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Area Cancer Consortium - Institutional

Applicability FHCC Institutional Policies

References Org Wide/ Institutional

Logo for FHCC Institutional Policies

## SRC Low Accrual Policy

### SCOPE:

This policy applies to all Fred Hutchinson Cancer Center ("Fred Hutch") workforce members supporting Cancer Consortium clinical research activities. As an extension, this policy also applies to all other consortium clinical research members including from University of Washington and Seattle Children's Hospital.

### PURPOSE:

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 Food and Drug Administration (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 Cancer Consortium (CC).

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 Cancer Center Support Grant (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 CC clinical trials are reviewed and evaluated by the Scientific Review Committee (SRC) for possible closure to further accrual because of poor accrual.

## 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 15/100,000
  - Disease is of uncommon clinical presentation (e.g., uncommon clinical subtypes of more common cancers)
  - The trial involves narrow molecular subtypes
- **Cancer Center Support Grant:** A P30 Cancer Center Support Grant and accompanying NCI designation for successfully meeting a spectrum of rigorous competitive standards associated with scientific and organizational merit. The CCSG supports research infrastructure that enhances collaborative, transdisciplinary research productivity. CCSG grants provide funding for formalized cancer research programs, shared research resources, scientific and administrative management, planning and evaluation activities, development of new scientific opportunities, and centralized clinical trial oversight and functions.
- **Cancer Consortium:** An NCI-designated Comprehensive Cancer Center that comprises Fred Hutch (Fred Hutch), University of Washington (UW) and Seattle Children's (SC).
- **Clinical Trial:** A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.
- **Conventional Accrual Track:** Trials that do not qualify for Alternative Accrual Track are reviewed under the Conventional Accrual Track.
- **Exempt Accrual Track:** Trials that meet one or more of the following criteria:
  - Involves rare, unpredictable, and infectious or non-infectious outbreak-related complications that result in episodic accrual such as with epidemics or pandemics.
  - From the Pediatric Oncology Research Group or enrolls pediatric patients.
  - No Consortium accrual and/or only affiliate site accrual where the Fred Hutch/UW/Seattle Children's Consortium is the coordinating center.
  - Where Fred Hutch/UW/Seattle Children's Consortium faculty serve as the National Chair or other leadership position for the entire NCTN trial.
- **Extension Trial:** A trial extending the treatment of a previously active trial. Also referred to as rollover, open-label extension, and long-term follow-up trials. The protocol will include reference to previous trial(s) patients participated on.
- **National Trials:** Studies supported by the NCI National Clinical Trials Network (NCTN) and

other NIH-supported National Trial Networks.

- **Protocol Review Monitoring System (PRMS):** The two-stage review process that consists of Research Group Review oversight and Scientific Review Committee oversight.
- **Research Groups (RG):** The first stage disease- and modality-focused groups that are responsible for the initial scientific review of concepts and protocols.
- **Scientific Review Committee (SRC):** A Cancer Consortium Committee that serves as the PRMS second stage review and provides the formal internal peer-review process required for cancer-related intervention studies under the terms of the Cancer Center Support Grant. The committee has a defined membership representing the major clinical research areas of the Consortium. The SRC has the authority to close a study for further accrual per the SRC Low Accrual Policy.
- **Target Accrual Rate:** The accrual goal divided by the expected duration of the trial. Within OnCore this is the RC Total Accrual Goal (Lower) divided by the Accrual Duration (Months).

## POLICY:

The SRC ensures that CC 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	Annual Accrual Requirements
Conventional	At least 50% of target accrual rate
Alternative	At least 1
Exempt	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</i>	At least 1
Expected annual accrual after two prior probations <i>Exempt: Exempt Accrual Track trials</i>	At least minimum annual accrual requirement ( <a href="#">Table 1</a> )
Expected accrual at end of anticipated trial duration <i>Exempt: Alternative and Exempt Accrual Track</i>	At least 50% of target accrual goal

## REQUIREMENTS:

In the CC, Research Groups (RG) review accrual and scientific merit prior to initial submission to the 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 CC 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](#).

## 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 that accrual has not met the criteria as defined in [Table 2](#), the trial will be closed to further accrual by the SRC.
- **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 Principal Investigator (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 the SRC Low Accrual Policy Job Aid and SRC Low Accrual PI Response Form for more information.
  - 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. Late or incomplete responses will not be accepted.

## 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 the accrual concerns were not sufficiently addressed or if the trial no longer has scientific merit, the SRC will close the trial to further accrual.

## 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 Clinical Trial Management System (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 Institutional Review Board (IRB) of record. The PI is also responsible for ensuring that the ClinicalTrials.gov record is updated appropriately, including reporting results data as needed, and uploading an informed consent form that was used to enroll at least one participant (when applicable).

## 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 incomplete appeals or appeals received after 30 calendar days will not be accepted. Only one closure appeal is allowed for any trial.

See the [SRC Low Accrual Policy Job Aid](#) and SRC Low Accrual Closure Appeal Form for more information.

- 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.

## REFERENCES:

- NCI/NIH: [PAR-21-321](#) – Cancer Center Support Grants (CCSGs) for NCI-designated Cancer Centers
- CC Plan: [Data and Safety Monitoring Plan of the Fred Hutch/University of Washington Cancer Consortium](#)

- CRS Definitions Dictionary
- CRS Job Aid: [PRMS.0002 SRC Low Accrual Policy Job Aid](#)
- CRS Template: [PRMS.0003 SRC Low Accrual PI Response Form](#)
- CRS Template: [PRMS.0004 SRC Low Accrual Closure Appeal Form](#)

## Attachments

[SRC Low Accrual Workflow.docx](#)

## Approval Signatures

Step Description	Approver	Date
	Natalie Simpson: Policy & Practices Mgr	06/2024
	Mari Schwab: Associate General Counsel, Sr	06/2024
	Kristi Stiffler: Vice President, Clinical Research	06/2024
	Kristi Stiffler: Vice President, Clinical Research	06/2024
	Nora Olsen: CR Reg Affairs&Compliance Dir.	06/2024

## Applicability

FHCC Institutional Policies