

**University of California, San Francisco
Helen Diller Family Comprehensive Cancer Center
Policy and Procedure**

PRMS Protocol Closure Policy

PRMS Procedure for Closing Studies for
Poor Accrual or Outdated Scientific Relevance

Purpose

Per CCSG Guidelines, it is particularly important for Centers involved in clinical research to establish a mechanism for assuring adequate internal oversight of the conduct of all cancer clinical trials in the institution or institutions that formally comprise the Center. The focus of the Protocol Review and Monitoring System (PRMS) is on *scientific merit, priorities and progress* of the clinical research in the Center. The PRMS should have the authority to open protocols that meet the scientific merit and scientific priorities of the center and to close protocols that do not demonstrate adequate scientific progress. The NCI requires that CCSG Competitive Renewal applications provide an account of how many protocols are monitored for progress and performance within a 12-month period and how many are closed, along with the reason for closure. At UCSF, the Program Site Committees are expected to review accrual and scientific merit regularly and to close trials that do not meet appropriate thresholds. In addition, the Protocol Review Committee (PRC) will independently review accrual and scientific merit of all open trials annually.

The purpose of this policy is to document the process by which studies are reviewed and evaluated by both the Program Site Committees and the PRC for possible closure for poor accrual or outdated scientific relevance.

Procedures

Program Site Committee Initiated Review

As specified in the PRMS Program Site Committee Review Policy, Program Site Committees are expected to review accrual. Trials which the Program Site Committee decides to close will be recorded in the electronic database but will not undergo review by the PRC full committee once they are closed.

Trials which the Program Site Committee wishes to keep open to accrual will have a corrective action plan formulated by the Program Site Committee to improve accrual. If after six months annual accrual does not meet the criteria in the table on page 2, the Program Site Committee is expected to close the trial to further accrual (and terminate the study, if possible). It is not required that these corrective action plans be reported to the PRC. However, should the PRC conduct independent review as described below in PRC Initiated Review and request a response to its concerns (including a corrective

action plan), the Program Site Committee can submit its existing corrective action plan in response to the PRC.

PRC Initiated Review

Studies are monitored for progress and performance annually once they are approved by the institutional IRB (Committee on Human Research, CHR) and are open to enrollment. Prior to each Protocol Review Committee (PRC) meeting the PRC Administrator identifies all trials that are open to enrollment for at least one year, are not PRC exempt, and are due for annual review.

Once identified, the following data is collected from the Cancer Center's electronic database for each identified study:

- Study Number
- PI Name
- Study Title
- Primary Objective
- Study Phase
- Research Type
- Date Opened to Accrual
- Anticipated Annual Accrual Rate
- Actual Accrual Rate for the Last Year
- Total Target Accrual Figure
- Total Accrual Figure to Date

At the meeting the full committee reviews accrual (see table below for accrual requirements) and scientific relevance.

Type of Trial	At least 5 patients accrued/year @ UCSF required?	Accrual completion within 3 years required?	Orphan disease accrual criteria (IF waiver granted)	>50% of yearly targeted accrual @ UCSF required?	>50 % of yearly national accrual required?
(UCSF) Investigator Initiated, Single Center	Yes*	Yes*	≥ 3 patients accrued per year, AND accrual completion within 5 years	Yes	N/A
(UCSF) Investigator Initiated, Multi-Center	Yes*	Yes*	≥ 1 patient per year accrued @ UCSF, or ≥ 3 patients per year accrued nationally, AND accrual completion within 5 years	Yes	Yes
Non-UCSF Investigator Initiated, Consortium or Coop Group (UCSF not lead)	Yes*	No	≥ 1 patient per year accrued @ UCSF	Yes	No
Industry	Yes	No	N/A	Yes	No

* Waivers to this requirement can be granted by the PRC chair, at the time of PRC initial protocol review only.

If the committee finds the accrual and/or scientific relevance acceptable, the study is approved for six months or one year from the date of the meeting, as determined by the committee. If the committee finds the accrual and/or scientific relevance unacceptable, the program PI and the relevant Program Site Committee Chair (and, in the case of cooperative group trials, the institutional PI) will be notified about this issue and requested to provide a response. Notification will cite a 30-day deadline for response, and will require the following information as applicable (will differ depending on whether the finding is low accrual or poor scientific relevance):

- Whether accrual figures in the Cancer Center's electronic database are accurate
- Whether there are patients on study treatment (and if yes, the plan for those patients)
- Whether the study will be closed to accrual
- Whether the study will be terminated (retired at the IRB)

- Whether there are extenuating circumstances that can be resolved with a revised recruitment action plan (which must be included with the response) and if so, whether the study still has scientific relevance

The Cancer Center's electronic database will send notifications every 7 days reminding the PI and the Protocol Project Manager that a response has not been received. If no response is received within 30 days of the initial correspondence, the PRC will recommend closure.

Responses received are reviewed at the next scheduled PRC meeting. Program Site Committee Chair responses will be accepted in place of a PI response. If the study will not be closed or retired, the committee will assess the response as follows:

- If the committee agrees fully with the response, the study is approved for one year from the date of initial review; if the committee agrees with conditions, the study is approved for six months from the date of initial review.
- If the committee does not agree with the response, it will recommend closure. Correspondence detailing the PRC's recommendation for closure will be sent to the program PI and the relevant Program Site Committee Chair (and, in the case of cooperative group trials, the institutional PI).

Appeals to PRC Recommendation for Closure

If 30 days elapse from the time PRC issues its recommendation for closure with no appeal from the PI or Program Site Committee Chair, then the PRC will close the study and inform the Director of Human Research Protection Program (HRPP) of the decision.

If, after receiving the PRC's recommendation for closure, the PI or Program Site Committee Chair appeals to the PRC within 30 days, then the trial will be referred to the PRC Chair for adjudication. If the PRC Chair cannot resolve the dispute, the PRC Chair will refer the trial to the Director of Investigational Trials Resource, who will convene an external grievance committee composed of three senior clinical leaders of NCI-designated Cancer Centers, preferably from within the University of California (UC) system.

The external grievance committee will decide via teleconference whether or not to uphold the PRC's determination. If the external grievance committee disagrees with PRC's determination, the study is approved for one year from the date of initial review. If the external grievance committee recommends that PRC's determination be upheld, then the PRC will close the study and inform the Director of HRPP of the decision.

Alternate Procedure

Alternate procedure may be used for cooperative group or consortium studies addressing rare malignancies such as pediatric malignancies. A program, PI or Program Site Committee Chair may submit their own annual assessment of accrual for all studies if this method is previously approved by PRC; PRC reviews the annual assessment for accrual and scientific relevance, and will issue correspondence if the PRC disagrees with the program or PI or Program Site Committee Chair assessment.

Policy Approval

This policy document was approved by the following personnel on the following dates:



Jeffrey A. Bluestone, PhD
Executive Vice Chancellor and Provost, UCSF

9/16/11

Date



Eric Small, MD
Director of Investigational Trials Resource

5/31/11

Date



Judith Luce, MD
Chair, Protocol Review Committee

7/6/11

Date



John Heldens, CIP
Director, Human Research Protection Program

7/18/11

Date