Externally Peer-Reviewed	No	Yes	Exempt from Review
	Institutional	Yes	No	Full or Expedited ¹
	Industry	No	Yes	Full or Expedited ¹
Observational including cancer patients and healthy populations	National	No	No	Exempt from Review
	Externally Peer-Reviewed	No	No	Exempt from Review
	Institutional	No	No	Exempt from Review
	Industry	No	No	Exempt from Review