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

PRMS Site Committee Review Policy

PRMS Procedure for Protocol Review by
Site Committee

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.

PRMS responsibilities at this institution are carried out on two separate levels to ensure optimal oversight of progress and performance. There is initial review by the applicable Site Committee(s), followed by independent review by the Protocol Review Committee (PRC). The purpose of this policy is to document the review process undergone by the programmatic Site Committees prior to review by the Protocol Review Committee.

Procedures

Meeting Schedule

All Site Committees are required to meet monthly at minimum. Larger groups may meet more than once per month if workload dictates. Phase I or otherwise high-risk/early phase clinical trials must be reviewed at weekly meetings.

Review Functions

Site Committees will be formed for each CCSG-funded program, and may be formed for non-CCSG-funded programs as well. There are specialized Site Committees established for interventional trials crossing many cancer sites, e.g., early phase and supportive care (symptom management/palliative care/survivorship). Each protocol must have one Site Committee designated as the responsible site committee. In some cases, varying levels of input from other Site Committees may be required. Please refer to the PRMS Site Committee Selection Policy for details.

Each committee is required to:

- Evaluate all new concepts. Committees must prioritize concepts of investigator initiated studies, and document approval status. Approved concepts will be developed into protocol format using standardized HDFCCC treatment and behavioral protocol templates to ensure the minimum set of guidelines and standards are met.
- Review and prioritize all protocols before they are submitted to the PRC.
- Ensure that protocols UCSF develops use the same HDFCCC treatment and behavioral protocol templates to ensure the minimum set of guidelines and standards are met.
- Ensure that all review concerns are adequately addressed and the protocol is appropriately revised prior to issuing Approval.
- Perform feasibility review and set targeted annual accrual expectations for each new clinical protocol prior to PRC submission.
- Evaluate accrual for all open studies.
- Close trials with poor accrual to ensure appropriate utilization of resources.
- Maintain two ongoing priority lists of: 1) all protocols and concepts under development and 2) all protocols open or planned for each patient population.
- Review all protocol amendments before they are submitted to the PRC (amended protocols will all be required to have a summary of changes per HDFCCC standards).
- Discuss all safety issues including review of current and prior SAEs and AEs (at least weekly for Phase I or otherwise high-risk/early phase clinical trials; at least monthly for all others).
- Maintain written records of all meetings using standardized forms wherever applicable, including attendance and decisions concerning accrual/priorities/new concepts/protocol review.
- Prepare quarterly reports tracking the cumulative number of concepts and protocols reviewed, rejected, and accepted by the committee.

Optional oversight:

- Evaluate and monitor non-therapeutic trials.

Review Conflicts

On all studies where the PI is also the committee Chair, it is considered a conflict and the Chair is prohibited from performing related committee business. In all such cases the Chair should defer to a formally appointed Co-Chair to conduct the committee business, and the Co-Chair is expected to complete and sign all applicable review forms. This applies to new concept reviews, new protocol reviews, contingent response reviews, protocol amendment reviews, and assignment of reviewers. Likewise, if the

Chair is unavailable and one of the appointed Co-Chairs is the PI, review must be deferred to another formally appointed Co-Chair who is not the PI.

On all studies where the PI is also a committee member, the PI cannot be assigned as a reviewer.

On all studies where the protocol statistician on an investigator-initiated protocol is also a committee member, that statistician cannot be assigned as a reviewer.

New Protocol Review Types

Studies exempt from PRC review (see PRMS Protocol Review Committee Review Policy for definitions) can also be exempt from Site Committee review at the committee's discretion, although individual site committees may choose to review such studies.

Likewise, studies allowed expedited review at PRC (see PRMS Protocol Review Committee Review Policy for definitions) may also receive an expedited review at the Site Committee, although the Chair or Co-Chair has the option to require full committee review whenever warranted. Expedited review consists of the Chair or Co-Chair assigning one reviewer to complete the Expedited Reviewer's Comments form, and the Chair or Co-Chair completes the Chair or Co-Chair Summary of Review form; the review does not need to be presented/discussed at a full committee meeting (unless the Chair or Co-Chair feels that committee discussion is warranted) but is nonetheless prioritized (meaning the study undergoing review is reflected in both the Competing Trials list and the Protocols in Development list).

All other protocols must undergo full committee review and prioritization as in New Protocol Review below; there is no Chair-only review format for new protocols.

New Protocol Review

A quorum is required for the conduct of every Site Committee meeting. Quorum is defined as 50% of the Core committee membership roster. Ad Hoc members should be recorded as such on the roster, but do not count toward quorum.

Reviewer assignments are made by the committee Chair (or designee). The PI cannot be assigned as a reviewer. Likewise, the statistician who was involved in developing the statistical sections of the protocol cannot be assigned as a reviewer. Each protocol requires reviewers to be assigned according to protocol type, as follows:

Institutional (investigator-initiated) trials*:

- Primary reviewer (presents study at full committee meeting)
- Secondary reviewer
- Statistical reviewer (except in cases of conflict).

Statistical review is required on all institutional trials, *unless* the committee statistician serves as the protocol statistician; in such cases, the protocol is exempt from site committee statistical review. In other words, the statistician

who wrote and/or designed the protocol's statistical sections cannot review that protocol at site committee. Statistical review will always occur at the PRC level.

* Please refer to the PRMS Reliance section below.

Industry trials:

- Primary reviewer (presents study at full committee meeting)
- Secondary reviewer
- *Optional*: Statistical reviewer.

No statistical review is required on Industry trials; however, the site committee Chair or designee can request statistical review due to specific concerns. Statistical review will always occur at the PRC level.

Primary reviewers are required to present the protocol, and must be faculty and committee members recorded on the roster. Secondary reviewers do not need to be faculty, but must be committee members recorded on the roster. Statistical reviewers must be statisticians, but do not need to be on the roster. The Principal Investigator or designee is required to attend committee discussions and to answer questions, but does not present the study to the committee.

All committees will use standardized forms approved by the Director of the ITR to ensure that all required concerns are discussed consistently across all programs and disease sites. There are separate forms for primary reviews, secondary reviews, statistical reviews, expedited reviews, Chair or Co-Chair summary of review, and contingent response review (**see http://cancer.ucsf.edu/itr/itr-forms**).

Primary, Secondary and Expedited reviewers will provide individual scores for clinical importance, trial design, innovation/science, UCSF involvement in development, potential for UCSF publication, and accrual/feasibility. An overall score is assigned, which takes the preceding scores into account but does not average them. The reviewing biostatistician provides an overall score as well. Non-reviewing members do not score. The NIH scoring system will be used. After presentation by reviewers, their scores will be averaged to determine the final overall score. It is recommended that priority be given first to institutional (investigator-initiated) protocols, followed by national group (cooperative group) clinical trials and lastly to industry/pharmaceutical-sponsored clinical trials.

In addition to completing the standardized review forms, it is each committee's responsibility to provide specific information for each study. The committee will identify the following information required for PRC submissions:

- Phase of study
- UCSF involvement
- UCSF total target accrual
- UCSF target accrual per year
- Total target accrual goal if UCSF is coordinating center for multicenter trial

- Target accrual goal justification or prior accrual for similar population
- All competing trials (must describe all competing trials for the patient population undergoing study, as well as how directly competing trials will be prioritized against the trial under review, if applicable; see Prioritization)
- Confirmation of submittal of all review forms, Chair or Co-Chair summary of review form, and numerical ranking list of all trials in development (see Prioritization)
- Additional feasibility review assessing: eligibility criteria, pharmacy or imaging requirements, visit schedule/participation duration, special personnel requirements, sufficient support staff, completion timeframe, and (for PI-initiated only) sponsor commitment or other funding source available
- Final overall score.

In completing the above information, the Site Committee should be mindful that the PRC will not approve any new applications upon initial review if the projected annual accrual does not meet the minimum requirements in **Table 1** below.

Table 1 – Required Minimum Annual Accrual

Type of Trial	Conventional Trial	Rare Cancer Status, Molecularly Defined Subsets, Unique Correlative Science
Institutional Single Center	5	3*
Institutional Multi- Center (includes multi-center consortia led by other centers)	5	1*
Cooperative Group/ National Group	3	1*
Industry	5	1*

*Waiver requests at the time of PRC review are allowed for these studies. Requests for waivers are submitted electronically by the Site Committee in an email to the PRC Administrator and must justify why it is necessary to open such a low accruing study. Waivers to these requirements can be granted on a case by case basis by the PRC, provided one of the following three criteria are met:

1. The disease being studied represents a rare cancer, consisting of a malignancy with an annual incidence in the U.S.A. of <10,000 new cases.

2. Molecularly defined subsets may be considered as rare cancers if there is a clear mechanistic rationale why the study treatment is predicated on that specific molecular characteristic.

3. Unique correlative science will be undertaken by a UCSF investigator that will be informative even with a small number of UCSF accruals.

No other justifications will be approved by the PRC. If the request for waiver is approved the protocol undergoes standard formal PRC review. If the request for waiver is declined the study is returned to the submitter without formal review.

Following discussion, the Site Committee will determine overall approval status, to be documented on the Chair or Co-Chair Summary of Review form:

1. Approval: If there are no changes that must be made to the protocol before it can be initiated, it can be approved and the site committee can forward to the PRC for review, with all requisite information.

2. Contingent Approval: Will include discussion of what concerns need to be addressed before approval is granted. Such memos enumerate each concern and require the PI or designee to respond to each concern point by point.

Responses to Contingent Approval go back to the original reviewers. Each original reviewer is responsible for ensuring that all concerns are adequately responded to, ensuring that the protocol is modified appropriately, and communicating their findings to the committee Chair or designee. Once all reviews are completed, the committee Chair or designee documents the review outcome using a Contingent Response Review form (**see http://cancer.ucsf.edu/itr/itr-forms**). The concerns requiring a response listed on the preceding Chair or Co-Chair Summary of Review Form should be identical to those listed on the Contingent Response Review Form. If there is conflict the Chair or Co-Chair should adjudicate. If the protocol gets Contingent Approval a second time, then the PI's second response goes directly to the Chair or Co-Chair for adjudication instead of going back to the original reviewers.

3. Disapproved: Includes a discussion of what concerns need to be addressed before approval is granted. Such memos enumerate each concern and require the PI or designee to respond to each concern point by point. If resubmitted, these protocols are reviewed by the entire site committee.

Responses to Disapproved get placed on the next full committee agenda and are reviewed as in New Protocol Review above, the only difference being that reviews are assigned to original reviewers if they are available. If original reviewers are not available the resubmission is assigned to replacement reviewers.

All above committee review outcomes will be issued by the committee Chair or Co-Chair using a standardized Chair or Co-Chair Summary of Review form. The Chair or Co-Chair Summary of Review form contains an indication of the committee's final overall score. Chair signature is required on the Chair or Co-Chair Summary of Review Form. If the Chair is the PI then the Co-Chair should sign the form. The approved Chair or Co-

Chair Summary of Review form signed by the Chair or Co-Chair (and the Contingent Response Review Form if applicable) serves as proof of Site Committee approval. For approved protocols, all applicable committee review forms, including individual review forms, Chair or Co-Chair summary of review forms, and contingent response review forms need to be submitted to the PRC as part of the application, to demonstrate the entire review history.

New Concept Review

Site committees are required to discuss new institutional (investigator-initiated) concept sheets/letters of intent prior to protocol development. Concepts need to be prioritized, and approval status must be documented. No specific reviewers should be assigned, but discussion outcome should address feasibility and scientific merit, and should be captured by the Chair, Co-Chair or designee on the Concept Review Form (a summary of review form -- **see http://cancer.ucsf.edu/itr/itr-forms**). Concepts can either be approved, rejected, or the committee can request the PI to make revisions and bring back for further discussion. If approved, the committee will request that the concept be written up as a formal protocol document and will provide standardized HDFCCC protocol templates for that purpose. Once in protocol format, the study goes back to the committee for formal review as in New Protocol Review above.

Protocol Amendment Review

Protocols exempt from initial Site Committee review do not require amendment review by the Site Committee. The review of all other protocol amendments is required. Review procedures will be in line with PRC's procedures (see PRMS Amendment Submission Policy and PRMS Amendment Review Policy). Amendments are any changes made to the protocol version which was originally approved by the Site Committee, over the life of the clinical trial, regardless of the nature of the change (e.g., editorial, administrative, scientific, etc.). At minimum amendments should be approved by the Chair, or designee; discussion by the entire committee or specific reviewers is at the Chair's discretion. Also at the Chair's discretion, approvals may be documented via Chair or Co-Chair summary of review forms as in New Protocol Review above. Chair signature is required on the PRC Amendment Submission Form. If the Chair is the PI then the Co-Chair should sign the PRC Amendment Submission Form. Once approved by the Site Committee, the amended protocol needs to be submitted to the PRC. All protocol amendment applications will need to follow the PRC submission requirements, and must subsequently be approved by the PRC and the institutional IRB (the Committee on Human Research, or CHR) prior to implementation. See the PRMS Amendment Submission Policy for full details.

Safety Issues

Safety issues will be reviewed at least weekly for Phase I or otherwise high-risk or early phase clinical trials. All other trials will have safety issues reviewed at least monthly. Risk definitions are as follows:

Risk Assignment	**Study Type**
High	Institutional Phase 1 therapeutic

	Institutional therapeutic using gene therapy or vaccines
Medium	Institutional Phase 2 therapeutic
	Institutional Phase 3 therapeutic
Low	Behavioral studies/early detection or diagnostic

For investigator-initiated studies, the Principal Investigator (PI) or designee will review all applicable grades of adverse events (AEs) and serious adverse events (SAEs) prior to the meeting. This list of all AEs/SAEs along with patient status and cohort accrual (if applicable) will be presented at the meeting and the minutes will reflect the committee review. For cooperative group studies, only ADEERS reports and patient status log will be prepared. For all non-cooperative group Phase I studies, Grades 1-5 AEs and patient status log will be prepared. For all other studies, only Grades 3-5 AEs and patient status log will be prepared. The summary of AEs for all trials will be signed by the committee Chair or designee and incorporated into the minutes.

For studies initially reviewed by any Site Committee serving interventional trials crossing many cancer sites, AE review will be conducted by the originating program, *not* the Site Committee which conducted the initial review.

Accrual Criteria

The Site Committees are charged with the responsibility of ensuring adequate accrual to clinical trials and for closing trials with poor accrual to ensure appropriate utilization of resources. All committees will review all enrolling studies for accrual progress at least annually.

The committee is required to determine if the study should stay open. If accrual is less than projected, the committee is charged with evaluating the potential reasons for the problems and with formulating a corrective action plan which is documented in the meeting minutes. In particular, if after one year of enrollment a clinical trial has accrued less than the required minimum (see **Table 1**), the committee will decide to either close the study or keep it open. If the intent is to keep the study open, the site committee must record a corrective action plan to indicate how it plans to improve accrual. (Corrective action plans can be submitted to the PRC in response to PRC queries.) If within six months of implementation the corrective action plan fails to increase accrual to a rate projected to meet the annual minimum in **Table 1**, the committee is expected to close the study to further accrual (or terminate the study if possible). Trials accruing the minimum projected annual accrual goal are re-reviewed annually until closed to enrollment.

While the Site Committees are charged with assessing all active protocols to ensure adequate resource usage and enrollment, and to close those not enrolling sufficiently, these committees cannot override the decision of the PRC. The ultimate recommendation for protocol closure falls under the purview of the Protocol Review Committee (see PRMS Closure Policy). Protocols allowed to continue enrollment by the relevant Site Committee are not exempt from annual progress and performance monitoring and closure by the PRC (see PRMS Protocol Closure Policy).

Prioritization

Three Prioritization Lists are maintained by each site committee:

1. Overall Prioritization. To ensure adequate ongoing review of progress and performance, all new protocols, concept sheets/letters of intent, and all protocol amendments which impact the budget or accrual or are otherwise urgent will be tracked in order of priority. Two separate lists will be maintained, defined by the required level of activation resource utilization. Each committee will numerically rank (whole numbers, please) the priority of each item relative to all other items on the same list. This prioritization of all protocols and concepts within a program or committee will be re-evaluated at each site committee meeting. The protocol to undergo review by PRC should be highlighted on the applicable list upon submission to PRC (applicability is defined by the level of resource utilization).

One list will consist of overall prioritization for all trials requiring moderate to significant resources for activation, whether ITR or programmatic resources (high-resource utilization list). The second list will consist of overall prioritization for all trials requiring few to no resources for activation, whether ITR or programmatic resources, e.g., CIRB-approved trials (low-resource utilization list). Depending on the resource intensity of the protocol being submitted to PRC, one of these two lists will be submitted to PRC with every new protocol application to be used in its review and prioritization, and both lists will be used by the relevant disease site program or committee to determine in what order trials should receive attention over others.

2. Prioritization of competing open and proposed protocols for each specific patient population. The purpose of this list is to provide the PRC with a complete picture of which, if any, existing or upcoming trials may compete with the trial under review. In addition to identifying all competing protocols for a patient population, a description of how competing trials will be prioritized is required. Where applicable, the Site Committee should include trials from outside their program provided those trials compete with the applicable patient population. This list, which only needs to reflect the patient population under study in the protocol being reviewed, will be submitted to PRC with every new protocol application to PRC, to be used to assess feasibility of trial completion. If there are no competing trials for that specific protocol application, please prepare a statement for PRC submission explaining why.

PRMS Reliance

As per NOT-CA-16-038, https://grants.nih.gov/grants/guide/notice-files/NOT-CA-16-038.html), and on a case-by-case basis, the HDFCCC PRC may choose to rely on the Lead Site's full committee PRMS review for multi-center investigator-initiated research protocols originating from other NCI-designated Cancer Centers. In all such cases, the core or originating institution (coordinating center, or Lead Site) must meet the following criteria:

- The Lead Site 1) has a fully approved PRMS, 2) has conducted a full committee review for scientific merit, prioritization and feasibility, and 3) has issued their full approval of the protocol document

- The Lead Site agrees to provide to the PRMS Manager with its CCSG renewal date and an assertion that its PRMS is fully approved
- The Lead Site can provide proof of full PRMS approval to the PRMS Manager, to include documentation of the approved protocol version.

The Site Committee must not make this determination on its own. Upon receipt of a protocol thought to meet the above criteria, the Site Committee Administrator should immediately contact the PRMS Manager, who will initiate communication with the Lead Site and obtain the required PRMS documentation. If the PRMS Manager confirms that the above criteria are met and that PRC will perform expedited review, then the Site Committee may proceed with its own expedited review. Otherwise the site committee must perform a full committee review.

Quarterly Reports

Each committee is required to submit quarterly reports to the PRC to document the cumulative number of concepts and protocols reviewed, rejected, and accepted by the committee per calendar year. A template is provided at **http://cancer.ucsf.edu/itr/itr-forms**.

Minutes

Each committee is required to maintain written minutes of all meetings, including attendance and decisions concerning accrual, priorities, new concepts, and protocol review. All reviews using standardized forms, all summary of review forms, and attendance records for each meeting will be maintained in centralized binders, and available for review. Additional written minutes should be prepared to document any committee activity not covered by existing forms.

Adjudication of Disputes

Disputes between the committee and a PI go back to the committee for review. If agreement cannot be reached there, then the dispute is referred to the Director of the Investigational Trials Resource, who will convene an ad hoc committee to carry out an appeals process. Disputes will be reviewed by the ad hoc committee within four weeks of submission.

Auditing

All Site Committees are subject to audit by the Cancer Center Clinical Research Oversight Committee to ensure compliance with Site Committee policies. The Cancer Center Clinical Research Oversight Committee will have the authority to withdraw Site Committee status if a committee does not satisfactorily carry out its responsibilities.

Alternate Procedure

None.

Policy Approval

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

Eric Small, MD
Director, Investigational Trials Resource

11/29/16
Date

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

Policy Revision Summary of Changes

Policy Title: **PRMS Site Committee Review Policy**

Version Date: November 18, 2016

Version Number: Revision 10

Notes: Page number corresponds to page number in updated version (Revision 10). 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 9 12/17/2015
New Text	Revision ~~9~~***10*** 1~~2~~***1***/1~~7~~***8***/201~~5~~***6***
Reason for Change	To reflect updated version number and date.

Page No.: 1	**Section**: Header
Original Text	PRMS Disease Site Committee Review Policy PRMS Procedure for Protocol Review by Site Committee
New Text	PRMS ~~Disease~~ Site Committee Review Policy PRMS Procedure for Protocol Review by Site Committee
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 1	**Section**: Purpose
Original Text	PRMS responsibilities at this institution are carried out on two separate levels to ensure optimal oversight of progress and performance. There is initial review by the applicable Disease Site Committee(s), followed by independent review by the Protocol Review Committee (PRC). The purpose of this policy is to document the review process undergone by the programmatic Disease Site Committees prior to review by the Protocol Review Committee.
New Text	PRMS responsibilities at this institution are carried out on two separate levels to ensure optimal oversight of progress and performance. There is initial review by the applicable ~~Disease~~ Site Committee(s), followed by independent review by the Protocol Review Committee (PRC). The purpose of this policy is to document the review process undergone by the programmatic ~~Disease~~ Site Committees prior to review by the Protocol Review Committee.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 1	**Section**: Procedures Meeting Schedule
Original Text	All Disease Site Committees are required to meet monthly at minimum. Larger groups may meet more than once per month if workload dictates. Phase I or otherwise high-risk/early phase clinical trials must be reviewed at weekly meetings.
New Text	All ~~Disease~~ Site Committees are required to meet monthly at minimum. Larger groups may meet more than once per month if workload dictates. Phase I or otherwise high-risk/early phase clinical trials must be reviewed at weekly meetings.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 1	**Section**: Procedures Review Functions
Original Text	Disease Site Committees will be formed for each CCSG-funded program, and may be formed for non-CCSG-funded programs as well. There are specialized Disease Site Committees established for interventional trials crossing many cancer sites, e.g., early phase and supportive care (symptom management/palliative care/survivorship).
New Text	~~Disease~~ Site Committees will be formed for each CCSG-funded program, and may be formed for non-CCSG-funded programs as well. There are specialized ~~Disease~~ Site Committees established for interventional trials crossing many cancer sites, e.g., early phase and supportive care (symptom management/palliative care/survivorship). ***Each protocol must have one Site Committee designated as the responsible site committee. In some cases, varying levels of input from other Site Committees may be required. Please refer to the PRMS Site Committee Selection Policy for details.***

Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now. Referred the reader to the new policy on how to select the designated Site Committee as well as ascertain the level of required input from outside Site Committees.

Page No.: 2	**Section**: Procedures Review Conflicts
Original Text	On all studies where the PI is also the committee Chair, it is considered a conflict and the Chair is prohibited from performing related committee business. In all such cases the Chair should defer to the Co-Chair to conduct the committee business, and the Co-Chair is expected to complete and sign all applicable review forms. This applies to new concept reviews, new protocol reviews, contingent response reviews, protocol amendment reviews, and assignment of reviewers. Likewise, if the Chair is unavailable and the Co-Chair is the PI, review must be delayed until the Chair becomes available; the Co-Chair cannot conduct committee business pertaining to a study for which the Co-Chair is PI.
New Text	On all studies where the PI is also the committee Chair, it is considered a conflict and the Chair is prohibited from performing related committee business. In all such cases the Chair should defer to ~~the~~***a formally appointed*** Co-Chair to conduct the committee business, and the Co-Chair is expected to complete and sign all applicable review forms. This applies to new concept reviews, new protocol reviews, contingent response reviews, protocol amendment reviews, and assignment of reviewers. Likewise, if the Chair is unavailable and ~~the~~***one of the appointed*** Co-Chair***s*** is the PI, review must be ~~delayed until the Chair becomes available; the Co-Chair cannot conduct committee business pertaining to a study for which the~~ ***deferred to another formally appointed*** Co-Chair ***who*** is ***not the*** PI.
Reason for Change	Added clarification; with only a single Co-Chair appointed, Site Committees had difficulty with committee coverage when the Chair and Co-Chair were both absent. Appointment of up to three Co-Chairs will allow additional coverage; the site committee should just ensure that the reviewing Co-Chair is not the PI.

Page No.: 3	**Section**: Procedures New Protocol Review Types
Original Text	Studies exempt from PRC review (see PRMS Protocol Review Committee Review Policy for definitions) can also be exempt from Disease Site Committee review at the committee's discretion, although individual site committees may choose to review such studies. Likewise, studies allowed expedited review at PRC (see PRMS Protocol Review Committee Review Policy for definitions) may also receive an expedited review at the Disease Site Committee, although the Chair or Co-Chair has the option to require full committee review whenever warranted. Expedited review consists of the Chair or Co-Chair assigning one reviewer to complete the Expedited Reviewer's Comments form, and the Chair or Co-Chair completes the Chair or Co-Chair Summary of Review form; the review does not need to be presented/discussed at a full committee meeting (unless the Chair or Co-Chair feels that committee discussion is warranted) but is nonetheless prioritized.
New Text	Studies exempt from PRC review (see PRMS Protocol Review Committee Review Policy for definitions) can also be exempt from ~~Disease~~ Site Committee review at the committee's discretion, although individual site committees may choose to review such studies. Likewise, studies allowed expedited review at PRC (see PRMS Protocol Review Committee Review Policy for definitions) may also receive an expedited review at the ~~Disease~~ Site Committee, although the Chair or Co-Chair has the option to require full committee review whenever warranted. Expedited review consists of the Chair or Co-Chair assigning one reviewer to complete the Expedited Reviewer's Comments form, and the Chair or Co-Chair completes the Chair or Co-Chair Summary of Review form; the review does not need to be presented/discussed at a full committee meeting (unless the Chair or Co-Chair feels that committee discussion is warranted) but is nonetheless prioritized ***(meaning the study undergoing review is reflected in both the Competing Trials list and the Protocols in Development list)***.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now. Added clarification to ensure that competing trials and prioritization are assessed on all expedited reviews.

Page No.: 3	**Section**: Procedures New Protocol Review
Original Text	A quorum is required for the conduct of every Disease Site Committee meeting. Quorum is defined as 50% of the Core committee membership roster. Ad Hoc members should be recorded as such on the roster, but do not count toward quorum.
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Page No.: 3	**Section**: Procedures New Protocol Review
Original Text	Institutional (investigator-initiated) trials: • Primary reviewer (presents study at full committee meeting) • Secondary reviewer • Statistical reviewer (except in cases of conflict). Statistical review is required on all institutional trials, *unless* the committee statistician serves as the protocol statistician; in such cases, the protocol is exempt from site committee statistical review. In other words, the statistician who wrote and/or designed the protocol's statistical sections cannot review that protocol at site committee. Statistical review will always occur at the PRC level.
New Text	Institutional (investigator-initiated) trials*****: • Primary reviewer (presents study at full committee meeting) • Secondary reviewer • Statistical reviewer (except in cases of conflict). Statistical review is required on all institutional trials, *unless* the committee statistician serves as the protocol statistician; in such cases, the protocol is exempt from site committee statistical review. In other words, the statistician who wrote and/or designed the protocol's statistical sections cannot review that protocol at site committee. Statistical review will always occur at the PRC level. **** Please refer to the PRMS Reliance section below.***
Reason for Change	Added an asterisk and a statement to refer to the PRMS Reliance section, which explains circumstances under which exceptions to full committee review may be allowed when a multi-center investigator-initiated protocol originates from another NCI-designated Cancer Center.

Page No.: 4	**Section**: Procedures New Protocol Review
Original Text	Primary, Secondary and Expedited reviewers will provide individual scores for clinical importance, trial design, innovation/science, UCSF involvement in development, potential for UCSF publication, and accrual/feasibility. An overall score is assigned, which takes the preceding scores into account but does not average them. The reviewing biostatistician provides an overall score as well. Non-reviewing members do not score. The NIH scoring system will be used. After presentation by reviewers, their scores will be averaged to determine the final overall score. It is recommended that priority be given first to institutional (investigator-initiated) protocols, followed by cooperative group clinical trials and lastly to industry/pharmaceutical-sponsored clinical trials.
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Reason for Change	Added NCI terminology for cooperative group trials.

Page No.: 5	**Section**: Procedures New Protocol Review
Original Text	• Confirmation of submittal of all review forms, Chair or Co-Chair summary of review form, and numerical ranking list of all trials (see Prioritization)
New Text	• Confirmation of submittal of all review forms, Chair or Co-Chair summary of review form, and numerical ranking list of all trials ***in development*** (see Prioritization)
Reason for Change	Added clarification on what type of prioritization is referred to.

Page No.: 5	**Section**: Procedures New Protocol Review
Original Text	In completing the above information, the Disease Site Committee should be mindful that the PRC will not approve any new applications upon initial review if the projected annual accrual does not meet the minimum requirements in **Table 1** below.
New Text	In completing the above information, the ~~Disease~~ Site Committee should be mindful that the PRC will not approve any new applications upon initial review if the projected annual accrual does not meet the minimum requirements in **Table 1** below.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 5	**Section**: Procedures New Protocol Review
Original Text	*Waiver requests at the time of PRC review are allowed for these studies. Requests for waivers are submitted electronically by the Disease Site Committee in an email to the PRC Administrator and must justify why it is necessary to open such a low accruing study. Waivers to these requirements can be granted on a case by case basis by the PRC, provided one of the following three criteria are met.
New Text	* Waiver requests at the time of PRC review are allowed for these studies. Requests for waivers are submitted electronically by the ~~Disease~~ Site Committee in an email to the PRC Administrator and must justify why it is necessary to open such a low accruing study. Waivers to these requirements can be granted on a case by case basis by the PRC, provided one of the following three criteria are met.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now. Added a space after the asterisk.

Page No.: 6	**Section**: Procedures New Protocol Review
Original Text	All above committee review outcomes will be issued by the committee Chair or Co-Chair using a standardized Chair or Co-Chair Summary of Review form. The Chair or Co-Chair Summary of Review form contains an indication of the committee's final overall score. Chair signature is required on the Chair or Co-Chair Summary of Review Form. If the Chair is the PI then the Co-Chair should sign the form. The approved Chair or Co-Chair Summary of Review form signed by the Chair or Co-Chair (and the Contingent Response Review Form if applicable) serves as proof of Disease Site Committee approval. For approved protocols, all applicable committee review forms, including individual review forms, Chair or Co-Chair summary of review forms, and contingent response review forms need to be submitted to the PRC as part of the application, to demonstrate the entire review history.
New Text	All above committee review outcomes will be issued by the committee Chair or Co-Chair using a standardized Chair or Co-Chair Summary of Review form. The Chair or Co-Chair Summary of Review form contains an indication of the committee's final overall score. Chair signature is required on the Chair or Co-Chair Summary of Review Form. If the Chair is the PI then the Co-Chair should sign the form. The approved Chair or Co-Chair Summary of Review form signed by the Chair or Co-Chair (and the Contingent Response Review Form if applicable) serves as proof of ~~Disease~~ Site Committee approval. For approved protocols, all applicable committee review forms, including individual review forms, Chair or Co-Chair summary of review forms, and contingent response review forms need to be submitted to the PRC as part of the application, to demonstrate the entire review history.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now. Removed an extra formatting space.

Page No.: 7	**Section**: Procedures Protocol Amendment Review
Original Text	Protocols exempt from initial Disease Site Committee review do not require amendment review by the Disease Site Committee. The review of all other protocol amendments is required. Review procedures will be in line with PRC's procedures (see PRMS Amendment Submission Policy and PRMS Amendment Review Policy). Amendments are any changes made to the protocol version which was originally approved by the Disease Site Committee, over the life of the clinical trial, regardless of the nature of the change (e.g., editorial, administrative, scientific, etc.). At minimum amendments should be approved by the Chair, or designee; discussion by the entire committee or specific reviewers is at the Chair's discretion. Also at the Chair's discretion, approvals may be documented via Chair or Co-Chair summary of review forms as in New Protocol Review above. Chair signature is required on the PRC Amendment Submission Form. If the Chair is the PI then the Co-Chair should sign the PRC Amendment Submission Form. Once approved by the Disease Site Committee, the amended protocol needs to be submitted to the PRC. All protocol amendment applications will need to follow the PRC submission requirements, and must subsequently be approved by the PRC and the institutional IRB (the Committee on Human Research, or CHR) prior to implementation. See the PRMS Amendment Submission Policy for full details.
New Text	Protocols exempt from initial ~~Disease~~ Site Committee review do not require amendment review by the ~~Disease~~ Site Committee. The review of all other protocol amendments is required. Review procedures will be in line with PRC's procedures (see PRMS Amendment Submission Policy and PRMS Amendment Review Policy). Amendments are any changes made to the protocol version which was originally approved by the ~~Disease~~ Site Committee, over the life of the clinical trial, regardless of the nature of the change (e.g., editorial, administrative, scientific, etc.). At minimum amendments should be approved by the Chair, or designee; discussion by the entire committee or specific reviewers is at the Chair's discretion. Also at the Chair's discretion, approvals may be documented via Chair or Co-Chair summary of review forms as in New Protocol Review above. Chair signature is required on the PRC Amendment Submission Form. If the Chair is the PI then the Co-Chair should sign the PRC Amendment Submission Form. Once approved by the ~~Disease~~ Site Committee, the amended protocol needs to be submitted to the PRC. All protocol amendment applications will need to follow the PRC submission requirements, and must subsequently be approved by the PRC and the institutional IRB (the Committee on Human Research, or CHR) prior to implementation. See the PRMS Amendment Submission Policy for full details.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 8	**Section**: Procedures Safety Issues
Original Text	For studies initially reviewed by any Disease Site Committee serving interventional trials crossing many cancer sites, AE review will be conducted by the originating program, *not* the Disease Site Committee which conducted the initial review.
New Text	For studies initially reviewed by any ~~Disease~~ Site Committee serving interventional trials crossing many cancer sites, AE review will be conducted by the originating program, *not* the ~~Disease~~ Site Committee which conducted the initial review.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 8	**Section**: Procedures Accrual Criteria
Original Text	The Disease Site Committees are charged with the responsibility of ensuring adequate accrual to clinical trials and for closing trials with poor accrual to ensure appropriate utilization of resources. All committees will review all enrolling studies for accrual progress at least annually
New Text	The ~~Disease~~ Site Committees are charged with the responsibility of ensuring adequate accrual to clinical trials and for closing trials with poor accrual to ensure appropriate utilization of resources. All committees will review all enrolling studies for accrual progress at least annually
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 8	**Section**: Procedures Accrual Criteria
Original Text	While the Disease Site Committees are charged with assessing all active protocols to ensure adequate resource usage and enrollment, and to close those not enrolling sufficiently, these committees cannot override the decision of the PRC. The ultimate recommendation for protocol closure falls under the purview of the Protocol Review Committee (see PRMS Closure Policy). Protocols allowed to continue enrollment by the relevant Disease Site Committee are not exempt from annual progress and performance monitoring and closure by the PRC (see PRMS Protocol Closure Policy).
New Text	While the ~~Disease~~ Site Committees are charged with assessing all active protocols to ensure adequate resource usage and enrollment, and to close those not enrolling sufficiently, these committees cannot override the decision of the PRC. The ultimate recommendation for protocol closure falls under the purview of the Protocol Review Committee (see PRMS Closure Policy). Protocols allowed to continue enrollment by the relevant ~~Disease~~ Site Committee are not exempt from annual progress and performance monitoring and closure by the PRC (see PRMS Protocol Closure Policy).
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 9	**Section**: Procedures Prioritization
Original Text	2. Prioritization of competing open and proposed protocols for each specific patient population. The purpose of this list is to provide the PRC with a complete picture of which, if any, existing or upcoming trials may compete with the trial under review. In addition to identifying all competing protocols for a patient population, a description of how competing trials will be prioritized is required. Where applicable, the Disease Site Committee should include trials from outside their program provided those trials compete with the applicable patient population. This list, which only needs to reflect the patient population under study in the protocol being reviewed, will be submitted to PRC with every new protocol application to PRC, to be used to assess feasibility of trial completion. If there are no competing trials for that specific protocol application, please prepare a statement for PRC submission explaining why.
New Text	2. Prioritization of competing open and proposed protocols for each specific patient population. The purpose of this list is to provide the PRC with a complete picture of which, if any, existing or upcoming trials may compete with the trial under review. In addition to identifying all competing protocols for a patient population, a description of how competing trials will be prioritized is required. Where applicable, the ~~Disease~~ Site Committee should include trials from outside their program provided those trials compete with the applicable patient population. This list, which only needs to reflect the patient population under study in the protocol being reviewed, will be submitted to PRC with every new protocol application to PRC, to be used to assess feasibility of trial completion. If there are no competing trials for that specific protocol application, please prepare a statement for PRC submission explaining why.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.

Page No.: 9-10	**Section**: Procedures PRMS Reliance
Original Text	Not applicable.
New Text	***PRMS Reliance*** ***As per NOT-CA-16-038, https://grants.nih.gov/grants/guide/notice-files/NOT-CA-16-038.html), and on a case-by-case basis, the HDFCCC PRC may choose to rely on the Lead Site's full committee PRMS review for multi-center investigator-initiated research protocols originating from other NCI-designated Cancer Centers. In all such cases, the core or originating institution (coordinating center, or Lead Site) must meet the following criteria:*** • ***The Lead Site 1) has a fully approved PRMS, 2) has conducted a full committee review for scientific merit, prioritization and feasibility, and 3) has issued their full approval of the protocol document*** • ***The Lead Site agrees to provide to the PRMS Manager with its CCSG renewal date and an assertion that its PRMS is fully approved*** • ***The Lead Site can provide proof of full PRMS approval to the PRMS Manager, to include documentation of the approved protocol version.*** ***The Site Committee must not make this determination on its own. Upon receipt of a protocol thought to meet the above criteria, the Site Committee Administrator should immediately contact the PRMS Manager, who will initiate communication with the Lead Site and obtain the required PRMS documentation. If the PRMS Manager confirms that the above criteria are met and that PRC will perform expedited review, then the Site Committee may proceed with its own expedited review. Otherwise the site committee must perform a full committee review.***
Reason for Change	Added new section on PRMS Reliance. The NCI has issued a Notice of Correction to the P30 CCSG in the form of Notice Number NOT-CA-16-038 (https://grants.nih.gov/grants/guide/notice-files/NOT-CA-16-038.html), which allows any center to rely on the Lead Site's full committee review, provided the Lead Site has a fully approved PRMS. This allowance to rely is negated if the Lead Site's PRMS is either conditionally approved or disapproved. The PRC will allow Expedited review for protocols meeting the terms of NOT-CA-16-038 in most cases, although it reserves the right to require full committee PRC review. Where Expedited review is allowed, the relevant Site Committee(s) may also conduct a formal Expedited review; however, Site Committees should not make this determination on their own, but rather inform the PRMS Manager, who will obtain the appropriate documentation from the Lead Site's PRMS, and inform the Site Committee on whether expedited review will be allowed. Should PRC require full committee review, the Site Committee will also be expected to conduct formal full committee review.

Page No.: 10	**Section**: Procedures Auditing
Original Text	All Disease Site Committees are subject to audit by the Cancer Center Clinical Research Oversight Committee to ensure compliance with Disease Site Committee policies. The Cancer Center Clinical Research Oversight Committee will have the authority to withdraw Disease Site Committee status if a committee does not satisfactorily carry out its responsibilities.
New Text	All ~~Disease~~ Site Committees are subject to audit by the Cancer Center Clinical Research Oversight Committee to ensure compliance with ~~Disease~~ Site Committee policies. The Cancer Center Clinical Research Oversight Committee will have the authority to withdraw ~~Disease~~ Site Committee status if a committee does not satisfactorily carry out its responsibilities.
Reason for Change	Deleted 'Disease' from the name for site committees, since some site committees cover modalities now.