Samuel Oschin Comprehensive Cancer Institute

Protocol Review and Monitoring System

Charter

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DOCUMENT VERSION HISTORY		
VERSION NUMBER	**DATE**	**CHANGES**
00	January 31, 2011	n/a
01	November 1, 2014	*ADDITION of:* Disease Research Group section PRMS Scope section PPC structure, policies, and procedures PRMC annual monitoring PRMC amendment review
01	December 26, 2014	*CLARIFICATION of:* *Tie vote language* *UPDATE of:* PRMC membership
01	January 21, 2015	*ADDITION of:* *PRMC review of significant protocol amendments* *CLARIFICATION of:* Protocol tracking within DRGs Voluntary study closure due to low accrual
02	November 17, 2015	*ADDITION of:* *PPC member responsibilities* *PPC membership term* *Scientific progress review for study annual review* *CLARIFICATION of:* *PRMC administrative review for peer reviewed Institutional research (IIS/IIT)* *IIS LOI two-stage review* *PPC Feasibility assessment* *PRMC meeting leadership when chair is recused* *PRMC amendment review process* *PRMC annual accrual monitoring minimum accrual requirements*
03	October 12, 2016	*ADDITION of:* *Table 3: Study types eligible for PRMS expedited review* *ADDITION of:* *PRMC chair responsibilities to include closing of studies that fail to meet accrual after 18 consecutive months of low accrual*

		ADDITION of: *PRMC Review Types to include Expedited Review* *MODIFICATION of:* *PRMC Review Outcome changed from maximum of 2 rounds to maximum of 3 rounds for deferrals pending PI response* *ADDITION of:* *Giving PRMS Coordinator authority to suspend study accrual when response is not provided during Accrual monitoring.* *MODIFICATION of:* *Study termination changed from having two thirds to having a majority for study termination* *ADDITION of:* *Provision that allows amendments to bypass scientific review for studies closed to accrual*
04	July 26, 2017	*REMOVAL of:* *Allowing PRMS Coordinator to obtain votes by email when quorum is not achieved during PRMC review* *FDA ok to proceed requirement for early phase trials and IITs* *MODIFICATION of:* *Slight modification of "Appendix 1: Detailed PRMS Review Scope" in accordance with CCSG guidelines dated 22 Dec.2016* *ADDITION of:* *Precision Medicine Classifications* *PPC approval maximums* *PRMC authority to terminate protocols that do not demonstrate scientific progress* *CLARIFICATION of:* *Appeal process for PRMC study closures*

I. INTRODUCTION

The Protocol Review and Monitoring System (PRMS) prioritizes and scientifically evaluates all prospective cancer research studies derived from and supported by institutional resources. The PRMS review is distinct from and yet complements the human subject protections review conducted by the Institutional Review Board (IRB). The PRMS is comprised of two distinct committees: Protocol Prioritization Committee (PPC) and Protocol Review and Monitoring Committee (PRMC).

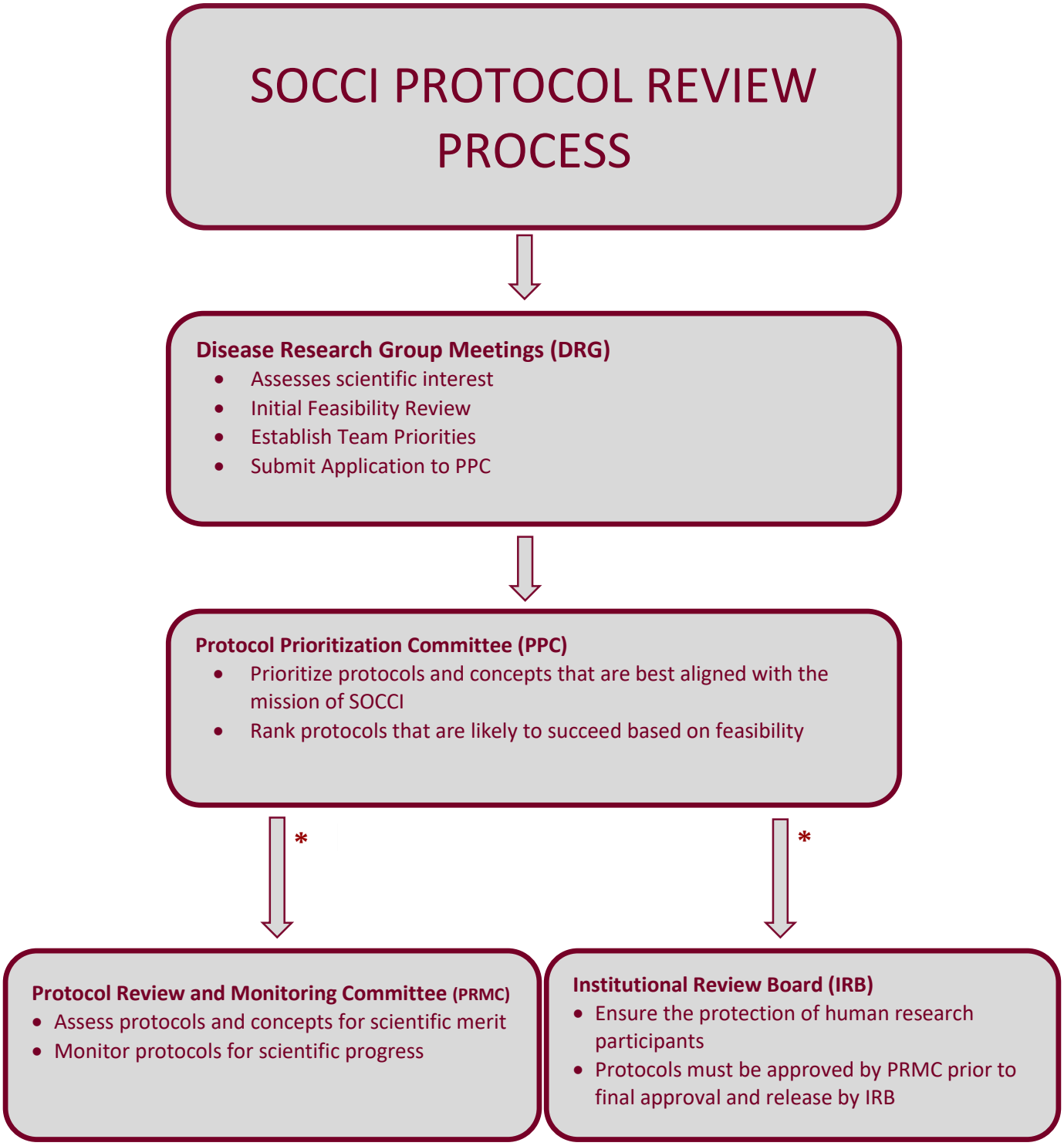
Protocols and concepts are initially evaluated for scientific merit as well as feasibility by the appropriate Disease Research Group (DRG). The DRGs are responsible for establishing group priorities, tracking the vetting of protocols, and determining whether or not to pursue the opening of trials based on group priorities, scientific interest, logistics and feasibility. All protocols vetted at the DRG level are tracked via the Clinical Research Office's (CRO) Protocol Vetting Tracker. Protocol information and final decisions regarding DRG trial approval or declination are chronicled on the tracker. The tracker is maintained by the CRO's clinical operations manager and the DRG team representatives are responsible for reporting protocol vetting information to the manager for inclusion on the tracker. Once protocols are vetted at the DRG level and approved to move forward, studies are then submitted to the PPC for consideration. The PPC is responsible for the prioritization of studies that are best aligned with the mission of the Samuel Oschin Comprehensive Cancer Institute (SOCCI) and consistent with the priorities set by the DRG. When ranking priority the PPC considers those studies that are likely to succeed, based upon a concurrent feasibility assessment, including an assessment of studies that may compete for the same patients, to foster the best use of resources.

Once ranked by the PPC and approved, the study is automatically forwarded to the PRMC for scientific review. The PRMC is responsible for assuring internal oversight of the scientific aspects of all prospective cancer research at SOCCI. Once a study is activated, the PRMC evaluates scientific progress of ongoing protocols through routine monitoring (including protocol accrual rates) to ensure timely completion of the research study and that the scientific aims of the study can be met.

SOCCI has elected to use a two stage review process for the evaluation of Investigator Initiated Studies (IIS). In Stage I, initial concepts (Letters of Intent) are reviewed by the PRMS for feasibility, prioritization and scientific merit. The first stage review also provides an opportunity for the PRMC to comment on the scientific design of the protocol. If approved at Stage I the protocol is then sent forward for full development through the SOCCI Protocol Development Core. At Stage II, fully developed protocols then follow the standard processing through the PRMS. This two-stage process ensures that limited resources are not directed towards protocols of lesser scientific merit or outside the priorities of the cancer center and improves development timelines.

Studies are processed electronically through the PPC Online and OnCore® ePRMS systems, eliminating the need to submit multiple applications. Flexible meeting schedules, including a virtual online forum for PPC and bi-weekly PRMC meetings, enables timely review of studies through the PRMS system.

Administrative leadership is provided by the Director of the Clinical Research Office while scientific leadership for PRMS is provided by the Associate Director for Clinical Research who supervises the academic activities of the DRGs and the Clinical Research Advisory Board (CRAB) who provides continuous oversight and evaluation of the clinical research infrastructure, including PRMS, to ensure efficiency and effectiveness.



** Most protocols are submitted concurrently to the PRMC and the IRB (i.e. standard industry and NCTN studies). Investigator Initiated Studies (IISs) are submitted serially to PRMC then IRB.*

II. DISEASE RESEARCH GROUPS

Multidisciplinary disease specific research groups (DRG) are composed of investigators, research nurses, clinical research coordinators (CRC), regulatory coordinators, basic research personnel, and other research professionals. These individuals work together to identify, develop, and maintain a portfolio of high quality cancer studies within a disease group that promotes and supports the mission of SOCCI: to make the best new cancer therapies available to patients and to enhance clinical research outcomes, consistent with NCI priorities for clinical cancer research.

Each DRG has a disease specific Program Leader (DRG Physician Lead) and a disease specific Lead Clinical Research Staff member (Research Nurse or CRC). The Clinical Research Office (CRO) designates Regulatory and Lead Clinical Research staff for each disease-specific team. The DRG Physician Lead, with the support of the staff lead, is responsible for convening DRG meetings and establishing the agenda. The agenda is based on a comprehensive template provided by the CRO. Prior to submission to submission for review through the PRMS the DRG reviews proposed studies for scientific interest, study conduct feasibility, the ability to accrue, and establishes the priority of the study within the disease specific portfolio. The DRG is also responsible for identifying any outliers within the study that may require additional resources including staffing, financial or ancillary department services, and logistical challenges. Protocols approved by the DRG should not compete with existing or planned studies and should have sufficient planned accrual to justify utilization of the shared resources.

The DRG is responsible for developing recruitment plans for each study and monitoring accrual and regulatory status and requirements, including pending changes to the protocol. The DRG Program Leader is also responsible for ensure the group maintains a balanced portfolio. In the event that the proposed portfolio exceeds the capacity of the CRO or the DRG, the DRG Program Leader and/or the investigator may be invited to present a plan to the PPC committee to obtain a manageable portfolio of protocols.

Once a study has been vetted through the DRG and approved to move forward, the DRG Program Leader must document the DRG support by signing off on the PPC application prior to submission to the committee for review.

III. PROTOCOL REVIEW AND MONITORING SYSTEM SCOPE

All prospective cancer research studies are required to be submitted to PRMS and reviewed by both the PPC and PRMC, including non-therapeutic interventions. However, observational or epidemiological studies enrolling *only* healthy human subjects are exempt from PRMS initial review. Determining whether a specific research project is defined as a "non-therapeutic intervention" versus an "observational" study, is not always straight-forward. Therefore, the PRMS will review all non-therapeutic cancer-related prospective research with those studies determined to be observational being exempt from future review and monitoring. Interventional and observational studies are defined ***Appendix 1*** and summarized below in ***Table 1***.

In addition, some studies may be eligible for an Administrative PRMC Review (***Table 2***) and others may be Exempt from PRMS review (***Table 3***).

Table 1

Study Types Requiring PRMS Review

TREATMENT Interventions	NON-TREATMENT Interventions	OBSERVATIONAL Studies
Hypothesis driven studies of therapeutic interventions administered to cancer patients or individuals at increased risk of cancer. Studies involving the following types of interventions: **Primary Therapy of Cancer** • Chemotherapy • Radiotherapy • Surgical Therapy • Transplants • Gene Therapy • Immunotherapy • Combined Modality Therapy • Alternative Therapy • Devices **Primary Cancer Prevention Therapy** • Chemoprevention • Surgical Prevention • Cancer Vaccine	**Primary Supportive Care Therapies** • Pain Prevention or Control • Infection Prevention or Control • Transfusion Support • Nutrition Support • Complementary Therapy **Other Interventions** • Physical Therapy • Behavioral • Educational • Detection/Screening • Diagnostic Methods • Imaging and Device trials (intended to improve diagnosis or detection of cancer)	**NON- INTERVENTIONAL** **Laboratory Studies** • Correlative • Ancillary **Epidemiologic** • Studies among cancer patients to determine the patterns, causes, and/or control of disease in groups of people leading to improved understanding of screening and detection, diagnosis, and treatment of cancer. * • Health Services Research **NOTE:** *Studies enrolling only healthy human subjects do not require PRMS review. Further, studies determined after initial review by the PRMC to be "observational" do not require additional monitoring.*

Studies which have undergone traditional peer review (See ***Appendix 3*** - Organizations with Approved Peer Review and Funding Systems) and those studies approved by NCI's Cancer Therapy and Evaluation Program (CTEP) as well as the Division of Cancer Prevention (DCP) are initially reviewed by the PPC for feasibility assessment and prioritization but are generally eligible for an administrative review by the PRMC Chair or Vice-Chair (***Appendix 4***). The following Study Types are eligible for administrative review by the PRMC; however, the PRMC leadership has the discretion to request a review by the full committee.

Table 2
Study types eligible for administrative PRMC review
• NCTN studies including the following CTSU studies: ACOSOG, AMC, ALLIANCE, BMTCTN, CALGB, COG, ECOG, GOG, IBCSG, MDA, NCCTG, NCIC, NCIMET, NSABP, RTOG, SCISF, SWOG, USMCI and WFUCCOP. See CTSU Protocol Menu for the most updated list. https://www.ctsu.org/
• U01, U10, P01, P50 funded studies* and other Peer Reviewed studies (See list of NCI approved agencies – Appendix 3)

* Under the two-stage review process for IIS/IIT, the LOI is eligible for administrative review if peer reviewed.

Table 3 outlines the study types are exempt from PRMS review:

Table 3
Study types eligible for PRMS expedited review
• For multi-site institutional trials with an NCI designated lead site (if lead institution PRMS has conducted scientific review of the protocol)

Table 4
Study types exempt from PRMS review
• Single Use IND (Compassionate Use)
• Retrospective Chart Reviews
• Institutional Registries and Specimen Banks
• Questionnaires that do not Test Interventions

As a means of ensuring that the scientific goals of the study can be met the all protocols approved by PRMS are monitored by the PRMC on an annual basis (aside from pediatric studies and low-risk observational studies - Section IV further details this process).

IV. PRTOCOL PRIORITIZATION COMMITTEE (PPC)

Objective

The purposes of the SOCCI PPC are to identify and prioritize cancer studies that are best aligned with the mission of SOCCI, to make the best new cancer therapies available to patients, and to enhance clinical study outcomes. Prioritization of SOCCI research goals begins within the individual disease research groups. When assessing high quality, relevant studies that meet SOCCI objectives, the PPC ensures that studies to be conducted are also consistent with the priorities set by the DRG.

The PPC ranks studies that are likely to succeed based on a concurrent feasibility assessment. The function of the PPC is distinct from that of the Protocol Review and Monitoring Committee (PRMC) the focus of which is scientific review and protocol monitoring. The PPC reviews protocols and assigns

priority scores prior to submission to the PRMC. The PPC does not consider scientific merit when reviewing studies and does not monitor the research following review.

A. PPC Committee Structure

1. PPC Leadership

The Chair and Vice-Chair of the PPC are appointed by the SOCCI Director from the membership of the SOCCI for a 36-month term.

The PPC Chair is responsible for:

- Ensuring that a quorum is in place for each meeting
- Assigning a primary reviewer to summarize the research
- Leading and facilitating the discussion at committee meetings
- Calling for committee recommendations and ensuring protocols are ranked
- Reconciling the committee's recommendation and recording a single score for each protocol presented for prioritization
- Monitoring the High Priority and Standard queues
- Initiating a portfolio review in the event that a proposed portfolio exceeds the capacity of the CRO or the DRG. This may also be done at the request of the committee or an investigator
- Appointing an Ad Hoc chair when the Chair and Vice-Chair are both unavailable to convene a meeting

The Vice-Chair of the PPC shall execute the responsibilities of the Chair in the absence of the Chair, or as delegated by the Chair.

2. PPC Membership

Voting Members of the PPC are appointed by the SOCCI Director and represent SOCCI leadership and major SOCCI programs, departments and divisions. In addition, representatives from SOCCI Administration, Biostatistics, Clinical Research Office (CRO), Imaging, Nursing, Pathology and Cancer Prevention and Control serve as Ad-Hoc members, and may be asked to participate in PPC meetings for purposes of providing context and assessing protocol feasibility for specific protocols. The SOCCI Director serves as an Ex-Officio member as needed. There are no alternates, however the PPC Online system allows voting members to review and discuss protocols virtually. The PRMS Coordinator is a non-voting member. The minimum term of appointment of voting members to the PPC is 24 months. The SOCCI Director will continuously reevaluate PPC membership.

a. Member Responsibilities

All regular members of the PPC are expected to routinely serve as a reviewer for protocols as assigned by the Chair and/or designee. Members are expected to attend a

minimum of 75% of committee meetings (i.e. 36 meetings) given the small membership group and commitment to rapid turn-around time.

3. PRMS Coordinator

The PRMS Coordinator is a non-voting member of the PPC who provides administrative support to the committee; s/he is responsible for all administrative tasks including receiving, cataloguing, and tracking all new protocols submissions made through the PPC Online system. The PRMS coordinator is also responsible for initial administrative review of all submissions to ensure completeness and identifies the need for ad-hoc members.

The PRMS coordinator is responsible for:

- Ensuring that all protocols submitted to the PPC are promptly reviewed and committee correspondence is returned to the investigator timely
- Compiling and distributing the agenda including each protocol to be reviewed
- Scheduling PPC meetings and routing meeting notifications as applicable
- Recording minutes, tracking protocols, and tracking committee votes in PPC Online
- Maintaining records of meeting attendance
- Managing all committee correspondence, including outcome letters, and all committee-related clerical duties
- Performing other committee related business delegated by the Chair
- Providing the committee with a status reports as needed
- Forwarding the protocol in OnCore® for PRMC review upon completion of PPC review

4. PPC Rules

a. Quorum

A quorum must be present for agreement to be reached and a priority score given. A quorum consists of 3 committee members: the Chair or the Vice-Chair plus two voting committee members.

b. Recusal

PPC voting members must recuse themselves from ranking priorities for those protocols in which they are listed as the principal investigator or sub-investigator, or where there is any other conflict of interest.

c. Ad-Hoc Members

Ad-hoc members may be asked to participate in individual reviews as necessary, to provide input regarding study feasibility as it relates to their particular area of expertise but are not considered in establishing a quorum and may not participate in the vote.

B. PPC Review Policy

1. Prioritization

All prospective cancer research studies are required to be reviewed by PPC, including non-therapeutic interventions as outlined in Table 1. For all submissions, the PPC assesses feasibility and sets an institutional priority; a priority score is assigned to every study (excluding Rapid Activation studies). The PPC uses a 9-point scale where a score of 1 indicates an exceptional study to be designated as High priority. A score of 5 is considered an average score. Each reviewer presents their score to the Chair or Vice-Chair of the PPC. If there is a lack of consensus, the Chair or Vice-Chair averages the scores and designates it as High Priority (1-3) or Standard Priority (≥ 4). A score of 10 indicates that the reviewer does not recommend the protocol for further activation or development. Investigators may elect to apply for use of the Rapid Activation process described below.

2. PPC Review Outcomes

The priority assigned to the study by the investigator or the DRG is considered during the PPC review. Protocol priority designation assigned by the PPC is used as a guide for enrollment strategies and balancing programs and resources at the Institute level. The PPC makes recommendations to the Clinical Research Office for processing the studies. The PPC Review outcomes are summarized below in ***Table 4*** and include Rapid Activation (RA), High Priority, Standard Priority, Deferred, or Not Recommended.

The PPC may, after deliberations, determine a study is not feasible and not recommend the study move forward. Reason for classifying a study as "not recommended" may include, but not limited to: logistical complexity, resource limitations, financial viability, inadequate patient population or investigator performance history in the same area. Those protocols not recommended for activation (or development in the case of IIS) may not move forward to PRMC or IRB.

Rapid Activation studies are processed by the CSMC Rapid Activation team and have essentially no waiting time. A limited number of studies are designated as High Priority, while the majority of studies are designated as Standard Priority. Those studies designated as Standard priority are processed in the order received by the CRO and are not displaced by High Priority studies. The CRO will alternately activate studies in the High Priority queue and the Standard Priority queue. That way, both queues advance, with the High Priority queue having a shorter average wait time. It is the responsibility of the PPC to monitor the volume of studies in the High Priority queue to ensure that the wait time there does not become excessive.

Table 4

PPC Review Outcomes		
Classification	**Score**	**Description**
Rapid Activation (RA)	RA	High Priority early phase trials and those approved through the Rapid Activation Request Review Process that meet the characteristics of RA
High	1-3	Studies that advance SOCCI research objectives and developmental goals
Standard	4-9	Majority of studies conducted at SOCCI

Deferral	N/A	Priority may be ranked but study cannot move forward to PRMC. Feasibility/ infrastructure or other issues will need to be addressed by the PI prior to activation. Do not send to PRMC unless the feasibility question is related to Therapeutic Intent of the protocol.
Not Recommended (NR)	10	Not recommended for further development

a. Rapid Activation (RA)

RA, as currently configured, is a highly intensive process, requiring that existing resources be diverted from other commitments from multiple departments (CRO, IRB, Grants and Contracts Office, Radiation Safety Committee, etc). Hence RA is a scarce resource that cannot be invoked for every study. If the investigator determines that their study meets the characteristics detailed in ***Table 5***, a formal request at PPC submission can be made for RA. These requests are immediately triaged to the Chair of the PPC and SOCCI Director for assessment and endorsement. Those studies determined to be eligible for RA are then sent to the RA leads at the CRO, IRB, Grants and Contracts Office, PRMC, and Radiation Safety to determine if resources are available to proceed. Details on the RA process, workflow, and tracking can be found at https://www.protocolrapidactivation.org/prat/index.php/site/index. Those studies determined not to be eligible for RA are sent through the routine PPC process.

Table 5

Characteristics of Rapid Activation Clinical Trials

- **Innovation**: Studies that offer access to cutting edge treatments
- **High Academic Impact**: Those studies that allow SOCCI investigators to participate at the level of trial design, completion, publication and presentation at the national level
- **Potential for Academic Collaboration**: Studies in which the sponsor seeks transdisciplinary collaboration with SOCCI/CSMC investigators and allows for the transition of scientific findings through the translation continuum
- **Impact within the Scientific Community**: Studies which positively impact our future relationships with the larger scientific community (external sponsors and CROs) such as access to First in Human, Investigator Initiated and Phase I trials

NOTE: *Trials that require review by the Biosafety Committee, such as infectious agent and recombinant genetic material studies, are currently excluded from being processed through the Rapid Activation process at this time.*

b. High Priority

Using the criteria below in ***Table 6***, the PPC reviews studies and designates a limited number as High Priority based on SOCCI scientific and strategic goals and the priorities established within the individual DRG's. The Committee may identify studies that are high priority but may not be feasible at the time of review.

Table 6

Characteristics of High Priority Clinical Trials

- Investigator Initiated and peer reviewed (as defined by NCI/CCSG Guidelines)
- Cooperative Group studies (NCTN) and CTSU status
- Investigator initiated studies (internal or peer reviewed) that meet SOCCI developmental goals
- Potential for High Scientific Output: investigator has a leadership role; likely scientific impact
- Studies preparatory to a cooperative group (NCTN) trial

c. Standard Priority

Protocols that do not qualify for RA or high priority and are scored between ≥4 and ≤10 are assigned standard priority to be activated as outlined above.

d. Deferral

In the event a protocol presents feasibility/ infrastructure or other issues will need to be addressed by the Principal Investigator prior to activation the committee may establish the priority and the protocol may be ranked but the study cannot move forward to PRMC until the issues are resolved. If a study is deferred for questions of Therapeutic Intent, the issue must be resolved by the PRMC and the application should continue.

e. Not Recommended

Protocols that are not feasible or do not meet the Institute's goals and/or priorities are not recommended for development or activation and do not proceed to PRMC or IRB.

3. Investigator Initiated Studies (IIS)

SOCCI has chosen a two-stage review for concepts and protocols initiated by SOCCI investigators (Investigator Initiated Studies (IIS)). The purpose, at both stages of review, is to ensure that the protocol concept is in line with SOCCI priorities; to provide an assessment, at each stage, as to whether the concept/protocol is feasible; and to rank the concept/protocol.

The first stage is the review of the investigator's concept or Letter of Intent (LOI) as detailed in ***Table 7***. In addition to ensuring the feasibility this is an opportunity for the PPC to comment on possible logistical, financial or other concerns (i.e. accrual rate) that may inhibit the success of the investigator's research. For this reason, peer reviewed LOIs are reviewed by the full committee. If a full protocol already exists, the first stage of the review will be waived and only the full protocol will be reviewed.

The second stage is the review of the final protocol by the process described above. The aims of this 2-stage review process are to reduce investigator and staff effort in developing protocols of lesser priority, and to improve the timeframe from concept approval to protocol activation. Listed below are the criteria which are used for review at both stages.

Table 7	
Stage I PPC Review of IIS LOI/Concept	
Concept Element	**PPC Review**
Disease type/Stage, Competing Research	Evaluate the availability of the patient population within SOCCI and the likelihood of success for the type and stage of disease to be studied
Sample size and projected accrual rates	Evaluate ability to accrue, in conjunction with the study design, registry data and experience of the investigator and investigator performance within this area
Funding Information	Evaluate appropriateness of proposed funding source and likelihood of successful funding request
Feasibility, logistics, and resources	Evaluates the reasonableness of dedicated shared resources against other competing SOCCI studies, feasibility of the study logistics

4. Expanded Access Trials

Expanded Access protocols, though not strictly research, are considered by the PPC as they may be conducted with SOCCI resources. In select cases, protocols that are designed for the purpose of making investigational agents available to patients who cannot participate in a controlled clinical trial may align with the mission of SOCCI. The review criteria in ***Table 8*** are considered when assessing the priority and feasibility of Expanded Access protocols.

Table 8
Review Considerations for Expanded Access Protocols
• Availability of alternative treatment options for the patients to be enrolled on the Expanded Access protocol
• Accessibility within the community for the agent offered by the protocol
• Active and proposed SOCCI clinical trials which may be available for the same patient population

5. PPC Feasibility Assessment

All priority assignments are reviewed within the context of the feasibility of the protocol. At the time that the investigator requests a PPC review, the investigator is asked to provide information that will allow the committee to assess the protocol feasibility, including a protocol prioritization description when research is competing for patients are under evaluation and program flow diagrams depicting current and planned research. As such, the committee will only review final protocol versions that

have been reviewed/approved (i.e. "Ok to proceed" letter or 30-day clinical hold met) by the FDA for IND/IDE external research. Early phase (Phase 1, Phase 1b) industry clinical trials may be submitted to FDA and PPC concurrently, with identical versions of the protocol being submitted to both entities. However, any substantive changes (see Table 11) require PPC re-review.

IIS/IITs follow a linear submission process which begins with PPC followed by FDA (if applicable), PRMC and ends with IRB review.

6. PPC Portfolio Review

In the event that a portfolio of protocols exceeds CRO or DRG capacity, the investigator may be requested to reconsider priorities and eliminate protocols from the queue. If this measure is inadequate to reduce the queue of protocols to a manageable number, the DRG Physician Lead of the research program may be invited to a PPC meeting to present a plan for adjusting the portfolio. If the DRG Physician Lead is unable to reduce the portfolio, the PPC may review the portfolio and withdraw select protocols.

In collaboration with the CRO, PPC will determine the capacity of the infrastructure and only approve a reasonable number of studies that can be successfully activated in a timely manner. The maximum number of PPC-approved studies to open each year will vary depending on staffing capacity and the absolute number will be determined by the CRO Advisory Board and will be assessed on annually. The PPC may extend this cap by 10% for high-priority or rapid activation trials. A 15% variance is acceptable for studies that may be processed outside of the central office (i.e. affiliates, additional local support/staff). A close review of capacity level and productivity of the DRG is necessary.

C. PPC Procedures

1. Meeting Calendar

The PPC is scheduled to meet weekly. Meetings can be conducted in person or virtually through the PPC Online system.

2. Submission of studies

a. Studies are submitted electronically through the PPC Online system. An interface with OnCore® eliminates duplication of efforts, streamlines submission, alleviates data entry burden and auto generates DRG portfolio reports for PPC review and discussion. Submissions are initiated in ePRMS, creating the initial record for the protocol and auto-emails are distributed as the study moves through the review process. The PRMS coordinator uses the PPC online system to assign reviewers, schedule meeting date and time, record ranking and overall outcome.

3. Review Process

The assigned reviewer provides a brief presentation of the study. All studies are reviewed within the context of the feasibility of the protocol to ensure that those protocols that are given priority are likely to be successfully conducted and achieve satisfactory accrual. The PPC considers the following criteria when assessing the protocol:

a. General Review
Overall adequacy of the application including: protocol synopsis; rationale; proposed priority score;

b. Principal Investigator and DRG Portfolio Review
Number of active studies for PI; proposed time/effort; number of active studies within DRG

c. Accrual Review
Adequate number of patients (tumor registry data, accrual history for similar studies); target enrollment; duration of accrual; active or planned competing research.

d. Logistics/Infrastructure Review
Budget assessment; required use of ancillary services; FDA approval status

e. Precision Trial Classifications
The PPC will verify precision medicine classifications according to the following standard definitions:

Table 9

Precision Medicine Definitions	
Umbrella	The umbrella design focuses on a single tumor type or histology. It involves a group of two or more enrichment designs, or sub-studies, that are connected through a central infrastructure that oversees screening and identification of patients.
Basket	Basket trials allow the study of multiple molecular subpopulations of different tumor or histologic types all within one study. They can include rare cancers that would be difficult to study individually in randomized trials. May include multiple treatments in which subjects are matched based on gene expression.
Targeted Therapy	Trials designed to evaluate treatments targeted at one or two molecular populations in single or multiple disease type but does not use the umbrella or basket design.
Other Adaptive Design	Other studies believed to be precision medicine trials based on non-traditional study design (that is not identified above), limited inclusion criteria and emphasis on individualized treatment.

Following robust discussion, each committee member reviews each protocol, considering the priority rank assigned by the investigator/DRG, and designates a PPC priority classification (High, Standard, Deferral or Not recommended) and summarizes feedback or comments for the investigator (as applicable). The PPC Chair or Vice Chair signs off on the final score.

Following the meeting the PRMS coordinator:

- Records the protocol priority designation and committee member comments
- Notifies the investigator of the assigned priority and comments from the PPC, when applicable
- Submits the outcome to the PRMC and CRO after the PI addresses committee recommendations (if any)

For protocols within the same DRG that have the same priority score, activation is based upon the first date approved by the PPC. In the event that all dates are the same the protocols are chosen randomly for activation.

4. PPC Appeals

If a protocol has been designated by the committee as "not recommended for further development", the investigator may appeal to the PPC responding to the committee's concerns outlined in the PPC review letter. Investigators who wish to appeal should address their responses to the Chair or Vice Chair of the PPC and email a copy of the response to the PRMS coordinator. Appeals are reviewed by the PPC at the next regularly scheduled committee meeting by the same criteria outlined above. Only one appeal per study is permitted.

V. PROTOCOL REVIEW AND MONITORING COMMITTEE (PRMC)

Objective

The Protocol Review and Monitoring Committee (PRMC) is a multidisciplinary committee responsible for peer review of all clinical research protocols at the Samuel Oschin Comprehensive Cancer Institute (SOCCI). The PRMC's objectives are:

- to foster development of SOCCI clinical research protocols
- to assure through peer review scientific quality, feasibility, timeliness and ethics
- to assign priorities in the use of SOCCI resources to support clinical research, and
- to monitor the progress of ongoing research studies

Establishment of research goals and scientific priorities begins at the Department or Division level or within each clinical or translational research program. The initial PRMC review will assess whether the protocol meets standards of scientific design, including scientific rationale, specific objectives, endpoints, biostatistical design and analysis, and the ability to accrue patients and meet endpoints. The PRMC will assess whether the data to be collected are appropriate to the study's goals, and will review important issues of social justice such as the inclusion of women and minorities.

The PRMC has the authority to:

- Approve or not approve the submission of protocols to the Institutional Review Board (IRB)
- Require modifications in any aspect of a study protocol prior to IRB approval

- Require supplemental supporting background information before completing review of a protocol
- Monitor study activity and if deemed appropriate request that the Principal Investigator close poorly performing studies.
- Open protocols that meet the scientific merit and scientific priorities of the center and to terminate protocols that do not demonstrate scientific progress. Unique considerations may apply to trials of rare diseases, or targeted therapies, which often do not accrue rapidly.

The function of the PRMC is distinct from that of the IRB whose focus is on human subjects' protection. Both PRMC and IRB approval are required for a protocol to go forward. This mission is consistent with, and derived from, National Cancer Institute (NCI) guidelines for Comprehensive Cancer Center Grant (CCSG) designation.

A. PRMC Committee Structure

1. PRMC Leadership

The Chair and Vice-Chair of the PRMC are appointed by the SOCCI Director from the membership of SOCCI. The terms of appointment of the PRMC Chair and Vice-Chair are 36 months; however, the Chair and/or Vice-Chair may continue to serve beyond the end of the 36-month term, at the discretion of the SOCCI Director.

The PRMC Chair is responsible for:

- Ensuring that an adequate number of members are appointed to the PRMC to allow timely review of submitted protocols
- Ensuring that all studies submitted to the PRMC receive a timely review
- Ensuring that a quorum is in place for each meeting
- Leading and facilitating the discussion at committee meetings and calling for recommendations
- Summarizing the Committee's comments and review outcome of a protocol in a letter to the Principal Investigator (PI)
- Reviewing the PI's responses to PRMC reviews and determining if administrative approval of a protocol is appropriate
- Closing studies that fail to meet accrual after 18 consecutive months of low accrual.

The Vice-Chair of the PRMC shall execute the responsibilities of the Chair in the absence of the Chair or as delegated by the chair.

2. PRMC Membership

The PRMC standing committee must include:

- Five or more physician members
- A translational medicine scientist
- A SOCCI biostatistician
- One or more oncology nurses
- An investigational pharmacist

Members of the PRMC may be drawn from the following disciplines:

- Medical oncology

- Surgical Oncology
- Gynecologic Oncology
- Pathology
- Pharmacology
- Imaging
- Nuclear Medicine
- Laboratory/Translational Science
- Clinical Research Office
- Prevention and Cancer Control
- Population-based Sciences

In addition, the PRMS Coordinator serves as a non-voting member of the committee.

The PRMC Chair shall make recommendations of individuals for membership on the committee to the SOCCI Director. Physician members of the PRMC are derived from the medical staff at Cedars Sinai Medical Center. Non-Cedars faculty/staff may be included on the PRMC as consultants who will attend PRMC meetings on an ad-hoc basis but will not have voting rights. The Director of the Cancer Institute has the responsibility of ensuring diversity in representation. The minimum term of appointment of physician members to the PRMC is 24 months. The SOCCI Director will continuously reevaluate PRMC membership.

a. Member Responsibilities

All regular members of the PRMC are expected to serve as a reviewer for a minimum of one protocol per quarter, and to attend a minimum of seventy-five percent of committee meetings, in order to remain in good standing. Attendance and review requirements for members designated as ancillary (those from specialties or departments anticipated to be needed less frequently) are at the discretion of the Chair. Members of the PRMC who consistently fail to meet their membership obligations as defined above are subject to dismissal by the PRMC Chair.

3. PRMS Coordinator

The PRMS Coordinator is responsible for receiving, cataloguing, and tracking all new protocols conducted under the auspices of the SOCCI. Following receipt of a protocol, the PRMS coordinator conducts an initial administrative review to ensure that all requisite components of the protocol are present before enlisting reviewers for the protocol or before forwarding the protocol to the PRMS Chair for reviewer assignment.

Following assignment of reviewers by the Chair, the PRMS coordinator is responsible for:

- Forwarding the protocol and relevant materials to the reviewers
- Scheduling PRMC meetings and notifying members of meeting time and agenda
- Recording all minutes and committee votes in written form and maintaining appropriate records and other documentation
- Based upon written reviews and meeting discussion, preparing draft letters to the investigators summarizing the review for review, editing and signature by the Chair
- Managing all committee correspondence and performing all committee-related clerical duties and maintenance of active files on all open protocols conducted under the auspices of the SOCCI

- Obtaining accrual data for the PRMC's annual accrual monitoring function
- Performing other committee-related business delegated by the Chair

4. PRMC Rules

a. Quorum

A quorum is defined as a number of full or ad hoc committee members in attendance equal to at least 50% of the number of full members. If this ratio is not achieved, the protocols cannot be reviewed and must be placed on a future meeting date. Proxy votes are not allowed. Any member who is out of the room is neither counted in the quorum nor counted in the vote.

b. Recusal

Members of the PRMC must recuse themselves from serving as a primary, secondary, or bio-statistical reviewer on protocols where they are listed as a co-investigator. Members with a conflict of interest may participate in preliminary discussions of a protocol, but they must also recuse themselves and not be present during concluding discussion and voting. In the event the Chair has a conflict the Vice-Chair should lead the meeting and discussions.

B. PRMC Review Policy

1. Scientific Review

a. Review Criteria

Studies are reviewed for validity of:

- Scientific rationale, including appropriate references to the medical literature
- Study design, including adequate scientific objectives, eligibility criteria, study endpoints, and treatment information
- Biostatistical design and evidence of an appropriate safety monitoring plan if applicable
- Study duration
- Evidence of ability to accrue to the protocol
- Scientific priority
- Adequacy of data collection forms and methods
- Therapeutic intent

b. Reviewers

Each protocol must be reviewed by three (3) "required" reviewers: (a) a primary reviewer, (b) a secondary reviewer, and (c) a biostatistician. The primary and secondary reviewers will be two physician reviewers or one physician reviewer and one translational research scientist reviewer, appropriately selected by discipline. In addition, each protocol should be reviewed by: (a) a member of the oncology nursing staff and (b) a research pharmacy representative. At least one of the two physician/scientist reviewers and the biostatistical reviewer are required to attend the meeting at which the submitted protocol is to be reviewed, in order to present a brief synopsis of the protocol. If either the primary or secondary physician/scientist reviewer is unable to attend the meeting at which the submitted protocol is to be reviewed, s/he will provide a written summary and review to the PRMS Coordinator

prior to the meeting. All committee members are expected to read the protocol and be prepared to give comments.

c. Meeting

The PRMC meets bi-weekly and may add additional meeting dates as required by volume. A maximum of five new studies are reviewed at each meeting to allow sufficient time for robust discussion of each study. The Chair/Vice Chair leads each meeting while all members are actively engaged and provide comments. The PRMS coordinator minutes each meeting and documents the committee's comments and/or concerns for inclusion into the outcome letter.

d. Vote

Following the presentation of a protocol for review by the primary and secondary reviewer and discussion among committee members, a vote is called by the Chair. A protocol must receive an affirmative vote from a majority of the voting members of the PRMC in order to receive approval. The PRMC Chair will vote only to break a "tie vote" by the PRMC. Proxy votes are not allowed. Any member who is out of the room is neither counted in the quorum nor counted in the vote.

2. PRMC Review Procedures

All protocols outlined in Table 1 must undergo review by the PRMC. Industry-authored studies may be submitted to IRB and PRMC concurrently as majority of these studies have been reviewed by the FDA and therefore risk of PRMC disapproval or significant protocol changes as a result of PRMC review is relatively low. This parallel process was implemented to accelerate the study activation process.

3. PRMC Types of Reviews

a. Full Committee

Protocols requiring Full Committee Review (Table 1) are reviewed as described above.

b. Administrative Review

Administrative Reviews are conducted by the PRMC Chair or Vice Chair and are generally limited to those studies identified as eligible for Administrative Review (Table 2).

c. Expedited Review

Expedited Reviews are conducted by the PRMC Chair or Vice Chair, one clinical reviewer, and one biostatistician. They are limited to those studies identified as eligible for Expedited review (table 3). Reviewers conducting expedited reviews can request full committee review.

4. PRMC Review Outcomes

The goal of the PRMC is to review all protocols in within four weeks of receipt of a complete PRMC application. After robust discussion and study analysis the committee may approve, defer or disapprove a study as detailed in ***Table 9***. The formal committee decision and any recommendations, concerns or committee comments is communicated to investigators in a letter which is distributed timely following the meeting in which the study was reviewed.

Table 9	
PRMC Review Outcomes	
Approved	Approved with no changes required.
Deferred pending PI response	The PI must respond to the Committee's concerns (responses may be reviewed at full committee or to the Chair as indicated on the Deferral letter). Upon receipt and review of the PI's response the committee may approve or not approve. A maximum of three rounds of review may occur.
Not approved	The study is not approved to move forward.

5. PRMC Appeal

There is no appeal process for those protocols not approved by the PRMC to move forward. PRMC has the final authority to close trials. This authority cannot be superseded by clinical or administrative leadership.

6. Investigator Initiated Studies (IIS)

As outlined in the PPC section related to IIS, SOCCI has chosen a two-stage review for concepts and protocols initiated by SOCCI investigators. The first stage is the review of the investigator's concept or Letter of Intent (LOI) as detailed in ***Table 10***. In addition to providing the review detailed in Table 10, the PRMC ensures that a faculty-level biostatistician is participating in the study as a co-investigator. Peer reviewed LOIs may be administratively reviewed as outlined in ***Table 2***.

The second stage is the review of the final protocol. The aims of this two-stage review process are to reduce investigator and staff effort in developing protocols of lesser scientific merit, and to improve the timeframe from concept approval to protocol activation. If a full protocol already exists, the first stage of the review will be waived and only the full protocol will be reviewed.

Table 10	
Stage I PRMC Review of IIS LOI/Concept	
Concept Element	**PRMC Review**
Study Synopsis	Evaluate the scientific merit of the concept
Rationale/Hypothesis	Evaluate the reasonableness of the rationale for performing the study and reason(s) for testing the agent (s)
Tumor type and specific disease	Identify known response to the agents in the proposal as well as other studies underway using the agent-disease combination
Performance measurement criteria/treatment plan/endpoint	Assess the reasonableness of the planned criteria; effectiveness of proposed treatment plan
Laboratory correlates	Evaluate the choice of targets and assays and (if appropriate) suggest alternatives or additional possible targets and assays

VI. PROTOCOL MONITORING POLICY

Scientific progress is monitored concurrently by the PRMC using annual progress reports as well as literature searches as appropriate.

1. **Amendments** [effective October 12 2016]

As a means of providing scientific oversight and ongoing monitoring the PRMC reviews applicable protocol amendments. An amendment is any change to a protocol subsequent to approval of the final protocol, including changes to the protocol that affect the scientific intent, study design, consent document, patient safety, or human subject protection. Protocol Amendments may be scientific, editorial, or administrative. Only protocol amendments with substantial scientific changes, as summarized in Table 11, require PRMC review. Other administrative and editorial changes do not require PRMC re-review. Early phase industry studies submitted concurrently to PPC and FDA may require PRMC re-review if substantial changes, as summarized in Table 11, are made to the protocol. This may occur prior to initial IRB approval.

In addition, protocol amendments may be exempt from scientific review if the study is closed to accrual and there are no patients on study or in follow up.

If protocols initially qualified for administrative review subsequent amendments also qualify for administrative review.

Table 11

Characteristics of Substantial Protocol Changes Requiring PRMC review

- Change in **objectives** (i.e. addition, or deletion of an objective)
- Change in **overall sample size** due as a result of interim analysis or change in objective
- **Addition/deletion of a study arm** (does not include arms where target accrual has been reached)
- Change in **statistical analysis plan** (outcome measures)
- Changes in the **disease population** under study
- Changes in **agent or administration** schedule
- An investigator-initiated trial to become **multi-center** in which **CSMC becomes the coordinating center**
- Other: PRMC discretionary trigger for reason(s) not identified above

2. PRMC Accrual Monitoring

As a means of ensuring that the scientific goals of the trial can be met, the PRMC monitors patient accrual to each SOCCI protocol on an annual basis. Additionally, monitoring of accrual to open protocols is conducted to ensure that continued use of SOCCI resources is warranted. Due to unique considerations pediatric studies are exempt from accrual monitoring however all other active cancer protocols (excluding observational studies) are subject to monitoring by the PRMC.

Accrual monitoring occurs annually from the study open to accrual date. Based on the projected accrual number and projected study duration provided by the Principal Investigator at the time of protocol submission the expected annual accrual for each protocol is established. If a protocol fails to accrue at a rate of 50% or greater of the expected annual accrual, the protocol may be subject to closure by the PRMC. Studies with annual accrual goals of odd number should round down for accrual assessment (i.e. if goal is 5/year, 50% is 2.5 therefore the minimum accrual to meet the 50% goal would be 2). The PI will be notified if accrual to any protocol is substandard at annual review and will be asked to provide a formal explanation of the basis for substandard accrual, or if appropriate, outlines revisions to the projected accrual goals. The formal explanation is due annually from the study open to accrual date. If a formal explanation is not provided within a reasonable timeframe (4 weeks) the PRMS Coordinator has the authority to suspend the study accrual until a response is provided.

a. Scientific Progress

A review of the study summary, study publications, new literature and new treatments (if applicable) will be reviewed in conjunction with accrual performance on an annual basis.

b. Extensions

The formal explanation and rationale for substandard accrual is reviewed by the PRMC to whether a six-month extension can be granted. If granted a second monitoring review will be conducted within six months of the first review (PRMC meeting date). If the rate of accrual is acceptable the protocol will continue to be

reviewed on an annual basis. Only one extension can be granted. If the protocol fails to meet the minimal accrual standard set by the PRMC during the allotted extension period, the PRMC Chair will require study closure.

c. Study Termination

All protocols that fail to meet the minimal accrual standard (including those which fail during the extension period) and for which an adequate explanation or revision is not provided will be reviewed by the PRMC. If evidence is not sufficient to continue accrual, as determined by majority vote of the PRMC, the PRMC has the authority to close the protocol to further accrual. A letter from the PRMC will be sent to the PI with copy to the IRB. The PI will be asked to initiate closure of the study to accrual to the IRB. The PI is responsible for maintaining appropriate IRB status if the study must remain open at the IRB for patient follow-up, data query resolution, or data analysis.

d. Voluntary Closure

In response to the PRMC annual accrual monitoring program investigators may elect to voluntarily close trials prior to the anniversary date due to low accrual. Such instances are tracked in OnCore as low performing studies with voluntary closure and further use of shared resources are discontinued as appropriate.

VII. PRMS ROUTINE REPORTING

As a means of ensuring research moves through the PRMS in a systematic and timely manner the PRMS continuously reviews its process and procedures to remain nimble and identify efficiencies. Further, the PRMS produces a routine performance report which includes at minimum the following metrics:

- Number of committee meetings held by year
- Number of protocols reviewed by year by committee (PPC and/or PRMC)
- Summary of protocols by PRMC Review Outcome (approved, not approved) and PPC Review Outcome (RA, high, standard priority)
- Summary of review types (full, administrative)
- Review timelines (i.e. number of days from submission to meeting date, days from meeting date to outcome letter distribution, etc)

Other analysis may be conducted as deemed appropriate by SOCCI Director, Associate Director of Research, CRO Director, and/or Clinical Research Advisory Board.

VIII. PRMS ELECTRONIC SYSTEMS

OnCore® ePRMS is a paperless committee management module within the OnCore® clinical trial management system (CTMS). ePRMS electronically facilitates the PRMS workflow through submission, review, and approval/disapproval. It is intended to save time and effort throughout the protocol review process through automation and eliminating redundancies. Some features include: automatic distribution of outcome letters, meeting calendar/scheduling, central registration of all research studies, single submission location, option to upload reviews/scores into the system, and extensive reporting functionality. The PPC Online is a web-based system with a built-in interface to OnCore® to allow streamlined submissions from PPC to PRMC. PPC Online also offers a virtual meeting space by which PPC members may review submissions, discuss, and vote electronically. PPC Online was designed to accelerate the PPC review process by eliminating redundancies, limiting data entry and facilitating the committee flow.

APPENDIX 1: Detailed PRMS Review Scope

PRMS Review Types: Full, Administrative, and Exempt from Review

Study Types Requiring FULL PRMS Review					
Category	**CCSG Full Definition (22Dec2016)**	**Primary Purpose**	**Primary Purpose Definition**	**Examples**	**CTMS: Protocol Type/ DT4 report type**
Interventional (INT)	Individuals are assigned prospectively by an investigator based on a protocol to receive specific interventions. The participants may receive diagnostic, therapeutic, behavioral or other types of interventions. The assignment of the intervention may or may not be random. The participants are followed and biomedical and/or health outcomes are assessed.	Diagnostic (DIA)	Designed to evaluate one or more interventions aimed at identifying a disease or health condition.	• Diagnostic methods • Imaging/device trials intended to improve diagnosis or detect cancer	Diagnostic / Interventional
		Health Services Research (HSR)	Designed to evaluate the delivery, processes, management, organization, or financing of health care		Health Services research/ Interventional
		Other (OTH)	Not in any other category	• Physical therapy • Behavioral • Educational	Other/ Interventional
		Prevention (PRE)	Designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition	• Chemoprevention • Cancer vaccine • Surgical prevention	Prevention/ Interventional
		Screening (SCR)	Protocol designed to assess or examine methods of identifying a condition (or risk factor for a condition) in people who are not yet known to have the condition(or risk factor).	• Detection methods	Screening/ Interventional
		Supportive Care (SUP)	Designed to evaluate one or more interventions where the primary intent is to maximize comfort, minimize side effects, or mitigate against a decline in the participant's health or function. In general supportive care interventions are not intended to cure a disease.	• Pain prevention/control • Infection prevention or control • Transfusion support • Nutritional support • Complimentary therapy	Supportive Care/ Interventional
		Basic Science (BAS)	Designed to examine the basic mechanisms of action (i.e. physiology, biomechanics) of an intervention.		Basic Science/ Interventional

Study Types Requiring FULL PRMS Review					
Category	**CCSG Full Definition (22Dec2016)**	**Primary Purpose**	**Primary Purpose Definition**	**Examples**	**CTMS: Protocol Type/ DT4 report type**
		Treatment (TRE)	Designed to evaluate one or more interventions for treating a disease, syndrome, or condition. Note: this equates to therapeutic in previous CCSG versions of the guidelines.	• Chemotherapy • Radiotherapy • Surgical therapy • Transplants • Gene therapy • Immunotherapy • Combined modality therapy • Alternative therapy • Devices	Treatment/ Interventional
Observational (OBS)	Studies that focus on cancer patients and healthy populations that involve no prospective intervention or alteration in the status of the participants. Biomedical and/or health outcome(s) are assessed in pre-defined groups of participants. The participants in the study may receive diagnostic, therapeutic, or other interventions but the investigator of the observational study is not responsible for assigning specific interventions to the participants of the study	Other (OTH)	Not in other categories	• Epidemiologic or other observational studies (i.e. outcomes) with cancer relevance. Those observational studies enrolling *only* healthy human subjects are exempt from PRMS review.	Other/ Observational

Study Types Requiring FULL PRMS Review (Cont'd)					
Category	**CCSG Full Definition (v.22Dec2016)**	**Primary Purpose**	**Primary Purpose Definition**	**Examples**	**CTMS: Protocol Type/ DT4 report type**
Ancillary (ANC)	Studies that are simulated by, but are not required part of, a main clinical trial/study, and that utilize patient or other resources of the main trial/study to generate information relevant to it. Ancillary studies must be linked to an active clinical research study and should include only patients accrued to that clinical research study. Only studies that can be linked to an individual patient or participant data should be reported.	Other (OTH)	Not in any other category		Other/ Ancillary
		Basic Science (BAS)	Designed to examine the basic mechanisms of action (i.e. physiology, biomechanics) of an intervention.	• Evaluation of circulating tumor cells (CTCs) in the blood to determine treatment efficacy • Biobanking of tumor tissue to identify relationship between response rate and tumor tissue characteristics • Defining and targeting specific populations of cells for therapy	Basic Science/ Ancillary
Correlative (COR)	Laboratory based studies using specimens to assess cancer risk, clinical outcomes, response to therapies, etc. Only studies that can be linked to individual patient or participant data should be reported.	Other (OTH)	Not in any other category		Other/ Correlative
		Basic Science (BAS)	Designed to examine the basic mechanisms of action (i.e. physiology, biomechanics) of an intervention.	• Evaluation of circulating tumor cells (CTCs) in the blood to determine treatment efficacy • Biobanking of tumor tissue to identify relationship between response rate and tumor tissue characteristics • Defining and targeting specific populations of cells for therapy	Basic Science/ Correlative

Study Types Eligible For: ADMINISTRATIVE Review or EXEMPT from Review		
Administrative	Expedited	Exempt
• NCTN Studies • U01s, U10s, P0Is, and P50 studies • NCI Studies-CTEP and DCP • Proprietary (Industry Sponsored) Registries/Tissue Banks must undergo full PPC Feasibility Review to ensure appropriate allocation of CRO resources. Once approved they may undergo an EXPEDITED review by PRMC	• For multi-site institutional trials with an NCI designated lead site (if lead institution PRMS has conducted scientific review of the protocol)	• Single Use IND • Chart Reviews • Institutional Registries, Tissue Bank • Questionnaires that do not test interventions • In vitro studies that utilize human tissues that cannot be linked to a living individual, tissue banking, and studies that do not require patient consent (e.g., retrospective chart reviews). • Observation/epidemiological studies that study healthy human subjects *only*. Studies that enroll cancer patients AND healthy human subjects as a control, require PRMS review but are exempt from ongoing monitoring*

* Studies that are both cancer related AND hypothesis driven are still required to be entered into OnCore and are assessed for Data Table 4 classification.

APPENDIX 2: Trial Phases

Translational- Exploratory trials, involving limited human exposure, with biological outcomes and minimal therapeutic or diagnostic intent (e.g., screening studies, microdose studies). See FDA guidance on exploratory IND studies for more information.

Dose-finding (phase I)- Includes initial studies to determine the metabolism and pharmacologic action of drugs in humans and the side effects associated with increasing dose may include healthy participants and/or patients.

Phase I/II - For trials that are a combination of Phases 1 and 2.

Safety/Activity (phase II) Includes controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks

Phase II/III (trial) - For trials that are a combination of phases 2 and 3

Comparative Efficacy (phase III) - Includes expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling

Post-marketing (phase IV) - Studies of FDA-approved drugs to delineate additional information including the drug's risks, benefits, and optimal use

Expanded Access - Expanded access is a means by which manufacturers make investigational new drugs available, under certain circumstances, to treat a patient(s) with a serious disease or condition who cannot participate in a controlled clinical trial.

Other - For trials that do not fit the above developmental paradigm

APPENDIX 3: Organizations with Approved Peer Review and Funding Systems

Eligibility criteria for applying for a CCSG application and for meeting the minimum standard to be considered a research program require specific minimum levels of "peer reviewed, funded research projects. To be considered as a "peer reviewed, funded project," the responsible funding agency or organization should meet the general NIH standards of peer review and funding: (1) a peer review system which uses primarily external reviewers and is free of conflict-of-interest; (2) a ranking or rating system in the review process based on the scientific merit of the proposed research; and (3) a funding system based primarily on the peer review ranking or rating of the research applications. In addition to research grants, contracts and cooperative agreements from the NIH, the organizations listed below generally employ a system of external review and funding that complies closely with the NIH standard. All funded, multi-year research projects (equivalent in size and complexity to an NIH R01) from these organizations (*excluding contracts, pilot projects, and feasibility studies*) are eligible (1) to count toward the minimum research base of a cancer center, (2) to have access to CCSG shared resources, and (3) to count toward the minimum number of grants needed to constitute a research program of the center as defined in the 2013 CCSG Guidelines. Approved agencies as of 05/07/13:

- Agency for Healthcare Research and Quality (AHRQ)
- American Association of Cancer Research (AACR)
- American Cancer Society (ACS), (national office only)
- American Foundation for AIDS Research (amfAR)
- American Institute for Cancer Research (AICR)
- California Institute for Regenerative Medicine (CIRM)
- Cancer Prevention Research Institute of Texas (CPRIT)
- Center for Disease Control and Prevention (CDC)
- Central Office of the Veterans Administration (VA) - excluding local/regional awards and "block" grants
- Environmental Protection Agency (EPA)
- The Flight Attendant Medical Research Institute (FAMRI)
- Florida Biomedical Research Program (FBRP)
- Food and Drug Administration (FDA)
- Howard Hughes Medical Foundation
- Leukemia and Lymphoma Society
- Melanoma Research Alliance (MRA)
- Multiple Myeloma Research Foundation (MMRF)
- National Institute for Occupational Safety and Health (NIOSH)
- National Science Foundation (NSF)
- New York State Department of Health Wadsworth Center/New York State Stem Cell Science Program
- Prevent Cancer Foundation
- Susan G. Komen for the Cure
- The California Breast Cancer Research Program (CBCRP)
- The California Tobacco Related Disease Research Program (TRDRP)
- U.S. Army (DOD) special research programs- ovarian, breast and prostate cancer

Please check the most recent list of Funding Organizations with Approved Peer Review and Funding Systems at http://cancercenters.cancer.gov/documents/NCIApprovedFundingOrganizations508C.pdf

APPENDIX 4: Studies Sponsored by these Groups are Eligible for Administrative PRMS Review

NCI Funded Programs Participating in the NCTN (CTSU Menu)	
ACOSOG	American College of Surgeons Oncology Group (legacy studies only)
ACRIN	American College of Radiology Imaging Network (legacy studies only)
AMC	Aids Malignancy Consortium
ALLIANCE	The Alliance for Clinical Trials in Oncology
BIG	Breast International Group
BMT CTN	Blood and Marrow Transplant Clinical Trials Network
CALGB	Cancer and Leukemia Group B (legacy studies only)
COG	Children's Oncology Group
ECOG –ACRIN	ECOG-ACRIN Cancer Research Group
ECOG	Eastern Cooperative Oncology Group (legacy studies only)
EORTC	European Organisation for Research and Treatment of Cancer
GOG	Gynecologic Oncology Group (legacy studies only)
IBCSG	International Breast Cancer Study Group
MDA	MD Anderson Cancer Center
NCCTG	North Central Cancer Treatment Group (legacy studies only)
NCIC	National Cancer Institute of Canada
NCIMET	National Cancer Institute Metabolism Branch
NRG	NRG Oncology
NSABP	National Surgical Adjuvant Breast and Bowel Project (legacy studies only)
RTOG	Radiation Therapy Oncology Group (legacy studies only)
SCISF	SunCoast CCOP at the University of South Florida
SWOG	SWOG Cancer Research Cooperative Group
USMCI	United States Military Cancer Institute
WFUCCOP	Wake Forest University CCOP

Note: the NCI may add additional groups to the CTSU menu. https://www.ctsu.org/

APPENDIX 5: Protocol Prioritization Committee Membership *[as of 26 July 2017*]*

Members

Robert Figlin, Chair	Medical Oncology, Urologic
Armando Giuliano, Vice Chair	Surgical Oncology, Breast
Monica Mita	Medical Oncology, Experimental Therapeutics
Barry Rosenbloom, Ad-Hoc Chair	Medical Oncology, Hematologic Malignancies/ Lymphoma/ BMT
Christine Walsh	Surgical Oncology, Gynecologic Oncology
Howard Sandler	Radiation Oncology, Urologic
Jaime Richardson	Oncology Certified Nurse, Cancer Clinical Trial Navigator

Ex Officio Members

Steven Piantadosi	SOCCI Director

Ad-Hoc Members

Janet Villarmia	Administration
Therica Miller	Clinical Research Office

** The current membership list is kept in file with the PRMS coordinator*

APPENDIX 6: Protocol Review and Monitoring Committee Membership *[as of 26 July 2017]**

Members

Alain Mita, Chair	Medical Oncology, Experimental Therapeutics / Lung
Mourad Tighiouart, Vice-Chair	Biostatistics
Regina Deck	Cancer Center Nursing
Omid Hamid	Medical Oncology, ET and Melanoma
David Hoffman	Medical Oncology, Kidney / Melanoma
Stephen Freedland	Medical Oncology, Urologic
Beatrice Knudsen	Translational Pathology / Biorepository
Suwicha Limvorasak	Investigational Pharmacy
Fataneh Majlessipour	Medical Oncology, Pediatrics
Franklin Moser	Radiology/Imaging
Stephen Pandol	Medical Oncology, Pancreas
Edwin Posadas	Medical Oncology, Urologic
Bobbie Rimel	Surgical Oncology, Gynecology
Andre Rogatko	Biostatistics
Greg Sarna	Medical Oncology
Richard Tuli	Radiation Oncology, Gastrointestinal
Yuliya Linhares	Hematology/Oncology
Marc Goodman	Prevention & Control, Epidemiology

** The current membership list is kept in file with the PRMS coordinator*