Protocol Review and Monitoring Committee

Policies and Procedures

Effective December 2014

Revised Dec 2014
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1. The Protocol Review and Monitoring Committee (PRMC)

A Protocol Review and Monitoring Committee (PRMC) is required for all National Cancer Institute (NCI)-designated Cancer Centers. NCI policies dictate that the purpose of a PRMC is to review, at a minimum, all research studies in areas of diagnosis, therapy, prevention and control of cancer that have not received traditional peer review for scientific merit. A PRMC also provides a mechanism for monitoring all cancer research studies in the institution for scientific progress, carrying with it the authority for closing any studies that are not meeting accrual or performance standards.

All human-subject, cancer-related initial submissions (new studies) being submitted to the Washington University Human Research Protections Office (HRPO) [serving as the IRB] must be reviewed and approved by the PRMC prior to final approval by HRPO. Renewals and amendments are reviewed and approved independently. Due to limited scientific contribution, the following do not need PRMC review: advertisements, case studies and single-patient studies.

The Director of the Siteman Cancer Center (SCC) appoints members of the PRMC. PRMC members are asked to serve for two years and may be reappointed for additional terms. PRMC members are selected based on the experience they have in designing or conducting clinical trials or based on special clinical expertise (nursing, pharmacology, etc.).

NCI Guidelines for a PRMC include the following:

- A qualified review and monitoring committee of sufficient size and breadth of expertise to conduct a critical, fair, scientific review of institutional research protocols involving human subjects;
- Clear criteria for scientific review that take into account the specific rationale, study design, duplication of studies already in progress elsewhere, adequacy of biostatistical input, and feasibility for completion within a reasonable time frame;
- Clear criteria for determining whether ongoing research is making sufficient scientific progress, including adequate subject accrual rates;
- A mechanism for overseeing the prioritization of competing protocols and, thus, for insuring optimal use of a center’s clinical resources for scientific purposes; and
- Authority and process for initiating, monitoring and terminating all cancer research protocols in the center.

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2. Goals and Responsibilities of the PRMC at the Siteman Cancer Center

The primary goal of the PRMC is to ensure that institutional and industry-initiated cancer research studies involving human subjects conducted under the auspices of the SCC are (1) scientifically and statistically sound; (2) appropriately designed; (3) feasible for completion; and (4) if applicable, in compliance with NIH guidelines for clinical trials, including monitoring for accrual and undue toxicity.

For purposes of this document, we define a clinical trial operationally as a prospective study involving human subjects designed to answer specific questions about the effects or impact of particular biomedical or behavioral interventions; these may include drugs, treatments, devices, or behavioral or nutritional strategies. Participants in these trials may be patients with cancer or people without a diagnosis of cancer but at risk for it.

In the area of molecular or imaging diagnostics, the SCC considers a study to be a clinical trial if it uses the information from the diagnostic test in a manner that somehow affects medical decision-making for the study subject. In this way the information from the diagnostic test may have an impact on some aspect of outcome, and assessment of this impact may be a key goal of the trial.

A behavioral trial is a study in which either (a) the intervention employs behavioral strategies, procedures, or theory, or (b) the primary outcomes involve behavior change on the part of patients, clinicians, families or larger systems (e.g. change in worksite policies). Interventions may pertain to cancer prevention, early detection, treatment, and survivorship. Observational studies and those that do not test interventions are not clinical trials (but may qualify for review).

Specific Responsibilities of the PRMC

The PRMC is responsible for:

- Providing scientific peer-review for all institutional and industry-initiated cancer research studies
- Reviewing all active cancer research studies for renewal/termination
- Reviewing accrual in all active cancer research trials
- Assessing protocol compliance in research trials
- Assessing for accurate and adequate reporting of toxicities and adverse events
- Providing information about study design and execution

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3. **Benefits an Investigator Derives from PRMC Protocol Review**

- The PRMC provides a formal peer-review mechanism for all cancer research studies. The PRMC reviews each study for scientific merit and to ensure quality research, and provides valuable feedback to investigators: e.g., suggestions for improving experimental design to better define or achieve research endpoints; opportunities for collaboration with other investigators; and better implementation strategies.
- Federal payors (all trial phases) and Missouri insurance plans (Phases II-IV) provide patient care reimbursements for all subjects participating in NCI-approved research studies. The Siteman Cancer Center is an NCI-designated Comprehensive Cancer Center, and all studies favorably reviewed and approved by the PRMC will be considered as NCI-approved.
- Siteman Cancer Center members, with Research or Research Associate designation, have access to all shared resources (see Appendix C) once their research study is approved by the PRMC. The Biostatistics Core and Clinical Trials Core are available for assistance in preparing the protocol prior to its submission to the PRMC. All investigators are strongly encouraged to consult with staff of these cores before submission of a study protocol for PRMC review.

4. **PRMC Policies and Procedures**

4.1 **Protocol Prioritization**

NCI guidelines require that a mechanism be established within a cancer center for prioritizing competing research studies that may enroll subjects with similar eligibility criteria. At the SCC, all clinical trials must be evaluated and approved by the corresponding Clinical Focus Group (see Appendix B) before submission to the PRMC. Evidence of this evaluation and approval is provided by signature and comments (when appropriate) by a Clinical Focus Group leader on the “Request for Initial Review of a Protocol” form (Appendix E). With the assistance of the SCC Clinical Trials Office, each Clinical Focus Group will maintain a list of active clinical trials (including patient eligibility criteria) to facilitate determination whether a new study will compete with an existing study. If a research study is deemed to be in competition with an on-going study, the Clinical Focus Group must determine whether the institution’s patient population can justify keeping both studies open for subject accrual, or if any competing study or studies will need to be closed. When a Clinical Focus Group determines that it is acceptable to have competing studies open, it should establish a prioritization rule for subject accrual to those competing studies: in general, the highest priority should be given to institutional studies, followed by cooperative group studies, and then by industry-initiated studies. Focus group leaders provide clear
rationale when there is more than one study for a specific population and prioritize the order in which studies are offered to patients.

4.2 PRMC Meetings

PRMC meets twice monthly for cancer study review (usually the second Thursday of every month and the fourth Wednesday of each month– see Appendix A for specific dates and deadlines). In order for a PRMC meeting to convene, there must be 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. At least one of the co-chairs and at least one statistical reviewer must be in attendance for constitution of the quorum. The PRMC has designed a Protocol Evaluation Form to facilitate the review and committee discussion of each study (See Appendix G). In addition, the PRMC uses a checklist, based on the NCI’s Investigator Handbook, as a reference in reviewing each research study to determine if the protocol is adequately presented (See Appendix H). Principal investigators are encouraged to review these documents to help them better understand the necessary components of a complete protocol and the criteria the PRMC will be using for protocol review.

4.3 Types of PRMC Review

There are two mechanisms for review by the PRMC – administrative review and full-committee review. The types of submissions that fall into these two categories and the procedures for their review are detailed below. There is also a flow diagram in Appendix J that illustrates the various paths a submission may take in the PRMC review process.

4.4 Submissions to Receive Administrative Review

- NCI-approved national cooperative group studies
- NCI Cancer Therapy Evaluation Program (CTEP)-approved and Division of Cancer Prevention (DCP)-approved studies
- Cancer studies that the PRMC co-chairs specify as not requiring scientific peer review. These include retrospective studies (chart reviews and existing specimen studies); compassionate-use protocols (only safety data being collected); case studies; studies in which subject participation involves only tissue/specimen collection; registry studies; and standard treatment protocols that are not designed to answer a scientific question or test a hypothesis but for which HRPO review and approval is desired by the principal investigator.
- Annual renewal of cancer studies previously reviewed by the PRMC.

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• Cancer studies included in any extramural grant submission for which subject accrual will NOT begin before completion of extramural peer review and funding. These applications are processed through the administrative review mechanism so that the HRPO approval can be granted in a timely manner as required for extramural review. Administrative review and approval of these studies does NOT authorize study activation and subject accrual. After funding has been obtained, such studies must undergo full-committee review before subject accrual begins. Documentation of this requirement from the grant agency must be provided.

• Study amendments/changes in protocols or risks of studies

All studies receiving administrative review and approval will be reported to the full committee each month.

4.4.1 Administrative Review Procedures

New Studies (subject accrual to be authorized after HRPO approval): Principal investigators will submit research studies that meet the requirements for administrative review to the SCC Protocol Office before submission to the HRPO. The submission should include:

- The HRPO application
- The complete protocol with all appendices
- The Investigational Brochure, when applicable
- The completed “Request for Initial Review of a Protocol” form with Clinical Focus Group leader signature if the study is a clinical trial (see Appendix E)

The PRMC staff will verify that the study meets administrative review requirements. The study will then be reviewed by one of the PRMC co-chairs. If the study is approved, the study team and HRPO will be notified of the approval. A copy of the study materials will be filed in the SCC Protocol Office, and study information will be logged into the SCC database. Once HRPO approval is obtained and an “open for accrual” date is received the study will be listed in the SCC publications and on the SCC World Wide Web page (unless permission is denied on the “Request for Initial Review of a Protocol” form).

New Studies (subject accrual NOT to begin until after extramural review and funding): These studies will be processed administratively as described above. If the study is approved by one of the PRMC co-chairs, the PRMC approval will specifically indicate that the study has been approved for HRPO review, but that study activation and subject accrual cannot begin until subsequent full-committee review by the PRMC.
**Annual Renewals:** All protocols are to be renewed through the PRMC until designated “in follow-up only” (all patients have completed treatment and off-treatment date is on record in the SCC Clinical Subject Registry). Principal investigators are asked to submit their annual HRPO renewal application along with a completed “PRMC Renewal request form” (Appendix F) no less than six weeks before the HRPO expiration date. The study team and HRPO will be notified of the approval.

**Study Accrual:** Monitoring of study accrual is performed in two ways. One way is review of accrual at renewal, starting when a study has been open to accrual for more than 12 months. If accrual is less than 25% of expected accrual, the principal investigator will be notified that the study will be closed by the full PRMC at its next regular meeting. The principal investigator may provide a justification as to why the study should remain open to accrual, along with a detailed plan for remediying the accrual problem. If no justification is received by the next submission deadline, the study will be closed at the next regular PRMC meeting. If justification is received, this will be reviewed by the Co-chairs of the PRMC, with either administrative approval with close follow-up and monitoring, or be brought to the full PRMC at its next regular meeting, and the committee will determine whether the study should be closed or can remain open to accrual. If accrual is more than 25% but less than 50% of expected accrual, a message will be sent to the principal investigator requesting an explanation. The explanation will be reviewed by at least one of the co-chairs. If the co-chair approves the explanation, the application for renewal will be approved. If the explanation is not considered satisfactory by the co-chairs, the matter will be referred to the full committee for resolution. If the principal investigator does not respond before the HRPO expiration date, the co-chairs will send a letter to the HRPO closing the study to further accrual. For therapeutic institutional studies undergoing annual review, PRMC approval for renewal also will take into consideration the results of the audit by the Quality Assurance and Safety Monitoring Committee (QASMC) (see Section 4.7) as well as evaluation of subject accrual.

Study accrual is also monitored on a quarterly basis. While the PRMC closely monitors current accrual rates compared to planned accrual rates, the PRMC and SCC Senior Leadership Clinical Research Subcommittee (SLCRSC) jointly assess overall accrual to all trials each quarter. Specifically, trials with zero accrual in the past 12 months are reviewed with the PRMC Lead Co-Chair and the Medical Director of the SCC Clinical Trials Office (CTO). In accordance with NCI guidelines, exceptions are made for trials focusing on rare tumor types. Justification for keeping the trial active is requested directly from each PI. Justifications are evaluated by the Medical Director of the SCC CTO and the Lead Co-Chair of PRMC and determinations to continue active enrollment or to formally request study closure are made. When PIs request to keep their study open after formal request for

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closure, the studies and PI justifications are reviewed by the PRMC Lead Co-Chair at the SCC Senior Leadership Clinical Research Subcommittee. Final decisions by the PRMC Lead Co-Chair (to close or continue accrual) made after consultation with SCC Senior Leadership Clinical Research Subcommittee are not subject to further appeals.

Amendments/Revisions: All protocols revisions are to be sent through the PRMC until the study is designated “in follow-up only”. Principal investigators are asked to submit the HRPO amendment application along with a completed “PRMC Amendment request form” (Appendix F) whenever changes are made to the study. The investigators and their study team are to highlight the requested changes or attach a clearly delineated list of changes and provide justification or explanation of the need for such changes. Without a clear explanation, the protocol will be returned for more information. The study team and HRPO will be notified of the approval.

If changes are made to data collection forms (CRFs) only (for institutional studies only), these should be submitted with a summary of changes (including a rationale for changes). Such submissions will be reviewed by either the SCC Education Program or QA Auditor. Notification of approval will be sent via email.

4.5 Studies to Receive Full-Committee Review

- New institutional cancer research studies: This category includes institutional studies that do not undergo extramural peer review. It also includes studies that were previously approved administratively by the PRMC to allow for HRPO approval that was needed for submission for extramural funding. Once funding has been secured such studies must undergo full-committee review by the PRMC before they can be opened for subject accrual.
- New industry-initiated cancer research studies.
- Survey/questionnaire studies (which are reviewed by BSS).

4.5.1 Full-Committee Review Procedures

All new studies that are received prior to the monthly deadline(s) will be placed on the agenda for that month’s meeting (See Appendix A). The submission must include:

- The HRPO application
- The complete protocol with all appendices
- The Investigational Brochure, when applicable
• The completed “Request for Initial Review of a Protocol” form with Focus Group leader signature if
the study is a clinical trial (see Appendix E)
• Data collection forms, if the study is an institutional clinical trial

In compliance with the Institutional DSM Plan and HRPO requirements, each protocol must contain a
Data and Safety Monitoring (DSM) plan. Specific requirements and suggested language are available in
the Quality Assurance and Safety Monitoring Committee (QASMC) policies and procedures available at

Research grant applications (which are typically limited in page length) lack sufficient detail to allow for
adequate review of the study by the PRMC. Accordingly, the submission to the PRMC for such studies
should include a detailed study protocol in standard protocol format to facilitate PRMC review. Principal
investigators who have not previously submitted to the PRMC are strongly encouraged to seek assistance
from the SCC Clinical Trials Office and Biostatistics Core.

Each study is reviewed by a primary and secondary reviewer (generally, both are physicians), by a
biostatistician, and by a data manager (institutional studies only); additional reviews are performed by a
pharmacist, a behavioral scientist, or a nurse (as appropriate). Review assignments are made by the co-
chairs to the individuals best qualified for review of each study. All review materials are posted on a
SharePoint web site to which all members have access. The primary reviewer is responsible for
summarizing the merits and weaknesses of the study for presentation to the full committee. If the primary
reviewer is unable to attend the meeting, the secondary reviewer or one of the co-chairs presents the
study. The reviewers are encouraged to contact the principal investigator before the meeting if there are
questions regarding study design or other issues. Principal investigators are welcome to attend the PRMC
meetings at which their studies are reviewed but are asked to leave the room during the final discussions
and formal vote. During committee discussion of a protocol for which a member of the PRMC is either
the principal investigator or a co-investigator, that member may be present for the discussion or asked to
leave the meeting for all or part of the discussion, at the discretion of the co-chairs. However, that
member must leave the room during the vote. For each study, the assigned reviewers complete the
Protocol Evaluation Form (Appendix G). These forms are kept on file in the SCC Protocol Office. The
reviewer comments also are forwarded to the principal investigator, along with a letter from the
committee stating the review action. After full-committee discussion, the committee will make one on the
following decisions:
1. **Approved – format revision only or comments not requiring principal investigator to respond.** The study team and HRPO will be notified of the approval.

2. **Contingent Approval – comments requiring minor revisions or clarifying responses from principal investigator.** The principal investigator will be notified of the PRMC’s decision following review. A review letter indicating the committee’s decision is sent to the principal investigator, along with a summary of the reviewers’ comments. The study team and HRPO will be notified of the approval after one of the co-chairs reviews and approves the principal investigator’s response to the PRMC’s comments. The co-chairs also may request that the original reviewers evaluate the adequacy of the investigator’s responses, as deemed necessary, or return the protocol back to the full committee for further evaluation and discussion of the changes.

3. **Deferred – deficiencies identified; substantial additional information or substantive revisions required.** The principal investigator will be notified of the PRMC’s decision following review. A review letter indicating the committee’s decision is sent to the principal investigator, along with a summary of the reviewers’ comments. Such studies must be re-reviewed by the full committee at the next monthly meeting after a response from the principal investigator is received.

4. **Disapproval – major deficiencies identified.** The principal investigator is notified of the PRMC decision following review. A review letter indicating the committee’s decision, along with a summary of the reviewers’ comments is sent to the principal investigator. To be reconsidered a detailed response with either a revised protocol or additional supplemental information must be submitted and reviewed by the full-committee. Otherwise the study remains disapproved.

4.5.2 **Response to Full-Committee Review**

For protocols that receive contingent or deferred status, investigators are expected to submit a response to the PRMC within 90 days. The response from the PI must be labeled with the PRMC number, address all concerns and include one redlined copy showing tracked changes of all revised documents. If no response is received within 60 days of the date of the letter to the principal investigator, the PRMC sends a reminder. If no response has been received at 90 days, the PRMC will close its file on the study. Written requests for extension of the 90-day response period will be considered on a case-by-case basis.

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When HRPO approval is obtained and an “open to accrual” date is received, the study will be listed both in the SCC publications and on the World Wide Web page (unless permission is denied on the “Request for Initial Review of a Protocol” form).

4.6 Behavioral Science Subcommittee (BSS)

The Behavioral Science Subcommittee (BSS) was created to review all behavioral science studies that involve cancer and that were previously reviewed by the Protocol Review and Monitoring Committee (PRMC) of the Siteman Cancer Center (SCC). The BSS provides appropriate expertise for the evaluation of protocols that focus on: (1) primary cancer prevention behaviors, (2) secondary cancer prevention behaviors, (3) quality of life in cancer patients, and (4) epidemiological data related to cancer control, prevention or incidence. The BSS will also evaluate studies that involve extensive use of psychological questionnaires. These examples are not exclusive, however, and decision as to review assignment will ultimately be decided by the PRMC co-chairs. The BSS makes recommendations to the PRMC regarding the studies it reviews. The appropriate NCI guidelines apply to both the PRMC and the BSS.

4.7 Quality Assurance and Safety Monitoring Committee

The Quality Assurance and Safety Monitoring (QASM) Committee functions to provide assurance that institutional studies are being conducted in accordance with the approved protocol and that data reported on clinical research forms accurately reflect the data as reported in the primary patient record. This committee reviews all institutional therapeutic studies and other studies designated by the PRMC (e.g., diagnostic trials). The PRMC will decide, at the time of initial approval, which institutional non-therapeutic research studies should be reviewed by the Quality Assurance and Safety Monitoring Committee. Separate QASMC Guidelines are available on the SCC Web Page (http://www.siteman.wustl.edu/prmc.aspx).

4.8 PRMC Review of Applications to the Research Development Committee

Cancer research studies submitted to the Siteman Cancer Center Research Development Committee for local funding opportunities (including the American Cancer Society Institutional Research Grant) must also be separately submitted to the PRMC for review. If the principal investigator intends to proceed with the research study only if an award by the Research Development Committee is granted, the study will not be reviewed by the PRMC until the Research Development Committee distributes notification of an
award. However, if the principal investigator intends to proceed with the study regardless of the action of the Research Development Committee, the principal investigator should submit the study simultaneously to the PRMC and to Research Development Committee. The study should be submitted to the PRMC in accordance with the “Full-Committee Review Procedures”.

The Research Development Committee limits the length of applications to 5 pages. In general, these applications often do not contain sufficient detail of study methods to allow for review by the PRMC. Hence, investigators are required to provide complete, detailed study protocols [in standard protocol format (see Appendix D)], rather than grant application format], including data collection forms, when submitting such studies for review by the PRMC.

Principal investigators should indicate on the Siteman Cancer Center Award Transmittal form whether the study will be initiated irrespective of SCC funding or only with such funding.

5. Human Research Protections Office Procedures

HRPO will not review any new cancer study without approval from the PRMC. If HRPO receives notice of accrual closure for any study by the PRMC, it will not approve the study for any further accrual. However, ongoing HRPO review may be required in order to allow for continuing data collection, for continuing treatment of any active patients enrolled in the study, or for continuing data analysis.

6. Siteman Cancer Center Protocol Office Responsibilities

The SCC Protocol Office will be responsible for the coordination of protocol issues for the Focus Group, PRMC, HRPO, and principal investigator and for record keeping (minutes, agenda, Protocol Evaluation Forms, committee correspondence, computer entry, generating reports, etc.). The SCC Protocol Office will serve as the office of record for all cancer-related research involving human subjects. Research personnel can contact this office at any time for clarifications or further information (see Appendix I).

7. Program for the Elimination of Cancer Disparities (PECaD)

Ensuring appropriate representation by gender and race/ethnicity in cancer clinical trials is mandated by the NCI: all research with human subjects must include adequate numbers of women and minorities to
allow for valid analyses of differences in the interventional effect; recruitment must be conducted so that no group is unduly burdened and that no group is unduly benefited; and any research proposal must describe the proposed study population in terms of gender and race/ethnicity as well as the rationale for inclusion. (http://orwh.od.nih.gov/inclusion/outreach.pdf)

The Program for the Elimination of Cancer Disparities (PECaD) monitors research accrual and supports investigators in their efforts to achieve appropriate representation. A PECaD representative is present at PRMC meetings when needed to ensure communication about specific trials.

Studies that are subject to PECaD review are: all ancillary trials that are investigator initiated (classified as "institutional, primary"), therapeutic trials, imaging studies, or any trial for which the SCC target sample size is ≥ 15 subjects. The patient population at the Siteman Cancer Center for a given study’s inclusion criteria is used as the standard for evaluation.

8. PRMC Co-Chair Responsibilities

One or both of the co-chairs will sign all PRMC review letters. At least one of the co-chairs will be present at each meeting. Each co-chair has the authority to approve all studies needing only administrative review and studies resubmitted after receiving a Contingent Approval by the full committee. The co-chairs will determine if a study requires administrative versus full-committee review and will assign reviewers for all full-committee study reviews. Amendments also will be administratively approved, unless deemed by the co-chairs to represent a substantive change. Such major amendments will be brought to the full committee for review.

9. Principal Investigator Responsibilities

Every investigator conducting cancer research studies is required to follow the PRMC policies and procedures. The principal investigator is responsible for making sure that all study participants are registered in the SCC Research Subject Registry (investigators and their staff members are encouraged to enter data directly into the SCC database. The principal investigator is responsible for notifying the SCC Protocol Office when a study is closed to accrual. The principal investigator should also submit any study amendments for review by the PRMC co-chairs.
10. Appendices

A. PRMC Monthly Meeting Schedule
B. SCC Clinical Focus Group List
C. SCC Shared Resources
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E. Request for Initial Review of a Protocol Form
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I. Contact Information
J. PRMC Review Process: Flow Diagram
Appendix A PRMC Monthly Meeting Schedule

For current meeting dates and submission deadlines, please see Schedule of PRMC Meetings and Deadlines at http://www.siteman.wustl.edu/prmc.aspx.
Appendix B. Research Focus Groups and Leaders

For current Focus Group membership information, please see Siteman Cancer Center Focus Groups and Leaders at http://www.siteman.wustl.edu/prmc.aspx.
Appendix C. Siteman Cancer Center Shared Resources

For current information regarding Shared Resources (Cores), please see Shared Resources at http://www.siteman.wustl.edu/prmc.aspx.
Appendix D. Protocol Format Outline*

Please include page numbers and protocol version/date in footer.

I. Cover page should include title, PI, collaborators (include statistician) and protocol version/date (include in footer on every page as well)

II. Table of Contents page

III. Background and Rationale

IV. Objectives

V. Eligibility criteria - inclusion and exclusion

VI. Registration procedure

VII. Research/Treatment plan

VIII. Study Procedure Calendar (if applicable)

IX. Drug Formulation and Procurement (if applicable)

X. Data and Safety Monitoring Plan

XI. Statistical Considerations

XII. Record Keeping

XIII. References

XIV. Special Considerations

* Refer to Appendix H for additional detail

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Appendix E. Request for Initial Review of a Protocol


Feb 2014
Appendix F. Amendment Form

For a current version of the Amendment Request form, please see PRMC Forms, at http://www.siteman.wustl.edu/prmc.aspx.
Appendix F. Renewal Form

For a current version of the Renewal Request form, please see PRMC Forms, at http://www.siteman.wustl.edu/prmc.aspx.
Appendix G PRMC Protocol Evaluation Form

PROTOCOL NUMBER: 
PROTOCOL TITLE: 
PI: 
MEETING DATE: 

I. Physician Scientific Review

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<tr>
<th>Section</th>
<th>Satisfactory</th>
<th>Unsatisfactory</th>
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<tbody>
<tr>
<td>A. Research Problem</td>
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<td>1. Background and Rationale</td>
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<td>2. Objectives and/or Hypothesis</td>
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<td>B. Design Characteristics</td>
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<td>1. Subject Assignment</td>
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<td>2. Trial Period</td>
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<td>3. Feasibility of Enrollment</td>
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<td>C. Treatment Characteristics</td>
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<td>1. Dose, Duration, Route</td>
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<td>2. Toxicity</td>
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<td>D. Subject Characteristics</td>
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<td>1. Selection Criteria</td>
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<td>2. Representative</td>
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<td>3. Inclusion/Exclusion of Children</td>
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<td>E. Data Collection</td>
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<td>1. Schedule-Study Calendar &amp; Forms</td>
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<td>F. Statistics</td>
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<td>1. Endpoints Clearly Defined</td>
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<td>2. Objectives achievable</td>
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<td>G. Data safety and monitoring plans</td>
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RECOMMENDATION: Approved ☐ Contingent ☐ Deferred ☐ Disapproved ☐

Overall Critique:

By completing this I indicate that neither myself, my spouse nor dependent children, have, or anticipate having, any income from or financial interest in the sponsor of the protocol, the supporting organization, or a company that owns/licenses the technology being studied that may reasonably affect the outcome of the research.
Appendix G PRMC Protocol Evaluation Form

PROTOCOL NUMBER:
PROTOCOL TITLE:
PI:
MEETING DATE:

II. Data Management Section

A. Are schema eligibility requirements consistent with eligibility requirements listed in protocol?
   Yes ☐ No ☐ NA ☐

B. Is schema treatment outlined clearly and accurately in comparison with treatment narrative section of protocol?
   Yes ☐ No ☐ NA ☐

C. Would addition/deletion of any information make the schema easier to interpret?
   Yes ☐ No ☐ NA ☐

D. Are the eligibility requirements clearly stated?
   Yes ☐ No ☐

E. Are the Registration, Data Submission, and Modality Review sections clear?
   Yes ☐ No ☐

F. Does the Data Submission Schedule coincide with the objectives of the protocol (i.e. f/u due at appropriate time, not excessive after progression/relapse)?
   Yes ☐ No ☐ NA ☐

G. Are modality review requirements listed in Data Submission section?
   Yes ☐ No ☐ NA ☐

H. Is the required Data section clear? Are the columns marked correctly with x’s and are footnoted items clear?
   Yes ☐ No ☐ NA ☐

I. Are ancillary studies (quality of life, specimen submission, etc.) listed on the Required Data section?
   Yes ☐ No ☐ NA ☐

J. In the Treatment Plan section, are specific premeds required?
   Yes ☐ No ☐ NA ☐

   Are certain prohibited drugs listed?
   Yes ☐ No ☐ NA ☐

   Is there a mechanism to assess for pt compliance?
   Yes ☐ No ☐ NA ☐

By completing this I indicate that neither myself, my spouse nor dependent children, have, or anticipate having, any income from or financial interest in the sponsor of the protocol, the supporting organization, or a company that owns/licenses the technology being studied that may reasonably affect the outcome of the research.
Appendix G PRMC Protocol Evaluation Form

PROTOCOL NUMBER:
PROTOCOL TITLE:
PI:
MEETING DATE:

II. Data Management Section (cont’d.)

K. If specific test requirements are listed in the Treatment section (i.e., blood test three times per week), are the same tests represented accurately in the Required Tests section?

Yes ☐ No ☐ NA ☐

L. Are dose modifications understandable?

Yes ☐ No ☐ NA ☐

M. Are doses to be re-escalated once they are reduced?

Yes ☐ No ☐ NA ☐

N. Is the NSC# listed for investigational drugs?

Yes ☐ No ☐ NA ☐

O. Are there any issues with the consent?

Yes ☐ No ☐

Please note that issues pertaining only to the consent document may not be identified as requiring a response from the study team; but will be passed along as comments to the study team. HRPO reviewers most likely will not see these comments.

P. Data safety and monitoring plan appropriate?

Yes ☐ No ☐

RECOMMENDATION: Approved ☐ Contingent ☐ Deferred ☐ Disapproved ☐

Overall Critique:

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Appendix G PRMC Protocol Evaluation Form

PROTOCOL NUMBER: 
PROTOCOL TITLE: 
PI: 
MEETING DATE: 

III. Nursing Section 

A. How many nursing hours of care will be needed for patient in addition to normal nursing care planned? _____

B. Will there be any special equipment needs? [ ] Yes [ ] No

C. Is nursing staff at each location adequate?

[ ] Yes [ ] No

If no, what do you recommend?

D. Is specialized education of nursing staff needed?

[ ] Yes [ ] No

If yes, in what area(s)?

Is there a contact person for this education?

[ ] Yes [ ] No

What are your suggestions?

E. Are the treatment sections clearly outlined and easy to follow?

[ ] Yes [ ] No

If no, what are your suggestions?

RECOMMENDATION: [ ] Approved [ ] Contingent [ ] Deferred [ ] Disapproved

Overall Critique: 

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Appendix G PRMC Protocol Evaluation Form

PROTOCOL NUMBER: 
PROTOCOL TITLE: 
PI: 
MEETING DATE: 

IV. Pharmacy Section

A. Does the study involve any drug therapy?
   ☐ Yes ☐ No

B. Does the protocol give adequate information about drug administration and evaluation of treatment toxicities?
   ☐ Yes ☐ No

C. Are there any drugs to be dispensed by the Pharmacy Department?
   ☐ Yes ☐ No
   If yes, please continue.

D. Are all non-standard drug therapies provided by the study sponsor?
   ☐ Yes ☐ No

E. Where should drugs be prepared and drug supplies and records be maintained?
   ☐ Barnes-Jewish Hospital Pharmacy
   ☐ Siteman Cancer Center Pharmacy
   ☐ Other (specify) _____

F. What is the estimated preparation time per patient? _____
   Specify criteria for estimate: _____

RECOMMENDATION: ☐ Approved ☐ Contingent ☐ Deferred ☐ Disapproved ☐

Overall Critique:

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**Appendix G PRMC Protocol Evaluation Form**

**PROTOCOL NUMBER:**
**PROTOCOL TITLE:**
**PI:**
**MEETING DATE:**

**V. Biostatistics Section**

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<tr>
<td>2. Objectives and/or Hypothesis</td>
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<th>B. Design Characteristics</th>
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<td>4. Control of Treatment-Related Bias</td>
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<td>5. Control of Extraneous Variables</td>
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<td>6. Dependent Variables</td>
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<td>7. Trial Period</td>
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<tr>
<th>C. Treatment Characteristics</th>
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<th>D. Subject Characteristics</th>
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<td>2. Representative</td>
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<th>E. Data Collection</th>
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<td>2. Quality Assurance</td>
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<td>3. Schedule</td>
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<th>F. Data Analysis</th>
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<td>2. Statistical Analysis</td>
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| G. Data safety and monitoring plans | | |

**RECOMMENDATION:** Approved □ Contingent □ Deferred □ Disapproved □

**Overall Critique:**

---

By completing this I indicate that neither myself, my spouse nor dependent children, have, or anticipate having, any income from or financial interest in the sponsor of the protocol, the supporting organization, or a company that owns/licenses the technology being studied that may reasonably affect the outcome of the research.
Appendix H. Protocol and Consent Development Checklist

All protocols should be dated, have numbered pages, and include a table of contents; subsequent versions (revisions or amendments) should also be dated and include a version number.

DISCLAIMER: Each protocol is unique. Thus, no protocol format (or checklist) will be applicable to all protocols. This checklist applies principally to therapeutic (drug) trials. Additionally, it contains many elements that may not be applicable to all therapeutic trials. It is provided to aid investigators in protocol development.

TITLE PAGE:

- Date of document
- Protocol number (e.g. 96-0001)
- Title of protocol
- Does title accurately represent or include all aspects of the protocol?
- Principal Investigator - name, name of institution, address and phone number
- List of other participating facilities
- Name of coordinating center if a multi-site trial
- Co-investigators or co-chairs for each modality (e.g. radiation, surgery, laboratory)
- Statistician

1.0 Introduction - Background and Rationale

- Is sufficient background given to understand the reason(s) for conducting this study and for estimating the expected risks and benefits of this study?
- Is the rationale clearly stated for correlations between tumor characteristics and outcome measurements?
- For therapeutic protocols, provide response data, toxicity and complications and supportive care measures from similar studies
- Is information provided to support all ancillary studies?
- Are references given for all statements for which they are needed?
- For Phase I studies, is the dose-limiting toxicity, pharmacokinetics/dynamics, either in animals or humans, adequately defined?

2.0 Objectives - Primary endpoints of study, listed and numbered individually.

- Are objectives stated clearly?
- Is study design appropriate to answer questions posed by these objectives?
3.0 Selection of Patients - Eligibility Criteria

Should include:

- Disease type/site
- Extent or stage of disease
- Whether disease must be measurable or evaluable and a definition of each

- What pathology is required - e.g. if protocol is for advanced disease, is recent biopsy proof of recurrent or metastatic disease required or only the initial biopsy of primary?
- What pathological materials, if any, are to be sent and where?
- Prior therapies permitted and/or not allowed
- Performance Status
- Required physiologic status laboratory parameters
- Age range specified (no upper age limit is permitted by the NCI unless justified scientifically)
- Statement regarding ineligibility if female subject is pregnant or lactating
- Statement advising women of childbearing potential and sexually active males to use effective contraception while on study
- Statement that patient must have signed informed consent of a HSC approved protocol prior to registration on study.

4.0 Patient Registration

- Are procedures for registration clear - what data are needed to register, who to call, etc.?
- If a multicenter trial, are patients registered through a central office?
- Does required information include description of randomization process, patient characteristics, and stratification factors?

5.0 Treatment Plan

5.1 Administration

- Administration - are instructions for mixture or preparation and administration of all drugs given in clear detail such that they can be followed by all research personnel?

Are the following clear?

- Route of administration (e.g. IM, SQ, IT, IV bolus, IV infusion, oral); time (over ___ minutes or hours; 3X per day at mealtime, etc.); days (e.g. days 1-5, 8 and 10).
- Hydration, urine alkalization, electrolytes, I & O
Appendix H. Protocol and Consent Development Checklist

_____ Treatment intervals (how often, e.g. q 3 weeks, daily for 28 days, etc).

_____ Total duration of treatment (for a maximum of ____ cycles or until progression, or other specified time e.g. IV infusion over 2 hours on days 1 and 5 q 3 weeks for a maximum of 4 cycles).

_____ Radiation therapy dose and schedule

_____ Integration of multimodality therapy (surgery, radiation therapy, chemotherapy)

5.2 Schema

_____ If a schema is given, is it complete and accurate when compared to this section? At a minimum, all treatment studies must have a schema.

5.3 Dose Modifications

_____ Are criteria for grading toxicities for dose modifications specified and included with the protocol, and are they described using NCI Common Toxicity Criteria?

_____ Is it clear when and how toxicity is to be assessed - whether by nadir counts or current values and at what points during therapy?

_____ Are instructions included for dose modification of each study drug?

_____ Are instructions included for each modality (chemotherapy, radiation therapy)?

_____ Are all reasonable measures included to monitor expected adverse events?

_____ Are instructions given for reporting Adverse Drug Reactions?

5.4 Duration of Therapy

_____ Are conditions given for taking patient off study (e.g., if grade 4 __________, patient should go off study; or, if treatment is held x times for toxicity, patient must go off study).

5.5 Supportive Care

_____ Are guidelines given for supportive care?

_____ Should special instruction sheets be included if patients are to give themselves injections?

_____ Are patient diaries included (if applicable) to record when drug is taken and any side effects?

6.0 Response Assessment

_____ Is “adequate course,” defined, i.e., how much therapy must a patient receive to be evaluable for response?

_____ Are criteria provided for assessing response for the following categories, depending on what is permitted in the protocol?
Appendix H. Protocol and Consent Development Checklist

_____ bidimensionally measurable disease
_____ unidimensional disease
_____ nonmeasurable evaluable disease
_____ leukemia/lymphoma

_____ Categories of response defined - What constitutes a complete response, partial response, minor response, stable disease and progression (NCI categories for Quarterly Reports)?

7.0 Study Parameters - Tabular format preferred

All required laboratory tests, imaging studies and measurements, ancillary laboratory tests, etc. should be included in chart format so that the times at which they are required are clear.

_____ Are all laboratory tests, imaging studies, etc. required in eligibility section listed here? Please list any that should be added.

_____ Do any tests seem unnecessary - e.g., SGPT is not included in standard SMAs.

_____ Is it clear from the charts how often test are to be done? Are intervals reasonable?

_____ Time limit for pre-study laboratory tests and imaging studies (how many days/weeks before beginning on study?)

8.0 Drug Formulation and Procurement - Is the following information given for each study drug?

_____ Other names, if any, for the drug

_____ Classification - type of agent

_____ Mode of action

_____ Storage and stability

_____ Dosing - Specific to this study

_____ Preparation - diluent to be used, etc.

_____ Route of administration - study specific

_____ Incompatibilities

_____ Availability - source of drug (NCI, pharmaceutical company, commercially available)

_____ Are agent ordering procedures clear if the agent (e.g., a drug) is provided?

_____ Side effects - for each drug

_____ Nursing implications

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Appendix H. Protocol and Consent Development Checklist

_____ Adequate description of Reported Adverse Events and Potential Risks given? Is an Investigator’s Brochure included if applicable?

9.0 Statistical Considerations Is the statistical section adequate with regard to the following?

_____ Method of randomization and stratification

_____ Sample size determinations

_____ Error levels (alpha and beta) in phase III studies

_____ Differences to be detected and size of the confidence interval

_____ Estimated accrual rate and/or study duration, with supporting documentation

_____ Early stopping procedures

_____ Primary endpoint for interim and final analyses

_____ Clear specification of primary and secondary (e.g., subset) hypotheses

_____ Maximum number of patients

_____ Statistical analysis

10.0 Recordkeeping

_____ Does protocol specify data to be collected, at what intervals, and to whom sent?

_____ Are intervals reasonable?

_____ Are data collection forms included?

_____ Are reporting guidelines and timing of data submission forms clear?

11.0 References

_____ Do references agree with numbers in the body of the protocol?

12.0 Special Considerations

_____ Are personnel identified?

_____ Are instructions re: methods of preparation and shipment (types of tubes, spun, frozen, on wet/dry ice or at room temperature, sent by overnight mail or batched, etc.) adequate
Appendix H. Protocol and Consent Development Checklist

For ancillary laboratory studies -

_____ Are personnel identified?

_____ Are instructions re: methods of preparation and shipment (types of tubes, spun, frozen, on wet/dry ice or at room temperature, sent by overnight mail or batched, etc.) adequate?

For patient self-administered drug:

_____ Are patient diaries or calendars for drug administration and recording side effects included?

12.0 Informed Consent

The following elements must be present in the informed consent document:

_____ Does the consent clearly state that the study involves research.

_____ State which drug(s), treatment(s), or delivery technique(s) is/are experimental?

_____ Clarify the study purpose(s) is layman’s terms (HSC suggests 6th Grade reading level)

_____ State the patient’s expected duration of participation in study (e.g., the patient will be treated until there is evidence that therapy is no longer effective).

_____ Give a brief description of the procedure(s) to be performed to monitor the patient during study (e.g., X-rays, lab evaluations, etc.). An exhaustive list is not necessary.

_____ Give a description of the experimental aspect(s) or new delivery techniques(s) of the study.

_____ State in specific terms the route of administration of each drug (e.g., I.V., oral, continuous infusion, etc.)

_____ State estimated time of delivery of each drug or time of procedure (e.g., 5 minutes, 30 minutes, 24 hours, etc.).

_____ State which risks are attributed to specific drug(s) or procedure(s).

_____ Clarify and describe expected benefit(s) to be derived from participation in this study.

_____ In general terms, discuss alternative treatment(s) to participation in this study (e.g., conventional chemotherapy, irradiation, hormonal therapy, surgery, etc.).

_____ State the extent to which confidentiality of records will be maintained.

_____ State if compensation for study-related injury will be provided by the institution or other insurer.

_____ Provide space in the form or list name(s) and number(s) of the contact person(s) (not involved in the research) for patients rights related questions.

_____ Include SCC Registry statement in consents for all trials (available at the HSC website).
Appendix H. Protocol and Consent Development Checklist

Additional Elements

The following elements may be appropriate for some studies:

_____ State that unforeseeable or unexpected risk(s) may be involved.

_____ State the circumstances under which the patient’s participation may be terminated by the investigator without the patient’s consent.

_____ State that additional costs may be incurred by the patient’s participation in the study.

_____ State the consequences of the patient’s decision to withdraw from the study.

_____ State that significant new findings that relate to the patient’s treatment will be discussed with the patient.

_____ State the approximate number of patients involved in the study.
Appendix I. Contact Information

For current contact information for PRMC or QASMC, please see the Protocol Office webpage at http://www.siteman.wustl.edu/prmc.aspx.
Appendix J. PRMC Review Process: Flow Diagram

Cancer Research Protocol Needing HRPO Approval

Is Protocol a Clinical Trial?

Protocol is reviewed by SCC Focus Group

Protocol is submitted to Protocol Office

Administrative Review
- NCI Cooperative Group protocols
- CTEP-approved protocols
- Chart reviews
- Compassionate use protocols
- Case studies
- Retrospective reviews
- Tissue/specimen studies
- Standard treatment protocols
- Annual renewal of protocol previously approved by PRMC
- Amendments

Approved

Submitted to HRPO

Approved

Open to Accrual

Administrative Review (To Allow For HRPO Review)
- Protocol to be reviewed by peer-reviewing agency (external or SCC) for funding AND accrual will NOT begin before completion of peer-review and funding

Approved

Submitted to HRPO

Approved

Submit to Funding Agency (When award notice is received, the protocol must then be submitted for Full Committee Review)

Funded

Full Committee Review
- Institutional trials (non-peer-reviewed)
- Industry-initiated trials
- Questionnaires, surveys, interviews

Approved

Submitted to HRPO

Approved

Open to Accrual

Behavioral Science Subcommittee

Program for the Elimination of Cancer Disparities

Revised April 2012