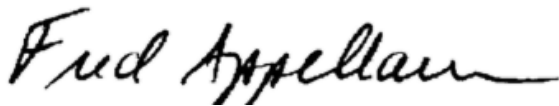



Approval

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Vice Dean, Research and Graduate Education, School of Medicine, University of Washington		Date:	07/23/2021
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Background

The National Cancer Institute (NCI) requires that Comprehensive Cancer Centers involved in clinical research establish a mechanism for assuring adequate internal oversight of the scientific aspects of clinical trials. As the site of practice for these trials, our institutions have the responsibility to protect patients, comply with FDA regulations, and act in a fiscally responsible manner as we integrate research with clinical care operations. Because of these obligations, the NCI mandates that Cancer Centers have a process, via the Protocol Review and Monitoring System (PRMS), to assure rigorous oversight of scientific aspects of all clinical trial research in the Consortium.

The two stage PRMS is expected to have the authority to open trials that meet the scientific merit and scientific priorities of the center and to terminate further accrual in those not demonstrating adequate scientific progress. The NCI requires that CCSG Competitive Renewal applications explain how many trials are monitored for progress and performance within a 12-month period and how many have been closed to further accrual.

The purpose of this policy is to document the process by which Cancer Consortium clinical trials are reviewed and evaluated by the SRC for possible closure to further accrual because of poor accrual.

Responsible Personnel

Principal Investigator

PRMS Medical Director

Directors, Research Groups

Chairs and Co-Chairs, Scientific Review Committees

Vice President, Clinical Research

Abbreviations and Acronyms

CCSG: Cancer Center Support Grant

CTMS: Clinical Trial Management System

NCI: National Cancer Institute

PI: Principal Investigator

PRMS: Protocol Review and Monitoring System

RG: Research Group

SRC: Scientific Review Committee

Definitions

Alternative Accrual Track: A rare disease trial that meets one or more of the following criteria:

- Disease incidence is equal to or less than 6/100,000
- Disease is of uncommon clinical presentation (e.g. uncommon clinical subtypes of more common cancers)
- The trial involves narrow molecular subtypes

Cancer Consortium: An NCI-designated Comprehensive Cancer Center comprised of Fred Hutchinson Cancer Research Center (FHCRC), University of Washington (UW), Seattle Children's (SC), and Seattle Cancer Care Alliance (SCCA).

Cancer Consortium Clinical Trial: A interventional clinical trial where the primary focus is cancer, or is cancer-related, and is conducted by a Cancer Consortium member.

Conventional Accrual Track: Trials that do not qualify for Alternative Accrual Track are reviewed under the Conventional Accrual Track.

Cooperative Group trials: Trials managed through the NCI National Clinical Trial Network (NCTN), Blood and Marrow Transplant Clinical Trials Network (BMT-CTN), and Cancer Immunotherapy Trials Network (CITN) are considered Cooperative Group trials.

Exempt Accrual Track: Trials that enroll only pediatric patients (under the age of 18 at the time of accrual) that are exempt from accrual monitoring.

Protocol Review Monitoring System: The two-stage review process that consists of Research Group Review oversight and Scientific Review Committee oversight.

Research Group: The first stage disease- and modality-focused groups that are responsible for the initial scientific review of concepts and protocols.

Scientific Review Committee: The second stage committee that reviews, approves, and monitors the scientific merit, feasibility and prioritization of cancer clinical trials conducted within the Cancer Consortium.

Target Accrual Rate: The accrual goal divided by the expected duration of the trial.

Policy

The Scientific Review Committee (SRC) ensures that Cancer Consortium clinical trials accrue patients according to the guidelines outlined in this policy.

Trials that do not meet the expected accrual per [Table 1](#) below will be reviewed by the SRC according to the procedures outlined in this policy.

Table 1 Minimum Annual Accrual Requirements for Trials

Accrual Track	Trial Type	Annual Accrual Requirements
Conventional	Cooperative group trials	At least 1
Conventional	Phase I	At least 2
Conventional	Industry-sponsored trials	At least 4
Conventional	Investigator-initiated multi-site trials (internal or external investigators)	At least 4
Conventional	Investigator-initiated single-site trials	At least 50% of target accrual rate
Alternative	Rare disease trials meeting defined criteria above	At least 1
Exempt	Pediatric trials	0

In addition to the requirements above, trials will be triggered for immediate closure if they do not meet the criteria outlined below in [Table 2](#).

Table 2 Accrual Criteria for Trials Triggering Closure

Additional Criteria	Expected Accrual
Expected accrual 12 months after activation <i>Exempt: Alternative and Exempt Accrual Track trials, and Cooperative group trials</i>	At least 1
Expected accrual at end of anticipated trial duration <i>Exempt: Alternative and Exempt Accrual Track trials</i>	At least 50% of target accrual goal

Procedures

In the Cancer Consortium, Research Groups (RG) review accrual and scientific merit prior to initial submission to the Scientific Review Committee (SRC). The RG proposes whether the trial should be considered under the Conventional, Alternative, or Exempt Accrual Tracks. The SRC then determines the appropriate accrual track for each trial at the time of initial review.

Annually, and more often as needed, the SRC reviews the accrual and scientific merit of Cancer Consortium clinical trials open to accrual or temporarily suspended to accrual with the intention to re-open. Low accrual reviews are not needed if the trial is closed to accrual or if the accrual data shows adequate accrual as defined in [Table 1](#).

1. Accrual Monitoring

Annual accrual monitoring result in one of the following outcomes:

- **Approval:** If the SRC finds that the accrual meets criteria in [Table 1](#), the trial is approved for the next year.
- **Closure:** If the SRC finds the trial failed to accrue in the initial year after opening to accrual, the trial will be closed to further accrual. If the SRC finds the trial failed to accrue at least 50% of the target accrual rate at the end of the anticipated trial duration, the trial will be closed to further accrual by the SRC as defined in [Table 2](#).
- **Low Accrual Review:** If the SRC finds that accrual has not met the target as defined in [Table 1](#), the SRC will notify the RG Director and the trial PI in a standardized letter. The SRC will require a detailed explanation for the low accrual, a corrective action plan for increasing accrual, and a justification for keeping the trial open to accrual (see [SRC Low Accrual Policy Job Aid](#)).
 - The RG Director or PI must respond within 30 calendar days of the SRC notification and responses will be reviewed at an assigned SRC meeting. If no response is received, the trial will be closed to accrual effective immediately.

2. Low Accrual Reviews

For underperforming trials undergoing a low accrual review, the SRC will assess the response as detailed below. Correspondence detailing the SRC determination will be sent to the applicable RG Director, the PI, and protocol contact.

- **12-month probation:** If the SRC determines that the response sufficiently addresses the concerns, the trial still has scientific merit, and a recruitment action plan is in place to increase accrual, the trial is approved for 12 months.
- **6-month probation:** If the SRC determines that the response only partially addresses the concerns or requires an update on the success of the recruitment action plan, the trial will be flagged for a mid-cycle review in 6 months.
 - At six months, data from the preceding twelve months are reviewed. If the trial is approved to continue accrual at a mid-cycle review, it will be reviewed yearly according to its originally scheduled cycle (i.e., the next review will be at the originally scheduled anniversary). Only one mid-cycle review is allowed for any trial.
- **Closure:** If during either the annual or mid-cycle review, the SRC determines that the proposed recruitment action plan did not address the accrual concerns sufficiently or if the trial no longer has scientific merit, the SRC will close the trial to further accrual, effective immediately.

3. Closure Process

When the SRC determines a trial should be closed to accrual, the RG Director, PI, and protocol contact will be notified via a SRC Result Letter. The trial status will be changed to closed to accrual in the OnCore CTMS.

The PI is responsible for ensuring consent documents are removed from the OnCore CTMS and for submitting a modification, updated status, or other appropriate reporting mechanism to the trial IRB of record.

4. Appeals after SRC Recommendation for Closure

The PI or RG Director may appeal a SRC closure notification within 30 calendar days of closure and the trial will be assigned and reviewed at a full SRC meeting. Expedited closure appeal reviews will not be granted, and appeals received after 30 calendar days will not be accepted. Only one closure appeal is allowed for any trial.

Appeals should include a detailed explanation for the low accrual, a corrective action plan for increasing accrual, and a justification for keeping the trial open to accrual (see [SRC Low Accrual Policy Job Aid](#)).

- If the SRC finds the appeal suitable, the trial will be reopened for accrual. The trial status will be updated to open to accrual. The PI is responsible for ensuring trial documents are reposted and the trial IRB of record is aware of the status change.
- If the SRC does not find the appeal suitable, the trial will remain closed to accrual with no further option to appeal.

SRC closure appeal outcomes will be communicated via SRC Result Letter and sent to the RG Director, the PI, and protocol contact.

Applicable Regulations & Guidelines

PAR-20-043 – Cancer Center Support Grants (CCSGs) for NCI-designated Cancer Centers

Attachments/Related References

[Data and Safety Monitoring Plan of the Fred Hutch/University of Washington Cancer Consortium](#)

[SRC Low Accrual Policy Job Aid](#)

Version Review History

Reviewer	Date
Frederick Appelbaum, MD, Deputy Director, FH	08/11/2015
John T. Slattery, PhD, Vice Dean for Research, University of Washington	08/11/2015
Frederick Appelbaum, MD, Deputy Director, FH	05/31/2017
John T. Slattery, PhD, Vice Dean for Research, University of Washington	05/31/2017
Frederick Appelbaum, MD, Deputy Director, FH	07/23/2021
John T. Slattery, PhD, Vice Dean for Research, University of Washington	07/23/2021