

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: 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. If a study is granted an approval period from the IRB of record that is less than 12 months, scientific progress review will occur annually. 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 or annual review date, the Office of Quality Assurance 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 15 business days of the Office of Quality Assurance request. The report will include completion of the *Scientific Progress Report* form (See Appendix A) and any supporting documentation. Scientific progress reviews will be waived for studies that have been open to accrual for fewer than 3 months.

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/ annually.
- Request that the status of the trial be re-evaluated prior to the next continuing review/ annually. 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/ annually, as applicable.
- The PLCS may request that the status of the trial be re-evaluated prior to the next continuing review/ annually. 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 Office of Quality Assurance staff will be responsible for issuing the “No Action Required Notice”, “Re- evaluation Prior to Next Scientific Progress 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 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 response will be provided to the PRC for review.

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 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 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 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.