UNIVERSITY OF MINNESOTA
MASONIC CANCER CENTER

DATA AND SAFETY MONITORING PLAN

Douglas Yee, M.D.
Director, Masonic Cancer Center
University of Minnesota

1.17.2012
**TABLE OF CONTENTS**

Executive Summary ................................................................................................................................. 3  
Accountability Units ............................................................................................................................... 4  
  1. Principal Investigator Responsibilities ............................................................................................. 4  
    1.1 Required Training .......................................................................................................................... 4  
    1.2 Protocol Design ............................................................................................................................ 4  
    1.3 Risk Assessment Plan .................................................................................................................... 4  
    1.4 Conflict of Interest ....................................................................................................................... 5  
    1.5 Trial Conduct ............................................................................................................................... 5  
    1.6 Required Reporting ....................................................................................................................... 5  
    1.7 Affiliate Site Management ............................................................................................................ 6  
    1.8 Trials Conducted Under an IND/IDE ............................................................................................ 6  
  2. Masonic Cancer Center Oversight ....................................................................................................... 6  
    2.1 Clinical Research Leadership Committee ...................................................................................... 6  
    2.2 Cancer Protocol Review Committee ............................................................................................ 6  
    2.3 Data and Safety Monitoring Council ........................................................................................... 7  
  3. University Oversight .......................................................................................................................... 8  
    3.1 PI Research Education Requirements ........................................................................................... 8  
    3.2 Institutional Review Board ........................................................................................................... 8  
    3.3 IND/IDE Oversight ........................................................................................................................ 9  
Oversight Processes ................................................................................................................................. 9  
  4. Monitoring Clinical Trials .................................................................................................................. 9  
    4.1 Monitoring Oversight ..................................................................................................................... 9  
    4.2 Monitoring Activities .................................................................................................................... 9  
    4.3 Monitoring Scope .......................................................................................................................... 10  
    4.4 Monitoring Extent and Frequency ................................................................................................. 10  
  5. Quality Assurance and Compliance Audits ....................................................................................... 11  
    5.1 Annual Audit Plan ......................................................................................................................... 11  
    5.2 Audit Findings ............................................................................................................................... 11  
Administrative Infrastructure .................................................................................................................. 12  
Definitions .................................................................................................................................................. 12  
Attachments ............................................................................................................................................. 14  
  Attachment 1: Clinical Trials Process ................................................................................................. 14  
  Attachment 2: Masonic Cancer Center Organizational Chart ......................................................... 15  
  Attachment 3: MCC Risk Assessment Checklist .................................................................................. 16  
  Attachment 4: Serious Adverse Event Reporting SOP ....................................................................... 17  
  Attachment 5: Masonic Cancer Center Affiliate Procedures Manual ............................................... 22  
  Attachment 6: MCC Clinical Trials Monitoring Plan ........................................................................... 49  
  Attachment 7: CRS Request for Services Form .................................................................................. 57
EXECUTIVE SUMMARY

The Masonic Cancer Center (MCC) at the University of Minnesota (UMN) places the utmost importance on minimizing risk for the individuals participating in cancer related investigations. The primary responsibility for ensuring this safety is held by the principal investigator (PI) for the clinical trial. This data and safety monitoring plan outlines the roles and responsibilities of the principal investigator, Masonic Cancer Center and the University of Minnesota in maintaining the safety of cancer related clinical investigations. Diagrams of the clinical trial process and MCC's organizational structure are found in Attachment 1: Clinical Trial Process and Attachment 2: Masonic Cancer Center Organizational Chart.

The MCC Data and Safety Monitoring Plan (DSMP) details the roles and responsibilities of the three accountable units (PI, MCC and UMN) and the processes that are utilized by these accountable units to ensure the highest quality clinical research is conducted while optimizing participant safety.

The PI is responsible for all aspects of trial conduct including clinical trial management, data acquisition and data and safety monitoring. The PI is responsible for the risk assessment of the trial. The monitoring and oversight of clinical trial conduct is directly based on risk assessment. This DSMP provides the detail necessary for the PI to provide the oversight necessary for compliance with local and federal regulations.

The Masonic Cancer Center has the responsibility of clinical research oversight through the Clinical Research Leadership (CRL) Committee. This committee has the authority to independently close clinical trials; however, the committee mainly delegates the responsibility for oversight of clinical research to the Cancer Protocol Review Committee (CPRC) and the Data and Safety Monitoring Council (DSMC) of the Masonic Cancer Center. The CPRC has the role of assessing scientific merit, confirming trial risk and prioritization of clinical trial conduct within the Masonic Cancer Center. The DSMC has the responsibility of ensuring the safe conduct of clinical trials and compliance with trial data and safety monitoring plans.

The Masonic Cancer Center exists and functions within the structure of the UMN and as such is subject to the University’s conflict of interest guidelines and regulatory standards. Links to these guidance documents are provided in the DSMP.
ACCOUNTABILITY UNITS

1. PRINCIPAL INVESTIGATOR RESPONSIBILITIES

The Masonic Cancer Center at the University of Minnesota places the highest priority on minimizing risk to individuals participating in cancer-related research. The PI of a clinical trial is responsible for the adequacy of the design and oversight of the trial. The PI holds full responsibility for personally conducting or supervising the conduct of the clinical study, including all clinical and regulatory activities.

The PI of a clinical trial may delegate tasks, but not responsibilities.

Principal Investigators must be aware of the specific responsibilities they undertake when conducting research. These responsibilities include all actions taken by anyone acting on the PI’s behalf, members of the research team, or any organization to whom the PI delegates tasks and activities. Regardless of who carries out a study-related activity, the PI is accountable for how the task is conducted.

1.1 REQUIRED TRAINING

UMN Required Training:

The University of Minnesota requires PIs to complete training in Human Subjects Protection and Responsible Conduct of Research per section 3.1 of the DSMP.

MCC Required Training:

Masonic Cancer Center requires PIs to attend a Fundamentals of Clinical Research educational session which is offered twice yearly, beginning in January 2013. PIs are required to attend this training within 6 months of submission of their first clinical trial concept.

1.2 PROTOCOL DESIGN

The PI must ensure the protocol contains an adequate data and safety monitoring plan prior to submission to the Cancer Protocol Review Committee. The protocol data and safety monitoring plan must include, but is not limited to the elements listed below. The data and safety monitoring plan or a supplemental protocol document must specify who is responsible for conducting onsite monitoring, extent, frequency, and scope.

- Management, quality assurance, storage, and access to data
- Adverse event collection and reporting
- Dose limiting toxicity
- Stopping rules

1.3 RISK ASSESSMENT PLAN

For investigator-initiated trials, in addition to the above, the PI is responsible for determining a trial’s level of risk prior to CPRC submission. Risk is determined by multiple factors including, but not limited to: trial phase, expected toxicities, conflict of interest, trial complexity, whether the trial is conducted under an IND/IDE, and PI experience.
leading clinical trials. Assigned trial risk determines if a trial meets the requirements for clinical trial monitoring and the frequency of DSMC review. (see Attachment 3: MCC Risk Assessment Checklist)

### 1.4 CONFLICT OF INTEREST

The potential for a conflict of interest arises when a member of the study team is in a position to influence research decisions or trial conduct in ways that could lead directly or indirectly to financial gain or advantage for the study team member or his or her family.

The UMN has established mechanisms to identify and manage potential conflicts, including annual disclosure requirements, research and sponsored project application questions, and informal communications. [http://www.compliance.umn.edu/conflictHome.htm](http://www.compliance.umn.edu/conflictHome.htm)

### 1.5 TRIAL CONDUCT

Prior to implementing a trial, the PI must receive written approvals from the CPRC, Institutional Review Board (IRB), and Food and Drug Administration (FDA) if applicable. If the PI is a member of any of the approval committees, the PI must recuse himself/herself from the review and vote. The PI must ensure the trial is conducted according to the approved protocol and relevant regulations. To adequately conduct and supervise the conduct of the trial, the PI must:

- Know and follow MCC and University requirements and applicable FDA regulations
- Ensure all study staff including investigators complete and document protocol training prior to conducting any protocol-related activity
- Ensure a delegation of authority log remains current throughout the trial
- Ensure continued scientific and clinical relevance and validity of the trial

### 1.6 REQUIRED REPORTING

The PI is responsible for ensuring the following reports are submitted appropriately and within their required timeframes:

- SAE reports, including events that occur at affiliate and satellite sites (see Attachment 4: Serious Adverse Event Reporting SOP)
  - Must submit to: IRB, FDA, DSMC SAE Coordinator, sponsor
- Protocol amendments
  - Must submit to: IRB, FDA, CPRC, sponsor
- Continuing review applications
  - Must submit to: IRB, FDA, CPRC
- DSMC progress reports
  - Must submit to: DSMC
- Suspension or termination of trial for safety or non-compliance
  - Must submit to: IRB, CPRC, FDA, DSMC, CRL, sponsor, NCI Program Director responsible for funding the trials
1.7 AFFILIATE SITE MANAGEMENT

Affiliate sites participation in investigator-initiated studies is the direct responsibility of the study PI. (see Attachment 5: Masonic Cancer Center Affiliate Procedures Manual)

1.8 TRIALS CONDUCTED UNDER AN IND/IDE

A PI who holds an IND/IDE holds all PI obligations as well as all sponsor responsibilities, including all commitments outlined in FDA Form 1572 or the Protocol Statement. [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312&showFR=1&subpartNode=21:5.0.1.1.3.4]

2. MASONIC CANCER CENTER OVERSIGHT

2.1 CLINICAL RESEARCH LEADERSHIP COMMITTEE

Responsibility:

The MCC’s CRL is responsible for overseeing all cancer-related clinical research. CRL membership includes: MCC Director*; Deputy Director*; Associate Directors for Administration*, Experimental Therapeutics*, and Cancer Prevention and Control*; CPRC Chairs; DSMC Chair; Clinical Research Services (CRS) Director; CRS Program Manager*; Biostatistics Core Leader; Director of Finance and Operations; and representatives from Pediatric Oncology and Blood and Marrow Transplant Program. (* Executive CRL membership) The CRL meets monthly and its responsibilities include:

- Approving the Masonic Cancer Center’s Data and Safety Monitoring Plan
- Appointing the committee chairs and membership for the Data Safety and Monitoring Council and Cancer Protocol Review Committees
- Semi-annually reviewing both CPRC and DSMC action summaries

The CRL Chair or CRL Executive Committee may take immediate action to suspend or close a trial if there appears to be excessive risk to subjects or the institution.

2.2 CANCER PROTOCOL REVIEW COMMITTEE

Responsibility:

The CPRC is responsible for reviewing cancer-related clinical trials for scientific merit and prioritizing protocols within the MCC. To ensure safety oversight throughout a trial, the CPRC must ensure the protocol data and safety monitoring plan includes all required elements, as referenced in section 1.2 of the DSMP. In addition, for investigator-initiated trials, the CPRC must confirm the assigned trial risk determined by the PI per section 1.3 of the DSMP.
The CPRC reviews all cancer-related protocols prior to IRB submission and continues to evaluate the scientific merit, priority, and progress towards accrual at least annually as long as a trial remains open to accrual.

The CPRC must close a trial to further accrual if the study:

- Is unlikely to meet its enrollment goal in the required timeframe
- No longer has scientific relevance

Membership:

The CPRC is a multidisciplinary committee whose members’ expertise includes Medical Oncology, Biostatistics, Epidemiology, Pharmacy, Surgical Oncology, Nursing, and others. Members are selected by area of expertise to form a diversified group of clinicians and other professionals able to provide rigorous scientific review of study rationale and design.

Conflict of Interest:

To preclude any conflicts of interest, when a member of the CPRC is the PI of a protocol under review, the member is recused from participating in the review and vote.

2.3 DATA AND SAFETY MONITORING COUNCIL

Responsibility:

The DSMC provides ongoing data and safety oversight for investigator-initiated clinical trials in the MCC. The DSMC reviews trial progress reports to assess trial conduct and safety-related events and to determine if the potential benefit to subjects continues to outweigh the risks. The frequency of DSMC review is based on the trial risk determined by the PI and confirmed by the CPRC per sections 1.3 and 2.2 of the DSMP.

The DSMC has authority to request clinical trial monitoring or DSMC review at more frequent intervals.

DSMC clinical trial reviews:

The DSMC reviews all investigator-initiated clinical trials at least annually from the time a protocol is opened to accrual until it is closed with the IRB. These trial progress reports cover trial activity at the Masonic Cancer Center and, if applicable, any affiliate site(s) and include:

- Assessment of expectancy, attribution, and seriousness of adverse events
- Monitoring findings
- Independent notification of safety concerns from the IRB, CPRC, CRL, PI, or local research community in its review

If the DSMC identifies serious safety concerns, the Chair communicates these in writing to the trial PI with a specified timeframe for the PI to respond or resolve the issues, or requests a for cause audit to be conducted of the trial.
Suspending or Closing trials:

The DSMC has the authority and responsibility to suspend or close a trial if the risk to subjects or the institution seems excessive relative to the benefit to the subject. The full DSMC or the DSMC Chair acting independently may temporarily close a trial. The full vote of the DSMC is required to permanently close a trial.

When the DSMC or DSMC chair rules to temporarily or permanently close a trial, the trial PI must communicate the decision to the CRL, CPRC, IRB, NCI Program Director, and, if applicable, the sponsor, FDA, or other appropriate bodies.

Serious Adverse Event (SAE) Review:

The DSMC reviews all SAE reports regardless of trial sponsor type or risk category to ensure that protocol and regulatory reporting requirements have been met. The PI is required to submit a corrective action plan if the number of SAE reports deficient in meeting these requirements is unacceptable.

Membership:

DSMC membership is multidisciplinary, and members are selected from diverse areas including, Biostatistics, Gynecologic Oncology, Medical Oncology, Nursing, Pediatric Oncology, Surgical Oncology, Pharmacy and others.

Conflict of Interest:

When a member of the DSMC is the PI of a protocol under review, the member is recused from participating in the review and vote to avoid any conflict of interest

3. UNIVERSITY OVERSIGHT

3.1 PI RESEARCH EDUCATION REQUIREMENTS

The University of Minnesota has developed a comprehensive curriculum for the responsible conduct of research. [http://www.research.umn.edu/training/] The Office of the Vice President for Research (OVPR) is responsible for ensuring investigators complete OVRP-required training. To be eligible to serve as principal investigator on a sponsored project, faculty, students, and staff must complete training workshops on the responsible conduct of research. Researchers must also complete continuing education requirements on a regular basis. In addition, Human Subject Protection Training for the principal investigator and all personnel involved with a study must be completed and its completion registered with Fostering Integrity in Research, Scholarship, and Teaching (FIRST) before Institutional Review Board approval is granted. The OVPR holds the PI responsible for ensuring all study staff working under the PI complete the required research training.

3.2 INSTITUTIONAL REVIEW BOARD

The Principal Investigator of a cancer-related trial may not submit the protocol to the UMN Institutional Review Board (IRB) until permission is granted by the CPRC.
The IRB provides comprehensive oversight of clinical research to ensure the safety of all human subjects. The IRB is responsible for reviewing and monitoring research involving human subjects to protect the rights and welfare of the trial participants. The IRB is responsible for reviewing and ensuring:

- Risks and benefits to subjects are appropriate
- Trial is conducted in compliance with Federal regulations for the protection of human subjects

The IRB reviews the protocol, consent forms, amendments, related adverse events, protocol and regulatory compliance, and accrual progress at least annually until the trial is terminated. The IRB has the authority to approve, require modifications in, or disapprove all research activities, including proposed changes in previously approved human subject research. The IRB can suspend or terminate research for serious or continuing non-compliance with the Common Rule, DHHS regulations, institutional requirements, FDA regulations, or the IRB’s own findings, determinations, and requirements.

If the IRB suspends or terminates a trial, the PI must notify the CRL, DSMC, CPRC, NCI Program Director, sponsor and other appropriate agencies.

### 3.3 IND/IDE OVERSIGHT

University faculty members who file an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) with the FDA must submit a copy of the IND/IDE application and other related documents (communications, safety reports, amendments, annual reports, etc.) to the IND/IDE Assistance Program (IAP).

Compliance with IND/IDE requirements is the sole responsibility of the PI; however, the IAP provides assistance with IND/IDE applications, tracks due dates, and reminds investigators of their reporting obligations.

The Office of the Vice President for Research (OVPR) is responsible for governing IND/IDE regulatory compliance and developing oversight processes to ensure IND/IDE holders meet their commitments and mitigate risks to faculty investigators and the institution.

### OVERSIGHT PROCESSES

### 4. MONITORING CLINICAL TRIALS

#### 4.1 MONITORING OVERSIGHT

The National Cancer Institute (NCI) mandates that NCI-designated Comprehensive Cancer Centers maintain a system for oversight of all clinical research conducted in the cancer center. Clinical trial monitoring is critical to ensuring appropriate trial conduct, the validity and integrity of data, protocol compliance, and patient safety. Quality assurance and compliance oversight is provided by MCC’s Clinical Research Services (CRS), the coordinated operation of the Clinical Trials Office (CTO) and Medical Informatics.

#### 4.2 MONITORING ACTIVITIES
The Masonic Cancer Center may delegate or contract monitoring activities to organizations external to the MCC. All monitoring of institutional trials must comply with the UMN MMC Clinical Trials Monitoring Plan, UMN MCC Clinical Trials Office SOPs, and the UMN Cancer Center Data and Safety Monitoring Plan. The CRS Quality Assurance and Compliance Manager (QAC Manager) is responsible for ensuring monitoring is conducted in compliance with these documents.

The QAC Manager is required to routinely review monitoring reports to identify common issues across trials, investigators, IND/IDE holders, and time and develop a targeted corrective action plan for improvement.

4.3 MONITORING SCOPE

Cancer-related clinical trials must be monitored as described in this plan if either of the following conditions is met:

- High or moderate risk MCC investigator-initiated study (see Attachment 3: MCC Risk Assessment Checklist)
  - Includes all trial/study types that meet the risk criteria
- Other high or moderate risk institutional trials where the sponsor organization has transferred monitoring responsibility to the MCC

The MCC does not monitor the following:

- Low risk trials, e.g. trials not meeting the definition of high or moderate risk (see Attachment 3: MCC Risk Assessment Checklist)
- Industry trials
- National Cooperative Group trials

4.4 MONITORING EXTENT AND FREQUENCY

The PI is responsible for determining a trial’s level of risk which is confirmed by the CPRC. (see section 1.3 of the DSMP) Trial risk determines the extent of clinical trial monitoring and frequency of DSMC review.

The MCC Monitoring Plan provides a detailed description of monitoring expectations with regard to extent. (see Attachment 6: MCC Clinical Trials Monitoring Plan) Complete and adequate monitoring visits must be conducted at least every six months and include:

- Review of regulatory documents
  - Including review of product accountability and integrity of the study blind
- Review of consent forms
  - 100% of subjects
- Verification of eligibility
  - 100% of subjects
- Verification of subject data against source records
  - 100% of subjects enrolled on high risk trials
  - 10% of subjects enrolled on moderate risk trials
- Protocol compliance (all tests and procedures completed in window)
  - 100% of subjects enrolled on high risk trials
  - 10% of subjects enrolled on moderate risk trials
• Adverse event and stopping rule reporting
  o 100% of subjects enrolled on high risk trials
  o 10% of subjects enrolled on moderate risk trials

At the end of each monitoring visit, a monitoring report is prepared and sent to the study PI. Monitoring reports include: 1) verification that all required essential documents and elements of the study were reviewed and 2) a list of any findings. The monitor works with the PI and research staff until all findings are resolved. The monitor forwards any significant and ongoing compliance issues in a written report directly to the DSMC and the CRS Quality Assurance and Compliance Manager.

5. QUALITY ASSURANCE AND COMPLIANCE AUDITS

Audits play a critical role in assuring that trials are conducted and data are collected, documented and reported in compliance with the protocol and all local and federal regulations. All active investigator-initiated trials may be subject to an internal audit of any aspect of trial conduct. Audits may include but are not limited to review of subject records, consent process and documentation, regulatory compliance, product accountability, PI oversight and protocol adherence.

5.1 ANNUAL AUDIT PLAN

The QAC Manager develops an annual audit plan approved by the DSMC and carried out by the DSMC Coordinator or designee for verifying monitoring integrity and the effectiveness of CRS training and policies. Annual audit plans include any routine and process audits as described below. These plans are intended to guide quality oversight throughout the year, but may be modified to achieve the goal of quality assurance and compliance throughout the CRS.

• Routine Audits focus on high risk investigator-initiated trials such as phase I trials or trials conducted under an IND or IDE. High risk trials enrolling three or more subjects within the first year of opening to accrual will be subject to an audit. A minimum of 3 subjects or 10% of enrollment at the time of the audit, whichever is greater, will be monitored.
• Process Audits are used to identify trends of non-compliance and guide in the implementation of change and training as needed.

Directed (for cause) audits occur at the directive of the DSMC. These audits are typically conducted when clinical trial monitoring identifies a single egregious finding of non-compliance or continual documented accounts of possible noncompliance, data discrepancies or concerns over the ethical conduct of the study by the investigator.

5.2 AUDIT FINDINGS

Audit reports are reviewed by the DSMC which categorizes the findings as acceptable, acceptable with follow up, or unacceptable. The PI is required to submit a corrective action plan for audit results not categorized as acceptable. The DSMC has the authority to suspend or terminate a trial at any time. (see section 2.3 of the DSMP)
ADMINISTRATIVE INFRASTRUCTURE

The Masonic Cancer Center Clinical Research Services provides the infrastructure necessary to assist investigators in the conduct of their clinical research. Specifically, the CRS provides administrative support to the Cancer Protocol Review Committees and the Data and Safety Monitoring Council, and in addition, provides trial management services including protocol development, regulatory management, IND/IDE support, study coordination, data management and budget management, etc. (see Attachment 7: CRS Request for Services Form, Attachment 1: Clinical Trial Process and Attachment 2: Masonic Cancer Center Organizational Chart)

The University of Minnesota requires all research support staff to complete training in Human Subjects Protection and HIPAA and Data Privacy. The Clinical Trials Office of the CRS requires training in Good Clinical Practice. Additionally, Clinical Trials Office staff are required to attend the Fundamentals of Clinical Research educational session referenced in section 1.1 within 6 months of hire.

DEFINITIONS

**Affiliate site**: Hospital, clinic, or other provider of medical services that participates in an MCC investigator-initiated trial under the jurisdiction of a local IRB. Affiliate sites agree to abide by the processes for affiliates outlined in this DSMP.

**Cancer Protocol Review Committee (CPRC)**: MCC committee that conducts scientific review of all clinical research protocols conducted in the MCC. The CPRC monitors the progress of trials and may terminate protocols if found deficient in accrual or scientific merit.

**Clinical Research Services (CRS)**: Coordinated operation of the Clinical Trials Office and Medical Informatics providing resources to investigators such as protocol writing, monitoring, regulatory services, recruitment, nursing, project management, budgeting, and data management.

**Closed trial**: Study that has been closed with the IRB and other regulatory agencies.

**Co-Investigator (or Sub-Investigator)**: Member of the study team who is directly involved in the treatment or evaluation of research subjects under the supervision of the PI.

**Completed trial**: Trial that has met its accrual goals and has a status of IRB closure or terminated.

**Correlative trial**: Laboratory based study using specimens to assess cancer risk, clinical outcomes, response to therapies, etc. The study must be linked to individual patient or participant data.

**DSMP**: Data and Safety Monitoring Plan: Describes how the PI will oversee research participant safety and welfare.

**IDE (Investigational Device Exemption)**: Authorization granted by the Food and Drug Administration (FDA) to use an investigational, non-commercial device in clinical trials. The FDA requires IDEs for significant risk devices.

**IND (Investigational New Drug)**: Authorization from the FDA to administer an investigational, non-commercial drug or biological product in clinical trials.

**Investigator-Initiated trial**: Trial planned and managed by the Principal Investigator.
**Monitoring**: Systematic, ongoing review of data integrity and investigator compliance with the protocol, GCPs, and regulatory requirements.

**Phase I trial**: Trial designed to determine the maximum tolerated dose of a new treatment, such as a new drug that has never before been tried in humans or a new combination of drugs that have never been tried together in humans.

**Phase II trial**: Trial designed to determine the response rate of a new therapy that has already been tested in Phase I trials.

**Pilot study**: Small scale preliminary study conducted before the main research to check feasibility or improve the design of the research.

**Principal Investigator**: Person responsible for the conduct of the study at the clinical trial site. If a trial is conducted by a team of individuals at a trial site, the PI is the responsible leader of the team.

**Satellite site**: Study site that uses the UMN IRB and agrees to abide by the Masonic Cancer Center DSMP.

**Toxicity grade**: Numeric scale, e.g. CTCAE v. 4, used to rate the severity of a toxicity.
ATTACHMENT 1: CLINICAL TRIAL PROCESS
ATTACHMENT 3: MCC RISK ASSESSMENT CHECKLIST

Check the following as applies to your trial:

- [ ] Phase I
- [ ] Grade 3 - 5 toxicities expected in >20% of subjects
- [ ] Unknown toxicities
- [ ] Trial involves agent, device or process initiated or developed by UMN faculty
- [ ] Faculty held IND/IDE

If you checked one or more of the risk criteria above, your trial will be assigned “high risk”.

If no boxes were checked, check the following as applies to your trial:

- [ ] Phase II
- [ ] Pilot
- [ ] Score of >2 on trial complexity scale (each of the following equals one point)
  - [ ] Involves pharmacokinetic studies
  - [ ] Requires use of a health care provider for infusion or administration of protocol directed therapy and/or direct monitoring for toxicity following study drug administration
  - [ ] Involves collection of biological samples for correlative science and/or observational studies
  - [ ] Has an unusual route of administration and/or safety issues regarding administration
  - [ ] Is an MCC multi-center trial with affiliate site(s)
- [ ] PI of < 2 completed clinical trials

If you checked one or more of the risk criteria above, your trial will be assigned “moderate risk”.

If no boxes were checked, your trial will be assigned “low risk”.

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Minimum Extent of Monitoring</th>
<th>Minimum Monitoring Frequency</th>
<th>Minimum DSMC Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>100% of subjects: consent forms, eligibility, protocol compliance and verification of subject data against source records*</td>
<td>Twice yearly</td>
<td>Quarterly</td>
</tr>
<tr>
<td>Moderate</td>
<td>100% of subjects: consent forms and eligibility 10% of subjects at each monitoring visit: protocol compliance and verification of subject data against source records</td>
<td>Twice yearly</td>
<td>Twice yearly</td>
</tr>
<tr>
<td>Low</td>
<td>Not required</td>
<td>Not required</td>
<td>Annually**</td>
</tr>
</tbody>
</table>

*For high enrolling studies, i.e. accrual goal >100 subjects, monitoring will consist of a review of 100% of subject data up to the first 50 subjects. If no significant compliance issues are identified, the DSMC may approve decreasing monitoring extent to 10% of subject data for the remaining enrollment.

**Excludes trials with protocol type of epidemiologic or observational. After initial DSMC review, low risk trials of other protocol types, e.g. ancillary, supportive care, etc., may have the annual review requirement waived by the DSMC.
ATTACHMENT 4: SERIOUS ADVERSE EVENT REPORTING SOP

1.0 Overview

This SOP outlines the process for reporting a serious adverse event (SAE) that occurs on any trial conducted by the Masonic Cancer Center (MCC). SAE reporting timelines and requirements are determined by UMN IRB, 21 CFR 312, and 21 CFR 812.

National Cancer Institute guidelines published by the Cancer Therapy Evaluation Program distinguish treatment related events from disease related events. Treatment related SAEs will be reported unless excluded by the protocol. If a protocol excludes certain events or limits SAE reporting to certain conditions or outcomes, only those targeted SAEs will be reported. Disease related events include relapse, disease progression, or other conditions that may result from the natural course of the disease. These will not be reported as SAEs unless specifically required by the protocol.

For any trial conducted under a locally-held IND, the Principal Investigator (PI) is responsible for analyzing the significance of each SAE in the context of the trial or protocol. The Local Sponsor is responsible for determining the significance of the event in light of previous SAEs, per FDA regulations. The Local Sponsor or Principal Investigator designated by the Sponsor determines if an event qualifies for submission to the FDA and for submitting IND safety reports.

Trial staff should be familiar with and refer to the protocol-specific reporting rules for all trials they support.

2.0 Definitions

External Sponsor: Industry, cooperative group, or other academic institution or cancer center which initiates the protocol or holds the IND/IDE under which the trial is conducted

Funding Sponsor: Industry that provides drug or funding for a locally sponsored trial

Local Sponsor: MCC faculty member who holds the IND/IDE under which the trial is conducted or who takes responsibility for and initiates the trial. This individual may be different from the study Principal Investigator; if the person who holds the IND/IDE is not the PI, the Sponsor is the individual who holds the IND/IDE.

UPIRTSO: Any problem or event which in the opinion of the local investigator was unanticipated, reflects new or increased risk to the subjects, and was possibly related to the research procedures

3.0 Procedure

3.1 Serious Adverse Event Reporting

1. Study Coordinator: Upon identifying or being notified of a potential SAE:
   a. Review the SAE section in the current approved protocol to determine the protocol definition of an SAE and the reporting requirements.
b. Gather relevant clinical information and initiate an SAE report in OnCore for local trials or on report template provided by External Sponsor.
   i. For local trials, complete all fields specified under the Help (?) icon in the upper right corner of the OnCore screen.
   ii. Do not complete expectedness and attribution; these require PI assessment.
   iii. For externally sponsored trials enter the minimum required information below:
       - Event Date
       - Reported Date
       - Reported by
       - Outcome
       - Category
       - Toxicity
       - Grade
       - Attribution

c. Print the SAE report:
   - Local trials - print from OnCore
   - Externally sponsored trials - use Sponsor’s SAE report template

d. Give the SAE report with relevant clinical information to the PI to assess, edit, sign, and date.

e. Record the following information from PI assessment in OnCore:
   - Attribution
   - Expectedness
   - Any other changes to the SAE report

f. Distribute the SAE as follows:
   i. For local trials email copy of the signed SAE report from OnCore to:
       - Regulatory Specialist
       - Funding Sponsor
   ii. For externally sponsored trials email copy of signed SAE form provided by Sponsor to:
       - Regulatory Specialist
       - Sponsor

g. Determine protocol-specific SAE reporting requirements. Inform the Regulatory Specialist if the SAE must be:
   - Reported to the regulatory authorities in an expedited timeframe
   - Included in the FDA annual report or IRB continuing review application

h. Enter the date sent to the Funding Sponsor and External Sponsor in OnCore. Distribution dates recorded in OnCore are considered source data and paper copies of fax reports, etc. do not have to be maintained.

i. File the original report in the SAE section of the subject binder.

2. **Regulatory Specialist:**
   a. Email a copy of the SAE report to:
       - Local Sponsor if PI and Local Sponsor are different
       - SAE Coordinator
       - Regulatory Manager
• Quality Assurance and Compliance Manager (QA Manager)
• CDA team – if the SAE occurs on a BMT trial

b. If the SAE meets the UMN IRB definition of UPIRTSO, submit the SAE report to the IRB in the required timeframe.
c. If CTO INDI/IDE Management Agreement is on file and the SAE requires expedited reporting, send the SAE report to the FDA.
d. Record the following in OnCore, if applicable:
   • Date the SAE report was received by Regulatory Specialist
   • Date SAE report was sent to SAE Coordinator, Regulatory Manager, and QA Manager
   • Date the SAE report was sent to BMT database
   • Date the SAE report was sent to IRB (If SAE does not meet UPIRTSO reporting criteria, leave blank and enter this date at time next continuing review is submitted.)
   • Date the SAE report was sent to Local Sponsor
   • Date the SAE report was sent to FDA (if there is a CTO INDI/IDE Agreement)

e. File copy of the SAE report in the regulatory binder.

3.2 Additional SAE reporting Requirements for Local Trials with Affiliate Sites

If the SAE occurs at the University of Minnesota or satellite site:

1. Regulatory Specialist: Ensure an SAE report is sent to the Affiliate Lead Regulatory Specialist if the SAE meets the IRB definition of UPIRTSO, FDA criteria for expedited reporting, or if directed by MCC PI or Local Sponsor.

2. Affiliate Lead Regulatory Specialist:
   a. Distribute the SAE report to all affiliate sites.
   b. Record date sent to affiliate sites in OnCore.

If the SAE occurs at an affiliate site:

3. Study Coordinator:
   a. Give copy of the SAE report to the MCC PI to review, edit, sign and date.
   b. Update the Subject SAE section in OnCore: If the MCC PI does not make any changes to the SAE report, note in the PI Comments field that the MCC PI reviewed and concurs with the report.
   c. If the MCC PI determination of attribution or expectedness differs from that of the Site PI, update the Toxicity section in OnCore:
      i. Change attribution or expectedness field(s) to reflect the MCC PI determination.
      ii. Document the Site PI determination in the Comments field; note MCC PI changes.
   d. Email the SAE report to Regulatory Specialist.

Comments in the Toxicity section in OnCore must reflect changes the MCC PI makes to the SAE report.
3.3 Data and Safety Monitoring Council (DSMC) Review

Per the MCC Data and Safety Monitoring Plan, the DSMC reviews all reportable SAEs regardless of trial sponsor. The DSMC delegates this responsibility to the Quality Assurance (QA) Manager or designee. SAEs are summarized in interim trial reports to the DSMC.

1. SAE Coordinator:
   a. Review the SAE report for omissions, errors, and appropriate and timely distribution.
   b. Return incomplete SAE reports to the reporting staff for completion or resubmission.
   c. For high or moderate risk local trials or other trials monitored by the DSMC:
      i. If there are urgent concerns, send the SAE report to the DSMC Chair for expedited review.
      ii. If there are no urgent concerns, include in the next trial progress report SAE summary.
   d. Record the following in OnCore
      • Date the SAE report was reviewed by the SAE Coordinator
      • Date the SAE report was reviewed by the DSMC Chair
      • Date the SAE report was summarized or presented to DSMC.
   e. Enter the date sent to the Funding Sponsor and External Sponsor in OnCore. Distribution dates recorded in OnCore are considered source data and paper copies of fax reports, etc. do not have to be maintained.

3.4 Follow-up SAE Reporting

This section applies to local trials only. Externally sponsored trials should follow Sponsor process for follow up reporting.

1. Study Coordinator:
   a. Initiate a follow-up SAE report for changes to any of the following (only):
      • Event name
      • Attribution
      • Expectedness
      • Outcome changes to fatal
   b. Ensure PI reviews and signs off on the follow-up report.
   c. Update OnCore to match the signed follow-up SAE report.
   d. Per Section 3.1, send follow-up report to Regulatory Specialist and Funding Sponsor.
   e. File original follow-up SAE report in the subject binder.

2. Regulatory Specialist:
   a. If the SAE changes to a UPIRTSO event, report to regulatory authorities as required.
   b. Per Section 3.1, send follow-up report to Local Sponsor if PI and Local Sponsor are different.
   c. Email a copy of the follow-up SAE report to the CDA team and the SAE Coordinator.
   d. Record dates in OnCore, per SAE SOP section 2(e).
   e. File copy of SAE follow-up report in the regulatory binder.

3. SAE Coordinator
a. Review follow-up SAE report and record review date in OnCore.
b. Update DSMC per section 3.11(c).

3.5 Quality Assurance

1. **SAE Coordinator:** Send a summary report of all SAEs not reported appropriately or within the required time frame regardless of sponsor or risk category to the QA Manager.

2. **QA Manager:** Review the SAE delinquency report for serious or persistent issues and report concerns to the DSMC. Ensure the MCC PI submits a corrective action plan to the DSMC if required by the council.
PROCEDURES FOR AFFILIATE INSTITUTIONS

November 7, 2011
**TABLE OF CONTENTS**

Clinical Trials Office (CTO) Key Personnel .................................................................................................................. 25

1.0 New Protocol Distribution and IRB Submission ........................................................................................................ 26

2.0 Other Requirements for Site Activation .................................................................................................................... 27

3.0 Study Initiation Meeting ........................................................................................................................................ 27

4.0 Amendment Distribution and IRB Submission ......................................................................................................... 27

5.0 Annual IRB Renewals ............................................................................................................................................. 27

6.0 Patient Registration and Data Submission ................................................................................................................ 28
   6.1 Patient Registration ................................................................................................................................................... 28
   6.2 Screening Logs ......................................................................................................................................................... 28
   6.3 Data Submission .................................................................................................................................................... 28

7.0 Serious Adverse Event Reporting ........................................................................................................................... 29

8.0 Other Required Reporting ................................................................................................................................... 30

9.0 Conference Calls ........................................................................................................................................................ 30

10.0 Outside Safety Reports ......................................................................................................................................... 30

11.0 Reimbursement ..................................................................................................................................................... 30

12.0 Clinical Trial Monitoring and Auditing ............................................................................................................... 31

Appendix A: Nondisclosure Agreement .......................................................................................................................... 32

Appendix B: Consent Form/HIPAA Authorization Preparation Checklist for Affiliate Institutions ........................................... 34

Appendix C: Affiliate Procedures Sign-off Sheet ........................................................................................................... 35

Appendix D: Significant Financial Conflict of Interest Disclosure Form ........................................................................... 36

Appendix E: Agreement to list affiliates in the National Cancer Institute PDQ Database .................................................. 37

Appendix F: Initial Regulatory Checklist for Affiliates .................................................................................................. 38

Appendix G: Ongoing Regulatory Submission Instructions for Affiliates ..................................................................... 39

Appendix H: Delegation of Authority Log .................................................................................................................... 40

Appendix I: Screening Log ............................................................................................................................................. 41

Appendix J: Finance/Contract Data Collection Form ..................................................................................................... 42

Appendix K: Fax Cover Sheet for reporting Serious Adverse Events to the University of Minnesota ................................... 43

Appendix L: Serious Adverse Event (SAE) Report for Affiliate Sites ........................................................................... 45
# Clinical Trials Office (CTO) Key Personnel

<table>
<thead>
<tr>
<th>Name</th>
<th>Phone</th>
<th>Fax</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical Director:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brenda Weigel, MD</td>
<td>612-626-5501</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Contract Administration:**   |               |                |                      |
| TBD for each study             |               |                |                      |

*Contact for: Contract, budget info unless otherwise directed*

| **Project Manager, Solid Tumor Studies** |               |                |                      |
| Project Manager, Heme/BMT Studies |               |                |                      |
| Project Manager, Phase I/CETI Studies |               |                |                      |

*Contact for: Study startup process guidance, initial contact for budget/contract and departmental negotiations, contact if others are not available*

| **Study Coordinator:**          |               |                |                      |
| TBD for each study              |               |                |                      |

*Contact for: Clinical inquiries, verification that new patient slots are still available, patient randomization assignments/sequence numbers and suggestions for protocol changes*

| **Regulatory/Affiliate Coordinator** |               |                |                      |
| Meadow Schroeder                 | 612-624-9487  | 612-625-6145   | schro051@umn.edu     |

*Contact for: Affiliate paperwork requirements, IRB/regulatory questions, study mailings and suggestions for protocol changes*
1.0 New Protocol Distribution and IRB Submission

Once final University of Minnesota (UMN) IRB approval is received, the Regulatory Coordinator will distribute the protocol and consent form to affiliates electronically with a consent form checklist included. Upon receipt of the email the affiliate institution is expected to do the following:

- **Within 30 days:**
  - Reply to the email indicating that the protocol was received.
  - Indicate whether the affiliate institution will participate.
  - If decision is not to participate, the affiliate PI or Protocol Coordinator must also contact the UMN PI with the reason for refusal. *(This can be done by contacting the PI directly using the contact information located on the first page of the protocol or by contacting the Regulatory Coordinator).*

- **As soon as possible after receipt of electronic documents:**
  - Adapt model consent to local consent format and submit to Regulatory Coordinator via email. Track revisions using Microsoft Word’s track changes tool. *(NOTE: Please contact the Regulatory Coordinator if you have questions or if you are unfamiliar with this tool.)*

  - Fax the completed and signed Consent Form Checklist to the Regulatory Coordinator at the time of submission of the adapted consent.

- **Within 14 days after site receives UMN approval of local consent**
  - Check with the Regulatory Coordinator to confirm that you have the most current version of the protocol when you are ready to submit for local IRB review.
  - Submit applicable study documents (protocol, consent, Investigator’s Brochure, etc.) to the local IRB.
  - Notify the Regulatory Coordinator when the study documents are submitted to the local IRB. In the notification, please include the version dates of all submitted documents.
  - If the affiliate IRB requests changes to the consent, these changes must be approved by the Regulatory Coordinator or other UMN CTO staff before they are submitted for final local IRB approval.

- **After receipt of affiliate institution IRB approval:**
  - Fax or email a copy of the IRB approval letter and the IRB-approved consent form to the Regulatory Coordinator.

  - *NOTE:* Local IRB approval letter must note version dates of all approved study documents.
2.0 Other Requirements for Site Activation

Refer to attached appendices for *INITIAL REGULATORY CHECKLIST FOR AFFILIATES*. Complete and submit required regulatory documents accordingly.

3.0 Study Initiation Meeting

Once affiliate IRB approval and all other required regulatory documentation is received, and the contract/budget finalized, the applicable UMN Nurse Manager will contact the site to schedule a study initiation meeting. Depending upon site location and study complexity, the meeting may be conducted as a teleconference or an on-site visit.

4.0 Amendment Distribution and IRB Submission

Once a protocol amendment has been approved by the UMN IRB, the Regulatory Coordinator will send the amended protocol and accompanying mark-up and clean versions of the model consent form (if applicable) to the affiliate institutions via email. The affiliate institution is expected to do the following:

- **Upon receipt of amendment documents:**
  - Reply to the email indicating that the amendment/consent was received and will be submitted to the local IRB.
  - Submit adapted local consent form to Regulatory Coordinator for UMN approval of changes. (Use same procedure as described in section 1.0.)
  - Submit amendment documents to local IRB as soon as possible. Notify the UMN Regulatory Coordinator when the amendment has been submitted to the local IRB.
  - If the affiliate IRB requests changes to the consent, these changes must be approved by the Regulatory Coordinator or other UMN CTO staff before they are submitted for final local IRB approval.
  - Must get affiliate institution’s IRB approval within 3 months from the date that the amendment was submitted to the local IRB. Delinquency may result in suspension of affiliate site’s ability to accrue new patients on study.

- **After receipt of affiliate IRB approval:**
  - Fax or email the affiliate IRB’s approval letter for the amendment and the amended consent form (if applicable) to the Regulatory Coordinator.
  - *NOTE: Local IRB approval letter must note version dates of all approved protocol documents.*

5.0 Annual IRB Renewals

Annual IRB renewal of approval letters/notices for affiliate institutions should be faxed or emailed promptly to the Regulatory Coordinator. If the institution’s IRB requires a new version of the consent form with the annual renewal, the consent form should be included with the renewal letter.
6.0 Patient Registration and Data Submission

6.1 Patient Registration

At the time of registration, the registering institution will:

- Confirm that the UMN CTO has record of their IRB’s current approval (within 1 calendar year) of the study. This approval must document the approved protocol and consent version dates. Sites that have not submitted this documentation will not be permitted to register new patients.

- Fax the completed, signed eligibility checklist, patient registration form (included in appendices) and signed consent form to the UMN Study Coordinator.

- Within 24 hours, the Study Coordinator will randomize/register the patient and send a confirmation of the patient’s assignment and protocol sequence number to the affiliate institution. This should be kept in the patient’s study chart at the affiliate site. **The date that the patient is randomized will be considered the patient’s “On-Study Date.”**

6.2 Screening Logs

Completed Screening Logs are to be faxed to the UMN CTO Study Coordinator on a monthly basis (unless the protocol outlines a different submission schedule). See the Screening Log (included in appendices) for further details.

6.3 Data Submission

Affiliate institutions are expected to send the appropriate Case Report Forms (CRFs) and, when requested, source documentation. These documents should be sent to the Study Coordinator. (See protocol for contact information.)

The CRF submission schedule will be included in the protocol.

Source documentation to be submitted may include, but is not limited to, the following items:

- Past Medical History
- Evaluations
- Response summaries
- Clinic/Visit Notes
- Other Treatment Notes
- Chemo/Treatment Order Forms
- Serious Adverse Event Reports
- Pathology Reports
- Radiology Reports
- Laboratory Reports
- PFT, EKG, ECHO, MUGA, etc.
- Communication/Correspondence related to patient treatment
- Home care referrals
- Any other applicable patient study chart documents and correspondence
7.0 Serious Adverse Event Reporting

SAE reporting will utilize either FDA Medwatch form or the Masonic Cancer Center’s Affiliate Site SAE Report form (included in appendices), according to instructions provided in the protocol.

- Within 24 hours of knowledge of the occurrence of any protocol-defined serious adverse event:
  - Notify The Clinical Trials Office (CTO) Study Coordinator of the event via phone or email.
  - 24-hour notification should include as much of the following information as is available:
    - Reporter’s name, site name and telephone number
    - Patient initials
    - Sequence number
    - UMN Cancer Center protocol number
    - Affiliate site study PI
    - Treating (registering) physician
    - Date of onset of SAE
    - Description of event (including grade of the event, whether or not the event required hospitalization or resulted in the death of the patient)
    - Attribution of event to protocol treatment, if known

- Within 10 working days of event occurrence:
  - Send final or follow-up SAE report with any relevant (de-identified) source documentation (lab results, etc.) to the UMN CTO Study Coordinator. This can be done electronically, by fax or by mail. Submit SAE report to the affiliate institution’s local IRB according to institutional guidelines.

- If submitted reports are incomplete, reports will be returned or sites queried for further information.

- Upon receipt, the SAE report will be reviewed by the UMN study PI and, if indicated, forwarded to the University of Minnesota IRB. All SAE reports will be handled in accordance with the University of Minnesota Masonic Cancer Center’s Data and Safety Monitoring Plan (available at [www.cancer.umn.edu/exfiles/research/dandsmplan.pdf](http://www.cancer.umn.edu/exfiles/research/dandsmplan.pdf)).

- Affiliate sites are responsible for submitting SAE reports to their local IRBs per their institutional guidelines. **Copies of all local IRB SAE submissions must be sent to the CTO Affiliate Regulatory Coordinator.**
8.0 Other Required Reporting

The following events must be reported to the UMN Study Coordinator within 48 hours of knowledge:

- Any serious accidental or unintentional change to the IRB-approved protocol that involves risk or has the potential to recur;
- Any deviation from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research subject;
- Any breach in confidentiality that may involve risk to the subject or others;
- Any complaint of a subject that indicates an unanticipated risk or that cannot be resolved by the research staff.

Affiliate institutions will be responsible for submitting reportable events to their local IRB and any other required local regulatory entities per institutional guidelines. Copies of correspondence to and from the local IRB must be sent to the CTO Affiliate Regulatory Coordinator.

9.0 Conference Calls

Conference calls will be scheduled as necessary. The UMN Study Coordinator will distribute a memo with the conference call information before the meeting. Affiliates should respond by the stated deadline and list all members participating. At these sessions accrual problems, adverse events, data questions, etc. will be reviewed.

10.0 Outside Safety Reports

All serious adverse events requiring immediate submission to the University of Minnesota IRB will be copied and sent to all affiliates for submission to their local IRB per their institutional guidelines. The University of Minnesota IRB’s policy dictates that only events which meet “UPIRTO” criteria, that is, events which are serious AND at least possibly related to the investigational element of the study AND unexpected require immediate submission for IRB review. CTO staff will be responsible for sending SAE reports to the study financial sponsor, FDA, etc., as required.

11.0 Reimbursement

In order to initiate a subcontract, complete and submit the Finance/Contract Data Collection Form (included in appendices) to the CTO Contract Administrator assigned to the study.

Contract study reimbursement is generally provided on a per patient accrual/registration basis. A list of patients (identified by sequence number or other data that do not include Protected Health Information) that the affiliate site is billing for should be attached to the invoice. Affiliate sites are generally required to submit billing vouchers/invoices quarterly or according to specific contract agreements.

Sites that have zero accrual for any quarter need not submit an invoice for that quarter.
12.0 Clinical Trial Monitoring and Auditing

The UMN CTO has oversight responsibility for trial monitoring at affiliate sites. Source documents and study records may be subject to monitoring at the discretion of the UMN Masonic Cancer Center Data and Safety Monitoring Council (DSMC). Affiliate sites may self-monitor following CTO affiliate site monitoring SOPs.

The CTO periodically selects and audits regulatory and/or subject documents to ensure UMN Masonic Cancer Center monitoring standards are met. UMN Masonic Cancer Center conducts these reviews for quality assurance and improvement, and for compliance with the Data and Safety Monitoring Plan and relevant UMN CTO Standard Operating Procedures. The DSMC may request additional audits of study monitoring activities and reports.

The audit may include but will not be limited to:

- All regulatory documentation
- Subject consent
- Eligibility and Pre Treatment Evaluation
- Treatment Administration
- Drug Accountability Report Forms
- Post Treatment Monitoring
- Toxicity Reporting
- Case Report Forms (CRFs)

Audits of affiliates located in the Twin Cities metro area may be done on-site. Affiliates outside the Twin Cities metropolitan area, if requested, will copy and forward all source documentation needed for the audit to the UMN Masonic Cancer Center Quality Assurance (QA) Coordinator. A written report of all audit deviations will be completed by the QA coordinator and reviewed with the PI and research nurse(s) at the affiliate site in person or by conference call. Final audit findings will be presented to the UMN Masonic Cancer Center DSMC and the severity of any instance of protocol non-compliance will be determined. The UMN Masonic Cancer Center DSMC will issue a letter to the PI and request a written corrective action plan for all major and/or multiple lesser deviations. Re-audits may be requested by the UMN Masonic Cancer Center DSMC for protocols with multiple major deviations. Failure of the PI to adequately address protocol deviations may result in suspension or termination of affiliate participation.
Appendix A: Nondisclosure Agreement

The Masonic Cancer Center, University of Minnesota Clinical Trials Office

This Agreement is entered into by _________________________________

Affiliate PI Name

with offices at ________________________________ hereinafter "Recipient") and the

Affiliate Site

Masonic Cancer Center, University of Minnesota Clinical Trials Office (hereinafter "Discloser").

WHEREAS Discloser possesses certain ideas and information relating to

__________________________________________

Protocol Title (and number, if applicable)

__________________________________________

that is confidential and proprietary to Discloser (hereinafter "Confidential Information"); and WHEREAS the Recipient is willing to receive disclosure of the Confidential Information pursuant to the terms of this Agreement for the purpose of participation in clinical oncology research trials as a member of the Masonic Cancer Center, University of Minnesota’s Affiliate Network;

NOW THEREFORE, in consideration for the mutual undertakings of the Discloser and the Recipient under this Agreement, the parties agree as follows:

1. Disclosure: Discloser agrees to disclose, and Receiver agrees to receive the Confidential Information.

2. Confidentiality.

   a) No Use. Recipient agrees not to use the Confidential Information in any way, or to manufacture or test any product embodying Confidential Information, except for the purpose set forth above.

   b) No Disclosure. Recipient agrees to use its best efforts to prevent and protect the Confidential Information, or any part thereof, from disclosure to any person other than Recipient's Institution's employees having a need for disclosure in connection with Recipient's authorized use of the Confidential Information.
c) Protection of Secrecy. Recipient agrees to take all steps reasonably necessary to protect the secrecy of the Confidential Information, and to prevent the Confidential Information, on from falling into the public domain or into the possession of unauthorized persons.

3. Limits on Confidential Information. Confidential Information shall not be deemed proprietary and the Recipient shall have no obligation with respect to such information where the information:

   a) was known to Recipient prior to receiving any of the Confidential Information from Discloser;

   b) has become publicly known through no wrongful act of Recipient;

   c) was received by Recipient without breach of this Agreement from a third party without restriction as to the use and disclosure of the information;

   d) was independently developed by Recipient without use of the Confidential Information; or

   e) was ordered to be publicly released by the requirement of a government agency.

4. Ownership of Confidential Information. Recipient agrees that all Confidential Information shall remain the property of Discloser, and that Discloser may use such Confidential Information for any purpose without obligation to Recipient. Nothing contained herein shall be construed as granting or implying any transfer of rights to Recipient in the Confidential Information, or any patents or other intellectual property protecting or relating to the Confidential Information.

5. Term and Termination. The obligations of this Agreement shall be continuing until the Confidential Information disclosed to Recipient is no longer confidential.

6. Survival of Rights and Obligations. This Agreement shall be binding upon, inure to the benefit of, and be enforceable by (a) Discloser, its successors, and assigns; and (b) Recipient, its successors and assigns.

7. This agreement shall be interpreted and construed in accordance with the laws of the State of Minnesota and any claims against Discloser will be adjudicated and enforced in Hennepin County, Minnesota district court.

__________________________________________
(Signature)

__________________________________________, Principal Investigator (at affiliate site)
(Print Name)

__________________________________________
(Date)

Affiliate Site:
Appendix B: Consent Form/HIPAA Authorization Preparation Checklist for Affiliate Institutions

The Masonic Cancer Center, University of Minnesota Clinical Trials Office

Affiliate consent forms must meet the following criteria:

1. □ Yes □ No Is the consent form written in lay language?

2. □ Yes □ No Does the title on the consent form match the title on the protocol?

3. □ Yes □ No Are the institution and the investigator clearly identified with contact phone numbers?

4. □ Yes □ No Are all of the risks associated with the treatment listed? These risks should be identical to the U of MN consent form.

5. Outline the site’s method of documenting IRB approval (in writing, notify the CTO which items apply):
   □ IRB approval stamp on consent document
   □ IRB approval letter references date of consent document.
   □ IRB approval date typed on consent document
   □ Other (describe):

Affiliate HIPAA Authorizations must include the following language:

If you decide to participate in this study, some private health information about you will be stored in a computer database at the Masonic Cancer Center, University of Minnesota. This information will include your name and medical record number, your date of birth, your diagnosis, your race/ethnicity, and information about your participation in this study. The purpose of storing this information is to assist the Cancer Center in creating reports about research and in making sure that research studies are being done correctly. Your information will not be used for any other purpose. There are no plans to erase information from the database. It will be stored indefinitely at the Masonic Cancer Center, University of Minnesota.

Parties Who May Receive or Use My Individual Health Information:

- The University of Minnesota Institutional Review Board (IRB), a group of people who review the research study to protect your rights;
- The Masonic Cancer Center, University of Minnesota Clinical Trials Office;
- Government agencies including the Food and Drug Administration (FDA), the Office for Human Research Protections, (OHRP), the National Cancer Institute (NCI). These agencies may review the research to see that it is being done safely and correctly.

NOTE: The U of MN Clinical Trials Office must approve the affiliate’s consent form and HIPAA authorization prior to submission to the affiliate’s IRB
Appendix C: Affiliate Procedures Sign-off Sheet

The Masonic Cancer Center, University of Minnesota Clinical Trials Office

All research nurses, data managers, regulatory coordinators and other personnel that work on the Masonic Cancer Center, University of Minnesota protocols at affiliate institutions are required to read the “Procedures for Affiliate Institutions” and sign below.

I, THE UNDERSIGNED, HAVE READ THE MASONIC CANCER CENTER, UNIVERSITY OF MINNESOTA PROCEDURES FOR AFFILIATE INSTITUTIONS AND AGREE TO COMPLY WITH THEM. I ALSO UNDERSTAND THAT IF I HAVE ANY QUESTIONS REGARDING THESE PROCEDURES THAT I MAY CONTACT THE UNIVERSITY OF MINNESOTA CLINICAL TRIALS OFFICE PROGRAM ADMINISTRATOR OR COORDINATOR FOR CLARIFICATION.

Signature: ___________________________ Date: ______________

Print Name: __________________________

Affiliate Institution: ___________________
Appendix D: Significant Financial Conflict of Interest Disclosure Form

The Masonic Cancer Center, University of Minnesota Clinical Trials Office

Study Title: ________________________  Affiliate Site: ________________________

Technology, process, product and/or business involved in this trial:

Conflict of Interest

Federal Guidelines emphasize the importance of assuring there are no conflicts of interest in research projects that could affect the welfare of human subjects. If this study involves or presents a potential conflict of interest, additional information will need to be provided. Examples of potential conflicts of interest may include, but are not limited to:

• A researcher or family member participating in research on a technology, process or product owned by a business in which the faculty member holds a financial interest
• A researcher participating in research on a technology, process or product developed by that researcher
• A researcher or family member assuming an executive position in a business engaged in commercial or research activities related to the researchers University responsibilities
• A researcher or family member serving on the Board of Directors of a business from which that member receives University-supervised Sponsored Research Support
• A researcher receiving consulting income from a business that funds his or her research

It is the responsibility of the investigator to contact the appropriate study personnel and institution regarding any changes to the following questions:

1. Do you have a business interest or a financial interest of $10,000 or more associated with this study?
   [ ] No  [ ] Yes
   If yes, complete question 4 below

2. Do you have ownership interests less than $10,000 when the value of interest could be affected by the outcome of the research?
   [ ] No  [ ] Yes
   If yes, complete question 4 below

3. Do you have compensation less than $10,000 when the value of the compensation could be affected by the outcome of the research?
   [ ] No  [ ] Yes
   If yes, complete question 4 below

4. If you answered yes to any of the above questions, please answer the following. Does the responsible Institutional Review Board (IRB) or participating institution have a Conflict Management Committee (CMC) to oversee/manage potential conflicts of interest among study investigators?
   [ ] Yes. Please attach a recommendation from the CMC regarding disclosure to subjects and management of the conflict. The responsible IRB may determine what disclosure language should be included in the consent form.
   [ ] No. Please contact the Affiliate Regulatory Specialist for instructions on how to manage this potential conflict of interest.

Investigators who answer “yes” to any of questions 1-3 above may not participate in any study activity until a plan to manage the potential conflict of interest is in place. Said plan must meet the approval of an institutional CMC or the responsible IRB. Documentation of this approval must be submitted to the University of Minnesota Masonic Cancer Center Clinical Trials Office.

Printed Name: ________________________

Signature: ________________________  Date: ______________
Appendix E: Agreement to list affiliates in the National Cancer Institute PDQ Database

I, ________________________________________ with offices at _____________________________________________________, an affiliate of the Masonic Cancer Center, University of Minnesota (MCC) participating in protocol #_________________, (title of protocol) ________________________________________, agree to allow the MCC to submit my name, phone number and affiliate site in the National Cancer Institute (NCI) Physician Data Query (PDQ) database for this protocol. Please review the following information about the NCI PDQ below before signing below.

______________________________________________
Signature of Affiliate Investigator

Date: ____________________

If you do not want to be listed in the NCI PDQ, please contact: smit4652@umn.edu

See the NCI’s Website at http://www.cancer.gov/cancertopics/pdq
Appendix F: Initial Regulatory Checklist for Affiliates

The Masonic Cancer Center, University of Minnesota Clinical Trials Office

Documents to be completed prior to the study initiation meeting. ALL ORIGINALS MUST BE RETAINED IN AFFILIATE SITE REGULATORY FILES EXCEPT FDA FORM 1572 IF THE STUDY IS UNDER AN IND. COPIES OF THESE DOCUMENTS SHOULD BE MAILED OR FAXED TO THE CTO AFFILIATE REGULATORY COORDINATOR

- Non-Disclosure Agreement, signed by Affiliate PI
- Financial Disclosure Form
- Investigator CV, signed and dated within 2 years
- Investigator medical license, current
- FDA Form 1572 (partially filled form provided by U of MN CC)
- NCI Physician’s Data Query (PDQ) Agreement
- MCC CTO Financial Disclosure form
- Affiliate IRB Federal-wide Assurance Number
- Affiliate laboratory values reference ranges
- Affiliate laboratory CAP certificate, current
- Affiliate laboratory CLIA certificate, current
- Documentation of affiliate’s submission of protocol and applicable study documents to their IRB
- Affiliate IRB’s approval of protocol and applicable study documents*
- Affiliate IRB’s approval of affiliate informed consent document*

NOTE: Affiliate sites must also retain documentation that U of MN CTO has approved the affiliate informed consent document PRIOR to it being submitted to the affiliate’s IRB.

*All correspondence from affiliate IRBs must include the following elements:
  * printed on IRB letterhead or equivalent
  * addressed to the affiliate PI
  * specify EXACTLY what is approved, including document title, version title/dates and, if applicable, description of the content
  * specify the date of the approval and be signed by the IRB chair or designee

Following the study initiation meeting, fax completed, signed and dated (by PI) Affiliate Site Personnel Delegation Log to PCRT Project Lead.
Appendix G: Ongoing Regulatory Submission Instructions for Affiliates

The Masonic Cancer Center, University of Minnesota Clinical Trials Office

Copies of these documents must be mailed or faxed to the CTO Affiliate Regulatory Coordinator.

ALL ORIGINALS MUST BE RETAINED IN AFFILIATE SITE REGULATORY FILES.

<table>
<thead>
<tr>
<th>Description of change</th>
<th>Submission requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol Amendment or change in informed consent document</td>
<td>• Documentation of submission of document to affiliate IRB</td>
</tr>
<tr>
<td></td>
<td>• Documentation of approval of document by affiliate’s IRB*</td>
</tr>
<tr>
<td></td>
<td>• Final revised informed consent approved by affiliate’s IRB</td>
</tr>
<tr>
<td>Any change to 1572 form (addition/deletion of PI, sub-investigator, clinical site or affiliate laboratory, change in address of PI, affiliate clinical site or affiliate laboratory)</td>
<td>• Original of revised 1572 form, signed and dated by PI. Keep a copy for your files.</td>
</tr>
<tr>
<td>Change in affiliate PI or addition of new affiliate sub-investigator</td>
<td>• PI/sub-investigator CV, signed and dated within 2 years</td>
</tr>
<tr>
<td></td>
<td>• PI/sub-investigator medical license, current</td>
</tr>
<tr>
<td>Change in study staff (addition or removal) or change in staff member’s responsibilities</td>
<td>• UPDATED Affiliate Site Personnel Delegation Log (Affiliate PI must sign/date with each revision. Do not need to submit unrevised pages.)</td>
</tr>
<tr>
<td>Addition of affiliate laboratory</td>
<td>• Affiliate laboratory values reference ranges</td>
</tr>
<tr>
<td></td>
<td>• Affiliate laboratory CAP certificate, current</td>
</tr>
<tr>
<td></td>
<td>• Affiliate laboratory CLIA certificate, current</td>
</tr>
<tr>
<td>EXPIRATION OF</td>
<td>• Submit replacement document</td>
</tr>
<tr>
<td>• IRB approval of study</td>
<td></td>
</tr>
<tr>
<td>• PI/sub-investigator medical license</td>
<td></td>
</tr>
<tr>
<td>• CAP/CLIA for any affiliate lab listed on 1572 form</td>
<td></td>
</tr>
<tr>
<td>Locally-occurring Serious Adverse Event (SAE)—see protocol for definition</td>
<td>• Documentation of submission of report to affiliate’s IRB including the following:</td>
</tr>
<tr>
<td></td>
<td>o Affiliate PI’s assessment of SAE attribution to study therapy</td>
</tr>
<tr>
<td></td>
<td>o Proposed changes to informed consent document as a result the SAE** (if any)</td>
</tr>
<tr>
<td></td>
<td>• Documentation of IRB review of SAE report (consult CTO regarding requested follow-up, if necessary)</td>
</tr>
<tr>
<td>Non-locally occurring SAE reports (Outside Safety Reports)—distributed to affiliates by CTO</td>
<td>• Documentation of submission of report to affiliate’s IRB including the following:</td>
</tr>
<tr>
<td></td>
<td>o Notation that SAE occurred off-site</td>
</tr>
<tr>
<td></td>
<td>o Notation of whether SAE occurred on this study or another study using the same agent</td>
</tr>
<tr>
<td></td>
<td>o Proposed changes to informed consent document as a result the SAE** (if any, either from affiliate PI or Sponsor/U of MN CTO)</td>
</tr>
<tr>
<td></td>
<td>• Documentation of IRB review of SAE report (consult CTO regarding requested follow-up, if necessary)</td>
</tr>
</tbody>
</table>

NOTE: Affiliate sites must also retain documentation that U of MN CTO has approved the affiliate informed consent document PRIOR to it being submitted to the affiliate’s IRB

**ALL proposed changes to informed consent documents must be approved by the U of MN CTO) PRIOR to submission to the affiliate IRB!
### Appendix H: Delegation of Authority Log

**UNIVERSITY OF MINNESOTA CANCER CENTER**

<table>
<thead>
<tr>
<th>NAME (printed)</th>
<th>SIGNATURE</th>
<th>ROLE</th>
<th>STUDY RESPONSIBILITY (CODE)</th>
<th>DATE TRAINED FOR STUDY</th>
<th>DATE STARTED WITH TRIAL</th>
<th>PI Initials</th>
<th>DATE ENDED WITH TRIAL</th>
<th>PI Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- A = Decide on subject eligibility
- E = Access IVRS, if applicable
- I = Perform study assessments
- M = Provide regulatory support
- B = Obtain informed consent
- F = Perform drug accountability and drug accountability
- J = Provide tumor measurements, if applicable
- N = Handle research laboratory samples
- C = Provide medical care of subjects
- G = Instruct subject on use of trial drug
- K = Handle dangerous goods, if applicable
- O = Train staff/investigators
- D = (1) Perform physical exam and (2) obtain medical history
- H = Prepare drug, if applicable
- L = Make CRF entries/corrections
- P:
Appendix I: Screening Log

Masonic Cancer Center, University of Minnesota
(RECORD ALL PATIENTS WHO SIGN THE CONSENT DOCUMENT)

- Study title:
- PI: _____________________________ Site name: ______________________________

<table>
<thead>
<tr>
<th>Consent signed date (mm/dd/yy)</th>
<th>Pt Initials (FML)</th>
<th>Eligible?</th>
<th>If no, give reason</th>
<th>Was Pt enrolled?</th>
<th>Date On-Study (mm/dd/yy) or N/A</th>
<th>If not enrolled, give reason</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes / No</td>
<td></td>
<td>Yes / No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*For affiliate use: Fax log to study coordinator at (fax)___________ on the first date of every month.*
## Appendix J: Finance/Contract Data Collection Form

<table>
<thead>
<tr>
<th>Site legal name</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact person for contracts/budgets</td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td></td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Phone</td>
<td></td>
</tr>
<tr>
<td>Fax</td>
<td></td>
</tr>
<tr>
<td>E-mail address</td>
<td></td>
</tr>
</tbody>
</table>

| Authorized signer for the site |   |
| Name |   |
| Address |   |
| Phone |   |
| Fax |   |
| E-mail address |   |

| Affiliate site Principal Investigator |   |
| Name |   |
| Address |   |
| Phone |   |
| Fax |   |
| E-mail address |   |

| Anticipated number of patients to be enrolled at site |   |
| IRB approval date |   |
Appendix K: Fax Cover Sheet for reporting Serious Adverse Events to the University of Minnesota
(see next page)
## FAX COVER SHEET

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>To:</td>
<td>Study Coordinator</td>
</tr>
<tr>
<td>University of Minnesota Masonic Cancer Center</td>
<td></td>
</tr>
<tr>
<td>Fax:</td>
<td></td>
</tr>
<tr>
<td>From:</td>
<td></td>
</tr>
<tr>
<td>Phone:</td>
<td></td>
</tr>
<tr>
<td>Email:</td>
<td></td>
</tr>
<tr>
<td>Fax:</td>
<td></td>
</tr>
<tr>
<td>Date:</td>
<td></td>
</tr>
<tr>
<td>Pages including cover sheet:</td>
<td></td>
</tr>
</tbody>
</table>

### Type of Report

- [ ] Serious Adverse Event (SAE) – initial report
- [ ] Serious Adverse Event (SAE) – follow-up report
- [ ] Report of Pregnancy (confirmed or suspected)

Confidentiality Note: Please be advised that the information contained in this facsimile message is privileged and confidential information intended only for the use of the individual or entity named above. If the reader of this message is not the intended recipient, or the employee or agent responsible to deliver it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please immediately notify us by telephone.
Appendix L: Serious Adverse Event (SAE) Report for Affiliate Sites

(see next page)
### Serious Adverse Event (SAE) Report for Affiliate Sites

**Masonic Cancer Center**  
**University of Minnesota**

<table>
<thead>
<tr>
<th>Date of Report:</th>
<th>Sequence Number:</th>
<th>Subject Initials:</th>
</tr>
</thead>
</table>

### Study Information

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>UMN Principal Investigator:</th>
<th>CPRC#:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Affiliate Site Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

### Study Therapy Information

<table>
<thead>
<tr>
<th>Study Therapy</th>
<th>Route</th>
<th>Dose</th>
<th>Schedule</th>
<th>Last Dose/Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SAE Information

<table>
<thead>
<tr>
<th>Date SAE Occurred:</th>
<th>Date Site Learned of SAE:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of Report</th>
<th>Initial</th>
<th>Follow Up # _____</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of SAE:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SAE Category:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severity Scale Used:</th>
<th>CTCAE V4.0</th>
<th>Modified Glucksberg Scale (AGVHD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CTCAE V3.0</td>
<td>Other __________________________</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Is SAE a DLT:</th>
<th>No</th>
<th>Yes - Complete DLT Stopping Rule Event Report, if applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Affiliate Site Study Coordinator:** Describe the SAE, treatment, and final outcome of the event in the space below or attach a typed narrative of the event to this report:

**Affiliate Site Study Coordinator:** Add relevant medical history, concomitant meds, and lab or test results:
### Serious Adverse Event (SAE) Report for Affiliate Sites
Masonic Cancer Center
University of Minnesota

<table>
<thead>
<tr>
<th>Date of Report:</th>
<th>Sequence Number:</th>
<th>Subject Initials:</th>
</tr>
</thead>
</table>

In the opinion of the **Affiliate Site Investigator**:

- Is the SAE:  
  - [ ] Expected  
  - [ ] Unexpected

- Is the SAE at least possibly attributable to study therapy:  
  - [ ] No  
  - [ ] Yes

  If Yes, Relationship to study therapy:  
  - [ ] Definitely Related  
  - [ ] Probably Related  
  - [ ] Possibly Related

**Treating Physician Comments:**

**Affiliate Site Principal Investigator Comments:**

**Affiliate Site Investigator Completing/Reviewing Report:**

- Name: ______________________  
  - Signature: ______________________  
  - Date: __ / __ / ___
Serious Adverse Event (SAE) Report for Affiliate Sites

Masonic Cancer Center

University of Minnesota

<table>
<thead>
<tr>
<th>Date of Report:</th>
<th>Sequence Number:</th>
<th>Subject Initials:</th>
</tr>
</thead>
</table>

--- NEXT SECTION TO BE COMPLETED BY UMN MASONIC CANCER CENTER STUDY STAFF ---

In the opinion of the UMN Masonic Cancer Center Principal Investigator:

<table>
<thead>
<tr>
<th>Is the SAE</th>
<th>❑ Expected</th>
<th>❑ Unexpected</th>
<th>Is SAE a DLT:</th>
<th>❑ No</th>
<th>❑ Yes - Date BMT database notified: <em><strong>/</strong></em>/___</th>
</tr>
</thead>
</table>

Is the SAE at least possibly attributable to study therapy: ❑ No ❑ Yes

If Yes, Relationship to study therapy: ❑ Definitely Related ❑ Probably Related ❑ Possibly Related

Has the overall risk-benefit relationship of the research changed in light of this SAE: ❑ No ❑ Yes

If Yes, explain:

Does SAE affect risk information in the consent form: ❑ No ❑ Yes

UMN Masonic Cancer Center Principal Investigator Comments:

SAE Report Forwarded to the Following Entities: (Check all that apply)

❑ FDA – Date sent: ___/___/___ ❑ IRB - Date sent: ___/___/___

❑ UMN IND Holder - Date sent: ___/___/___ ❑ Other: ___________________ - Date sent: ___/___/___

UMN Masonic Cancer Center Principal Investigator:

Signature: __________________ Date: ___/___/___
UNIVERSITY OF MINNESOTA

Masonic Cancer Center

Clinical Trials

Monitoring Plan

Revision Date: May 5, 2012
1.0 Purpose of Monitoring Plan

2.0 Definitions

3.0 Minimum Elements Reviewed

3.1 Protocol Compliance

3.2 Subject Screening and Enrollment

3.3 Informed Consent & HIPAA

3.4 Eligibility

3.5 Data Verification

3.6 Adverse Event and Deviation Review

3.7 Essential Document Review

3.8 Investigational Product Accountability

4.0 Required Review and Reporting

4.1 Extent and Frequency

4.2 CTO Quality Assurance Oversight

4.3 Monitoring Reports

5.0 Acronyms
1.0 Purpose of Monitoring Plan

This document describes monitoring requirements for investigator-initiated clinical trials conducted in the Masonic Cancer Center (MCC). The Data and Safety Monitoring Plan (DSMP) defines the scope of trials that require monitoring. The MCC encourages compliance with good clinical practice guidelines; however the standard to which all trials are held is compliance with FDA regulations, CRS SOPs, and IRB requirements.

2.0 Definitions

Authorized designee: Individual authorized by the Principal Investigator to perform specific tasks documented on the Delegation of Authority log

Clinical Research Services (CRS): Department within the MCC that supports clinical research. The CRS offers Clinical, Finance, Protocol Development, Regulatory, and Technology support.

Enrollment: Enrollment occurs when the subject signs the consent form, regardless of eligibility or participation in the study

Investigator-initiated trial: Trial planned and managed by the Principal Investigator

Source document: The first permanent medium where data are recorded (e.g. medical records, subject research file, lab reports, etc.). Shadow charts or printed copies of medical records are not considered source documents

Subject research file: Collection of source documents that are not maintained in the medical record such as outside medical records, RECIST documentation, subject interview forms, documentation of telephone discussions, performance status (Karnofsky, Lansky, ECOG). Subject research files may also contain consent, HIPAA, and SAE forms. Subject research files are not shadow charts and do not contain printed medical records.

3.0 Minimum Elements Reviewed

Monitoring includes review of consent, HIPAA, and eligibility forms, regulatory documents, and subject case report forms to ensure compliance with the protocol, CRS SOPs, and local and FDA regulations. Consent, eligibility, and subject data must be verified against source documents.

The study elements reviewed as part of a monitoring visit are described below:

3.1 Protocol Compliance

a. The monitor must verify:
   • Protocol required visits and procedures have been conducted appropriately
   • All submissions to oversight entities (IRB, FDA, etc.) have been made appropriately and within the required timeframes
   • No deviations from the protocol have been made without prior IRB approval except where necessary to eliminate an immediate hazard to subjects or when the change is only logistical or administrative

3.2 Subject Screening and Enrollment

a. The monitor must verify:
   • Enrollment does not exceed number of subjects approved by the IRB
   • Enrollment and Subject Screening logs are maintained (Screen failures are documented)
3.3 INFORMED CONSENT & HIPAA

a. The monitor must review all applicable consent, assent and HIPAA forms and verify:
   • Subject name is printed, labeled, or imprinted on the form
   • Subject signed and dated the correct version of the form
   • Consent was signed prior to any protocol-specific procedures and this is documented in the subject’s medical record or other source document (e.g. subject research file)
   • All fields or blank lines on the form are complete
   • Legal guardianship is recorded in source documents.

3.4 ELIGIBILITY

a. The monitor must verify each subject met all eligibility requirements as documented in:
   • Medical record
   • Subject research file
   • Eligibility checklist signed by investigator or designee. Note: A signed eligibility checklist may serve as source documentation for some requirements such as life expectancy, birth control discussion, etc.

3.5 DATA VERIFICATION

a. The monitor must verify:
   • All case report forms (CRFs) are completed by the investigator or authorized designee
   • All required CRFs are complete, legible, and well organized
   • CRF data are accurate and supported by source documentation
   • All data corrections are initialed and dated appropriately

3.6 ADVERSE EVENT AND DEVIATION REVIEW

a. The monitor must verify:
   • Adverse events are documented and reported as required
   • Other UPIRTSO events (e.g. breach of confidentiality, deviations that meet UPIRTSO criteria) are reported appropriately
3.7 ESSENTIAL DOCUMENT REVIEW

Essential documents may be maintained in the regulatory binder, OnCore, CRS central file, or subject research file or binder.

a. The monitor must verify all of the following essential documents are well maintained, complete, and current, if applicable.

- 1572
- Adverse event logs and reports
- Correspondence with:
  - Affiliate sites
  - Investigators
  - Monitors
  - Sponsors (IND/IDE holder or funding sponsor)
- Investigational product accountability documents
- Investigator qualification documentation (License, CV, or CV letter)
- Lab certifications
- Monitoring log
- Randomization procedure
- Regulatory applications, reports, and correspondence. IRB approval letters must specify the version of the documents approved
- IRB approved documents
  - Protocol
  - Assent
  - Consent
  - HIPAA
  - Materials provided to subjects
  - Other IRB-approved documents
3.8 INVESTIGATIONAL PRODUCT ACCOUNTABILITY

As part of essential document review, the monitor must verify disposition of investigational products, including those managed by the Fairview Investigational Drug Service (IDS). The monitor must verify:

- Study files contain guidelines and instructions for handling product
- Study documents describe how subjects are instructed on using, handling, storing, and returning product
- Logs indicate name of person who received, used, or disposed of product

- Product disposition records are accurate and complete, including:
  - Shipping receipts (name and address of consignee, type and quantity of the product, date of shipment, batch number or code)
  - Dispensing log
  - Product return and disposal/destruction logs
- Investigational products are not stored with non-investigational products
- Investigational products are stored under conditions specified in labeling or packaging
- Investigational products have not been stored beyond the specified shelf life
- Labels on individual patient bottles/medical devices comply with the requirements for investigational drug or device labeling

The MCT Quality Assurance Director is responsible for quality assurance oversight of products developed or modified by the Cell Therapy Clinical Laboratory. This includes oversight of chain of custody, lot release criteria, etc.

4.0 Required Review and Reporting
4.1 EXTENT AND FREQUENCY

The DSMP defines the minimum extent and frequency of monitoring for investigator-initiated studies in the MCC. More frequent or extensive monitoring may be conducted at the discretion of the DSMC or CTO management.

4.2 CTO QUALITY ASSURANCE OVERSIGHT

a. The designated monitor schedules monitoring visits to meet monitoring requirements and sends an updated monitoring tracker monthly.

b. The tracker includes all trials subject to monitoring in the MCC.

c. The tracker clearly indicates all of the following for each trial:
   - Previous dates trial was monitored in last 12 months
   - Total subjects on trial
   - Percentage of subjects fully monitored to date and at last visit
   - Percentage of consent and eligibility monitored to date
   - Number of new subjects enrolled since last monitoring visit
   - Number of subjects that currently require monitoring

d. The DSMC or CTO management may change monitoring priorities.

e. Masonic Cancer Center trials conducted at a facility other than MCC must follow this monitoring plan.

f. The CTO may permit sites to self-monitoring or allow monitoring to be conducted by an entity other than the MCC; however, all monitoring must comply with Clinical Trials Office SOPs, and the MCC Data and Safety Monitoring Plan.
4.3 MONITORING REPORTS

a. All monitoring activities must be documented on a CTO-approved monitoring report template.

b. Each monitoring report must specify all essential documents and elements of the study the monitor reviewed at the visit.

c. Each monitoring report must document all findings, including those resolved during the visit.

c. The monitor must send a monitoring report to the Principal Investigator, Nurse Manager, Regulatory Manager, and other CTO managers as requested within two weeks of any monitoring activity.

ACRONYMS

CRF    Case Report Form
CRS    Clinical Research Services
CTO    Clinical Trials Office
DSMC   Data and Safety Monitoring Council
DSMP   Data and Safety Monitoring Plan
GCP    Good Clinical Practice
HIPAA  Health Insurance Portability and Accountability Act
IDE    Investigational Device Exemption
IDS    Investigational Drug Service
IND    Investigational New Drug
MCC    Masonic Cancer Center at the University of Minnesota
MCT    Molecular and Cellular Therapeutics lab
NCI    National Cancer Institute
RECIST Response Evaluation Criteria in Solid Tumors
UPIRTSO Unanticipated Problems Involving Risk to Subjects or Others (See IRB website for more details)
**CLINICAL TRIALS OFFICE**

**Masonic Cancer Center**

**Request for Services**

**UNIVERSITY OF MINNESOTA**

### PROJECT MANAGER

### PROTOCOL

- [ ] Draft/Concept
- [ ] Final

- **CPRC/MT#:**
- **Phase:**
- **Site:**
- **Protocol Type:**
- **Program Area:**

### Full Title

### Short Title

### INVESTIGATOR INFORMATION

- **PI Contact:**
- **Co-investigators:**

### MANAGEMENT GROUP

- **Primary:**
- **Secondary:**

### Comments:

---

### ISC TEAM

- [ ] N/A
- **Phase IV/emes/BMT:**
- **Solid Tumor:**
- **ISC Team approval:**

- **Competing protocols?**
  - [ ] Yes
  - [ ] No

- **If yes, specify CPRC/MT#:**

---

### TRIAL SCOPE and ACCRUAL GOALS

- **Scope:**
- **Trial Duration:**
- **Total national accrual goal:**
- **Total local accrual goal:**
- **Annual local accrual goal:**
- **Estimated trial open date:**

---

Version 05/10/2013
**INVESTIGATIONAL PRODUCT/ INVESTIGATIONAL DEVICE**

<table>
<thead>
<tr>
<th>Name</th>
<th>Provided by manufacturer</th>
<th>Use considered SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**STUDY SITES**

- Masonic Cancer Clinic
- Adult BMT Clinic
- Women's Health Clinic
- Breast Center
- Urology/Prostate Clinic
- Peds/Journey Clinic
- Other

**LABS USED**

- N/A
- MCT
- TTL
- PI Lab
- Other

Affiliate sites (site's institutional IRB has oversight)

If yes, list sites

Satellite sites (UMN IRB has oversight)

If yes, list sites

**CTO SUPPORT**

- Protocol Writer
- Regulatory Specialist
- Clinicaltrials.gov

- Research Nurse
  - Start up only
  - Start-up to closure
  - Post start-up only

- CRA

- Contract/SPA

- Budget Development

- Case Report Form Development

- Biostatistics

Version 05/10/2013
ADDITIONAL SCIENTIFIC COMMITTEES

IBC □ Yes □ No  
AURPAC □ Yes □ No  

IND/IDE  
□ N/A  
Will trials be conducted under an IND/IDE □ Yes □ No If yes, trial will be conducted under  
IND/IDE Sponsor  
Would you like CTO assistance with IND/IDE submission and maintenance □ Yes □ No  

FUNDING  
Funding Plan  
EFS Account  

ADDITIONAL INFORMATION  
Comments