

**Approval**

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Clinical Research Oversight Committee Chair or Designee		Date:	<u>5/31/17</u>
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Vice Dean, Research and Graduate Education, School of Medicine, University of Washington		Date:	<u>6/19/17</u>
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**Background**

NCI requires Comprehensive Cancer Centers involved in clinical research to 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 to monitor the scientific progress of clinical trials and to close trials when accrual does not meet a standard.

The focus of the Protocol Review and Monitoring System (PRMS) is on *scientific merit, priorities and progress* of clinical trial research in the center. The 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 enrollment 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 enrollment. In the UW / FHCRC Cancer Consortium, Research Groups are expected to review accrual and scientific merit prior to initial submission to Scientific Review Committee (SRC). Annually, and more often as needed, SRC reviews the accrual and scientific merit of therapeutic trials open to enrollment.

The purpose of this policy is to document the process by which Cancer Consortium clinical trials are reviewed and evaluated by both the Research Groups and the SRC for possible closure to further enrollment because of poor accrual or outdated scientific relevance.

### Responsible Personnel

*Medical Director, Clinical Research Support*

*Directors, Research Groups*

*Chairs and Co-Chairs, Scientific Review Committees*

### Abbreviations and Acronyms

CCSG: Cancer Center Support Grant

PI: Principal Investigator

PRMS: Protocol Review and Monitoring System

SRC: Scientific Review Committee

### Definitions

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

**Cooperative Group Studies:** Studies managed through NCTN, BMT-CTN, and CITN are considered Cooperative Group Studies. Other cooperative groups that provide documentation of NCI (SRC or PRMS) initial review will also be considered Cooperative Group for the purposes of accrual monitoring.

**Protocol Review Monitoring System:** The PRMS consists of Research Group Review oversight and Scientific Review Committee oversight.

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

**Pediatric Studies:** Studies that enroll only patients that are under the age of 18 (at the time of enrollment) are considered pediatric studies.

**Alternative Accrual Track:** A study qualifies for Alternative Accrual Track if the SRC determines that it 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

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

### Policy

The SRC is required to ensure that Cancer Consortium Clinical Trials accrue patients according to the guidelines outlined in this policy. Trials that do not meet the expected enrollment per this policy will be reviewed and closed to further accrual by the SRC according to the procedures outlined in this policy.

Expected enrollment per year—Conventional Accrual Track	
Phase I	At least 2
Industry-sponsored trials	At least 4
Cooperative group trials	At least 1
Investigator-initiated multicenter trials (internal or external investigators)	At least 4
Investigator-initiated single center trials	At least 50% of projected
Expected enrollment per year—Alternative Accrual Track	
All trials	At least 1
Expected enrollment per year— Pediatric Studies	
All trials	Exempt from SRC low accrual review

### Procedures

#### Research Group Initiated Review

The Research Group proposes whether the study should be considered under the Conventional Accrual Track or the Alternative Accrual Track.

#### SRC Initiated Review

The SRC determines the appropriate accrual track for each study at the time of initial review. The SRC annually reviews trials open to enrollment for at least one year that are *not* SRC exempt.

The following data are collected and entered into the Cancer Center’s electronic database for each study:

- Study Number
- PI Name
- Study Title
- Study Phase
- Sponsor
- Date Opened to Accrual
- Any temporary closure and re-opened dates
- SRC Annual Review (Continuing Review) expiration date
- Review Type (Initial, Annual, 6-Month Follow-Up)
- Accrual review track (conventional or alternative)
- Protocol (Total) Target Accrual Goal

- Center's Total Target Accrual Goal
- Center's Actual Accrual to Date

If the SRC finds that the accrual meets criteria in the table and that the trial still has scientific merit, the study is approved for the next year.

At annual reviews, if the SRC finds that accrual has not met the target in the above table or that scientific merit is questionable, the SRC will request a response from the Research Group Director (or designee) and the trial PI. The SRC will require the following information as applicable:

- Whether the annual target accrual goal was met
- Whether accrual figures in the Cancer Center's electronic database are accurate
- Whether any patients are continuing study-related activities
- Whether the study is or will be closed to accrual
- Whether the study is or will be closed by the IRB
- Whether any extenuating circumstances can be resolved with a revised recruitment action plan (which must be included with the response), and if relevant, whether the study still has scientific merit.
- Whether accrual can be increased

For Alternative Track Accrual Review studies, the following will also be considered

- For multi-center studies, enrollment will be assessed across the entire study. If there has been little or no enrollment across the entire study, rigorous scientific justification will be required to keep the study open.
- Whether important scientific objectives can still be met if enrollment of the first patient is delayed beyond the first year or if enrollment is much lower than originally planned

The Research Group Director (or designee) and PI must both respond within 30 days of the SRC request.

Research Group and PI responses will be reviewed in an assigned SRC meeting. If the study will not be closed to accrual or closed by the Research Group or PI, the SRC will assess the response as follows:

- If the SRC determines that the response sufficiently addresses the concerns, the study is approved for one year.
- If the SRC determines that the response only partially addresses the concerns, the study will be flagged for a mid-cycle review in six months. At six months, data from the preceding twelve months are reviewed. If the study 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 ever allowed for any study.
- If during either the annual or mid-cycle review, the SRC determines that the proposed changes do not address the concerns sufficiently, the PI does not respond to the request, SRC will close the study to further accrual, effective immediately.

Correspondence detailing the SRC's determination will be sent to the relevant Research Group Director (or designee) and the PI.

**Closure process**

When the SRC determines a trial should be closed to accrual, the Research Group and PI will be notified by email. The trial status will be changed as appropriate in the CRS database status.

Consent documents will be removed from FYI, and the study status in FYI will note that the study is closed to further accrual.

The PI will be responsible for submitting a modification, updated status at annual renewal, or other appropriate reporting mechanism to the trial IRB of record.

**Appeals after SRC Recommendation for Closure**

If, after receiving the SRC’s closure notification, the PI or Research Group Director appeals to the SRC within 30 days, the trial will be referred to the SRC Chair for determination of whether the appeal is appropriate.

**Applicable Regulations & Guidelines**

*None*

**Attachments/Related References**

*None*

**Version Review History**

Reviewer	Date
Frederick Appelbaum, MD, Deputy Director, FHCRC	8/11/2015
John T. Slattery, PhD, Vice Dean for Research, University of Washington	8/11/2015
Frederick Appelbaum, MD, Deputy Director, FHCRC	5/31/2017
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