Data and Safety Monitoring (DSM) Plan

Ensuring Patient Safety and the Validity and Integrity of Clinical Research Data

Summary

The Alvin J. Sitemap Cancer Center places the highest priority on ensuring the safety of patients participating in clinical trials.

The Protocol Review and Monitoring Committee (PRMC) is responsible for the scientific review of all cancer-related trials at initial submission, amendment and annual renewal. Decisions regarding study continuation are made by the PRMC. A Quality Assurance and Safety Monitoring Committee (QASMC), which serves as the SCC Data and Safety Monitoring Committee (DSMC), provides independent oversight and review of quality assurance audits, reportable adverse event (RAE) reporting, and interim data and safety monitoring (DSM) reports for institutional trials. RAEs encompass Serious Adverse Events (SAEs) and additional institutional reporting requirements (see RAE section p. 3). The QASMC appoints study-specific ad hoc Data and Safety Monitoring Boards (ad hoc DSMBs) as federal requirements indicate.

Oversight of data and safety monitoring is the responsibility of the Sitemap Cancer Center PRMC and QASMC. Every clinical trial conducted at the Sitemap Cancer Center must also include a plan for data and safety monitoring. The development of protocol monitoring plans and reporting requirements are dependent upon the degree of risk encountered by patients on the study, the study sponsor, the nature of an investigational agent, and the phase of trial.

NCI/CTEP-sponsored phase I/II studies rely upon monitoring of the trial by the PI with reporting to NCI/CTEP using the Clinical Trials Monitoring Service (CTMS), the Clinical Data Update System (CDUS), and/or the Adverse Event Expedited Reporting System (AdEERS).

Phase I, II, III, and other clinical trials sponsored by the NCI Cooperative Group Program (at the SCC this includes ACRIN, ACOSOG, AMC, CALGB, COG, GOG, NSABP, RTOG, and other studies open through the CTSU) are monitored by long-standing and established systems for cooperative group data submission, reporting, review, and monitoring.

Industry-sponsored (drug and medical device) trials require data and safety monitoring plans that adhere to industry, Washington University IRB (known as the Human Research Protection Office or HRPO) and FDA-specified guidelines.

All local, investigator-initiated clinical trials are required to have specific data and safety monitoring plans tailored to the size and complexity of each trial.

Local, investigator-initiated Phase I trials are required at a minimum to be continuously monitored by the PI and audited annually. Studies run by the Clinical Trials Core (CTC) Developmental Therapeutics (DT) program receive weekly monitoring. Semi-annual data and safety monitoring reports are submitted to the QASMC coordinator for subsequent submission to and review by the QASMC. The PRMC and the QASMC may require more frequent reporting (monthly) for early Phase I studies of agents that may pose higher risks to patients.
Local, investigator-initiated Phase II protocols require regular monitoring by the PI of the study with semi-annual DSM reports submitted to the QASMC coordinator for subsequent submission and review by the QASMC.

Local, investigator-initiated randomized Phase III clinical trials are monitored by protocol-specific ad hoc data and safety monitoring boards (ad hoc DSMBs) that meet semi-annually, or more frequently as needed. Formal ad hoc DSMBs consist of at least two clinical investigators and a biostatistician; these members must be independent of the investigators and biostatisticians involved in the design and conduct of the trial. Data and safety monitoring is specified in the protocol with the ad hoc DSMB’s semi-annual reports to be forwarded to the QASMC (DSMC).

All data and safety monitoring reports for local, investigator-initiated studies must include, at a minimum, the number of patients entered, number of patients treated, summary of adverse events reported to date, a specific list of adverse events requiring reporting and ALL reportable adverse events (RAEs). Significant literature (if applicable) that reports developments that may affect the safety of participants or the ethics of the study should be submitted to the QASMC on an annual basis or as the need arises.

As above, for each local, investigator-initiated clinical trial, the investigator is required to submit to the QASMC coordinator a semi-annual data and safety monitoring report summarizing study safety experience. Regular data and safety monitoring activities for each study will continue until all patients have completed their treatment and all patients are beyond the time point at which study-related adverse events would likely be encountered as defined in the protocol. However, even if patients are past the period during which study-related adverse events are likely, any adverse events likely attributable to the study must still be reported to the QASMC.

Trial PIs with DSM reports that are delinquent 30 days from the due date receive a warning notice from the QASMC. A second warning is sent at 60 days after the due date. If the delinquent DSM report is not received within 90 days of the initial warning notice (a total of 120 days from the due date), the trial is suspended or closed at the discretion of the PRMC and QASMC.

Multi-institutional, collaborative consortia trials centrally managed by SCC investigators must have a study-specific DSM plan that requires RAE reporting from all sites to the PI, distribution of RAE reports to all participating sites, and preparation of semiannual DSM reports that summarize the adverse events and responses (when appropriate) from all sites. Multi-institutional, collaborative consortia trials managed by investigators who are not SCC investigators should have a similar DSM plan.

All reportable adverse events for all clinical trials conducted at the SCC are submitted both to the QASMC and the Washington University IRB. RAE reports are reviewed at the monthly QASMC meeting.

Acknowledgements

The SCC is greatly indebted to efforts of the National Institutes of Health, particularly the National Cancer Institute, whose data and safety monitoring policies and plans formed the basis of our data and safety monitoring plan. We also acknowledge the generosity of the Ohio State University Comprehensive Cancer Center and the Yale Comprehensive Cancer Center for willingly sharing their data and safety monitoring plans when this plan was first developed in 2001.
Data and Safety Monitoring Plan

Introduction

The Alvin J. Siteman Cancer Center (SCC) places the highest priority on ensuring the safety of patients participating in clinical trials. All clinical trials conducted at the Siteman Cancer Center must include provisions for data and safety monitoring.

The extent of monitoring varies by the degree of risk encountered by patients on the study, the study sponsor, the type of agent or agents involved, and the phase of the clinical trial.

The Siteman Cancer Center Data and Safety Monitoring Plan was developed to coordinate and provide oversight for data and safety monitoring for all cancer-related trials consistent with the National Institutes of Health Policy for Data and Safety Monitoring dated June 10, 1998 (http://grants.nih.gov/grants/guide/notice-files/not98-084.html) with further guidance issued on June 5, 2000 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html). The National Cancer Institute issued a policy on June 22, 1999 for data and safety monitoring of all trials with the additional requirement that randomized phase III trials be monitored by ad hoc Data and Safety Monitoring Committees (ad hoc DSMBs) (http://deainfo.nci.nih.gov/grantspolicies/datasafety.htm). The NCI published the essential elements of a Data and Safety Monitoring plan on April 1, 2001 (http://www.nci.nih.gov/clincialtrials/conducting/dsm-guidelines/page3).

Currently, all SCC clinical trials undergo data and safety monitoring. Study investigators and clinical trials staff forward all reportable adverse event reports to the Washington University Institutional Review Board (IRB), Siteman Cancer Center Quality Assurance and Safety Monitoring Committee (QASMC), and the study sponsor. While these activities have always been a vital and important role for the PRMC, the current NIH guidelines require a more comprehensive and detailed data and safety monitoring plan.

Reportable Adverse Events (RAEs)

Reportable adverse events (RAEs) are untoward clinical research medical occurrences, such as those resulting in death, hospitalization, or prolonged hospitalization, which must be reviewed by the QASMC and the IRB. The definition of what must be reported to QASMC and the IRB changes over time and may be more extensive than those incidences defined as “serious adverse events” by Good Clinical Practice.

Organization and Administration

As the specific types of monitoring and reporting vary by the nature of the individual trial, the responsibility to ensure that monitoring is timely and effective is shared by a number of SCC offices. The Director and the Associate Director of Translational and Clinical Investigation hold the overall responsibility for data and safety monitoring within the Siteman Cancer Center. Other individuals and units with responsibilities in data and safety monitoring include the Protocol Review and Monitoring Committee (PRMC), the Quality Assurance and Safety Monitoring Committee (QASMC), the Washington University Institutional Review Board (IRB), individual ad hoc data and safety monitoring boards (ad hoc DSMB) for trials (defined in ad hoc DSMB section, pages 16-17),
the principal investigators of NIH grants, and other principal investigators of individual clinical trials. Appendix 1 summarizes each committee’s reporting and role in data and safety monitoring.

Staff members in the PRMC and QASMC assist in trial monitoring and quality control. Staff members:

1. Collect centralized patient registration information for all approved Siteman Cancer Center clinical trials that are not managed by the Clinical Trials Core (PRMC for initial data collection; QASMC for monitoring).

2. Collect, maintain update, and/or review data on patients enrolled in clinical trials including data on accrual, toxicity, and adverse events. PRMC collects accrual information; QASMC (staff members may provide assistance to PIs to complete semi-annual data and safety monitoring reports that are to be reviewed.

3. Provide information to and assist in the review and monitoring of clinical studies by the QASMC.

4. Perform annual audits to assure protocol compliance and data integrity to ensure that cancer-related clinical trials are conducted in accordance with federal, state, and institutional regulations. Materials audited include, but are not limited to, consents, protocols, regulatory approvals, participant eligibility, study management, and intervention compliance (QASMC).

All RAE reports for all clinical trials conducted at the Siteman Cancer Center are submitted both to the QASMC and the Washington University IRB. All SAE reports from the previous 30 days are reviewed at the monthly QASMC meeting.

Protocol Review and Monitoring Committee (PRMC)
The Protocol Review and Monitoring Committee (PRMC) is comprised of a representative group of basic, clinical research, and population scientists and staff; including medical, surgical, and radiation oncologists; data managers; behavioral scientist(s); a biostatistician; nurses; a pharmacist; and a patient advocate.

The SCC Protocol Review and Monitoring Committee (PRMC) meets once monthly (unless protocol volume requires an additional meeting) and plays a vital role of protocol review and monitoring to assure that clinical trials are scientifically sound and that approved studies maintain adequate patient accrual and scientific progress. The PRMC reviews all cancer related clinical trials conducted at the Siteman Cancer Center and/or at the Washington University Medical Center (Washington University School of Medicine, Barnes-Jewish Hospital, and St. Louis Children’s Hospital). Beginning in 2007, the PRMC also reviews all cancer-related trials conducted through the St. Louis University (SLU) School of Public Health, in accordance with the Siteman/SLU Consortium, signed in April 2007. Trials that have undergone CTEP, NIH, or similar peer-review are administratively reviewed by one of the PRMC Co-Chairs. All other cancer-related trials, including non-therapeutic trials, investigator-initiated trials (sponsored or unsponsored), and industry-initiated studies undergo full PRMC review. Registries, retrospective studies, chart reviews, tissue/specimen collections, and other studies that are not trials are administratively reviewed by one of the PMRC Co-Chairs. As part of the review process, the PRMC reviews and approves protocol-specific data and safety monitoring plans on cancer-related trials prior to protocol review by the Washington University IRB. No study receives PRMC approval without a data and safety monitoring plan, or where appropriate, a DSM plan with identified ad hoc DSMB. The PRMC also reviews case report forms for institutional trials to verify that data pertinent to the study objectives will be collected.

All trial protocols are initially prioritized by the disease-oriented SCC Working Groups (WGs, formerly known as Focus Groups). Each trial protocol regardless of source must be approved and
prioritized by the appropriate working group leader prior to submission to the PRMC and IRB. Authority for final prioritization based on population, significance of studies, competition, etc. rests with the PRMC, which can accept or decline the initial prioritization by the WGs.

The Working Groups are:

| Breast Oncology | Leukemia/Lymphoma/Transplant |
| Endocrine Oncology | Melanoma & Skin |
| Lower Gastrointestinal | Musculoskeletal |
| Upper Gastrointestinal | Neuro-Oncology |
| Genitourinary Oncology | Pediatric Oncology |
| Gynecologic Oncology | Thoracic Oncology |
| Head and Neck Oncology | Developmental Therapeutics |

All studies are prioritized as follows:

1. Investigator-initiated local studies (with or without external sponsorship), and cooperative group studies for which a SCC member is the national PI
2. Cooperative group studies or other NCI-approved multi-center studies
3. Industry-initiated studies

Within these larger categories of studies, the working group selects and prioritizes studies in order to focus on high-priority science, to ensure an appropriate patient population for each study, and to minimize competition for a given patient population. Authority for final prioritization based on population, significance of studies, competition, etc. rests with the PRMC, which can accept or decline the initial prioritization by the WGs.

**Behavioral Science Subcommittee (BSS)**

The Behavioral Science Subcommittee (BSS) was created in January 2006 to review all behavioral science studies that involve cancer. 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 also evaluates studies that involve extensive use of psychological questionnaires. These examples are not exclusive, however, and the decision as to review assignment is ultimately made by the PRMC Co-Chairs. The BSS makes recommendations to the PRMC regarding the studies it reviews which the PRMC Co-Chairs either accept (no subsequent PRMC review) or deem to require an additional and overriding formal PRMC review. The appropriate NCI guidelines apply to both the PRMC and the BSS. The subcommittee meets monthly and is comprised of several psychologists, a biostatistician, a medical oncologist, and an oncology nurse.

**Quality Assurance and Safety Monitoring Committee (QASMC) [functions as the SCC Data and Safety Monitoring Committee, or DSMC]**

The Quality Assurance and Safety Monitoring Committee (QASMC) serves as the SCC Data and Safety Monitoring Committee (DSMC) and provides independent oversight of clinical trials conducted at the SCC. The Committee is comprised of medical oncologists, a surgical oncologist, a radiation oncologist, a biostatistician, and a pharmacist. At its monthly meeting, the QASMC reviews the following:
1. **Quality assurance audits.**
   Audits are conducted for all institutional therapeutic trials, and for diagnostic or other non-therapeutic studies at the request of the QASMC or PRMC. All cancer-related clinical trials are entered into the SCC administrative database along with HRPO approval information for each study. Audits are conducted for all institutional therapeutic trials and for other studies at the request of the QASMC or PRMC. QASMC staff query the database to select studies requiring audit. During review of each audit, the Committee determines when the next audit should occur: 6 months, 1 year, 2 years, or based upon accrual as deemed necessary.

   The audit team consists of a faculty advisor (a member of the QASMC and the Quality Assurance (QA) auditor. The number of cases selected for review is determined by the enrollment to the study. All cases are reviewed if current enrollment is ≤ 10; 10 cases are reviewed for enrollment of 11-100; and 10% of cases (up to maximum of 50) are reviewed for studies enrolling more than 100 patients. Cases are selected randomly by the SCC Biostatistics Core Director and divided in a 3:7 ratio between those enrolled prior to and since the last audit. The audit process includes a review of all data forms for accuracy and completeness; outpatient and inpatient records; regulatory requirements including IRB approvals and renewals, adverse event reporting, consents, and investigational drug logs (if applicable). Following the audit, an audit report is prepared by the audit team and presented to the QASMC at the monthly meeting. Suggestions from all members of the Committee are incorporated into the final report and the report is sent to the PI. The reply from the PI is reviewed at a subsequent QASMC meeting. A summary of the audit report, PI response, and final recommendations by the QASMC are then forwarded to the PRMC for final approval.

   Materials audited include, but are not limited to, consents, protocols, regulatory approvals, participant eligibility, study management, and intervention compliance.

2. **Reportable adverse events**
   Each month, reportable adverse events (RAEs) (regardless of phase of study or sponsor) are reviewed and approved by a faculty member of the QASMC, and if there are any specific concerns, discussed at the QASMC meeting. If needed, letters requesting clarification of an RAE are sent to the PI/study coordinator following the meeting. All communications regarding review of RAEs by the QASMC are copied to the Washington University IRB, to ensure that both committees review the same information. The QASMC regularly updates the definitions of a RAE and the mechanism, timeframe, and requirements for reporting these. The CTC also has an educational program that provides training in this area.

3. **Interim data and safety monitoring (DSM) reports.**
   Data and safety monitoring reports are prepared at least semi-annually by the PI in accordance with each individual trial’s data and safety monitoring plan. These reports go beyond the RAE report in listing all adverse events, measures of efficacy, and recent literature relevant to the continued conduct of the trial. The QASMC QA auditor in the Protocol Office is available to assist principal investigators in preparing the necessary documents. Oversight of the documents is the responsibility of the QASMC. Trial PIs with DSM reports that are delinquent 30 days from the due date will receive a warning notice from the QASMC. A second warning letter is distributed at 60 days of delinquency. If the delinquent DSM report is not received within 90 days after the initial warning notice (a total of 120 days from the due date), the trial will be suspended or closed at the discretion of the QASMC with input as needed from the PRMC.

   Based upon information from the DSM reports, annual audits, and/or RAE reviews, the QASMC recommends that the study continue with no modification or that a revision is required. In the event that the QASMC feels that a revision is warranted, the Committee notifies the PI of the study. Once QASMC approval has been granted, the revisions are sent to PRMC for final approval. The
QASMC has the authority to suspend and/or close trials to patient accrual should the risk to patients be excessive or outweigh the potential benefits of the study.

**SCC 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](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 therapeutic trials, imaging studies and ancillary trials that are investigator initiated (classified as "institutional, primary"), 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.

1. **Initial Protocol Submission to PRMC**
   As a part of the submission of a cancer-related protocol to the SCC Protocol Review and Monitoring Committee (PRMC), principal investigators (PIs) estimate the target number of patients that will be enrolled by race and gender. Demographic information is provided on the PECaD website to help investigators. These projections are reviewed by the PECaD Clinical Studies Outreach team, in parallel with PRMC review so that the processing of applications through the PRMC will not be delayed. The PECaD Clinical Studies Outreach team must approve the accrual estimates prior to the protocol's submission to the IRB.

2. **Annual Renewal**
   When protocols are submitted to the PRMC for annual renewal, the Clinical Studies Outreach team reviews aggregate accrual data by gender and race for those studies that meet the criteria stated above. Each study’s accrual is compared to the overall incidence of eligible participants at Siteman Cancer Center.

   These studies receive one of the following ratings:
   - **Commendable** - Annual minority accrual that is 10% or more above the target minority accrual receives specific commendation by the SCC Senior Leadership.
   - **Satisfactory** - Annual minority accrual that is within 10% of the target minority accrual is considered "satisfactory."
   - **Needs follow-up** - Annual minority accrual that is from 10% to 30% below the target minority accrual goal as determined by the SCC disease demographics requires follow-up. PIs are contacted by PECaD to offer guidance or to facilitate assistance from appropriate SCC resources (e.g., the SCC Health Behavior, Communications & Outreach Core).
   - **Unsatisfactory** - Annual minority accrual that is more than 30% below the target minority accrual is deemed “unsatisfactory” and requires submission of a corrective action plan. A warning letter is sent to the PI if a corrective action plan has not been submitted within 90 days of renewal. If the corrective action plan has not been submitted within 30 days after the designated deadline (so a total of 120 days after it was originally due), accrual to the trial will be suspended immediately, and actions up to and including study closure will be decided by the Senior Leadership of the Siteman Cancer Center.
If a study has continued problems reaching proportional accrual, and if the PI does not demonstrate effort to improve minority accrual, PECaD may return the protocol to the full PRMC for discussion. The PRMC may then close the study immediately and/or require other remedial steps from the PI. Also for very flagrant violations, the PRMC can immediately suspended or close a study after discussion between PECaD and PRMC co-chairs. The PRMC and PECaD may also send studies to the Senior Leadership of the Siteman Cancer Center if needed.

As a part of this process, PECaD can offer guidance and link investigators to appropriate internal and community resources. Internal resources will provide assistance to SCC members at nominal cost (funded studies) or no cost (unfunded studies).

Occasionally there are studies that do not fall into these rigid guidelines. There are many unique factors within any clinical trial that can affect the level of minority participation. Therefore, PECaD will consider these factors and reserve the right to assign a rating based on all available information.

**Washington University Institutional Review Board (IRB)**

The Washington University IRB (known as the Human Research Protection Office or HRPO) reviews all research involving human subjects at the Washington University Medical Center and its affiliated hospitals. The IRB ensures that research meets ethical standards and is conducted in accordance with federal, state, and local regulations. The initial review of a cancer-related trial by the IRB can only take place after PRMC review and approval. Likewise, annual renewal and amendment requests are submitted to the IRB only after PRMC approval.

As part of the annual review process, the IRB examines trials for accrual and reviews study progress. The IRB reviews RAE reports as they are received and reviews aggregate adverse event reports annually.

**Investigator Requirements and Responsibilities**

The PI of each study is responsible for the design, conduct, and final analysis of their protocol. It is the expectation that the study PI is monitoring data and safety continuously throughout the conduct of the study. The study PI is responsible to ensure that:

- All protocols must include a data and safety monitoring (DSM) plan and procedures for its implementation.

- An additional ad hoc data and safety monitoring board (ad hoc DSMB) is established if the proposed study meets any of the following criteria:
  
  a. The study is a randomized, Phase III clinical trial.
  
  b. The study is multi-institutional.
  
  c. The study is determined to be a high-risk intervention (for example, gene therapy or high-risk cancer vaccine).
  
  d. The study includes a blinded treatment arm.
e. The study has a large expected accrual (n > 300).

Note: PIs for studies that do not meet the above criteria requiring an ad hoc DSMB may still propose to have an ad hoc DSMB if they feel it would be useful for a study.

- All studies must have a structured adverse event determination, monitoring and reporting system, including standardized forms and procedures for referring and/or treating subjects experiencing adverse events. Published forms such as AdEERS or MedWatch should be used in appropriate circumstances.

- The schedule for reporting adverse events to the ad hoc DSMB (if one is established), the QASMC, PRMC, the IRB (or IRBs in the case of multi-institutional studies), and/or the NIH or FDA must be described.

- Substantive scientific changes to a protocol must be reviewed by the PRMC as well as the IRB prior to implementation except in rare cases generally mandated by the NCI or FDA that study-specific procedures must be implemented immediately.

- Protocols must be accompanied by the proposed human subjects consent form and describe procedures for protection of human subjects.

- All blinded studies should describe a randomization scheme, and specific criteria and procedures for unblinding.

- If an independent ad hoc DSMB is required for adequate subject safety, the protocol should indicate the proposed frequency of ad hoc DSMB meetings (not less than semi-annually) and include a proposed list of data items to be provided to the ad hoc DSMB. If possible, the PI should nominate prospective ad hoc DSMB members (including a curriculum vitae or biosketch). The PRMC will assist investigators in naming qualified members of the ad hoc DSMB who are free of any conflict of interest. These nominations are subject to approval by the Chair of the QASMC and the Co-Chairs of the PRMC.

- Investigators and ad hoc DSMB members are subject to the Washington University School of Medicine policies regarding standards of conduct. Investigators and individuals invited to serve on the ad hoc DSMB will disclose any potential conflicts of interest to the trial PI and/or appropriate university officials, in accordance with institution policies. Potential conflicts that develop during a trial or a member’s tenure on a ad hoc DSMB must also be disclosed. Conflict of interest can include professional interest, financial interest, proprietary interest, and miscellaneous interest as described in the NIH Grants Policy Statement, Page II-12, and 45 CFR Part 94. Decisions concerning ad hoc DSMB membership for individuals with potential conflicts of interest will be made in accordance with institution policies.

- In specific cases where an outside agency is the sponsor of the test agent, i.e., holder of the Investigational New Drug (IND) application, PIs must submit individual adverse event reports to the funding agency (as sponsor) in accordance with agency and FDA regulations.

The Nature of Clinical Trials and Monitoring Required

The NCI Operational Definition of a Clinical Trial

For purposes of this document, a clinical trial is defined 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. By contrast, studies that do not use information from the diagnostic test in any manner that can affect the outcome of study subjects, but whose objective is only the gathering of data on the characteristics of a new diagnostic approach, are not clinical trials and are not covered by this DSM policy, unless performing the diagnostic test itself imposes some risk on study subjects.

- 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 by BSS).

The extent of the monitoring and reporting period varies by the degree of risk encountered by patients on the study, the study sponsor, the type of agent or agents involved, and the phase of the clinical trial.

Given the great diversity of clinical trials underway at the Siteman Cancer Center, trial data and safety monitoring, by necessity, reflects that diversity. The SCC’s Data and Safety Monitoring Plan is tailored to (1) ensure monitoring of all clinical trials, (2) meet the reporting requirements of individual trial sponsors, and (3) eliminate excessive or redundant monitoring and reporting.

The individual trial sponsor or sponsoring group dictates data and safety monitoring and reporting. Trial sponsors include the National Institutes of Health, National Cancer Institute, drug and medical device industries, the SCC, and/or the individual departments of the Washington University School of Medicine (WUSM).

Sponsor: National Institutes of Health

The National Institutes of Health sponsor trials at the Siteman Cancer Center using a number of mechanisms, each with their particular data and safety monitoring requirements. The primary mechanisms are national cooperative oncology group grants and contracts, P01 (program project) grants, R01 grants, R21 grants, and Quick-trial (specialized R21) grants.

National Cooperative Oncology Groups

The SCC conducts clinical trials of the American College of Radiology Imaging Network (ACRIN), the American College of Surgery Oncology Group (ACOSOG), the AIDS Malignancy Consortium (AMC), the Cancer and Leukemia Group B (CALGB), the Children’s Oncology Group (COG), the Gynecologic Oncology Group (GOG), the National Surgical Adjuvant Breast and Bowel Project
Each of these national groups conducts a range of therapeutic (phase I, II, and III) and non-therapeutic clinical trials. Arrangements (grant, contract, or consortium) with the PIs (all of whom are SCC research members or clinicians) clearly specify the data and safety monitoring requirements for each study. Since these trials are multi-institutional, specific data management systems using a variety of computer and communications technology allow safety and efficacy data to be closely monitored for each study by site and for the group as a whole. The SCC does not place additional reporting requirements on staff supporting these trials, but relies on mandated reporting mechanisms to monitor patients on these studies.

Nevertheless, all RAES on subjects enrolled in SCC trials are required to be reported to the QASMC and IRB. Aggregate RAES reports from multi-institutional trials also need to be submitted when received. As such, these RAES are included in the monthly RAES report generated by the QASMC coordinator for review by the QASMC. Based on local or national/external RAES reported, the QASMC or the Washington University IRB has the authority to close any active study to further local accrual and/or require more detailed reporting of RAES observed and mandate steps that need to be taken to minimize patient risk and maximize the safety of participating patients.

**Other NCI Grants and Contracts (e.g. Quicktrials, R21)**

In the event a Siteman Cancer Center PI conducts a trial under the auspices of a grant or contract from the NCI, each protocol will include specific plans for data and safety monitoring using established NCI data and safety monitoring systems. For example, if a PI is testing an investigational new drug for which the IND is held by the NCI, the CDUS and AdEERS reporting system should be used. A matrix of reporting requirements and schedules is available at the CTEP website at [http://ctep.info.nih.gov](http://ctep.info.nih.gov). Reporting requirements and timing of reporting are dependent upon the phase of trial, grade of adverse event, attribution, and whether the event is expected or unexpected.

Nevertheless, all RAES on subjects enrolled in SCC trials are required to be reported to the QASMC and IRB. Aggregate RAES reports from multi-institutional trials also need to be submitted when received. Based on local or national/external RAES reported, the QASMC or the Washington University IRB has the authority to close any active study to further local accrual and/or require more detailed reporting of RAES observed and mandate steps that need to be taken to minimize patient risk and maximize the safety of participating patients.

Local monitoring is reviewed and approved by the PRMC on a study-by-study basis. Any action taken by the QASMC, PRMC, IRB, sponsor, or the investigator him/herself resulting in temporary or permanent suspension of an NCI funded clinical trial must be reported to the NCI grant program director responsible for the grant. These actions include for example, any FDA actions that affect NCI funded trials.

For all NIH-sponsored trials, prior to the IRB expiration date, the local PI must submit a renewal report to the PRMC and IRB that states the number of patients entered on the trial (at WUMC and overall); the race, sex, and ethnicity of enrolled subjects; the number of patients treated; and a summary of RAES reported to date. The QASMC will review semi-annual data and safety monitoring reports and make recommendations on whether the study should continue unchanged, be closed based on unacceptable risk to participants, or be suspended while protocol changes are requested of the study sponsor. Literature reporting significant developments that may affect the safety of participants or the ethics of the study should be submitted to the QASMC as soon as the PI or study staff becomes aware of it.
**Sponsor: Industry**

All clinical trials conceived and initiated by drug and medical device industry sponsors with subsequent SCC participation require data and safety monitoring plans that have been reviewed and approved by both the PRMC and Washington University IRB. These protocol-specific plans must adhere to industry and FDA-specified guidelines. Local reporting for data and safety monitoring for industry-sponsored trials requires RAEs to be reported to the QASMC coordinator and IRB using either industry-specified report formats or the FDA MedWatch reporting form.

The QASMC coordinator distributes RAEs to the members of the QASMC once per month for review. Aggregate adverse event (AE) reports are forwarded to the QASMC as they become available (in the same way as individual AEs) and are included in the same way as individual AEs for standard reports.

Prior to the IRB expiration date, the local PI must submit a renewal report to the PRMC and IRB that states the number of patients entered on the trial (at WUMC and overall); the race, sex, and ethnicity of enrolled subjects; the number of patients treated; and a summary of RAEs reported to date. Literature reporting significant developments that may affect the safety of participants or the ethics of the study should be submitted to the QASMC as soon as the PI or study staff becomes aware of it.

**Sponsor: Consortium Trials**

Therapeutic clinical trials often require more patients than a single institution would be able to enroll. This has led to the formation of collaborative agreements between investigators and institutions to conduct studies in a multi-institutional setting. A notable example is that of the national cooperative oncology groups. However, collaborative consortia of investigators interested in specific diseases and modalities exist outside the usual cooperative group system. Trials conducted in these settings may not have been subjected to the rigorous review and reporting requirements imposed by NIH funding. As noted previously, investigators must be aware of NIH policy "Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials" (NIH Guide for Grants and Contracts, June 11, 1999), "NIH Policy on Data and Safety Monitoring" (NIH Guide for Grants and Contracts, June 10, 1998), and "Further Guidance on a Data and Safety Monitoring for Phase I and Phase II Trials" (NIH Guide for Grants and Contracts, June 5, 2000). All of these documents are relevant to multi-institutional trials. Multi-institutional, collaborative consortia trials managed by Siteman Cancer Center investigators must have a study-specific DSM plan and ad hoc DSMB that requires RAE reporting from all sites to the PI, distribution of RAE reports to all participating sites, and preparation of semi-annual DSM reports that summarize the adverse events and responses (when appropriate) from all sites. Multi-institutional, collaborative consortia trials led and managed by investigators who are outside of Siteman Cancer Center, Washington University, and Barnes-Jewish Hospital (e.g., the overall study PI is at another cancer center) should have a similar DSM plan. However, a Siteman Cancer Center ad hoc DSMB is not required, and monitoring will be overseen by the QASMC in its role as SCC DSMC.

Prior to the IRB expiration date, the local PI must submit a renewal report to the PRMC and IRB that states the number of patients entered on the trial (at WUMC and overall); the race, sex, and ethnicity of enrolled subjects; the number of patients treated; and a summary of RAEs reported to date. Literature reporting significant developments that may affect the safety of participants or the ethics of the study should be submitted to the QASMC as soon as the PI or study staff becomes aware of it.
**Sponsor: Local, Investigator-Initiated Studies**

Local, investigator-initiated studies, which include many studies with NIH sponsorship, often rely only upon SCC Research Development Grant support, local departmental funding, American Cancer Society Institutional Research Grant support, or limited industry funding. Since these trials frequently have no external requirements for data and safety monitoring, they require particular attention for local monitoring. These studies receive the highest priority for local oversight.

Local, investigator-initiated trials include studies that may receive partial or full external funding. Each such study is reviewed by the PRMC to determine if data and safety monitoring plans are complete and appropriate. In the event that no monitoring is specified by external agencies, the study PI is required to develop a local data and safety monitoring plan that adheres to the following plans based on the phase of trial.

**Overall PRMC Responsibilities**

Prior to activation of any local, investigator-initiated trial, the PRMC and the IRB review the risks of the intervention proposed in the protocol. For protocols including interventions that could cause potential harm, if any required information is missing in the protocol, the PRMC Co-Chairs or the IRB will notify the PI of what items are missing and indicate that the SCC will not activate the study until this information is received, reviewed, and approved by the PRMC and IRB.

If the study is approved by the PRMC on scientific grounds and the PI has not proposed an *ad hoc* DSMB, the PRMC will determine whether or not an *ad hoc* DSMB is required for adequate subject safety. If an *ad hoc* DSMB is required, the PRMC will request the PI to nominate an *ad hoc* DSMB with an appropriate monitoring plan.

**Prior to protocol approval and activation, the PRMC must:**

- Review and approve the protocol data and safety monitoring plan.
- Institute any other appropriate conditions needed for subject safety (e.g. data reporting formats and schedules, restrictions on expenditure of funds pending completion of particular activities).

**Following protocol activation, the PRMC:**

- At least annually (and more frequently if necessary), reviews rationale for continuation of study, and terminates the study if recommended by the QASMC, the *ad hoc* DSMB, the IRB and/or the SCC Director (e.g., inadequate recruitment, retention or compliance, or excessive adverse events).
- The following policy was approved by the Siteman Senior Leadership at the May 25, 2010 meeting.

  *The official registering physician ("registering MD") is the physician who signs the patient consent. This is the person documented as overseeing explanation, eligibility assessment, and the overall consent process for the patient.*

**Following protocol activation (and on a continuing basis), the QASMC:**

- Requests additional data from investigators as needed on safety issues arising over the course of the study.
• Monitors that the protocol receives appropriate annual (or more frequent) review by the IRB.

The QASMC semi-annually (every six months):

For trials without an ad hoc DSMB:

• Reviews the DSM reports submitted by the PI to the QASMC coordinator.

For trials with an ad hoc DSMB:

• Reviews DSM reports (or more frequently if additional ad hoc DSMB meetings are needed for a particular study) submitted by the ad hoc DSMB to the QASMC coordinator.

The QASMC annually (every year):

• Determines the necessity to perform and review QA audits based on accrual, performance, and risk. Risk is assessed on a study-specific basis, and implemented based on frequency of audit required. For example, early phase studies that involve first-in-human drugs or devices; gene therapy, and other particularly novel interventions are generally audited more frequently than studies, such as diagnostic imaging.

Phase I Studies

These studies involve limited numbers of subjects (usually fewer than 30) to determine a safe and maximum tolerated dose of drug/regimen and evaluate adverse events/toxicity. Occasionally, phase I trials evaluate feasibility endpoints in the case of medical devices and procedures. Nevertheless, due to the unknown safety and relatively high risk to the patient of the agent, regimen, or device/procedure under study, these trials require particular attention in monitoring patient safety.

For phase I studies, the PRMC requires the study PI to provide regular monitoring of patient safety. The study PI must provide a monitoring report to the QASMC coordinator every 6 months, or, for early Phase I studies of agents with little existing data on toxicity that may pose higher risks to patients, the PRMC, and the QASMC may require more frequent reporting. The frequency of reporting is determined on a protocol-by-protocol basis. The data to be reported includes summary data similar to those submitted by investigators using the NIH/NCI CDUS reporting system. The QASMC reviews these semi-annual reports and recommends that the study continue with no modification or that a revision is required. In the event that the QASMC feels that a revision is warranted, the Committee notifies the PI of the study. Once QASMC approval has been granted, the revisions are sent to PRMC for final approval. The QASMC has the authority to suspend and/or close trials to patient accrual should the risk to patients be excessive or outweigh the potential benefits of the study.

The reporting schedule for individual trials may be modified over the course of the study based on the safety experience of patients treated. Studies under a semi-annual schedule may be required to initiate more frequent reporting should the rate of accrual, frequency or severity of adverse events so warrant. However, due to the dose escalation nature of phase I studies, trials initiated with a monthly reporting schedule should only rarely have the reporting period lengthened.
In the event of an RAE experienced by a patient on a local, investigator-initiated phase I trial, the study PI is required to report the RAE to the QASMC, IRB, study sponsor (if applicable), and FDA (if applicable) using appropriate reporting forms and guidelines.

For each local phase I trial at the Siteman Cancer Center, the study PI is required to submit information on patients entered on the trial overall); the race, sex, and ethnicity of enrolled subjects; the number of patients treated; a summary of all adverse events reported to date; a specific list of serious adverse events requiring immediate reporting; and significant literature (if applicable) reporting developments that may affect the safety of participants or the ethics of the study. The QASMC coordinator forwards these interim reports to the QASMC.

**Phase II**

Phase II studies also involve limited numbers of patients (usually fewer than 50) to assess the efficacy of an agent, regimen, device, or procedure. While more is known concerning the risks and benefits of the study treatment as compared to Phase I studies, more patients are exposed to the study regimen. The disease process often confounds assessment of toxicity and outcomes. While some variation may exist in monitoring, the PRMC will normally require PIs of local, investigator-initiated phase II studies to provide regular monitoring of patient safety with at least semi-annual reporting of summary data to the QASMC coordinator for QASMC review.

For each local phase II trial at the Siteman Cancer Center, the study PI is required to submit information on patients entered on the trial overall); the race, sex, and ethnicity of enrolled subjects; the number of patients treated; a summary of all adverse events reported to date; a specific list of serious adverse events requiring immediate reporting; and significant literature (if applicable) reporting developments that may affect the safety of participants or the ethics of the study. The QASMC coordinator forwards these interim reports to the QASMC.

The QASMC reviews these semi-annual reports and recommends that the study continue with no modification or that a revision is required. In the event that the QASMC feels that a revision is warranted, the Committee notifies the PI of the study. Once QASMC approval has been granted, the revisions are sent to PRMC for final approval. The QASMC has the authority to suspend and/or close trials to patient accrual should the risk to patients be excessive or outweigh the potential benefits of the study.

In the event of an RAE experienced by a patient on a local, investigator-initiated phase I trial, the study PI is required to report the RAE to the QASMC, IRB, study sponsor (if applicable), and FDA (if applicable) using appropriate reporting forms and guidelines.

**Phase III**

The large number of patients required for comparative randomized phase III trials dictates special concerns in ensuring patient safety. While the risk to individual patients may be less than that encountered in phase I and II trials, the longer period of treatment and exposure to investigational regimens may pose significant risks to patients.

Commensurate with risk, all local phase III clinical trials require the establishment of an independent ad hoc Data and Safety Monitoring Board (ad hoc DSMB) prior to the initiation. Members of an ad hoc DSMB may not be associated with the trial. The PRMC requires the PI to nominate an ad hoc DSMB with an appropriate monitoring plan described in the section on “Investigator Requirements and Responsibilities.”
Multi-institutional, collaborative consortia trials managed by Siteman Cancer Center investigators must have a study-specific *ad hoc* DSMB and a DSM plan that requires RAE reporting from all sites to the PI, distribution of RAE reports to all participating sites, and preparation of semi-annual DSM reports that summarize the adverse events and responses (when appropriate) from all sites. Multi-institutional, collaborative consortia trials led and managed by investigators who are outside of Siteman Cancer Center, Washington University, and Barnes-Jewish Hospital (e.g., the overall study PI is at another cancer center) should have a similar DSM plan. However, a Siteman Cancer Center *ad hoc* DSMB is not required, and monitoring will be overseen by the QASMC in its role as SCC DSCM.

The following policies describe Siteman Cancer Center requirements for local, investigator-initiated Phase III trials. They do not replace existing regulations on protection of human subjects, policies and guidelines for conduct of clinical research, inclusion of women and minorities, research project administration, reporting, and financial management, or requirements of local Institutional Review Boards (IRBs). DHHS regulations for the protection of human subjects are described in 45 CFR46. The implementation of these regulations for PHS research grants involving human subjects is found in the PHS 398 form, available on the NIH home page (http://www.nih.gov/grants/forms.htm). This policy document describes further steps to be taken to ensure the protection of human subjects when the study involves a potentially harmful intervention, and for other phase III studies to ensure that participants receive an appropriate share of the benefits. In individual cases, the Siteman Cancer Center may find it beneficial to have additional levels of involvement or oversight beyond those described in these policies.

Therapeutic protocols should state (on the IRB submission form) whether the proposed study intervention could have harmful effects and the basis for that opinion. The PRMC will review the risks of the intervention then forward it to the Washington University IRB for review and approval. If the proposal for a study with a potentially hazardous intervention does not include the required information for such studies (described below), the PRMC will forward the protocol to the Washington University IRB until this information is received, reviewed, and approved. The PRMC may obtain additional consultation from Siteman Cancer Center staff, QASMC, or external advisors.

The QASMC reviews these semi-annual reports and recommends that the study continue with no modification or that a revision is required. In the event that the QASMC feels that a revision is warranted, the Committee notifies the PI of the study. Once QASMC approval has been granted, the revisions are sent to PRMC for final approval. The QASMC has the authority to suspend and/or close trials to patient accrual should the risk to patients be excessive or outweigh the potential benefits of the study.

Protocols for any intervention study should clearly state whether the proposed study meets NIH's criteria for a NIH-defined Phase III trial and the basis for that opinion. The PRMC Chair will review this information. If the protocol deemed by the PRMC to be a Phase III trial does not include the required information for such studies (described below), the protocol will not be approved and activated until this information is received and reviewed by the PRMC Chair.

*Ad Hoc Data and Safety Monitoring Board (Ad hoc DSMBs)* [Note: only applies to phase III studies]

*Ad hoc* DSMB membership:
An ad hoc DSMB consists of no fewer than 3 members including 2 clinical investigators and a biostatistician who are not involved with the study. The PRMC reserves the right to appoint additional members to an ad hoc DSMB to include scientific expertise in topic areas relevant to the trial such as biostatistics, ethics, or patient advocacy.

The PRMC assists investigators in identifying qualified members of the ad hoc DSMB who are free of any conflict of interest. These nominations are subject to approval by the Chair of the QASM C and the Co-Chairs of the PRMC.

Like investigators, ad hoc DSMB members are subject to the Washington University Medical School policies regarding standards of conduct. Individuals invited to serve on the ad hoc DSMB must disclose any potential conflicts of interest, including financial conflicts, to the trial PI and/or appropriate university officials in accordance with institution policies. Potential conflicts that develop during a trial or a member's tenure on an ad hoc DSMB must also be disclosed.

Ad Hoc DSMB Responsibilities:

The ad hoc DSMB must meet on a regular schedule (not less than twice a year) over the course of study (with additional meetings as needed) to:

- Review data (including blinded data) over the course of the trial relating to efficacy, recruitment, randomization, compliance, retention, protocol adherence, trials operating procedures, forms completion, intervention effects, gender and minority inclusion, and subject safety.

- Identify problems relating to safety over the course of the study. Inform study PI via written report who in turn will ensure that all clinical collaborative site PIs receive this report.

- Identify needs for additional data relevant to safety issues and request these data from the study investigators.

- Propose appropriate analyses and periodically review developing data on safety and endpoints.

- At each meeting, consider the rationale for continuation of the study, with respect to recruitment, progress of randomization, retention, protocol adherence and compliance, data management, safety issues, outcome data, if relevant, and make a recommendation for or against continuation of the trial.

- Provide the PI, QASMC, and PRMC written reports following each ad hoc DSMB meeting. The PI will then forward the report to the IRB at the time of the trial annual renewal, or immediately if any urgent needs or problems are identified.

- Provide advice on issues regarding data discrepancies found by the data auditing system or other sources. If the QASMC Chair requests this advice, it should be provided by the ad hoc DSMB in writing within one month of the date of the request.

- If there is more than one clinical site, the study PI is responsible for sending the reports to individual site PIs, who in turn are required to distribute the report to their local IRBs, as detailed in the NIH "Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials" (NIH Guide for Grants and Contracts, June 11, 1999).
**Ad Hoc DSMB Meetings**

*Ad hoc* DSMB meeting coordination is the responsibility of the research team. Data must be provided to the *ad hoc* DSMB members by the research team prior to the meeting. *Ad hoc* DSMB meetings will be divided into an opened and closed session. First is an open session during which members of the clinical trial team may be present, at the request of the *ad hoc* DSMB, to review the conduct of the trial and to answer questions from members of the *ad hoc* DSMB. Issues discussed may include accrual, protocol compliance, and general toxicity. Outcome results must not be discussed during the open session. Following the open session, a closed session involving the *ad hoc* DSMB and study statistical staff will be held to allow the *ad hoc* DSMB opportunity to discuss the general conduct of the trial and all outcome results, including toxicities and adverse events, develop recommendations, and take votes as necessary.

**Ad Hoc DSMB Recommendations**

*Ad hoc* DSMB recommendations should be based on results for the trial being monitored as well as on data available to the *ad hoc* DSMB from other studies. It is the responsibility of the PI to ensure that the *ad hoc* DSMB is kept apprised of non-confidential results from other related studies that become available. It is the responsibility of the *ad hoc* DSMB to determine the extent to which this information is relevant to its decisions related to the specific trial being monitored.

A written copy of *ad hoc* DSMB recommendation(s) is given to the trial PI and QASMC and PRMC. If the *ad hoc* DSMB recommends that a study be changed for patient safety or efficacy reasons, or that a study be closed early because of slow accrual, the trial PI must act to implement the change as expeditiously as possible. In the unlikely situation that the trial PI does not concur with the *ad hoc* DSMB, then the PRMC Co-Chairs must be informed of the reason for disagreement. The trial PI, *ad hoc* DSMB Chair, and the QASMC Chair will be responsible for reaching a mutually acceptable decision about the study. Confidentiality must be maintained during these discussions (see confidentiality below). However, in some cases, relevant data may be shared with other selected trial investigators and/or PRMC members to seek advice to assist in reaching a mutually acceptable decision. The SCC Director holds ultimate decision making authority if this group cannot reach a mutually acceptable agreement.

If a recommendation is made to change a trial for reasons other than patient safety or efficacy reasons or for slow accrual, the *ad hoc* DSMB will provide an adequate rationale for its decision.

Confidentiality: All *ad hoc* DSMB discussions and decisions are confidential. The integrity of this safeguarded information is maintained by double-locking of all hard-copy materials and role-restricted, password-protected access to electronic materials.

**Release of Outcome Data**

In general, outcome data should not be made available to individuals outside of the *ad hoc* DSMB until accrual has been completed and all patients have completed their treatment. At this time, the *ad hoc* DSMB may approve the release of outcome data on a confidential basis to the trial PI for planning the preparation of manuscripts and/or to a small number of other investigators for purposes of planning future trials. Any release of outcome data prior to the *ad hoc* DSMB’s recommendation for general dissemination of results must be reviewed and approved by the *ad hoc* DSMB.
Confidentiality Procedures

No communication, either written or verbal, of the deliberations or recommendations of the ad hoc DSMB will be made outside of the ad hoc DSMB except as provided for in this policy. Outcome results are strictly confidential and must not be divulged to any non-member of the ad hoc DSMB. Each member of the ad hoc DSMB including non-voting members must sign a statement of confidentiality.

Conflict of Interest

Ad hoc DSMB members are subject to the Washington University Medical School and Siteman Cancer Center policies regarding standards of conduct. Individuals invited to serve on the ad hoc DSMB as either voting or non-voting members will disclose any potential conflicts of interest, including financial interests, whether real or perceived, to the trial PI and the appropriate SCC official(s), in accordance with the institution's policies. Conflict of interest can include professional interest, proprietary interest, and miscellaneous interest as described in the NIH Grants Policy Statement, Page II-12, and 45 CFR Part 94. Potential conflicts that develop during a member's tenure on an ad hoc DSMB must also be disclosed. Decisions concerning whether individuals with potential conflicts of interest or the appearance of conflicts of interest may participate in a ad hoc DSMB are made in accordance with the institution's policies.

A Principal investigator, co-investigators, and any member of the study team may be present during general discussion of protocols at PRMC and QASMC meetings. However, a study PI, co-investigators, and any member of the study team must leave the room for final discussion, deliberation, and voting.

IRB Review and Approval of Data and Safety Monitoring Plans

According to NIH policy, individual protocol data and safety monitoring plans require Washington University IRB review and approval.
Sitemap Cancer Center Data and Safety Monitoring Plan Reporting

Summary

**PI**
- Ongoing trial management

**Working Groups (all trials)**
- Preliminary Study Prioritization

**PRMC (all trials)**
- Initial clinical trial review and approval
  - Scientific focus
- Annual review and renewal
  - Scientific focus
- Study amendments
  - Scientific focus
- Power to close studies
- Study Prioritization

**WUMC Human Research Protection Office (IRB)** (all trials)
- Initial clinical trial review and approval
  - Safety and ethical focus
- Annual review and renewal
  - Safety and ethical focus
- Study amendments
  - Safety and ethical focus

**QASMC (all trials) [the SCC DSMC]**
- Adverse event monitoring
- Safety monitoring
- Audit review
- DSM report review
- Power to close studies

**Ad Hoc DSMBs**
- Trial-specific oversight
- Trial management
- Safety monitoring
- Efficacy review

Communication