

DATA AND SAFETY MONITORING PLAN

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VERSION DATE: DECEMBER 12, 2022

NCI APPROVAL DATE: DECEMBER 15, 2022



Masonic Cancer Center

UNIVERSITY OF MINNESOTA

Comprehensive Cancer Center designated
by the National Cancer Institute

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EXECUTIVE SUMMARY

The Masonic Cancer Center (MCC), 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.

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 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 MCC has the responsibility of clinical research oversight through the Executive Clinical Research Leadership (CRL) Committee. This committee oversees the function of 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, assessing trial risk and confirming 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 MCC 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, 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 UMN REQUIRED TRAINING

The University of Minnesota requires PIs to complete training in Human Subjects Protection and Good Clinical Practice (GCP) per [Section 3.1](#) of the DSMP.

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

The CPRC is responsible for determining a trial's level of risk. Risk is determined by multiple factors including, but not limited to: trial phase, 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 1: 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 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 as applicable for the scope and design of the trial per University and Federal guidelines:

Report	Must Submit To
SAE Reports, including events that occur at Fairview Community sites and any participating sites (see Attachment 2: Serious Adverse Event (SAE) Reporting)	IRB of Record, FDA, SAE Coordinator, Sponsor
Protocol Amendments	IRB of Record, FDA, CPRC, Sponsor
Continuing Review Applications	IRB of Record, FDA, CPRC
DSMC Progress Reports	DSMC
Suspension or termination of trial for safety or non-compliance, i.e. serious findings that would threaten the protection of the subjects or the integrity of the study results	IRB of Record, CPRC, FDA, DSMC, Executive CRL, Sponsor, NCI Program Director responsible for funding the trials

1.7 MULTISITE MANAGEMENT

Oversight of MCC investigator-initiated trials with participating sites is the direct responsibility of the PI. (see [Attachment 3: Procedures Manual for Participating Sites](#))

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. [FDA CFR 21](#)

2. MASONIC CANCER CENTER OVERSIGHT

2.1 EXECUTIVE CLINICAL RESEARCH LEADERSHIP COMMITTEE

Responsibility

The MCC's Executive Clinical Research Leadership (CRL) Committee is responsible for overseeing all cancer-related interventional clinical research. The Executive 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

Membership

Director, MCC; Chair, Executive Clinical Research Leadership and Deputy Director, MCC; Co-Associate Directors for Clinical Research, MCC; Executive Director and Associate Director for Administration, MCC; Medical Director, Clinical Trials Office, Cell, Gene and Immunotherapy Initiative, MCC; Medical Director, Clinical Trials Office, Solid Tumor Unit, MCC; Associate Director of Cancer Prevention and Control, MCC; Oncology Service Line Co-Leads, Fairview Health Services; Director of Cancer Survivorship Services and Translational Research, MCC; Operations Director, Clinical Trials Office-Solid Tumor Unit (CTO-STU); Operations Director, Clinical Trials Office-Cell, Gene and Immunotherapy (CTO-CGI); Clinical Directors, Clinical Trials Office, MCC; Senior Regulatory Manager, Clinical Trials Office, MCC; and Finance Manager, MCC. (see Attachment 5: Executive Clinical Research Leadership Roster)

2.2 CANCER PROTOCOL REVIEW COMMITTEE

Responsibility

The Cancer Center Protocol Review Committee (CPRC) is responsible for reviewing cancer-related clinical trials for scientific merit and prioritizing protocols within the MCC. (see [Attachment 5: Clinical Trial Oversight](#)) 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, the CPRC assigns a risk level to all investigator-initiated trials which determines the frequency of DSMC review and extent of trial monitoring. (see [Attachment 1: MCC Risk Assessment Checklist](#))

The CPRC reviews investigator-initiated and industry sponsored 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 has the authority and responsibility to 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 Adult and Pediatric Hematology, Oncology, Blood and Marrow Transplantation, Radiation Oncology, Surgery and Surgical Subspecialties, Primary

Care, Pharmacology, Epidemiology, Tobacco Research, Biostatistics, 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. (see [Attachment 6: CPRC Roster](#))

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. (see [Attachment 5: Clinical Trial Oversight](#))

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 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 interventional investigator-initiated clinical trials regardless of protocol type, e.g. therapeutic, supportive Care, etc. at least annually from the time a protocol is opened to accrual until it is closed to accrual and all subjects have completed treatment. These trial progress reports cover trial activity at the Masonic Cancer Center and, if applicable, any participating site(s) and include:

- Assessment of expectancy, attribution, and seriousness of adverse events
- Monitoring findings
- Protocol deviations
- Dose limiting toxicities and stopping rule events
- Independent notification of safety concerns from the IRB, CPRC, Executive CRL, or PI

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 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.

When the DSMC or DSMC chair rules to temporarily close a trial, the trial PI must communicate the decision to the Executive CRL, CPRC, IRB, 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, Adult and Pediatric Hematology, Oncology, Blood and Marrow Transplantation, Surgical Oncology, Pharmacology, and others. (see [Attachment 7: DSMC Roster](#))

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.

Data and Safety Monitoring Boards

A Data and Safety Monitoring Board (DSMB) is required for any investigator-initiated trial meeting the following criteria:

- Trial generating blinded, randomized data
- Single or multi-institutional, randomized phase II or phase III trial presenting more than minimal risk

DSMBs are required to have a charter which includes:

- Confidentiality statement
- Plan for maintaining the study blind, including process for emergency unblinding
- Breakdown of all blinded personnel

DSMBs are required to meet at least annually or more often depending on the activity and nature of the clinical trial being monitored. The trial PI must submit all DSMB reports to the DSMC and IRB for review.

Multi-Site Investigator-Initiated Trials

Participating sites of multi-site Investigator-Initiated trials for which Masonic Cancer Center is the lead site are required to enter subject data, including adverse event and serious adverse events (SAEs), dose-limiting toxicities and stopping rule events into MCC's Clinical Trials Monitoring System, OnCore. In addition, participating sites are required to submit SAE reports electronically to the MCC Clinical Trials Office. SAE and outside safety reports meeting the FDA's criteria of a reportable SAE are distributed to all participating sites. (see Attachment 3: Procedures Manual for Participating Sites)

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. Principal Investigators and study staff must complete training in Human Subjects Protection and Good Clinical Practice 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) or other IRB of record 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 DSMC, CPRC, and study sponsor.

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 Office of the Vice President for Research (OVPR).

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.

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 the coordination of MCC's Clinical Trials Office (CTO) and Cancer Informatics Shared Services (CISS).

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 CTO Quality Assurance (QA) Manager is responsible for ensuring monitoring is conducted in compliance with these documents.

The QA 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 are met: (see [Attachment 1: MCC Risk Assessment Checklist](#))

- High or moderate risk MCC investigator-initiated study
- 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
- Industry trials
- National Clinical Trials Network trials

4.4 MONITORING EXTENT AND FREQUENCY

The CPRC is responsible for assigning a risk level to each trial under its review. (see [Section 1.3](#)) The risk level assigned 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 8: 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
 - 100% of subjects enrolled on high risk trials
 - 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 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 to the QA Manager who forwards to the DSMC as appropriate.

Multi-Site Investigator-Initiated Trials

Participating sites may self-monitor on multi-site Investigator-Initiated trials for which Masonic Cancer Center is the lead site. They are required to follow the MCC Monitoring Plan or, if an NCI Designated Cancer Center, they may follow their own NCI approved Data and Safety Monitoring Plan. Alternatively, an external monitoring entity can be used to monitor the trial if the MCC Monitoring Plan is followed. In cases where MCC has contracted with a clinical research consortium to coordinate a multi-site Investigator-Initiated trial, extent and frequency of clinical trial monitoring may be modified to accommodate the consortium's policy and/or practice.

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, protocol adherence and PI oversight. Adequate PI oversight includes, but is not limited to, ensuring that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

5.1 ANNUAL AUDIT PLAN

The QA Manager develops an audit plan approved by the DSMC and carried out by the QA Manager or designee for verifying monitoring integrity and the effectiveness of CTO training and policies. 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 CTO.

- **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 will be subject to an audit after enrolling three or more subjects. A minimum of 3 subjects will be audited.

- **Process Audits**

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.

Routine audits of high risk investigator-initiated trials will not be conducted at Masonic Cancer Center participating sites; however, participating sites are subject to directed audits as appropriate.

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](#)).

ADMINISTRATIVE INFRASTRUCTURE

The Masonic Cancer Center Clinical Trials Office provides the infrastructure necessary to assist investigators in the conduct of their clinical research. Specifically, the CTO 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.

The University of Minnesota requires all research support staff to complete training in Human Subjects Protection, Good Clinical Practice (GCP) and HIPAA and Data Privacy

DEFINITIONS

DSMB: (Data and Safety Monitoring Board): An impartial group established to oversee a clinical trial and review the results to determine if they are acceptable. Members of a DSMB must be multidisciplinary and include members with relevant clinical and statistical expertise.

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.

Participating site: Hospital, clinic, or other provider of medical services that participates in an MCC investigator-initiated trial under the jurisdiction of a local IRB.

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.

ATTACHMENT 1: MCC RISK ASSESSMENT CHECKLIST

POLICY | 718.1pl

MCC Risk Assessment

PURPOSE

The purpose of this policy is to define the criteria utilized by the Masonic Cancer Center (MCC) for risk assessment evaluation and the resulting level of monitoring and Data and Safety Monitoring Council (DSMC) review.

SCOPE

This policy is applicable to all Investigator-Initiated studies under MCC oversight.

POLICY

Risk Assessment

<input type="checkbox"/> High Risk	Studies meeting one or more of the following criteria are High Risk: <ul style="list-style-type: none"> • Phase I/Pilot study for possible Phase I study • Trial involves agent, device, or process initiated or developed by UMN faculty • Faculty held IND, IDE, or ITP
<input type="checkbox"/> Moderate Risk	Studies that do not fit into the High Risk category, with one or more of the following applicable criteria, are Moderate Risk: <ul style="list-style-type: none"> • Phase II or Pilot for possible Phase II • Score of >2 on trial complexity scale (each of the following equals one point): <ul style="list-style-type: none"> – 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 – Has an unusual route of administration and/or safety issues regarding administration – Is an MCC multi-center trial with participating site(s) • PI of < 2 completed clinical trials - applies to interventional drug, biologic and device trials only
<input type="checkbox"/> Low Risk	Interventional or Ancillary/Correlative studies that do not fit into any of the previous risk categories are Low Risk.
<input type="checkbox"/> Minimal Risk	Observational studies that do not fit into any of the previous risk categories are Minimal Risk.

Monitoring & DSMC Review Frequency

Risk Level	Minimum Extent of Monitoring	Minimum Monitoring Frequency	Minimum DSMC Review
High	100% of subjects: consent forms, eligibility, protocol compliance and verification of subject data against source records*	Twice Yearly	Quarterly
Moderate	100% of subjects: consent forms and eligibility 10% of subjects at each monitoring visit: protocol compliance and verification of subject data against source records	Twice Yearly	Twice Yearly
Low	Not required	Not Required	Annually**
Minimal	Not required	Not required	Not required

* 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.

** 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.

Revision Tracking	
New Version # & Date	Summary of changes
v.1 09DEC2022	Initial stand-alone policy document. Previous versions were only found in the MCC Data and Safety Monitoring Policy as an appendix.

STANDARD OPERATING PROCEDURE | 407

Serious Adverse Event (SAE) Reporting

PURPOSE

The purpose of this Standard Operating Procedure is to outline the process for reporting a serious adverse event (SAE). SAE reporting timelines and requirements are determined by [UMN IRB Investigator Manual](#), [21 CFR 312.32: IND Safety Reporting](#), and [21 CFR 812.150: IDE Reports](#).

SCOPE

This procedure applies to the Primary Clinical Research Coordinator (PCRC), Regulatory Specialist, Multisite Program Manager (if applicable), SAE Coordinator, and Data and Safety Monitoring Council (DSMC) Coordinator.

DEFINITIONS

1. **External sponsor:** Industry, National Clinical Trials Network (NCTN), or other academic institution or cancer center which takes responsibility for or initiates the trial.
2. **Local sponsor:** University of Minnesota faculty member who holds the IND under which the trial is conducted or who takes responsibility for and initiates the trial. This individual may be the same or different from the study Principal Investigator.
 - a. There may be instances where a University of Minnesota faculty members takes responsibility for and initiates the trial, but Industry, or NCTN, etc. holds the IND under which the trial is conducted. These are considered to be local trials.
3. **Participating Site:** Hospital, treatment facility, and/or research facility that is not a formal part of the University of Minnesota or Fairview Health Services.
4. **Community Site:** Any Fairview Health Services hospital or medical clinic.

PROCEDURE

Monitoring for SAEs

Monitoring for SAEs will begin with the initiation of study therapy and continue for 30 days after cessation of study therapy unless otherwise indicated in the study protocol.

1. Study therapy is defined as any protocol directed investigational or non-investigational agent. This would include standard of care therapy directed by the protocol (e.g. preparative regimen for a transplant.)

SAE Aware Date

The date that any individual on the Delegation of Authority (DOA) Log becomes aware of a serious adverse event. This includes the Principal Investigator, Co-Investigators, and CTO Study Staff.

24 Hour Initial Notification

Twenty four hours will be considered one business day unless otherwise specified in the protocol or sponsor contract.

1. If the SAE Aware Date occurs on a business day, the count for one business day starts that day and stops

- at the end of the following business day.
- If the SAE Aware Date occurs on a non-business day, the count for one business day starts the first business day after the SAE Aware Date and stops at the end of the following business day.

Documentation of SAE Aware Date

The SAE Aware Date will be recorded on the Adverse Event Log in the “If SAE: Aware Date” field. This form will serve as the original source documentation of the date of notification.

Initial SAE Notification

Upon discovery of a potential SAE:

- If the study PI is unaware of the SAE, inform the PI and confirm that the event is an SAE.
 - In addition, inform the Co-I if they will be completing the SAE Report on the PI’s behalf, and are delegated this authority.
- Notify the study sponsor(s), if different from study PI, within the [One Business Day Reporting Requirements](#) listed above.

Initial SAE Reporting

Within 5 business days of the SAE Notification Date:

- Enter the SAE into the OnCore database, completing all required fields.
- Review event with the PI or Co-I to determine if Unexpected and/or Increased Risk.
 - Initial documentation of the PI/Co-I assessment will be documented in OnCore during this timeframe and later signed off by the PI/Co-I on the Adverse Event Log.
- Submit the SAE Report:
 - To the study sponsor(s) if the report includes additional information from that previously submitted in the initial notification.
 - To appropriate regulatory authorities, i.e. Food and Drug Administration (FDA), Institutional Review Board (IRB), Institutional Biosafety Committee (IBC), etc.:
 - Expedited Reporting:** Determine if the SAE meets the criteria for expedited reporting to any regulatory authorities and submit within the appropriate timeline. Note: SAEs that are neither fatal nor life-threatening must be reported to the FDA within 15 calendar days.
- File copies of all SAE submissions to regulatory authorities in the regulatory binder.
- File the original report in the subject research file.

Additional SAE Reporting Requirements for Local Trials with Participating Sites

If the SAE occurs at the University of Minnesota or one of its community (Fairview Health Services) sites:

- Distribute the SAE Report to all participating sites if the SAE meets criteria of expedited submission to a regulatory authority, or if directed by the MCC PI or sponsor.

If the SAE occurs at a participating site:

1. Send a copy of the Participating Site SAE Report to the MCC PI to review and to complete the Masonic Cancer Center Principal Investigator Assessment at the end of the SAE Report.
2. File the Participating Site SAE Report containing the original MCC PI assessment in the appropriate participating site folder.

Revision Tracking	
New Version # & Date	Summary of changes
v.1 26APR2010	Initial document.
v.2 03JAN2012	
v.3 07MAY2012	
v.4 17MAR2012	
v.5 27MAR2013	
v.6 01MAY2015	
v.7 01MAY2018	
v.8 01NOV2018	New numbering system and formatting. Formerly numbered: 402.00.
v.9 03SEP2020	Added Multisite Program Manager to the scope. Revised requirement for filing copies of SAE Reports in the regulatory binder. Revised requirements for MCC PI's assessment of SAEs when an SAE occurs at an affiliate site. Clarified reporting timelines. Combined policies 203.1pl and 211.1pl into this document and archived the policies.
v.10 07MAY2021	Changed name of Adverse Event Flow Sheet to Adverse Event Log.



Procedures Manual for Participating Sites

Protocol Title: Click or tap here to enter text.

Protocol Number: Click or tap here to enter text.

Version Click or tap to enter a date.

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Masonic Cancer Center Key Study Contacts

	Phone	Fax	Email
Principal Investigator: Insert name	Insert #	Insert #	Insert email
Multisite Program Manager: Insert name	(612) 626-5174	(612) 625-2652	affiliates@umn.edu
	Contact for: Point of contact for study startup process guidelines, study questions, CRF questions, IRB submissions, regulatory updates, data and monitoring requirements, recipient of local SAEs and deviations, verification that new patient slots are available		
Program Manager: Insert name	Insert #	Insert #	Insert email
	Initial contact for budget/contract and departmental negotiations; contact if others are not available		
Study Coordinator: Insert name	Insert #	Insert #	Insert email
	Contact for: Urgent clinical inquiries		
Insert other key contacts as applicable, such as the research lab or other shared services			
OnCore and other databases as applicable Help	oncore@umn.edu		
	Contact for: OnCore and other databases as applicable technical support (training, reset password, etc.)		

PROCEDURES MANUAL SIGNATURE PAGE

Protocol Title: Click or tap here to enter text.

Protocol Number: Click or tap here to enter text.

Procedures Manual for Participating Sites Version: Click or tap here to enter text.

Sponsor Name: Masonic Cancer Center, University of Minnesota

Declaration of Investigator

I confirm that I, and the study staff that I have delegated tasks to, have read the Procedures Manual for Participating Sites for the above-mentioned study. I agree to conduct this trial in accordance with all stipulations of the protocol and procedures manual.

Participating Site Principal Investigator Name: _____

Participating Site Principal Investigator Signature: _____

Date Signed: _____

Introduction

The purpose of this manual is to provide guidance for institutions participating in Masonic Cancer Center, University of Minnesota investigator-initiated trials, hereby referred to as participating sites. This manual ensures appropriate oversight and consistency for clinical research conducted at all participating sites taking part in the study.

All investigators, research nurses, data managers, regulatory specialists, and other study staff that are involved in the conduct of the study are required to read the Procedures Manual for Participating Sites.

Failure to conduct the study in accordance with the protocol and the Procedures Manual for Participating Sites will result in the participating site being contacted by the Data and Safety Monitoring Committee for resolution. Continuing noncompliance may result in suspension of the site.

Study Overview

Schema



Site Initiation

Site Selection

Before the Study Start-up Packet (containing the final protocol and other study documents) can be sent to a site, the following documents must be completed, signed by the participating site's local Principal Investigator, and returned to the Masonic Cancer Multisite Program Manager:

- Confidentiality/Non-Disclosure Agreement
- Study Feasibility Questionnaire
- Contact information for one or more key study start-up personnel (i.e. project manager, regulatory specialist, study coordinator) to whom the Study Start-Up Packet is sent

If further information is needed before deciding to participate, the site may contact the Masonic Cancer Center Multisite Program Manager or the Principal Investigator (PI) to discuss the protocol and participation concerns and/or logistics.

Budget and Contract

Budgeting and contracting occurs during the time the study is going through the regulatory approval process. A fully executed contract should be in place before the Site Initiation Meeting occurs.

If a budget is required for IRB submission, please contact the Masonic Cancer Center Multisite Program Manager.

[Insert additional language if the study is industry-funded. Suggested template language is as follows: The multisite portion of this research study is being funded by [insert drug company's name], therefore a sub-contract between the U of M and each of the participating sites will be used and will include a statement of work, payment terms and scientific, administrative, financial, and reporting requirements].

Study Start-Up Packet and Essential Regulatory Documents

Once the Masonic Cancer Center Multisite Program Manager has received the signed Confidentiality/Non-Disclosure Agreement and the Study Feasibility Questionnaire, they will email an initial study start-up packet to the participating site's local Principal Investigator and research staff.

As soon as possible, the participating site must respond to the Multisite Program Manager's Study Start-Up Packet email with the following:

- Acknowledge receipt of the initial start-up packet
- Indicate whether or not the institution will participate, as follows:
 - If the decision is to participate, please provide an estimated time for submission to the local IRB.
 - If the decision is to not participate, please provide the reason for refusal

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If further information is needed before making a decision, the participating site may contact the Masonic Cancer Center Multisite Program Manager or the Principal Investigator (PI) to discuss the protocol and participation concerns and/or logistics.

If no response is received within 30 days of providing the initial start-up package, it will be assumed that the site is not participating.

Reviews of Local Consent Documents

The Masonic Cancer Center provides a template consent form in Word format to allow editing to meet the site's local institutional consent form format.

In general, the consent form wording should remain the same as the Masonic Cancer Center template with the site's local institutional information added where indicated. The HIPAA language may be presented in a separate document or incorporated into the consent based on the site's local institutional preferences.

The edited consent form with the changes tracked must be approved by the Multisite Program Manager or designee before the participating site submits the study to the local IRB. The Multisite Program Manager is typically able to review the consent form within one week. Participating sites must retain documentation that Masonic Cancer Center has approved the participating site's consent document in the site's Regulatory Binder.

Note: The participating site may proceed with any institutional reviews (i.e. scientific review) that do not require submission of the consent document(s) while preparing the consent.

Initial IRB Approval

At the time of IRB submission, the participating site is expected to email the Multisite Program Manager the submission date and expected date of review.

If any local review committee submission results in stipulations or questions, the participating site is welcome to contact the Multisite Program Manager for assistance in a response. If a local review committee requires further changes to the Masonic Cancer Center approved consent form, the updated consent form must be reviewed and approved by the Multisite Program Manager before re-submission.

Upon receipt of local IRB approval, the participating site emails the approval letter, documentation of the study documents that were approved by the IRB (if not listed in the approval letter) and the IRB approved consent form to the Multisite Program Manager.

Identification of Study Staff

Included in the study start-up packet will be an excel spreadsheet for the participating site to complete with contact information for key personnel. The key personnel spreadsheet should be completed and emailed back to the Multisite Program Manager as soon as possible to assist in beginning to initiate the site.

The Delegation of Authorities Log is used by each participating site to specify the names of staff who will be responsible for implementing specified protocol activities (see the Essential Documents checklist). This document will be completed prior to site initiation. When staff join or leave the participating site's study team, the Delegation of Authorities Log must be updated and a copy sent to the Multisite Program Manager.

OnCore Access

The Masonic Cancer Center uses OnCore® Enterprise Research as its clinical research database. Access to the Masonic Cancer Center OnCore database will be required for all study staff, even if the participating site uses OnCore locally as its own clinical database. Participant enrollment, clinical data capture (via electronic case report forms (eCRFs), serious adverse event reporting, regulatory tracking, and study monitoring are some of the functions performed in the Masonic Cancer Center OnCore database.

The Multisite Program Manager will send an electronic OnCore Access Request Form to site staff to complete to obtain access to the Masonic Cancer Center OnCore database.

OnCore navigation training and study-specific eCRF training is provided by the Masonic Cancer Center OnCore support staff around the time of activation of the study at the participating site.

For OnCore technical support, email oncore@umn.edu. For protocol-specific questions, email the Multisite Program Manager.

Essential Regulatory Documents Checklist

The Participating Site will not be permitted to enroll patients until the essential documents are received. The Initial Essential Documents Checklist identifies the documents that must be in place prior to site activation (see Appendix A).

Site Initiation Meeting

Once the contract/budget is finalized and all initial essential documents are received, or an agreed-upon plan is in place to finalize and obtain all remaining items, the Multisite Program Manager will contact the site to schedule a Study Initiation Meeting.

Site Activation

A Site Activation email will be sent to the participating site and the institution's status changed to "Open to Accrual" in OnCore when all requirements are met. At this point patient screening/enrollment may begin.

Participant Screening and Enrollment

Informed consent must be obtained prior to initiation of any screening procedures that are performed solely for the purpose of determining eligibility for research. The informed consent process must be documented thoroughly in the participant's research chart. The original signed consent form(s) must be kept in the participant's research chart.

Screening Log

Participating sites are required to maintain participant screening records in OnCore in a real-time basis. Screening records must be entered in the Pre-Screening Console (click the "new" button to start entering information on a new participant).

It is recommended that the site contact the Multisite Program Manager and Masonic Cancer Center Principal Investigator to verify the current enrollment status and confirm that there is a slot available, especially once the study gets close to meeting the accrual goal.

If a participant signs consent but doesn't meet the eligibility requirements, the participant's ineligibility status must be documented in OnCore. If the study has a waiting list, notify the Multisite Program Manager and Masonic Cancer Center Principal Investigator to have the participant removed from the potential patient list.

Eligibility Checklist

The study's eligibility checklist is included as an appendix to the protocol and is also available in OnCore's Documents tab. OnCore Enrollment will occur after the consent has been signed and eligibility is confirmed.

Participant Enrollment

Enrollment in OnCore is done by the participating site. As detailed in the study's consent and HIPAA documents, the participant's name and demographics are entered into OnCore.

The date that the site PI signs the eligibility checklist is considered to be the participant's "On-Study Date."

Assignment of a Sequence Number: All patients [add: "and donors", if applicable] who sign consent, including screen failures, must be assigned a Sequence ID Number. The Sequence ID Number is used in place of the participant's direct identifiers on all

documents and samples sent to the Masonic Cancer Center. The Participating Site assigns the sequence number. The format for the sequence number is the abbreviated OnCore Protocol No (insert Protocol No. here), a 3-letter acronym for the study site (i.e. "OSU" for Ohio State University), followed by a 3-digit number beginning with 001. For example, the second patient enrolled on the study protocol number 2016LS056 at the Ohio State University would be assigned the sequence number 16056-OSU-002. Sequence numbers are consecutive and will not be re-used.

Upon completing the participant enrollment, OnCore will automatically generate an email notifying key study personnel of the enrollment.

Regulatory Requirements

Participating sites are responsible for the maintenance of local essential regulatory documents for the conduct of the study at the site. The participating site must submit updated regulatory documents to the Multisite Program Manager.

Institutional Review Board (IRB) Reviews

Participating sites must submit the protocol, future protocol amendments, consent/assent documents, and other applicable materials to the local IRB. Prior to protocol activation at each participating site, the site must submit documentation of initial IRB approval to the Multisite Program Manager.

The Multisite Program Manager will distribute protocol amendments and other required documents to participating sites. Upon receipt of protocol documents, the participating site performs the following:

- 1) Submit edited local consent form in tracked-changes format to the Multisite Program Manager for Masonic Cancer Center approval prior to submission to the local IRB.
- 2) Submit protocol documents to local IRB as soon as possible.
- 3) If the local IRB requests changes to the consent, these changes must be approved by the Multisite Program Manager before re-submitting for final local IRB approval.
- 4) Email the local IRB's approval letter, citing the version date of the documents approved, and the approved consent documents (if applicable) to the Multisite Program Manager.
- 5) The Multisite Program Manager will update the OnCore > Institution > IRB Reviews tab.

Amendments must be approved by the participating site's IRB **within 3 months** from the date that the amendment was received by the participating site. Delinquency may result in suspension of a participating site's ability to enroll new patients to the study.

Throughout the conduct of the study, all IRB approval documentation (i.e. annual continuation reviews, amendments, SAEs, deviations, etc.) must be submitted to the Multisite Program Manager.

Re-consenting of participants occurs when the Masonic Cancer Center or local IRB determines that the addition of new information (e.g. risks, additional tests) needs to be shared with study participants that are already on study. The informed consent process must be documented thoroughly in the participant's research chart. The original signed consent form(s) must be kept in the participant's research chart.

Deviation Reporting

Deviations may be defined as (1) any departure from the protocol or (2) any action associated with the conduct of a clinical trial that does not comply with IRB or federal regulations. Both the Seriousness and Expectedness of the deviation are used to determine the timeline for reporting deviations to Masonic Cancer Center, as follows:

- **Seriousness:**
 - **Major Deviation:**
 - Causes participant harm, significantly increases risk to participant or requires medical intervention to prevent harm
 - Done to eliminate apparent immediate harm caused by the protocol
 - Affects participant rights or welfare
 - Non-adherence to significant protocol requirements, regulations, or GCP guidelines
 - Repeated instances of a minor deviation, suggesting continuing noncompliance
 - **Minor Deviation:**
 - Departure from protocol (usually inadvertent) that does not affect soundness of the protocol or participant safety, rights, or wellbeing
 - Administrative oversight
- **Expectedness:**
 - **Planned deviation:** In rare circumstances, it may be permissible for the Masonic Cancer Center PI and the participating site's local IRB to approve the departure from protocol *prior* to the deviation.
 - **Unplanned deviation:** IRB approval is not obtained prior to departure from protocol. (e.g. Follow-up visit missed).

All deviations must be reported to the Masonic Cancer Center by entering the event in OnCore's Deviations tab (training will be provided) within the timeframe detailed below. For Major Deviations the participating site prints a copy of the OnCore Deviation Report and obtains the site PI's signature. The OnCore Deviation Report does not have to be

printed and signed for Minor Deviations, unless repetitive minor deviation events suggest continuing noncompliance.

[Mention additional study-specific event reporting procedures if applicable.]

In addition to reporting deviations to the Masonic Cancer Center, participating sites are responsible for reporting deviations to their local IRB and other local regulatory oversight agencies as per local requirements.

Reporting Protocol Deviations Timeframe:

1. Deviations that are both **Major** and **Unplanned** must be entered in OnCore and reported to the Multisite Program Manager within 5 working days of knowledge.
2. Deviations that are **Major** and **Planned** must be discussed with the Masonic Cancer Center Principal Investigator and Multisite Program Manager prior to deviating from the protocol. The participating site enters the deviation in OnCore and notifies the Multisite Program Manager upon local IRB approval of the planned deviation.
3. Minor deviations are not reported to Masonic Cancer Center in real time, unless the events suggest continuing noncompliance. Minor deviations should still be recorded in OnCore and are to be addressed during monitoring visits.

Participant Safety Oversight and Event Reporting Requirements

Adverse Event and Serious Adverse Event Reporting

Clinical research studies must be monitored for safety and potential risk to the participant. Monitoring of participant safety is described in detail in the protocol.

Assessment of adverse events is performed by the site Principal Investigator, and includes determination of the following: severity, and attribution of the event. It is the site Principal Investigator's responsibility to ensure that adverse events are accurately recorded in the participant's research chart and to ensure adequate reporting of adverse events, Serious Adverse Events, and all other reportable events as detailed in the protocol Section [insert section #].

Serious Adverse Events are defined in the protocol. All Serious Adverse Events are recorded by completing the SAE Form within the timeframe described in the protocol. [Include reporting instructions per protocol, such as "A subset of SAEs are to be reported expeditiously to the Masonic Cancer Center. Any event that is both serious and unexpected and at least possibly related to the study treatment requires expedited reporting."] [Include additional industry-supporter language, if applicable. Sample language is as follows: "In addition to reporting SAEs to Masonic Cancer Center, a subset of SAEs are expeditiously reported to Miltenyi Biotec, Inc."] Within the timeframes defined in the protocol, the participating site's Study Coordinator begins the SAE Report

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Form, the site Principal Investigator reviews, completes, and signs the form, and the Study Coordinator emails the form along with relevant de-identified source documentation to the Multisite Program Manager.

[Include additional study-specific details as needed. Suggested template language is as follows:

Targeted Toxicities – Adverse event collection will start on Day 1 of the 1st dose of study drug and will focus on targeted adverse events and unexpected adverse events at specific time points in relation to the study drug. This protocol also uses a targeted toxicity form to be completed at times specified in the study and entered into OnCore. This avoids over reporting of events related to standard of care treatment/procedures while focusing on the investigational element of the study.

Dose Limiting Toxicities and Early Study Stopping Events – In addition to monitoring and recording adverse events as defined in the protocol, this protocol also had dose limiting toxicities (DLTs) and early study stopping rule event reporting. Such events may not constitute an adverse event, however they do require immediate reporting by completing the applicable form in OnCore (Stopping Rules or Dose Limiting Toxicities eCRF) and by notifying the Multisite Program Manager.]

IND Safety Reports

All SAEs, whether originating from the Masonic Cancer Center or a participating site, will be reviewed by the Masonic Cancer Center Principal Investigator to confirm the treating physician's determination of relatedness and expectedness. All SAEs that have a reasonable possibility of having been caused by the study procedures and that are both serious and unexpected are reported to the FDA in an IND Safety Report by the Masonic Cancer Center IND Sponsor. The Multisite Program Manager distributes IND Safety Reports, along with a description of modifications to the study if applicable, to the participating sites. Participating sites are responsible for submitting the IND Safety Report to their local IRB or other regulatory oversight committees per local institutional guidelines.

Data Management

Data Collection Database

The Masonic Cancer Center uses OnCore® Enterprise Research as its data entry and data management database. The Masonic Cancer Center OnCore support staff provides OnCore navigation training and study-specific electronic Case Report Form (eCRF) training.

Case Report Form (CRFs) Completion Deadline

Study personnel must complete all CRFs for a participant within the timeline indicated in the study's OnCore Subject Registration and User Guide and eCRF Completion Manual.

Conference Calls

Within the protocol's Conduct of Study section will be the plan for communication between the Masonic Cancer Center and the participating sites. To make these communications meaningful, it is important that OnCore be kept current especially in regards to enrollment, serious adverse events and stopping rule/dose limiting toxicity events.

A regular conference call with the study PI and all participating sites will be scheduled at an agreed upon time. The Multisite Program Manager will distribute an agenda with the conference call information before the meeting. A typical agenda for conference calls will include review of screening/accrual, adverse events, eCRF completion, regulatory updates and any issues, including study deviations. The Multisite Program Manager will distribute minutes from each conference call.

Participating Site Monitoring Plan

Participating sites are responsible for monitoring their own participant data and protocol compliance. Participating sites will be expected to self-monitor following the Masonic Cancer Center's Data and Safety Monitoring Plan (DSMP) unless otherwise arranged. All sites are expected to comply with the Masonic Cancer Center's DSMP when fulfilling these monitoring obligations, as the University of Minnesota in its capacity as the study coordinating center is responsible for FDA reporting and communication.

For this study, complete and adequate monitoring visits must be conducted at least every [specify number] months. The first monitoring visit is due 1 month after the first patient is enrolled at the site or 6 months of opening to accrual, whichever occurs first. For a detailed description of monitoring expectations, refer to the Masonic Cancer Center's DSMP located at <https://www.cancer.umn.edu/for-researchers/clinical-investigator-resources/mcc-dsmp>.

Monitors must record their visits in a Monitoring Log (template available upon request). This document should be retained in the participating site's study regulatory binder.

Participating sites are expected to resolve monitoring findings promptly. Failure of the site PI to adequately address protocol deviations/issues may result in suspension or termination of site participation.

Source documents and study records may be subject to a Masonic Cancer Center audit at the discretion of the Masonic Cancer Center Data and Safety Monitoring Council (DSMC).

Awards and Payments

In order to initiate a sub-award agreement, the participating site completes and submits the Collaborator and Contact Information Form, Statement of Work, Budget/Payment Terms and Schedule, and Audit Certification and Financial Questionnaire (if applicable) to the CTO Contract Administrator assigned to the study.

Study reimbursement and other compensation may be provided for the conduct of the study and shall be made according to the budget and payment schedule of the sub-award agreement. Participating sites are required to submit itemized invoices according to sub-award agreement terms with necessary back up information, such as a list of patients (identified by sequence number or other data that do not include Protected Health Information) that the participating site is billing for. Final invoice must be submitted no later than thirty days after sub-award end date or after receiving notice of termination from primary site. Final invoice must be marked "FINAL." If invoices are not received within thirty days after notification and request of final invoice, the primary site cannot guarantee payment for services performed by participating sites.

Site Close-Out

Study close-out with the local IRB will occur after all participants have completed the study related follow-up and all data has been submitted. All final regulatory documents should be submitted to the Multisite Program Manager, including the IRB closure notice, and the final study delegation log.

Appendix A: Initial Essential Documents Checklist

This checklist can be used to guide collection of documents to be reviewed by the Masonic Cancer Center Multisite Program Manager for activating a participating site planning to take part in a Masonic Cancer Center investigator initiated clinical trial. The essential documents listed here are among the core documentation required by Good Clinical Practices (GCP) that must be in place before the site is activated.

Principal Investigator:

Participating Site:

Protocol Number:

DOCUMENTS TO BE COMPLETED BY SITE PRIOR TO ACTIVATION:

- ☐ **FDA Form 1572**
- ☐ **Laboratory Certification(s)**
- ☐ **Medical Licenses and CVs** (Principal Investigator and Sub-Investigators)
- ☐ **Financial Disclosure Statements** (Principal Investigator and Sub-Investigators)
- ☐ **IRB approval letter**, documenting the version date(s) of the documents reviewed and approved
- ☐ **IRB approved consent form(s)**
- ☐ **Procedures Manual for Participating Sites Signature Page**
- ☐ **Delegation of Authorities Log**

A Delegation of Authorities Log is to be used by each site. A template log will be provided for each site's use; alternatively, the site may use their own log if the site provides their DOA log policy to the MCC Multisite Program Manager.

- ☐ **Protocol Training Documentation**

It is required that protocol training for all study personnel be documented. The protocol training documentation is started at the Site Initiation Meeting. Documentation of training for any staff who were not present at the Study Initiation Meeting must be obtained. Templates for documenting training will be provided; alternatively, the site may use their own training documentation method.

- ☐ **OnCore Access Request Form** (completed electronically)

It is required that, at a minimum, the Study Coordinator obtains access prior to activation. It is acceptable for all other staff to obtain access soon after activation. The Multisite Program Manager will route the electronic access request form upon receipt of the name and email address of study staff members who require access.

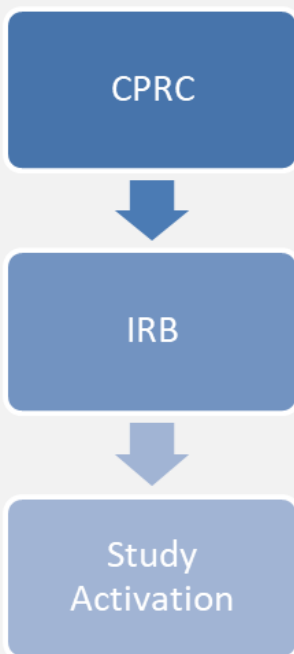
Send the completed essential documents to the Multisite Program Manager via email or fax.

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ATTACHMENT 4: EXECUTIVE CLINICAL RESEARCH LEADERSHIP ROSTER

Director, Masonic Cancer Center
Deputy Director, Masonic Cancer Center
Associate Director of Clinical Research, Masonic Cancer Center
Executive Director and Associate Cancer Center Director for Administration, Masonic Cancer Center
Medical Director, Clinical Trials Office, Cell, Gene and Immunotherapy Initiative
Medical Director, Clinical Trials Office, Solid Tumor Unit
Associate Director for Translational Research
Associate Director of Cancer Prevention and Control, Masonic Cancer Center
Associate Director for Community Outreach and Engagement, Masonic Cancer Center
Co-Directors, Cancer Protocol Review Committee
Oncology Service Line Director, Fairview Health Services
Director of Cancer Survivorship Services and Translational Research, Masonic Cancer Center
Director, Informatics Innovation Dissemination, Core Faculty, Institute for Health Informatics
Executive Director, Masonic Cancer Center - Clinical Trials Office
Clinical Director, Masonic Cancer Center - Clinical Trials Office, Clinical Trials Office, Cell, Gene and Immunotherapy Initiative and Solid Tumor Unit
Clinical Director, Masonic Cancer Center - Clinical Trials Office, Pediatrics
Director of Regulatory Affairs, Masonic Cancer - Center Clinical Trials Office
Director of Quality Assurance, Masonic Cancer - Center Clinical Trials Office
Director, Community Outreach and Engagement
Director, Minnesota Cancer Clinical Trials Network
Finance Director, Masonic Cancer Center

INITIAL REVIEW



PERIODIC REVIEWS

DSMC

Safety Profile

- Data Quality
- Protocol Compliance
- **Authority to close trials**

CPRC

Scientific Merit

- Feasibility
- Prioritization (if competing trials)
- **Authority to close trials**

IRB

Subject Welfare

- Withdrawals
- Monitor Reports / Compliance Review
- **Authority to close trials**

ATTACHMENT 6: CANCER PROTOCOL REVIEW COMMITTEE ROSTER

Name	Expertise/Specialty	Academic/Staff Appt.
Brenda Weigel, MD, MSc (Co-Chair)	Pediatric solid tumor cancers and early-phase drug development	Professor of Pediatrics, Division of Pediatric Hematology/Oncology
Rachel Vogel, PhD (Co-Chair)	Outcomes and survivorship	Associate Professor, Department of Obstetrics, Gynecology and Women's Health (OBGYN)
Ajay Prakash, MD, PhD	GI oncology	Assistant Professor of Medicine, Division of Hematology, Oncology and Transplantation
Ashish Gupta, MBBS, PhD	Pediatric BMT	Assistant Professor of Pediatrics, Division of Blood and Marrow Transplantation
Emily Greengard, MD	Pediatric solid tumor cancers	Associate Professor of Pediatrics, Division of Pediatric Hematology/Oncology
Erin Marcotte, PhD	Epidemiology	Assistant Professor, Epidemiology and Clinical Research
Evidio Domingo-Musibay, MD	Melanoma/sarcoma	Assistant Professor of Medicine, Division of Hematology, Oncology and Transplantation
Heather Beckwith, MD	Breast cancer	Assistant Professor of Medicine, Division of Hematology, Oncology and Transplantation
Irina Stepanov, PhD	Tobacco research	Mayo Professor, Environmental Health Sciences
Jacob Ankeny, MD	Surgical oncology	Assistant Professor, Division of Surgical Oncology, Department of Surgery
Kathryn Dusenbery, MD	Radiation oncology	Professor and Department Head, Department of Radiation Oncology
Lucie Turcotte, MD	Pediatric hematology/oncology and outcomes research	Associate Professor of Pediatrics, Division of Pediatric Hematology/Oncology
Mark Yeazel, MD, MPH	Family medicine	Professor of Medicine, Department of Family Medicine and Community Health
Sasha Skendzel, DNP	Survivorship	Clinical Assistant Professor, School of Nursing
Sally Mullany, MD	Gynecologic oncology	Assistant Professor of Medicine, Department of OBGYN
Steven Fu, MD, MSCE	Internal medicine	Professor of Medicine, Department of Medicine
Anne Eaton, PhD, MS	Biostatistics	Assistant Professor, Department of Biostatistics, School of Public Health
Connor Demorest, MS	Biostatistics	Core Staff, MCC Biostatistics Shared Resource
Katelyn Tessier, MS	Biostatistics	Core Staff, MCC Biostatistics Shared Resource
Lin Zhang, PhD	Biostatistics	Professor, Department of Biostatistics, School of Public Health
Nathan Rubin, MS	Biostatistics	Core Staff, MCC Biostatistics Shared Resource
Ryan Shanley, MS	Biostatistics	Core Staff, MCC Biostatistics Shared Resource
Thomas Murray, PhD	Biostatistics	Assistant Professor, Division of Biostatistics, School of Public Health
Xianghua Luo, PhD	Biostatistics	Professor, Division of Biostatistics, School of Public Health

ATTACHMENT 7: DATA AND SAFETY MONITORING COUNCIL ROSTER

Name	Expertise/Specialty	Academic/Staff Appt.
Frank Ondrey, MD, PHD, FACS (Co-Chair)	Head and neck malignancies	Professor, Department of Otolaryngology, Head and Neck Surgery
Naomi Fujioka, MD (Co-Chair)	Thoracic malignancies Head and neck malignancies Lung cancer chemoprevention	Associate Professor of Medicine
Boris Winterhoff, MD, MS	Gynecologic oncology	Associate Professor, Department of Obstetrics, Gynecology and Women's Health (OBGYN)
Shernan Holtan, MD	Immunotherapy Allogeneic hematopoietic cell transplantation Graft versus host disease Long-term survivorship	Associate Professor of Medicine, Division of Hematology, Oncology and Transplantation
Paul Orchard, MD	Pediatric Blood and Marrow Transplant Metabolic Disorders	Professor, Department of Pediatrics
Stuart Bloom, MD, MSC	Breast Cancer Prostate Cancer Doctoring skills Medical burnout	Associate Professor of Medicine, Division of Hematology, Oncology and Transplantation
Ashley Petersen, PhD	Biostatistics	Assistant Professor, Division of Biostatistics
Qing Cao, MS	Biostatistics	Senior Biostatistician, Biostatistics Core
Connor Demorest, MS	Biostatistics	Staff, Biostatistics Core
Jen Braun, DNP, APRN	Clinical Research	Clinical Director, Pediatrics, Clinical Trials Office
Elizabeth Kerr, BA, RN	Clinical Research	Clinical Director, Solid Tumor Unit and Cell and Gene Therapy Initiative, Clinical Trials Office
Megan Johnson, BS	Clinical Research	Director of Quality Assurance, Clinical Trials Office

MASONIC CANCER CENTER

**Clinical Trials
Monitoring Plan**

Revision Date: March 14, 2020

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1.0 Purpose of Monitoring Plan

This document describes monitoring requirements for investigator-initiated clinical trials conducted in the Masonic Cancer Center (MCC). The NCI approved MCC 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, IRB requirements and MCC Clinical Trials Office (CTO) SOPs.

2.0 Definitions

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

Clinical and Translational Science Institute: Department within the MCC that supports clinical research. Services offered include 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, CTSI and CTO 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 and legible
 - 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 a regulatory binder or a secure electronic file, e.g. Box Secure Storage.

- 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
- Financial disclosure documents
- Screening and enrollment log
- Delegated tasks authorization log Training documentation

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 Molecular and Cellular Therapeutics (MCT) Quality Assurance Director is responsible for quality assurance oversight of products developed or modified by the MCT 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

- The designated monitor maintains a monitoring tracker.
- The tracker includes all trials subject to monitoring in the MCC.
- 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
- The designated monitor schedules monitoring visits to meet monitoring requirements.
- The DSMC or CTO management may change monitoring priorities.
- MCC trials conducted at a facility other than MCC must follow this monitoring plan unless otherwise stated in the MCC DSMP.
- 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 the MCC DSMP.

4.3 Monitoring Reports

- All monitoring activities must be documented on a CTO-approved monitoring report template.
- Each monitoring report must specify all essential documents and elements of the study the monitor reviewed at the visit.
- Each monitoring report must document all findings, including those resolved during the visit.
- The monitor must send a monitoring report to the study's Principal Investigator, Regulatory Specialist, Clinical Research Coordinators, and CTO Quality Assurance team within two weeks of any monitoring activity.

5.0 Acronyms

CRF	Case Report Form
CTO	Clinical Trials Office
CTSI	Clinical and Translational Science Institute
CV	Curriculum Vitae
DSMC	Data and Safety Monitoring Council
DSMP	Data and Safety Monitoring Plan
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IDE	Investigational Device Exemption
IDS	Investigational Drug Service
IND	Investigational New Drug
IRB	Institutional Review Boards
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
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
UPIRISO	Unanticipated Problems Involving Risk to Subjects or Others (See IRB website for more details)