

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

PRMS Amendment Review Policy

PRMS Procedure for Review of Protocol
Amendments by the Protocol Review and Monitoring Committee

Purpose

The purpose of this policy is to document the process by which all protocol amendments must be reviewed by the Protocol Review and Monitoring Committee (PRMC).

Background

Per the Cancer Center Support Grant (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 research studies 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. At UCSF PRMS functions are carried out by the Site Committees and the Protocol Review and Monitoring Committee (PRMC). All protocols initially requiring PRMC approval must have all amendments reviewed by the PRMC.

Definitions

Protocol amendments are any revisions made to a protocol after it has been submitted to or reviewed by *any* regulatory body, regardless of the nature of the change, which can be typographical, editorial, administrative, scientific, etc. At the UCSF Helen Diller Family Comprehensive Cancer Center, regulatory bodies include, but are not limited to, the Site Committees, PRMC, the UCSF IRB or IRB of record, Radiation Safety Committee, Biosafety Committee, and the FDA.

Procedures

What Needs to be Reviewed by PRMC

All protocol amendments created after initial Site Committee submission but prior to initial PRMC approval must be submitted to the PRMC as part of the Initial Review PRMC submission, as per query instruction from the PRMC Administrator. All amendments made after initial PRMC approval must be submitted to the PRMC as amendments (Change Reviews), as per the [PRMS Amendment Submission Policy](#).

Protocols exempt from PRMC review do not require amendment review by the PRMC.

Review Process

Submissions are reviewed as a whole packet. The review outcome will apply to all documents submitted, and to all changes contained within the Summary of Changes and unmarked protocol document.

The PRMC Administrator will review each amendment submission. If the changes are deemed administrative and do not encompass any of the bullet points below (i.e., they do not affect the scientific intent of the study or study design), then the PRMC Administrator can approve the amendment. If the changes are deemed to encompass any of the bullet points below, then the PRMC Administrator will forward the amendment to the PRMC Chair or Vice Chair for review. If the Chair is the Principal Investigator (PI), then the amendment will be given to the Vice Chair or, in the event of a conflict with both the PRMC Chair and Vice Chair, to a designated Alternate Chair. The PRMC Chair, Vice Chair or Alternate Chair has the prerogative to refer any amendment for PRMC full committee review. In cases where the amendment significantly changes the study design, the PRMC Chair, Vice Chair or Alternate Chair may request Site Committee assessment of the amendment, which may include feasibility assessment.

Amendments that require review by the PRMC Chair, Vice Chair or Alternate Chair:

- change in dose – includes changes to dose reduction doses
- change to response criteria
- addition or removal of a new study/treatment arm – includes adaptive design platform protocols – in some instances the PRMC Chair, Vice Chair or Alternate Chair may require ad hoc full review
- addition of a study site to a multi-center study where UCSF is the coordinating center
- change from institutional single-center study to multi-center study where UCSF is the coordinating center.

Amendments that require review by the PRMC Chair, Vice Chair or Alternate Chair which may trigger review by the full committee:

- change in study design (including addition of follow-up phase)
- other treatment changes (except prophylaxis regimens, e.g., prophylaxis for infections in leukemia and transplant patients)
- change in sample size
- change in stopping rules
- change in statistical plan.

Expedited review of amendments by the PRMC Chair, Vice Chair or Alternate Chair are documented via a completed amendment review form. Amendments going to full committee are reviewed by a Primary, Secondary and Biostatistical reviewer using three separate full committee amendment review forms specific to each reviewer role. All amendment reviews (by either the PRMC Administrator, PRMC Chair, Vice Chair,

Alternate Chair, or Primary, Secondary and Biostatistical reviewers at full committee) are documented in OnCore (the Cancer Center's secure electronic web-based database) and issued via electronic notification from OnCore.

Review Outcome/Approval Process

After review by either the PRMC Administrator, PRMC Chair, Vice Chair or Alternate Chair, the PRMC Administrator will either prepare a review outcome memo (for Contingent Approval) or an approval notification using OnCore, or prepare the submission for full committee review, depending on the outcome.

A review outcome memo (for Contingent Approval) will include a discussion of which revisions were not acceptable and why, and may contain suggestions on how the PI can make those revisions acceptable. In cases where the amendment significantly changes the study design, the review outcome memo may contain a request for the Site Committee [Protocol Amendment Review Form](#). The review outcome memo will be issued to the PI, Protocol Project Manager (PPM), and the submitter. Approval will not be granted until all of the concerns are met. The PI's response to Contingent Approval must follow the "Responding to Contingent Approval of an Amendment" submission criteria outlined in the [PRMS Amendment Submission Policy](#).

If approved, amendment approval notification will be issued to the PI, Protocol Project Manager (PPM), and the submitter via OnCore. If there are suggestions provided with the amendment approval notification, they are recommendations only. The PI may choose to respond by submitting a separate amendment application, but this is not required.



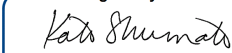
All protocol amendments must be approved by the institutional IRB (the Committee on Human Research, or CHR) prior to implementation.

Alternate Procedures

There are no alternate procedures to this policy.

Policy Approval

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

<p>DocuSigned by:  7FCB32D327E3438...</p> <hr/>	<p>11/2/2020</p> <hr/>
<p>Eric Small, MD Deputy Director and Chief Scientific Officer, Helen Diller Family Comprehensive Cancer Center</p>	<p>Date</p>
<p></p> <hr/>	<p>10/27/2020</p> <hr/>
<p>Jennifer Clarke, MD, MPH Chair, Protocol Review and Monitoring Committee, Helen Diller Family Comprehensive Cancer Center</p>	<p>Date</p>
<p>DocuSigned by:  80D38159E89D41B...</p> <hr/>	<p>11/2/2020</p> <hr/>
<p>Kate Shumate, MPA, CCRP Chief of Staff and Director, Administration & Planning Helen Diller Family Comprehensive Cancer Center</p>	<p>Date</p>

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

Policy Revision Summary of Changes

Policy Title: PRMS Amendment Review Policy
Version Date: October 27, 2020
Version Number: Revision 5

Notes: Page number corresponds to page number in updated version (Revision 5).
 New text in modified paragraphs is shown as ***bold italics*** and deleted text is shown as ~~strikethrough~~.

Page No.: All pages		Section: Footer
Original Text	Revision 4 09/25/2019	
New Text	Revision 45 109/257/2019 20	
Reason for Change	Updated text to reflect revised version number and date.	

Page No.: 1		Section: Policy Sub-Title
Original Text	PRMS Procedure for Review of Protocol Amendments by the Protocol Review Committee	
New Text	PRMS Procedure for Review of Protocol Amendments by the Protocol Review <i>and Monitoring</i> Committee	
Reason for Change	Added “and Monitoring” to the full name of the PRC, which is now PRMC.	

Page No.: 1		Section: Purpose
Original Text	The purpose of this policy is to document the process by which all protocol amendments must be reviewed by the Protocol Review Committee.	
New Text	The purpose of this policy is to document the process by which all protocol amendments must be reviewed by the Protocol Review <i>and Monitoring</i> Committee (<i>PRMC</i>).	
Reason for Change	Added “and Monitoring” to the full name of the PRC, and added the acronym, which is now PRMC.	

Page No.: 1	Section: Background
Original Text	Per the Cancer Center Support Grant (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 research studies in the institution or institutions that formally comprise the Center. The focus of the Protocol Review and Monitoring System (PRMS) is on <i>scientific merit, priorities and progress</i> of the clinical research in the Center. At UCSF PRMS functions are carried out by the Site Committees and the Protocol Review Committee (PRC). All protocols initially requiring PRC approval must have all amendments reviewed by the PRC.
New Text	Per the Cancer Center Support Grant (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 research studies in the institution or institutions that formally comprise the Center. The focus of the Protocol Review and Monitoring System (PRMS) is on <i>scientific merit, priorities and progress</i> of the clinical research in the Center. At UCSF PRMS functions are carried out by the Site Committees and the Protocol Review and Monitoring Committee (PRMC). All protocols initially requiring PRMC approval must have all amendments reviewed by the PRMC.
Reason for Change	Changed the name of PRC to PRMC (and added “and Monitoring” to the full name).

Page No.: 1	Section: Definitions
Original Text	Protocol amendments are any revisions made to a protocol after it has been submitted to or reviewed by <i>any</i> regulatory body, regardless of the nature of the change, which can be typographical, editorial, administrative, scientific, etc. At the UCSF Helen Diller Family Comprehensive Cancer Center, regulatory bodies include, but are not limited to, the Site Committees, PRC, the UCSF IRB, Radiation Safety Committee, Biosafety Committee, and the FDA.
New Text	Protocol amendments are any revisions made to a protocol after it has been submitted to or reviewed by <i>any</i> regulatory body, regardless of the nature of the change, which can be typographical, editorial, administrative, scientific, etc. At the UCSF Helen Diller Family Comprehensive Cancer Center, regulatory bodies include, but are not limited to, the Site Committees, PRMC, the UCSF IRB or IRB of record , Radiation Safety Committee, Biosafety Committee, and the FDA.
Reason for Change	Added IRB of Record to UCSF IRB, and changed the name of PRC to PRMC.

Page No.: 1-2	Section: Procedures What Needs to be Reviewed by <i>PRMC</i>
Original Text	<p><u>What Needs to be Reviewed by PRC</u></p> <p>All protocol amendments created after initial Site Committee submission but prior to initial PRC approval must be submitted to the PRC as part of the Initial Review PRC submission, as per query instruction from the PRC Administrator. All amendments made after initial PRC approval must be submitted to the PRC as amendments (Change Reviews), as per the PRMS Amendment Submission Policy.</p> <p>Protocols exempt from PRC review do not require amendment review by the PRC.</p>
New Text	<p><u>What Needs to be Reviewed by <i>PRMC</i></u></p> <p>All protocol amendments created after initial Site Committee submission but prior to initial <i>PRMC</i> approval must be submitted to the <i>PRMC</i> as part of the Initial Review <i>PRMC</i> submission, as per query instruction from the <i>PRMC</i> Administrator. All amendments made after initial <i>PRMC</i> approval must be submitted to the <i>PRMC</i> as amendments (Change Reviews), as per the PRMS Amendment Submission Policy.</p> <p>Protocols exempt from <i>PRMC</i> review do not require amendment review by the <i>PRMC</i>.</p>
Reason for Change	Changed the name of PRC to <i>PRMC</i> .

Page No.: 2	Section: Procedures Review Process
Original Text	The PRC Administrator will review each amendment submission. If the changes are deemed administrative and do not encompass any of the bullet points below (i.e., they do not affect the scientific intent of the study or study design), then the PRC Administrator can approve the amendment. If the changes are deemed to encompass any of the bullet points below, then the PRC Administrator will forward the amendment to the PRC Chair or Vice Chair for review. If the Chair is the Principal Investigator (PI), then the amendment will be given to the Vice Chair or, in the event of a conflict with both the PRC Chair and Vice Chair, to a designated Alternate Chair. The PRC Chair, Vice Chair or Alternate Chair has the prerogative to refer any amendment for PRC full committee review. In cases where the amendment significantly changes the study design, the PRC Chair, Vice Chair or Alternate Chair may request Site Committee assessment of the amendment, which may include feasibility assessment.
New Text	The PRMC Administrator will review each amendment submission. If the changes are deemed administrative and do not encompass any of the bullet points below (i.e., they do not affect the scientific intent of the study or study design), then the PRMC Administrator can approve the amendment. If the changes are deemed to encompass any of the bullet points below, then the PRMC Administrator will forward the amendment to the PRMC Chair or Vice Chair for review. If the Chair is the Principal Investigator (PI), then the amendment will be given to the Vice Chair or, in the event of a conflict with both the PRMC Chair and Vice Chair, to a designated Alternate Chair. The PRMC Chair, Vice Chair or Alternate Chair has the prerogative to refer any amendment for PRMC full committee review. In cases where the amendment significantly changes the study design, the PRMC Chair, Vice Chair or Alternate Chair may request Site Committee assessment of the amendment, which may include feasibility assessment.
Reason for Change	Changed the name of PRC to PRMC.

Page No.: 2	Section: Procedures Review Process
Original Text	<p>Amendments that require review by the PRC Chair, Vice Chair or Alternate Chair:</p> <ul style="list-style-type: none"> • change in dose • change to response criteria • addition of a new study/treatment arm • addition of a study site to a multi-center study where UCSF is the coordinating center • change from institutional single-center study to multi-center study where UCSF is the coordinating center. <p>Amendments that require review by the PRC Chair, Vice Chair or Alternate Chair which may trigger review by the full committee:</p>
New Text	<p>Amendments that require review by the PRMC Chair, Vice Chair or Alternate Chair:</p> <ul style="list-style-type: none"> • change in dose – <i>includes changes to dose reduction doses</i> • change to response criteria • addition <i>or removal</i> of a new study/treatment arm – <i>includes adaptive design platform protocols – in some instances the PRMC Chair, Vice Chair or Alternate Chair may require ad hoc full review</i> • addition of a study site to a multi-center study where UCSF is the coordinating center • change from institutional single-center study to multi-center study where UCSF is the coordinating center. <p>Amendments that require review by the PRMC Chair, Vice Chair or Alternate Chair which may trigger review by the full committee:</p>
Reason for Change	<p>Changed the name of PRC to PRMC; clarified that changes to the dosing levels discussed in dose reduction sections qualify as dose changes; modified the new study/treatment arm criteria to include removal of treatment arms, and added that some adaptive platform protocol amendments which add or remove treatment arms, at the Chair or Vice Chair's prerogative, may require ad hoc full review.</p>

Page No.: 2-3	Section: Procedures Review Process
Original Text	<p>Expedited review of amendments by the PRC Chair, Vice Chair or Alternate Chair are documented via a completed amendment review form. Amendments going to full committee are reviewed by a Primary, Secondary and Biostatistical reviewer using three separate full committee amendment review forms specific to each reviewer role. All amendment reviews (by either the PRC Administrator, PRC Chair, Vice Chair, Alternate Chair, or Primary, Secondary and Biostatistical reviewers at full committee) are documented in OnCore (the Cancer Center's secure electronic web-based database) and issued via electronic notification from OnCore.</p>
New Text	<p>Expedited review of amendments by the PRMC Chair, Vice Chair or Alternate Chair are documented via a completed amendment review form. Amendments going to full committee are reviewed by a Primary, Secondary and Biostatistical reviewer using three separate full committee amendment review forms specific to each reviewer role. All amendment reviews (by either the PRMC Administrator, PRMC Chair, Vice Chair, Alternate Chair, or Primary, Secondary and Biostatistical reviewers at full committee) are documented in OnCore (the Cancer Center's secure electronic web-based database) and issued via electronic notification from OnCore.</p>
Reason for Change	Changed the name of PRC to PRMC.

Page No.: 3	Section: Procedures Review Outcome/Approval Process
Original Text	<p>After review by either the PRC Administrator, PRC Chair, Vice Chair or Alternate Chair, the PRC Administrator will either prepare a review outcome memo (for Contingent Approval) or an approval notification using OnCore, or prepare the submission for full committee review, depending on the outcome.</p> <p>A review outcome memo (for Contingent Approval) will include a discussion of which revisions were not acceptable and why, and may contain suggestions on how the PI can make those revisions acceptable. In cases where the amendment significantly changes the study design, the review outcome memo may contain a request for Site Committee assessment of the amendment, which may include feasibility assessment. The review outcome memo will be issued to the PI, Protocol Project Manager (PPM), and the submitter. Approval will not be granted until all of the concerns are met. The PI's response to Contingent Approval must follow the "Responding to Contingent Approval of an Amendment" submission criteria outlined in the PRMS Amendment Submission Policy.</p>
New Text	<p>After review by either the PRMC Administrator, PRMC Chair, Vice Chair or Alternate Chair, the PRMC Administrator will either prepare a review outcome memo (for Contingent Approval) or an approval notification using OnCore, or prepare the submission for full committee review, depending on the outcome.</p> <p>A review outcome memo (for Contingent Approval) will include a discussion of which revisions were not acceptable and why, and may contain suggestions on how the PI can make those revisions acceptable. In cases where the amendment significantly changes the study design, the review outcome memo may contain a request for <i>the</i> Site Committee Protocol Amendment Review Form assessment of the amendment, which may include feasibility assessment. The review outcome memo will be issued to the PI, Protocol Project Manager (PPM), and the submitter. Approval will not be granted until all of the concerns are met. The PI's response to Contingent Approval must follow the "Responding to Contingent Approval of an Amendment" submission criteria outlined in the PRMS Amendment Submission Policy.</p>
Reason for Change	<p>Changed the name of PRC to PRMC; deleted the action required by the Site Committee and replaced it with the name of the form (with a link to the form), as the action required of the Site Committee is covered by the use of the form.</p>

Page No.: 4	Section: Policy Approval
Original Text	<p>_____ Date _____ Jennifer Clarke, MD, MPH Chair, Protocol Review Committee, Helen Diller Family Comprehensive Cancer Center</p>
New Text	<p>_____ Date _____ Jennifer Clarke, MD, MPH Chair, Protocol Review and Monitoring Committee, Helen Diller Family Comprehensive Cancer Center</p> <p>_____ Date _____ Kate Shumate, MPA, CCRP Chief of Staff and Director, Administration & Planning Helen Diller Family Comprehensive Cancer Center</p>
Reason for Change	<p>Changed the name of PRC to PRMC in the Chair's signatory section, and added Chief of Staff as new signatory.</p>