EMORY | WINSHIP CANCER INSTITUTE | Clinical Trials Office

National Cancer Institute-Designated Comprehensive Cancer Center

WINSHIP CANCER INSTITUTE DATA AND SAFETY MONITORING PLAN

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DSMP Version 01/2022: Revisions of the DSMP include the following changes:

- Reporting structure: DSMC Chair directly reports to Winship Executive Director
- Cooperative Group, NIH and NCI trials will no longer be monitored by the DSMC, new Quality Management Department will provide monitoring.
- Added authority of DSMC to suspend trials at other sites for multi-center studies.
- Added Discontinuing Protocol Monitoring Process
- Added Assuring Data Accuracy and Protocol Compliance
- Added Temporally or Permanent Suspension Reporting
- Added Training and Education of DSMC members and Research Personnel
- Added Role of Investigational Pharmacy
- Updated/revised all web links
- Updated/revised spelling, grammar and/or formatting errors
- Added description of the Winship Cancer Institute management services for regulatory, study startup and quality assurance tasks
- Added description of the Treatment Modality Working Groups (TMWG) that define priority trials and set the trial portfolio for all cancer specific interventional trials, specifically investigator-initiated trials that will be monitored under this DSMP
- Updated Clinical Protocol and Data Management (CPDM) Organization Chart (Appendix D)
- Added Treatment Modality Working Group (TMWG) Leaders and Meeting Schedule (Appendix F)
- Updated Protocol Review and Monitoring Committee (PRMC) Membership (Appendix G)
- Updated Data and Safety Monitoring Committee (DSMC) Membership (Appendix H)
- Added Forms (Appendix K - BB)

These items have been approved by the Data and Safety Monitoring Committee at Winship Cancer Institute, Emory University.

This DSMP last approval date by the NCI: 01/16/2015
This DSMP has been revised to reflect process improvements to meet changing compliance for study monitoring.

This DSMP was submitted to the NCI for approval: 03/10/2022
This DSMP was revised under advisement of the NCI to: N/A

VERSION HISTORY

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02/20/2003

Revisions
Version Date
07/09/2008
05/28/2010
08/24/2010
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INTRODUCTION

This document is intended to provide investigators with expert guidance, policies, procedures, and processes that will ensure appropriate oversight and monitoring of the conduct of all cancer-related clinical trials to ensure the safety of participants and the validity and integrity of the data in accordance with National Institutes of Health (NIH) and National Cancer Institute (NCI) requirements. The NIH/NCI suggests that institutions sponsoring a significant number of clinical trials formulate their own Data Safety and Monitoring Plan (DSMP) that can be broadly applied to the individual trials in their portfolio.

The Winship Cancer Institute of Emory University (Winship) has designed the following Data and Safety Monitoring Plan (DSMP) to help ensure the safety of all clinical research participants, the ethical conduct of human studies, and the achievement of scientific goals by ensuring high quality data collection. This DSMP specifies the process for monitoring and auditing those studies which are investigator-initiated and for which a DSMP does not already exist. The Data Safety and Monitoring Committee (DSMC) is the DSMB of record for all interventional, cancer-related clinical research studies which do not have an external DSMB. The DSMP also defines the guidelines for the appropriate and timely suspension or closure to accrual of trials with significant safety, protocol compliance issues, or if the trial cannot be completed successfully due to safety/risk concerns. Winship has implemented a process for routine, real-time data monitoring and safety review of investigator-initiated, interventional trials. The Winship DSMP is in line with recent recommendations from the NIH and the FDA, as detailed at the following web sites:

- 45 CFR 46.111(a)(6) - Criteria for IRB approval of research: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.111
- NIH Policy for Data and Safety Monitoring: http://grants.nih.gov/grants/guide/notice-files/not98-084.html
- Further Guidance on Data and Safety Monitoring For Phase I and Phase II Trials: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html
- Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials: http://grants.nih.gov/grants/guide/notice-files/not99-107.html
- The Establishment and Operation of Clinical Trial Data Monitoring Committees for Clinical Trial Sponsors: http://www.fda.gov/regulatoryinformation/guidances/ucm127069.htm

The DSMP was developed with reference to the *FDA Guidance for Clinical Study Sponsors on the Establishment and Operation of Clinical Study Data Data/Safety Review Committees* (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/establishment-and-operation-clinical-trial-data-monitoring-committees ,
National Institutes of Health Policy for Data and Safety Monitoring dated June 10, 1998 (http://grants.nih.gov/grants/guide/notice-files/not98-084.html) with further guidance issued on June 5, 2000 (https://grants.nih.gov/grants/guide/notice-files/not-od-00-038.html). The National Cancer Institute (NCI) issued a policy on September 30th, 2014, for Data and Safety Monitoring of Clinical Trials (https://deainfo.nci.nih.gov/grantspolicies/datasafety.pdf)
Policy on Peer Review of Data and Safety Monitoring in Cancer Center Support Grants (https://cancercenters.cancer.gov/documents/PolicyforDSMPReview508.pdf)

The Winship DSMP is created and maintained by the Chair of the DSMC. The Winship DSMP will be reviewed annually by the Chair of DSMC and the full DSMC. All revisions will be approved by the Winship Executive Director. Approved revisions and reviews will be documented with an attestation in the current DSMP. Winship faculty and staff are required to review the DSMP and complete an attestation after review. Documentation is maintained in the Data Safety Monitoring (DSM) Office. Winship members are not permitted to lead an interventional, IIT unless the review and attestation has been completed.

Winship also would also like to acknowledge and thank the many other cancer centers who provided their DSMPs as models. We have freely used their language where appropriate. This specific DSMP, however, reflects the practice at Winship. The current DSMP is maintained and available within the Winship Clinical Trials Office intranet and SharePoint.

SCOPE

The Data and Safety Monitoring Committee (DSMC) is responsible for providing oversight to oncology-specific therapeutic/interventional clinical trials conducted by a Winship investigator. Every interventional clinical trial conducted through Emory University's Winship Cancer Institute will have a plan delineated for safety, adverse event reporting, and monitoring. Industry-sponsored trials, National Clinical Trials Network (NCTN), and other studies funded through the NIH/NCI mechanism (i.e., ETCTN) are not under the direct purview of the DSMC. The Winship Clinical Trials Office, Quality Management Department will monitor all NCTN, ETCTN and NCI interventional clinical trials providing final monitoring reports to the Winship DSMC and Emory Clinical Trials Audit and Compliance (CTAC) department. The frequency of monitoring by the DSMC will be dependent upon degree of risk to patients, expected accrual rate, type of study (whether IND/IDE is held by a Winship Investigator), and anticipated safety profile of the investigational interventions. The initial monitoring frequency will be determined at the outset of the study initiation during the scientific review process, and included in the study protocol, although the committee may monitor more or less frequently based on ongoing activity and study conduct. For Winship interventional Investigator-initiated trials (IIT), the protocol-specific monitoring plan will be reviewed and approved by the Protocol Review and Monitoring Committee (PRMC) and DSMC prior to study activation. The Principal Investigator is responsible for notifying the DSMC should any revisions be made to the protocol-specific monitoring plan after initial DSMC approval.

ORGANIZATIONAL OVERVIEW

The organizational structure and reporting scheme for the DSMC within Winship and Emory are outlined below. The Winship DSMC ensures the safety of all research subjects, the ethical conduct of studies, and the achievement of scientific goals by ensuring high quality data collection. IITs, regardless of sponsor, submitted to the Protocol Review and Monitoring Committee (PRMC) must include a DSMP. The DSMP requires data monitoring and safety review of IITs utilizing the Essential Elements of the National Cancer Institute (NCI) guidelines, the FDA regulations, Good Clinical Practice (GCP) Guidelines, and other DSM plans and programs approved by the NCI. DSMC functions independently within Winship to conduct internal monitoring functions to ensure that research being conducted by Winship investigators produce high-quality scientific data in a manner consistent with GCP and appropriate regulations that govern clinical research. The DSMC consists of physician investigators, pharmacist, a biostatistician, and as appropriate, additional clinical staff engaged in clinical research (i.e., nurses, advanced practice providers) who review the results of internal monitoring, and full-time staff that monitor individual charts on the studies the DSMC has identified as needing to be monitored. Required voting members of the DSMC include physicians, a pharmacist,

biostatistician and a non-Winship member. Additional members who may be appointed at the discretion of the DSMC chair and who may have voting rights include advanced practice providers, nurses, patient/family advocates. Clinical research coordinators and regulatory specialists will be appointed to the committee but will not be voting members. In addition, the DSMC dedicated administrative staff prepares reports and correspondence in support of the DSMC. The DSMC is distinct in its leadership and organization from the Clinical Trials Office (which consists of staff involved in the conduct of research and associated supervisory personnel), and the PRMC.

The DSMC and PRMC have distinct and non-overlapping roles in reviewing clinical research conducted by Winship investigators and separate staff and membership. DSMC and PRMC communicate with each other in matters that are relevant to their respective missions. PRMC's purpose is to provide scientific oversight for the conduct of clinical research involving cancer patients at Emory University as part of the Protocol Review and Monitoring System (PRMS) for Winship. The PRMC is responsible for reviewing all new clinical trials involving cancer patients and subjects at risk for cancer. The level of risk associated with each clinical trial is determined during the PRMC review based on set parameters as outlined in this DSMP. An evaluation of the adequacy of the trial-specific data and safety monitoring plan is done by the DSMC. The DSMC will review and approve the protocol specific monitoring plan for all investigator-initiated interventional studies by a Winship investigator, during the PRMC scientific review process. PRMC approval will not occur prior to the protocol-specific monitoring plan being approved by the DSMC. The Principal Investigator is responsible for notifying the DSMC should any revisions be made to the protocol-specific monitoring plan after initial DSMC approval.

The DSMC review for studies is independent of the internal Quality Management (QM) [Quality Assurance (QA)/Quality Control (QC)] process in effect within the Clinical Trials Office and other processes within Emory University. The DSMC, which has the authority to recommend suspension of accrual to studies with problems in data quality, unfavorable risk-benefit ratio, compliance with Emory policy, or compliance with GCP, communicates these administrative recommendations to the PRMC as suspension to accrual on a specific study will affect the ability of that study to meet its scientific objectives and may affect prioritization of accrual onto competing studies. The PRMC, which has the authority to recommend suspension of accrual of studies that have limited accrual or address scientific questions that have been superseded by new data, communicates these administrative recommendations to the DSMC as suspension to accrual on a specific study will affect the schedule for monitoring. When necessary, communication of monitoring reports from the DSMC to the IRB occurs following review of internal monitoring reports by the DSMC. In situations in which immediate reporting to the IRB is indicated, such as unanticipated problems (UPs), serious adverse events (SAEs) which are life-threatening or fatal, and regulatory non-compliance, The PI or designee is responsible for expedited reporting to the IRB.

For pediatric studies, the role of Aflac Cancer and Blood Disorders Center's Data and Safety Monitoring Board (DSMB) is to protect the interests of subjects and the scientific integrity for all therapeutic investigator-initiated clinical trials unless it is provided by another external entity. The pediatric DSMB membership consists of five voting members and four *ad hoc* members if additional expertise is needed. Voting members include physicians, statisticians, other scientists based on their experience and expertise in the design and conduct of pediatric oncology clinical trials. To objectively review trial data and avoid financial influence, DSMB members must be free of conflicts of interest. Committee members with a conflict of interest will not review the trial and follow the standard full disclosure of conflicts per Emory COI policy. On a bi-annual basis, the DSMB reviews trial safety data for stopping rules, deviations, study amendments, accrual rates and

monitoring reports for IITs and any other trial as deemed necessary. *Ad hoc* meetings may be necessary as new safety information becomes available. The Clinical Research Coordinator (CRC) will record meeting minutes for all scheduled and *ad hoc* DSMC meetings. The CRC will distribute meeting minutes to the appropriate parties. For each study reviewed, the DSMC will provide a recommendation for study continuation as planned or suspension. The study's PI will be notified in writing of recommendations generated during the committee meetings. The Compliance Monitor (CM) will carry out the internal monitoring functions for studies under the DSMC's purview. The independent review by the CM ensures subject safety and that the trial is conducted in accordance with protocol parameters, GCP, applicable regulatory requirements as well as accurate and complete reporting of data. Components of the monitoring review include informed consent, eligibility, response, toxicity, source documentation compared to case report forms, data entry timeliness, drug accountability, and essential documents. The frequency of internal monitoring is determined by the rate of accrual for the therapeutic investigator-initiated trials. Additional monitoring may be performed if deemed necessary.

DATA AND SAFETY MONITORING COMMITTEE

Membership

The DSMC consists of a Chair, Vice-Chair, voting members, non-voting members and support staff. Voting members consist of physicians engaged in the care of patients at Winship and at least one non-Winship Cancer Institute Emory faculty member, and a statistician. Additional voting members of the DSMC may include advanced practice providers, clinical and research nurses, and other clinical team members with expertise in clinical research as recommended by the chair of the DSMC. At least one of the voting members of the DSMC are from outside of Winship. Other members of the clinical trials team (including coordinators and research specialists) may be appointed as non-voting members. The Chair of the DSMC will be appointed for a three-year term, renewable twice, by the Executive Director of the Winship Cancer Institute. Committee members will include a Chair, Vice-Chair and members who are active investigators appointed to a three-year term, by the Winship Cancer Institute following recommendations from the Chair of DSMC. The Vice-Chair will serve as a committee member and in this role for three years, renewable twice (Appendix E). The Winship Executive Director reviews membership composition, attendance, and expertise at least annually to ensure appropriate diversity and balance of members. The DSMC will request the presence of non-members on an *ad hoc* basis if additional expertise is necessary for the full review of trial conduct.

At the beginning of every meeting, the DSMC Chair will discuss confidentiality to the DSMC members confirming that decisions and discussions regarding studies reviewed by the DSMC are not shared with anyone outside of meetings. Members may be directed to seek clarification from the PI regrading a study, but actual review decisions are only communicated by the DSMC Chair or Vice-Chair.

Suresh Ramalingam, MD, FACP, FASCO, serves as executive director of Winship Cancer Institute of Emory University (Winship) and associate vice president for cancer of Woodruff Health Sciences Center. **Ramalingam** plays an active role in national clinical trial efforts. He has held multiple leadership roles in the NCI National Clinical Trials Network (NCTN) and ECOG-ACRIN Cancer Research Group, such as the Chair of the Thoracic Malignancies Committee and Deputy Chair of Therapeutics Programs. **Ramalingam** is board certified in medical oncology with national recognition as an investigator and a physician in the area of small cell and non-small cell lung cancer. He has authored over 300 scientific publications and serves as editor-in-chief of CANCER, a peer-reviewed journal of the American Cancer Society. He is a Fellow of the American Society of Clinical Oncology and a Georgia Cancer Coalition Distinguished Cancer Scholar. He has served

as a PI on investigator-initiated as well as high impact, multi-institutional trials for lung cancer, receiving numerous recognitions for this work including as a recipient of an NCI Cancer Clinical Investigator Team Leadership Award. In his role as Executive Director, Ramalingam is responsible for leading Winship's clinical research enterprise including directing the establishment and implementation of the Data Safety and Monitoring Plan (DSMP) through coordinated activities of CPDM, Protocol Review and Monitoring System (PRMS), Data Safety and Monitoring Committee (DSMC), research programs, affiliate sites, and cancer disease-specific working groups. Ramalingam sets the direction and continuously works to strengthen Winship's overall clinical research efforts across all oncology-related disciplines. Ramalingam is supported by a team of highly qualified faculty and staff leaders who implement and manage all Winship clinical trials.

Jonathon Cohen, MD., MS., Chair of Data Safety and Monitoring Committee. Associate Professor of Hematology and Medical Oncology, Co-Director of lymphoma program. **Cohen**'s clinical focus is on the treatment of lymphomas, where he manages both newly diagnosed patients as well as those requiring stem cell transplantation, cellular therapies, and treatment for relapsed disease. He has served as director of the lymphoma clinical trials working group since 2015, is a co-investigator on Winship's NCTN Lead Academic Participating Site (LAPS) award and serves as PI for several investigator-initiated trials at Emory. He is a key member of the ECOG/ACRIN lymphoma core committee, where he is the lead PI for PrE0404 and the ECOG lead for the upcoming clinical trial in elderly patients with untreated MCL (AO52101). He is mentor for several junior faculty members and trainees and has served as faculty of the ASH Clinical Research Training Institute and the Lymphoma Research Foundation (LRF) Clinical Research Mentorship Program. **Cohen** serves as the Chair of the DSMC working with **Ramalingam** to ensure compliance to the DSMP. The Senior Administrator, DSM works directly with **Cohen** to ensure the DSMP is followed, and clinical trials are monitored following the DSMP.

Manali Bhave, MD is the Vice-Chair of the DSMC. She is an Assistant Professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine. Board certified in medical oncology and internal medicine; Dr. Bhave specializes in breast oncology. She is an active member of the Breast Cancer Working Group and the Phase I Clinical Trials Unit and collaborates with other Winship members in clinical trials.

Kristie Blum, MD, is a Professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine. A board-certified hematologist, Dr. Blum has extensive experience in the clinical development of novel therapeutics for patients with aggressive B-cell non-Hodgkin's lymphoma and Hodgkin's lymphoma. Prior to joining Emory in 2017, Dr. Blum was Professor in the Division of Hematology in the Department of Internal Medicine at The Ohio State University - James Cancer Hospital and Solove Research Institute where she was also the Director of the Lymphoma Clinical Research Program. Dr. Blum is co-chair of the NCI Lymphoma Steering Committee. She is also a member of the Lymphoma Research Foundation Scientific Advisory Board, the AllianceCo-Operative Group Lymphoma Committee, the American Society of Hematology Clinical Research Mentoring Program, and the National Comprehensive Cancer Network Hodgkin's Lymphoma Panel. She developed and chaired the first two Lymphoma Research Foundation Clinical Research Mentoring Programs from 2013-2015.

Robert Lyles, PhD, is a is a Professor in the Department of Biostatistics and Bioinformatics in Emory University's Rollins School of Public Health. He is currently Director of the Biostatistics and Bioinformatics Core of Emory's Center for AIDS Research and is a member of the Program Office analytic team for the Bill and Melinda Gates Foundation-funded Child Health and Mortality Prevention Surveillance (CHAMPS)

Network. Dr. Lyles is a Fellow of the American Statistical Association with ongoing interests in statistical methods applicable to epidemiological studies, including missing and mis- measured data problems encountered with surveillance data obtained in mortality and morbidity studies and with laboratory assay data used in HIV and environmental research.

Tamara Miller, MD is an Assistant Professor in the Department of Pediatrics at Emory University. She treats hematology/oncology patients at the Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta. In addition, she conducts research that focuses on improving adverse event reporting and supportive care for pediatric cancer.

Kevin Hall, PharmD is a Bone Marrow Transplant Clinical Pharmacist. He has extensive experience in hematologic/oncology. His practice area is in bone marrow transplants and his research interest is hematologic malignancies.

Stephanie Pouch, MD, MS is an Assistant Professor of Medicine at Emory University. She is actively engaged in the management of infections in solid organ and stem cell transplantation, with a primary research emphasis on multi-drug resistant Gram-negative infections in transplant recipients.

Jill Remick, MD is an Assistant Professor in the Department of Radiation Oncology at Emory University School of Medicine. Dr. Remick practices general radiation oncology and specializes in the treatment of head and neck, and gynecologic cancer. She treats patients at Emory University Hospital and Emory University Hospital Midtown. Dr. Remick's research interests include identifying optimal treatment strategies to improve outcomes while minimizing acute and chronic side effects from radiation therapy.

Jim Zhong, MD, is an Assistant Professor and board-certified radiation oncologist in the Department of Radiation Oncology at Emory University School of Medicine in Atlanta, GA. Dr. Zhong practices general radiation oncology and specializes in the treatment of central nervous system malignancies, including brain and spine tumors, and head and neck cancer. He treats patients at Winship Cancer Institute's Clifton campus and Emory Proton Therapy Center.

Non-voting members:
Stephanie deRijke, RN, MSN, FNP, CIP is the Senior Director for Emory University's Clinical Trials Audit and Compliance Department. She has extensive clinical research experience which includes serving as an investigator of gastroenterology trials at the NIH Clinical Center. In addition, she previously worked to develop the Emory Institutional Review Board Education and Quality Assurance program.

Amanda Lesinski, BS, is the Assistant Director, Regulatory Affairs Maintenance, Clinical Trials Office for Winship Cancer Institute of Emory University. She is responsible for the oversight of regulatory maintenance in the Clinical Trials Office at Winship Cancer Institute. Prior to her appointment at Winship, she served as a clinical trials auditor with an NCI-designated comprehensive cancer center.

Susan Rogers, RPh is a Registry Pharmacist at Winship Cancer Institute. She is the Director of Emory Investigational Drug Service. She coordinated and developed the Emory University Investigational Drug Service. Dr. Rogers directed the department's growth from the beginning of the IDS in the 1980's managing

the daily operations which provided investigational drug services to investigators from all medical/surgical divisions.

Conflict of Interest

DSMC members are subject to Emory's Conflict of Interest Policy. Members of the DSMC may not have any other professional or personal involvement with the study that they are over-seeing, such as serving as a principal investigator, co-investigator, research coordinator, or as a study subject. Individuals invited to serve on the DSMC as either voting or non-voting members will disclose any potential personal, professional or financial conflicts of interest, whether real or perceived, and will abide by the Emory University's Conflict of Interest policy found at http://www.coi.emory.edu/policies/index.html. In addition, financial conflicts of interest must be disclosed to the Conflict-of-Interest Review Office as indicated by Emory's policy. DSMC members with a conflict of interest will recuse themselves from any deliberations or administrative review responsibilities for the study with which they are conflicted. In cases in which the Chair is conflicted, a non-conflicted DSMC member will assume responsibility for administrative review of the study in question. In cases regarding the review of trials in which the Executive Director of Winship serves as the PI, the Vice-President of Research for the Woodruff Health Science Center of Emory University, will assume the responsibility of leading the committee meeting and review, in order to mitigate an conflicts of interest.

Meetings

The DSMC convenes monthly and voting member quorum is required for all monthly meetings. To constitute a quorum, 60% of the DSMC membership must be present, including the DSMC Chair or Vice-Chair at the time the DSMC Chair initiates the meeting. If the DSMC chair or vice-chair are not available for a meeting or are conflicted on a specific trial, the Chair shall appoint a committee member to lead the meeting in his or her absence. During the meetings, the DSMC reviews available aggregate safety data, monitoring report findings with investigator responses in addition to any other supplemental material provided by the investigator that may assist with ensuring an accurate review of the data and safety of the trial. If non-member expertise is warranted for a particular trial during a monthly meeting, the individual will not be present during any DSMC discussions or deliberations to maintain confidentiality. Meeting minutes will be prepared by the designated administrative support staff. The designated Data and Safety Monitoring (DSM) support staff is responsible for maintaining and archiving meeting minutes. Minutes are reviewed and approved by voting members at each monthly meeting. *Ad hoc* meetings may be held to address specific issues that require immediate attention for assurance of subject safety. For decisions regarding dose escalation in Phase I trials, a sub-committee comprised of the DMSC chair, vice-chair, clinical pharmacist, and biostatistician reviews requests and votes electronically on an *ad hoc* basis.

Responsibilities

The DSMC will serve as the DSMB for interventional IITs approved by the PRMC. The DSMC will review and monitor trial safety and progress for investigator-initiated trials. If appropriate, the DSMC will designate and monitor corrective action(s) based on review outcome. Critical protocol violations can result in immediate termination and/or suspension. Major violations can result in suspension with required Corrective and Preventative Action (CAPA). Multiple minor violations and/or predetermined significant data deficiency can result in suspension with required CAPA. The DSMC will have the authority to recommend amending or suspending protocols based upon issues of safety at the local institution or at participating study sites for multi-site trials. In addition to a comprehensive review of available toxicity data, the DSMC reviews all internal monitoring and quality management reports of trials under its purview and requests a corrective and preventive action plan (CAPA) from the PI for identified significant trial conduct deficiencies when necessary.

The frequency of monitoring studies by the DSMC is determined through risk assessment. Monitoring frequency will be determined at the outset of the PRMC review and included in the study protocol, although the DSMC may determine to monitor a study more frequently or less frequently based on ongoing activity and study conduct. The Principal Investigator is responsible for notifying the DSMC should any revisions be made to the protocol-specific monitoring plan after initial DSMC approval. For studies under the DSMC's purview, the protocol-specific monitoring plan must be commensurate with guidance outlined in this DSMP; the responsibility for approval of these monitoring plans resides with the DSMC. Any major irregularities in the conduct of a clinical trial or compliance with study protocol will be reported by the monitors to the DSMC for review. The DSMC Chair will notify, in writing, the PI and the Winship Executive Director of any findings that could be considered an unanticipated problem (UP) involving risk to subjects or others, or serious or continuing non-compliance that affects the rights, welfare, or safety of current or future subjects. Examples of such problems include data insufficiency or data inaccuracy that compromises the scientific validity of the study; serious non-compliance in the conduct of the study or regulatory requirements; or significant deviations in Good Clinical Practice (GCP). Deficiencies in data quality or data completion that could affect the scientific validity of the study will be communicated to the Chair of the PRMC for review by the PRMS.

In the event of major protocol violations, significant or ongoing non-compliance, unfavorable risk-benefit ratio to study participants, or potential unanticipated problems involving risk to subjects or others the DSMC may recommend trial suspension or termination. The DSMC Chair is responsible for notifying, in writing, the recommendation of suspension or termination to the PI and the Winship Associate Director for Clinical Research. The PI is responsible for providing the written DSMC recommendation to the IRB in a timely manner. A decision to halt accrual or all research activities will be made by the Winship Executive Director and will be reported, in writing, to the PI, IRB, the Winship Executive Director, the NCI (when applicable), and other regulatory agencies as needed. The Winship Executive Director has the authority to terminate trials for cause. If the Winship Executive Director decides to accept the DSMC recommendation for trial termination, the Winship Associate Director for Clinical Research will communicate the decision in writing to the PI, IRB, the Winship Cancer Institute Director, the NCI, (when applicable), and other regulatory agencies, as needed.

Serious findings related to deficiencies with protocol compliance, regulatory compliance, data quality or data completion in the DSMC monitoring report may lead to a recommendation by the DSMC Chair to the Winship Executive Director to halt accrual or all research activities pending the development and implementation of a CAPA. The CAPA may include any or all the following: suspension of accrual to the study; additional training for faculty and/or staff involved in the conduct of research; implementation of new procedures; improved procedures for data capture including completion of outstanding case report forms; or required modifications or amendments to the study. If Winship Executive Director approves to halt accrual the PI will notify the IRB. The PI will communicate the CAPA with timeline, in writing, to the DSMC Chair.

Following implementation of the CAPA, the DSMC will determine if it is appropriate to re-monitor the study to ensure that previously identified deficiencies have been adequately addressed. For cases in which accrual to the study or research activities have been suspended, the DSMC will review the PI's response to determine if all items sufficiently address the committee's concerns. The DSMC may accept the response and recommend trial continuation, in writing, to the PI and the Winship Executive Director. If the PI's response is deemed unacceptable or inadequate, the DSMC may request further action be taken to address and resolve significant issues prior to recommending trial continuation. The DSMC will communicate this *further action*

request, in writing, to the PI and the Winship Executive Director. Upon review of the DSMC recommendation, the Winship Executive Director will decide if the trial may be re-opened or if suspension should continue. The Winship Executive Director will communicate the decision in writing to the individuals and entities as previously mentioned above.

At Winship, early phase studies that involve dose escalations are usually conducted and reviewed by the Phase I Clinical Trials Working Group. For Phase I, IITs that are conducted by other working groups, any decision regarding dose escalation/de-escalation will be reviewed and approved by the DSMC prior to implementation. The PI holds the responsibility to notify the DSMC in writing with the supportive data that justifies dose escalation/de-escalation. The committee will review the information provided by the PI and make recommendations for dose escalation or de-escalation.

For studies that include cohorts (e.g., a Simon 2-stage Phase 2 design or a trial with expansion cohort), the PI will submit the toxicity and applicable efficacy data to the DSMC for approval of moving to the next enrollment cohort. For studies that include interim analysis, the analysis needs to be reviewed by the DSMC before accrual can be resumed.

Recommendations and Ratings

The DSMC has authority to request additional information to be provided to the committee, an internal audit of patient record(s) and regulatory information, or protocol amendments(s). The PI will be required to provide any additional information within a specific time frame as determined by the committee. DSM staff will follow-up and provide the DSMC Chair with the required information. The DSMC Chair will review the information and uphold the review outcome or make further recommendations. All DSMC decisions are conveyed in writing to the investigator using disposition forms. DSMC will state specific reason(s) for the decision. Principal investigators may appeal DSMC decisions in writing to the DSMC Chair within five (5) working days. The PI must respond to each reason(s) in the decision. Appeals will be distributed to (2) members of the DSMC not involved in the original review. Reviewers will have five (5) working days to complete their review and return comments to the DSMC Chair. The DSMC Chair will convey the results in writing to the PI. Appeal decisions will be final. The DSMC committee will meet annually to review processes and receive training if needed. The DSMC will make one of the following recommendations:

- **Study Continuation as Planned**: no further action deemed necessary
- **Study Continuation with Stipulations and/or Protocol Modifications**:
  - Stipulations and/or modification are expected to be formally addressed by the PI with a response provided to the DSMC within two weeks
- **Study Suspension with Stipulations and/or Protocol Modifications**:
  - Stipulations and/or protocol modifications are expected to be formally addressed by the PI with a response provided to the DSMC prior to study resumption
- **Study Termination**

Data Safety and Monitoring Administrative Support

Designated DSM support staff provides further support by arranging committee meetings, creating the meeting agenda, and distributing meeting agenda, minutes, and monitoring reports to committee members. All records, including database management, of DSMC activities are maintained by a designated DSM

support staff. The designee will draft the committee recommendation letter for review and approval by the DSMC Chair or Vice-Chair and distribute the approved letter to the study PI, along with other pertinent individuals. If the committee requests additional follow-up or response from the PI, a member of the monitor team or a designated administrative support staff will follow-up to ensure submission of requested documentation.

Interaction with the FDA and NCI
The Winship Associate Director for Clinical Research and the Director of the Clinical Trials Office are the primary contacts for the FDA, NCI, and Cooperative Group (NCTN) for all trial-related activities. The sponsor and investigator responsible for maintaining compliance with the IND/IDE regulations.

RISK-BASED MONITORING

Clinical Trial monitoring is critical to ensuring appropriate trial conduct, the validity and integrity of data, protocol compliance, and patient safety. All clinical trials conducted at Winship, and the affiliate sites are subject to internal monitoring, including those protocols sponsored by NCI, pharmaceutical industry, or other sponsors. The goals of the monitoring process are to ensure and confirm ongoing protocol compliance in accordance with Winship guidelines, policies and procedures and US federal regulations.

The overall objective of the DSMP is to provide oversight and monitoring of all cancer relevant IITs ensuring patient safety, data integrity and collection. Under the direction of the DSMC Chair, the committee is responsible for providing oversight for the cancer center's therapeutic/interventional clinical trials. Monitoring activities are a continuous process conducted by experts in all scientific disciplines needed to interpret the data, ensure patient safety, and review related trial toxicities. Clinical trial experts, biostatisticians, and clinicians knowledgeable about the disease and treatment under study are part of the monitoring group or available when warranted. Participants in monitoring outcomes of the trial are not associated with the trial. The DSMC will implement monitoring activities to ensure that all sites are complying with regulatory and protocol requirements, data quality, and subject safety. The method and degree of monitoring investigator-initiated trials is related to the type of trial and degree of risk involved. The DSMC does not monitor non-interventional clinical trials.

The DSMC is supported by full-time clinical trials monitors and administrative support staff. The internal monitoring team is independent from any study protocol and does not perform any trial-related specific duties to uphold an unbiased approach to study monitoring. Oversight of the monitoring process and identification/assignment of studies for monitoring is provided by the Senior Administrator, DSM, Senior Clinical Trials Monitors, and Clinical Trials Monitors.

A qualified and trained individual will perform trial monitoring. The monitor will have appropriate experience to perform these duties. The monitors will be familiar with the investigational product(s), protocol, written informed consent, SOPs, GCP, and any other applicable regulatory requirement(s). The Senior Administrator, DSM is responsible for ensuring monitoring is conducted in compliance with these documents. Monitors can ask the DSMC Chair (or a designee) or Associate Director for Clinical Research for guidance and resolution of medical questions. Monitoring will be conducted according to the plan defined in the DSMP. These procedures shall assure that monitoring activities meet the FDA's requirements as delineated in 21 CFR 50, 21 CFR 56, 21 CFR 812 for studies conducted under an IDE and 21 CFR 312 for studies conducted under an IND.

Determining the Level of Risk

Determining the level of risk, includes the complexity of the study design, study endpoints, clinical complexity, study population, geography, experience of the participating investigators, experience of the sponsor in conducting these types of trials, data capture requirements, known safety profile of the investigational product, IND/IDE status, accrual rates, stage of the study and follow-up status. The level of risk associated with each trial under the DSMC's purview will be determined during PRMC review in conjunction with the protocol-specific monitoring plan approval by the DSMC. See Table 1 below for details of risk determination. For Winship interventional institutional studies, the protocol-specific monitoring plan is reviewed and approved by the DSMC during the PRMS review process. As part of the initial review of investigator-initiated protocols by the PRMC, the PRMC Chair and assigned reviewers will ensure that each interventional trial is accompanied by an adequate Data and Safety Management Plan. The content of the plan must be commensurate with the level of risk and complexity of the study. The study specific DSMP will be reviewed and approved by the PRMC as part of the initial study review. Upon PRMC approval, protocols utilizing the DSMC are forwarded to the DSMC Chair who then reviews the PRMC's risk-surveillance level recommendation for concurrence. The DSMP now defines the level of risk as high, moderate, or low for Winship institutional trials. Based on that, the frequency of internal monitoring is determined.

A schedule of studies that require DSMC review is maintained by the internal monitoring staff to ensure compliance with the monitoring plan. The monitoring staff are independent and are not associated with any protocols (i.e., do not perform any trial-related duties). Responsibilities of the internal monitors include, but are not limited to, the following: verifying compliance with the protocol and any amendments, informed consent process, eligibility criteria, maintenance of essential regulatory documents, capturing and reporting of adverse events, and accuracy and timeliness of data entry. The DSMC internal monitors perform the monitoring and then present the findings to the committee at the monthly meetings.

Table 1. Guidelines for the Assessment of Protocol Risk

Risk Category	Study Project Characteristics	DSMC Progress Reporting
Low	• Biomarker • Non-Interventional	**None**
Moderate	• Non-therapeutic IITs with IND/IDE (sponsor is Emory faculty) • Phase II interventional or therapeutic IIT with IND/IDE (sponsor is Emory faculty) • Phase I/II IIT of FDA approved agents and other Phase II trials (i.e., commercially available agents or devices; IND Exempt or Abbreviated (Nonsignificant Risk IDE)	**Annual** • Initial study monitoring will occur within 1-year from date of 1st subject accrued to study. • At that time, 2 of the 1st 5 subjects accrued will be monitored. ○ Thereafter, subsequent monitoring will occur in 1 year if any subjects were accrued. The population continuing to receive intervention will be monitored on a study-by-study basis. • At minimum, 10% of subjects accrued since previous monitoring will be reviewed. • An additional subject (or subjects) may be selected based on previously noted monitoring deficiencies or at DSMC discretion.

		• Continued monitoring will occur in twelve-month intervals for the population continuing to receive intervention on a study-by-study basis. • Review of investigator regulatory files, at first and close-out
High	Phase I (toxicity/dose finding) or gene transfer therapeutic IITs with institution or PI as IND/IDE holder (Emory faculty as sponsor) and not routinely monitored by a CRO	**Every Six Months** • Initial study monitoring will occur within 6 months from date of 1st subject accrued to study. o at that time, 2 of the 1st 5 subjects accrued will be monitored. • Thereafter, subsequent monitoring will occur in six-month intervals if any subjects were accrued. The population continuing to receive intervention will be monitored on a study-by-study basis. o at minimum, 10% of subjects accrued since previous monitoring will be reviewed. o an additional subject (or subjects) may be selected based on previously noted monitoring deficiencies or at DSMC discretion. • Continued monitoring will occur in six-month intervals for the population continuing to receive intervention on a study-by-study basis. • Monitoring will include but not limited to: • Review of credentials, training records, the delegation of responsibility logs • Comparison of a "sample" of case report forms (CRF)/EDC will be reviewed to source documentation for accuracy and completion, EDC access will be utilized if available • Review of documentation of all adverse event • Review of informed consent process and eligibility • Monitoring of critical data points (eligibility, study endpoints, etc.) • Laboratory review of processing and storage of specimens • Review of accountability logs, dispensing records, and participant records • Review of investigator regulatory files, at first and close-out

Frequency of Monitoring

Based on a comprehensive review of available toxicity data, efficacy, and internal monitoring reports, the DSMC makes one of the following recommendations: study continuation as planned with no further action deemed necessary; study continuation with stipulations and/or protocol modifications (stipulations and/or modifications are expected to be formally addressed by PI with response provided within two weeks); study

suspension with stipulations and/or protocol modifications (stipulations and/or modifications are expected to be formally addressed by the PI with a response provided prior to study resumption); or study termination. A schedule will be prepared by the internal monitoring staff to ensure that trials under the DSMC's purview are reviewed according to the DSMP or until the DSMC determines there are no subject safety concerns that require further monitoring. Once a study is scheduled/selected for monitoring (i.e., notification sent to PI and applicable study team members), deferment will not be allowed without the approval of the DSMC Chair or Vice-Chair. The DSMC, institution and regulatory authorities' expectation is for study documentation, including data entry, to be maintained contemporaneously throughout trial conduct in a high-quality manner. Thus, the DSMC does not consider monitoring deferment acceptable. See Table 2 below for details of monitoring frequency for trials conducted at Winship sites.

Table 2: Frequency of DSMC Study Review According to Study Risk

Low Risk	Moderate Risk	High Risk
Not reviewed	Monitoring, progress report and toxicity review annually	Monitoring, progress report and toxicity review semi-annually For dose escalation trials not run by the Phase I Working Group, upon completion of each dose level must be approved by expedited review before moving to the next dose level. Phase I trials with an expansion cohort and Simon 2-stage Phase 2 design studies must be approved by expedited review before moving to the next enrollment cohort.

Designated monitors may conduct visits, especially with multi-site trials, to ensure that participating sites PIs and study team members are compliant with the protocol, regulations, and institutional policies, that data are of high quality and integrity, and facilities and staffing are adequate for continued participation in the trial. The participating sites may be required to submit source documents for remote monitoring. The participating sites may be subject to onsite monitoring. Many trials may include a combination of remote and onsite monitoring. The DSMC Chair or committee members may recommend more frequent monitoring, based on study population and/or design for trials that are determined to be high risk or for trials with unanticipated adverse events or compliance issues. Source data verification will be done on 20% of the data. Source data verification for phase I subjects during the DLT period will be done on 100% of the data. Regulatory review is performed annually regardless the chart review frequency.

Monitoring Elements and Structure

Monitoring activities are intended to protect the safety of subjects and ensure the validity of the data and the integrity of the study. Monitoring activities include, but are not limited to, source verification of the following: eligibility requirements of all participants, informed consent procedures and compliance, adverse events and all associated documentation, study drug administration / treatment, regulatory records and site trial master files, protocol deviations, pharmacy records, response assessments, and data management. There are two major monitoring components for investigator-initiated studies:

Central Elements: Used for patient monitoring and includes:

- **Subject Eligibility:** participants who are enrolled onto the study must meet all protocol-defined eligibility criteria, and appropriate source documentation must support eligibility.
- **Consent:** verification that informed consent was obtained appropriately using a consent process and a consent document approved by the IRB. Additionally, each participant must have signed

a HIPAA form authorizing use of their protected health information. If re-consent is required, a review is performed to ensure that subjects were appropriately re-consented with an updated, IRB-approved consent form in a timely manner.

- **Data Quality:** the timeliness, completeness, and accuracy of the data must be sufficient for evaluation of the safety and welfare of study participants.

Study Conduct Elements: Used for study monitoring and includes:

- **Accruals:** adequacy of compliance with goals for recruitment and subject retention are assessed.
- **Treatment and/or Study Procedures:** adherence to the protocol is evaluated. When applicable, appropriate accountability and administration of the investigational agent is determined.
- **Toxicity:** interim/cumulative data are reviewed for evidence of anticipated and unanticipated adverse events. Evaluation, documentation, and appropriate reporting and attribution of adverse events, subject deaths, and withdrawals (i.e., the patient or the physician chooses to discontinue study participation or treatment for that patient) are assessed.
- **Study Outcome:** interim/cumulative data are reviewed to determine whether there are factors that might affect the study outcome, impact the likelihood that the study will lead to generalizable knowledge, or compromise the confidentiality of the trial (e.g., protocol violations).

Close out monitoring is conducted by the Quality Management (QM) Team when all participants have completed the study, including treatment and follow-up assessments. At the closeout monitoring assessment, the QM monitor is responsible for ensuring that the investigator conducted the study according to the protocol and in compliance with Good Clinical Practices and federal and state laws and regulations. The QM monitor will also ensure that the investigator is aware of his/her continued obligations. The closeout assessment visit is to finalize all the necessary procedures to conclude the clinical investigation at a specific investigator site especially when a trial is multi-site. A closeout final report will be generated by the QM monitor and reviewed by the DSMC then sent to the PI of record at each study site.

Monitoring of Multi-Site Investigator-Initiated Trials

A summary of the DSMP for the collaborative trial must be submitted to the PRMC. The PRMC will review the DSMP as part of the scientific review process. The PRMC will ensure that monitoring meets the minimum requirements of the Winship DSMP. If it does not, the Winship DSM support staff will monitor this study for Winship. For trials led by Winship principal investigators that include other sites (Winship is the coordinating site) Winship DSM support staff will monitor these trials including conduct at external sites. For studies led at other sites where Winship is a subsite, Winship DSMC will only monitor those studies that don't have adequate external monitoring from the lead (coordinating) site. For these studies Winship DSMC will only monitor the patients enrolled at Winship. Monitoring will be according to the requirements for an institutional trial of comparable type, including reporting for AEs and SAEs according to Winship standard and through the appropriate channels when the Winship PI does not hold the IND or IDE relevant to the trial. Monitoring requirements are as above based on the Phase and level or risk of the trial (Table 2). The DSMC will monitor the non-Winship site(s) within 6 months of the first subject enrollment at the unaffiliated site. Monitoring frequency at unaffiliated sites will be done according to this DSMP and frequency of monitoring at each site may be increased based on the determination by the DSMC Chair. Subsequent frequency of monitoring will be determined by the DSMC Chair for each activated participating trial site. If the Chair determines that an unaffiliated trial site requires more monitoring based on prior findings, the site will be monitored per the recommendations of the DSMC Chair or possibly suspended if safety issues are identified until an approved corrective action plan (CAPA) is in place.

The formation of a Multi-Site Program enables the Winship CTO to effectively provide oversight for the management of Winship faculty-sponsored trials conducted at participating institutions. The established multi-site SOPs ensure adequate monitoring of trial activities and conduct at participating institutions. The Multi-Site Coordinator (MSC) will carry out the monitoring activities in accordance with GCP, multi-site SOPs and the protocol specific monitoring plan. Winship is responsible for assurance that the MSC is qualified to perform monitoring tasks through training and experience. Furthermore, the ultimate responsibility for overall subject safety as well as quality and integrity of the trial data lies with the Winship sponsor.

Following onsite or remote as applicable monitoring at the participating institution by the MSC, a monitoring follow-up letter will be generated for submission to the sponsor as well as the participating site's PI. The monitoring follow-up letter will also be provided to the Manager of the Internal Monitors for review. Should any serious or significant issues arise that indicate compliance problems or affect subject safety, the MSC's monitoring report will be escalated for full DSMC review. For instances where local internal monitoring is no longer warranted but participating site monitoring continues, the trial data will be reviewed on the original schedule and will include the data for all sites with active subjects. Specifically, the DSMC will review deviations and toxicity data, including SAEs, that occur at the participating institution.

Discontinuing Protocol Monitoring Process(es)
If a trial is closed to accrual, no subjects are receiving treatment, interventions, or follow-up evaluations and the DSMC receives a final summary of the trial progress no additional monitoring will be performed. A closeout form will be submitted to the DSM support staff, a summary of the study status, toxicity data for the remaining patients and any unanticipated problems to be. The DSMC Chair will approve discontinuing monitoring and DSMC oversight. A notice of discontinuation is sent to the PI and the PI notifies the IRB of record. Documentation of the discontinuation is kept in the trial regulatory binder within Complion®. The DSMC monitors all moderate and high-risk trials until all subjects on the protocol have been off study treatment for a minimum of 3-months. The DSMC Chair reserves the right to reject the request and/or reopen monitoring activities should conditions warrant.

Cooperative Group (NCTN, ETCTN), NIH, NCI, and Consortium Studies
Recognizing the benefits of identification of protocol implementation or regulatory compliance problems in real-time, the CPDM has implemented an internal quality management (QM) program. The QM program, led by a Senior Administrator, Quality Management, internal monitoring and cooperative group monitoring, network monitoring, and an audit/inspection preparation will provide monitoring for cooperative group (NCTN, ETCTN), NIH, NCI, and consortium studies providing monitoring reports to DSMC and CTAC for review. The QM team uses a multidisciplinary approach to continued monitoring of cooperative group (NCTN, ETCTN), NIH, NCI, and consortium studies activated in Winship. The QM team ensure protocol compliance with all Winship policies and procedures, FDA regulations, IRB policies, ICH-GCP and adherence to the protocol through monitoring activities throughout the year. The QM team track and evaluate adherence to performance standards and requirements from monitoring, working with the Training, Education and Outreach (TEO) team to for continuous education of research staff and investigators. The QM, DSMC, TEO team, Assistant Directors of clinical operations and Assistant Directors of regulatory meet monthly to evaluate quality trends to revise training curriculum and competency trainings for Winship staff. The QM team will audit patients enrolled on NCTN, ETCTN, NCI, and NIH clinical trials. Frequency of audits depends on the type of protocol, protocol risk, and rate of accrual per the PRMC. Key quality indicators audited against standard operating procedures include informed consent process; eligibility criteria/screening; interim medical history, concomitant medications, identification, and reporting of adverse events, and serious

adverse events; lab test/procedures; deviations/violations; case report form completion; pharmacy/investigational agents; and regulatory compliance. Based upon audits, the QM Coordinator identifies areas in need of corrective action and educates the research staff and investigators. The QM team is responsible for providing CAPAs from audit findings, SOP development and annual reviews or renewals. Audit findings are reported to IRB and DSMC as per institutional policies and procedures. Quarterly audit reports are prepared and submitted to the CTO Director, CTO Medical Director, and Associate Director for Clinical Research for review, approval, and input on further corrective action. Major findings, recommended suspensions, and/or termination of trials will be reviewed addressing major findings and recurrent findings. The CTO Director presents audit findings quarterly to the Clinical Trials Leadership Committee. The QM Coordinator reviews audit findings and corrective action plans with the Treatment Modality Working Group (TMWG). QM will submit all monitoring reports to DSMC and CTAC for NCTN, ETCTN and NCI trials.

Responsibilities and Procedures

The DSMC will identify trials to be monitored at the time of initial PRMC approval. The internal monitors will focus solely on IITs with Emory/Emory faculty as sponsor and trials sponsored by collaborating institutions in which the collaborating site's DSMP does not meet Winship's requirements. Once a trial is selected for monitoring, the assigned DSM monitor will randomly select subject(s) for review based on parameters in Table 1 as noted above. The DSMC Chair, can recommend increasing number of monitored subjects (i.e., findings related to consent, eligibility, incorrect dosing). Although the principal investigator and applicable study team members will receive notification of trial monitoring in advance, the subject selection will not be revealed in advance of the monitoring visit.

The DSM monitors will review (but not limited too):

1. Regulatory documentation including conformance to IRB, informed consent requirements, maintenance of delegation log.
2. Pharmacy operations and use of DARFS or accountability logs
3. Individual subject case
    a. Inclusion/Exclusion criteria to ensure eligibility
    b. Review of data integrity
    c. Rate of data completion
    d. Determination that AEs and SAEs
    e. Toxicity assessment
    f. Tumor response evaluation
    g. Treatment delivery or intervention
    h. Review of credentials, training records, the delegation of responsibility logs
    i. Comparison of case report forms (CRF) to source documentation for accuracy and completion
    j. Monitoring of critical data points (eligibility, study endpoints, etc.)
    k. Laboratory review of processing and storage of specimens
    l. Review of accountability logs, dispensing records, and participant records
    m. Review of investigator regulatory files, at first and close-out

The pre-monitoring meeting is optional. During the pre-monitoring meeting the PI, and any study team members in attendance, will be informed of items and subjects monitored for the DSMC review.

The site prepares for the monitoring by gathering all source documentation pertaining to the selected subject case (or cases for subsequent monitoring). The regulatory binder and records regarding the disposition of investigational drugs, specifically copies of drug orders, return receipts, transfer forms, and DARFs are available to the DSM monitor. The Principal Investigator and his/her study team are available during the monitoring visit to answer any questions and help the DSM monitors locate necessary information in the source documents. Source documents are used to verify specific data related to the clinical trial.

Winship components are evaluated against source documentation and deficiencies are rated using the Cancer Therapy Management Branch (CTMP) standard system of assessment.

- **Critical Deficiency**: Any condition, practice, process, or pattern that adversely affect the rights, safety, or wellbeing of the patient/study participant and/or the quality and integrity of the data; includes serious violation of safeguards in place to ensure safety of a patient/study participant and/or manipulation or intentional misrepresentation of data
- **Major Deficiency**: A variance from protocol-specified procedures or practices that makes the resulting data questionable.
- **Lesser Deficiency**: Finding does not have significant impact on the outcome or interpretation of the study and is not described above as a major deficiency. An unacceptable frequency/quantity of lesser deficiencies should be treated as a major deficiency when determining the final assessment of a component

If the site is found to have a critical or major deficiency, the Winship site PI will be required to submit a written response and/or corrective and preventative action (CAPA) plan to the Winship Quality Management Team.

A copy of the internal monitoring report will be sent to the site to document findings, and copies of the audit will be sent to the PI, CTO Director, and DSMC Chair. Offsite monitoring reports will be forwarded to the PI.

Assuring Data Accuracy and Protocol Compliance
Winship uses the OnCore™ Clinical Trials Management System which serves as a centralized database for clinical trial patient-related data for Winship. Winship requires that data on all cancer clinical trial accruals is entered into this database. The internet-based Clinical Trials Management System was developed by Forte Inc. Data entry is accomplished online using web-based forms, consoles, and entry screens. Winship CTO staff also utilizes OnCore™ for accurate and timely reporting on protocol and patient- related information.

Edit checks for valid entry are done during the process of data entry. Additional edit checks and cross validations are run separately during monitoring interim visits. The web-based case report forms and entry screens have been designed specifically for the needs of Winship researchers and the CTO. Standardized pull-down lists are used when appropriate to facilitate data entry and reduce error. The OnCore™ system allows access from multiple sites, including Winship and affiliated institutions. Users are trained and given appropriate system access and permissions. In the secure OnCore™ system, each user account has a specific access level reflecting the user's role within Winship and his/her needs. This privilege is verified and assigned by the OnCore™ administrator. Users can perform authorized operations (e.g., inserts and/or updates) to records as per their access granted by the administrator. Lead personnel in the CTO can lock data records so they cannot be modified. The OnCore™ application has the following features: (1) a two-factor authentication system for users to log into a secure server, resulting in improved protection of protocol information (2) system audit tables are maintained to track when a user logs in and out of the system; and

(3) application audit tables are maintained to track changes made to the database itself. The OnCore™ database is characterized by the ease of use, accuracy, completeness, timeliness, security, flexibility, and efficiency.

Temporary or Permanent Suspension Reporting
For investigator-initiated trials (IITs), any action resulting in a temporary or permanent suspension of an IIT for which for a study drug is provided by industry, will be reported by the Winship PI to the drug manufacturer within 5 working days. If Winship holds the IND, the temporary or permanent suspension will also be reported to the Food and Drug Administration (FDA). A note to file must document that the manufacturer (and FDA, if applicable) has been notified.

Reporting internal adverse events and deviations
Adverse Events (AEs) are events occurring to patients while on study. Further, as defined by the NIH and NCI, an AE is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. AEs encompass both physical and psychological harms.

AE documentation is the responsibility of the PI, sub-investigator and clinical research nurses who may be participating in the care of the subjects and delegated to perform this activity. A report is prepared by the PI with the clinical research nurse or research coordinator, as required by regulation and the IRB of Record.

An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. In therapeutic interventional trials, each AE is graded on the NCI Common Terminology Criteria for Adverse Events (CTCAE) scale from 1 to 5 and are defined by three sets of terms, expected/unexpected, serious/non-serious, or unlikely/possibly/probably/definitely attributed to the protocol. Expected AEs are those listed as such in the protocol.

Serious AE (SAEs) includes toxicities, which cause the following outcomes, (i) death, or (ii) a life-threatening adverse event, resulting in inpatient hospitalization or a prolongation of existing hospitalization, or (iii) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or (iv) a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Attribution of the AE will be made by the protocol PI in the case of serious or unexpected AE, and by the assigned research nurse in other cases. AE reporting procedures are specified in detail in each individual protocol, depending on the type of study, the type and severity of the AE, the trial sponsor, the IRB of Record, and existence of an IND/IDE.

All events that fall under the definition of serious or unexpected AE including the ones occurring within 30 days following the last treatment date, must be reported to the sponsor within the specified time frame in the protocol and the requirements of the IRB of Record.

For all trials with an external sponsor, internal AEs from Winship are to be reported to both the protocol sponsor and the IRB of record. The Emory University IRB policy may be found at http://www.irb.emory.edu/policies/index.html. For IITs, all unexpected deaths (related or unrelated), Grade 3 and 4 toxicities (with attribution), SAEs, AEs documented for that reporting period (either every three or six months) are submitted to the DSMC for review, who then reports to the IRB with the appropriate recommendations to either continue the protocol as is, amend the protocol, or terminate the protocol, for safety reasons. For studies with >1 Arm, these will be broken down by Arm, comparing toxicities between Arms is required to determine if terminating one Arm is warranted. For multicenter trials, coordinated by Winship, the Regulatory Affairs Office also submits copies of all documentation to the PI at the participating sites, as well as any feedback documentation generated by the DSMC, the IRB, and subsequent responses by the Winship PI. It will be the responsibility of the PIs at the various sites to submit this information to their respective IRBs.

For trials of an investigational agent for which NCI is *not* the IND holder: The controlling regulations are those of the Food and Drug Administration (21 CFR, Part 312.32: Expedited Safety Reporting Requirements for Human Drug and Biological Products) and are available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.32. They describe the responsibilities of the investigator and the IND holder. Additional sponsor or institutional requirements may be appropriate for specific agents and included in the pertinent protocol sections.

For trials involving commercially available agents (no INDs involved): Serious adverse events that occur with commercially available agents/devices are reported through Food and Drug Administration MedWatch (http://www.fda.gov/Safety/MedWatch/default.htm).

For trials involving Recombinant DNA molecules: In addition to the reporting requirements for investigational agents, investigators should adhere to NIH Guidelines for Research Involving Recombinant DNA Molecules (Gene Transfer). (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html)

Food and Drug Administration reporting requirements of serious adverse events for post-marketing trials of vaccines: Serious adverse events must be reported according to applicable FDA regulations (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarketing-safety-reporting-human-drug-and-biological-products-including-vaccines).

INVESTIGATOR RESPONSIBILITIES

Winship 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.

The Principal Investigator is required to provide ongoing supervision and evaluation of the activities of the study, including the frequency and severity of adverse events and whether new risks have been identified

and whether appropriate progress is being made. The DSMP must describe how the PI will perform the supervision and evaluate the progress of the trial, including periodic assessments of data quality and timeliness, subject recruitment, accrual and retention, participant risk versus benefit, and other factors that can affect study outcome. Ongoing oversight should also involve consideration of factors external to the study when interpreting the data, such as scientific or therapeutic developments that may have an impact on the safety of the subjects or the ethics of the study.

The PI is responsible for ensuring that:

- Protocol includes the data and safety monitoring plan and procedures for its implementation.
- All studies have a structured adverse event determination, monitoring, and reporting system, including standardized forms and procedures for referring and/or treating participants experiencing adverse events.
- Protocols describe procedures for protection of human subjects.
- All masked studies describe a randomization scheme, and specific criteria and procedures for unmasking.
- In specific cases where an outside agency is the sponsor of the test agent, i.e., holder of the Investigational New Drug (IND) application, the Principal Investigator submits individual adverse event reports to the funding agency (sponsor) in accordance with agency and FDA regulations.
- Regularly submits reports as designated and required by this plan.
- Protocol amendments are submitted per this plan for review prior to IRB submission and approval.
- The appropriate committees of the research oversight system and applicable personnel are informed of actions, if any, taken by the IRB as a result of Continuing Review or any other IRB submission (e.g., Reportable New Information).
- All decisions made by the research oversight committees are adhered to (e.g., protocol suspensions or closures).
- The informed consent document is complete and accurately reflects the risks and other essential information as part of the initial submission to the PRMC. If a waiver of consent will be requested, a justification must be submitted to the IRB.
- Protocol serious adverse events, adverse events and protocol deviations are submitted to the IRB of Record and the Sponsor of the trial.
- With the assistance of CTO staff, participating sites enrolling in multi-center trials are kept informed of unanticipated SAEs and/or any problems identified by the DSMC or IRB.
- The PI is responsible for following all protocol-specific early stopping rules.
- In accordance with NIH policy released September 22, 2000, entitled “Notice to NIH Grantees/Contractors Regarding Letters Or Notices From The Food And Drug Administration (FDA),” the Lurie Cancer Center requires the PI of any IND or IDE trial receiving federal funds to inform the awarding Institute of significant communications from FDA.
- As per NCI requirements, the NCI Program Director responsible for funding a trial must be informed of any communication affecting the status of NCI-sponsored trials (e.g., trial suspension or closure).
- In accordance with federal policy, the PI is responsible for clinicaltrials.gov trial registration and reporting. The responsible party for an applicable clinical trial (ACT) must register the trial and submit results information. The responsible party is defined as: The sponsor of the clinical trial, as defined in 21 CFR 50.3; or The principal investigator (PI) of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the PI is responsible for conducting the trial, has access

to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements for the submission of clinical trial information FDAAA 801 and the Final Rule - ClinicalTrials.gov

Required Training
Winship requires PIs to complete training in Human Subjects Protection, Good Clinical Practice (GCP) through Collaborative Institutional Training Initiative (CITI) training modules and Winship Investigator Training through the Winship CTO Training/Education/Outreach Department.

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 family. Winship has established mechanisms to identify and manage potential conflicts, including annual disclosure requirement, research and sponsored project application questions, and informal communications.

Trial Conduct
Prior to implementing a trial, the PI must receive written approvals from the PRMC, 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 Emory University requirements and applicable FDA regulations
- Ensure continued scientific and clinical relevance and validity of the trial

DSMP AND PRMS PURVIEW OVER CANCER-RELATED CLINICAL RESEARCH CONDUCTED AT WINSHIP CANCER INSTITUTE OF EMORY UNIVERSITY
All clinical research conducted at Emory University that involves interventions specifically targeted towards cancer patients or patient populations specifically identified as being at risk for cancer (Interventional Preventative and Interventional Diagnostic) will be entered into the Central Winship Cancer Institute Clinical Research database. All cancer-related clinical research studies will be reviewed by the PRMC as part of the PRMS of the Winship Cancer Institute and all interventional studies will be monitored by the DSMC as part of the DSMP of the Winship Cancer Institute. Faculty in all departments conducting interventional research conducted at Emory University will be responsible for ensuring that the studies are conducted in accord with FDA human subject's protections regulations 45 CFR 46, 21 CFR 50, 21 CFR 56, 21 CFR 312 for studies conducted under an IND and with 21 CFR 812 for studies conducted under an IDE.

The PRMC is a multidisciplinary committee (see Appendix G) charged with providing peer review of the scientific merit of all cancer-related clinical research. For the purpose of this committee "cancer- related" is defined as any study designed to diagnose, prevent, or treat cancer; or provide supportive care to patients with cancer. The primary goal of the PRMC is to ensure that all Winship cancer-related clinical research involving human subjects are:

1. Scientifically meritorious
2. Appropriately designed, specifically from biostatistics perspective
3. Prioritized within Winship Treatment Modality Working Groups'(TMWG) research portfolios to avoid competing trials as well as aligned with Winship's overall institutional priorities for clinical research

4. Feasible for completion or in meeting institutional accrual goals
5. Assessed for the adequacy of the data and safety monitoring plans based on the risk level of the study
6. Monitored regularly for accrual and scientific progress. In the context of the PRMC, a cancer research study is defined as a formal research plan with a hypothesis and aims intended to evaluate an untested, unproven, or unknown regimen or procedure for the screening, diagnosis, staging, treatment, support, outcome, prevention, control, or characterization of human subjects regarding cancer.

The PRMC has the authority to open cancer research studies of high scientific merit and to suspend or close cancer-related research studies based on a lack of scientific progress, including low accrual. Only cancer related studies initially approved by the PRMC may proceed to review by the IRB of record. IIT, peer-review grant supported trials are submitted to the Emory IRB, and NCI-sponsored NCTN trials are submitted to the Central IRB (CIRB). The appropriate committee maintains a copy of all reviews of protocols, which may be requested or reviewed by the NCI.

Scientific amendments to IITs will be reviewed by the Chair of the PRMC, or in the absence, the Co-Chair of the PRMC. The DSMP is distinct from, and complements, the activities of the Protocol Review and Monitoring System (PRMS) and the Clinical Protocol Data Management (CPDM) functions of Winship. The Winship DSMP covers all clinical research activities of Winship. The PRMS, which encompasses the disease-specific treatment modality working groups (TMWG) and the Protocol Review and Monitoring Committee (PRMC), is an essential component of the conduct of cancer clinical research at Winship. The PRMC has the authority to open protocols that meet the scientific merit and scientific progress of Winship and to close protocols that do not demonstrate scientific progress. The PRMC works with the TMWGs to approve and prioritize these studies. The PRMC assigns the risk of approved protocols, which is one criterion for the frequency of ongoing monitoring by the DSMC. The DSMC is responsible for ongoing real-time monitoring of IITs at Winship and is responsible for monitoring patient safety and closing trials for safety reasons. The Executive Director of Winship holds overall responsibility for overseeing data and safety monitoring and is assisted by the DSMC for all Winship investigator-initiated, interventional trials.

CLINICAL TRIALS OFFICE (CTO)

The Winship Clinical Trials Office oversees the Clinical Trials operations at Emory University, Winship Cancer Institute, which provide an infrastructure (e.g., clinical research nursing, clinical research coordination, data management, regulatory affairs, protocol review analysts, quality assurance and financial aspects) to support investigators conducting cancer clinical trials. With its in-depth expertise in coordinating, managing, and monitoring different types of studies including complex phase I and IITs, the CTO plays a crucial role in this important research area. The CTO is responsible for providing oversight, performance monitoring and training of their staff. Additional education and training e.g., with OnCore™ Clinical Trials Management System are provided by the CTO. The CTO synchronizing and centralizing the clinical trials-related activities, policies, and Standard Operating Procedures (SOPs). Both CTUs utilize the same database (OnCore™) for patient and trial-related information. All cancer clinical trials, whether supported by CTUs or not, are required to use the OnCore™ database.

Clinical research nurses/coordinator review all subjects on clinical treatment protocols covered by the DSMP. Subjects are evaluated during treatment and at protocol specified follow-up visits. Toxicities that occur are

assessed and reported to their respective committees each week. Serious adverse events (SAEs) are reported to the attending physician, the principal investigator (PI), the respective IRBs per their policies, sponsor and to the appropriate agency. The CTO QM staff performs quality assessments to ensure accurate and timely collection and reporting of data, as well as compliance with all applicable regulations.

The CTO functions, as related to Cancer Center Support Grant (CCSG)-mandated functions and to NCI guidelines, are overseen centrally by the Winship CTO Director, Medical Director and Administrative Director, who provide coordination and oversight of the CTO to ensure alignment of procedures and compliance with Winship policies.

Treatment Modality Working Group (TMWG)
TMWGs include a multidisciplinary team of Winship members from across departments and schools interested in pursuing research in the working group disease or treatment modality. The TMWGs review all clinical research proposals related to the disease or treatment modality regardless of PI specialty or department. TMWG manage the research portfolio across Winship main and affiliate sites (Table 1). TMWGs meet at least once monthly to coordinate the development of interventional treatment and non-interventional clinical trials in collaboration with CCSG programs. The 15 TMWGs represent Winship's clinical activity and are responsible for determining study priority prior to the PRMS submission and review trial portfolios for scientific relevance and alignment with the needs of the catchment area as outlined in the COE initiatives. TMWGs are a forum to plan therapy and consider patients for clinical trial participation. The working group Assistant Directors, CROM, CRTS, CRN, CRC, and regulatory specialist attend the meetings. The CRS facilitate the meeting with the TMWG leader and PRMC staff to promote standardization within the TMWG and movement of protocols through the PRMS and IRB review. The Feasibility Checklist seeks to enhance implementation of the clinical trial and improve communication. This review occurs prior to the working group meeting by the CROM of clinical operations, CROM of Regulatory Affairs and PI of the trial.

Clinical Trials Office
The Winship CTO encompasses the administrative/regulatory and implementation aspects of clinical protocol management at Winship. The CTO supports all essential services necessary to perform clinical research in compliance with all regulations of Good Clinical Practice (GCP). The CTO administrative and regulatory activities related to data and safety monitoring summarized below:

Clinical Operations Unit

- Hires and supports clinical staff responsible for coordinating and implementing studies
- Reviews proposed protocols as part of disease specific clinical work group for procedural nursing issues
- Coordinates clinical research activities in compliance with sponsor and regulatory requirements
- Screens patients for clinical studies
- Assists with consenting patients to clinical trials
- Reviews eligibility criteria and implementation of study criteria
- Assesses patient safety
- Coordinates study treatment administration
- Tracks all protocol deviations
- Conducts patient follow-ups
- Collects research data

- Resolves monitoring queries

Regulatory Affairs

The Regulatory Affairs team provides technical and administrative support for consent and HIPAA authorization form development and all IND/IDE forms needed for IRB and FDA submission. Regulatory Specialists provide support from initial protocol submission to PRMC, IRB, and Office of Sponsored Programs, trial activation, management of amendments, continuing IRB reviews, external reporting of serious adverse events, and management of IND/IDE applications. Winship uses three IRBs: the NCI Central IRB for NCI-sponsored studies; Western IRB for industry-sponsored randomized phase III trials; and Emory IRB for all other trials including institutional trials. In addition to working with IRBs, the regulatory specialists prepare studies for review and approval by other site-specific regulatory bodies, i.e., research oversight committees, ethical and religious oversight committees, and VA Privacy Board.

The CTO administrative and regulatory activities related to data and safety monitoring summarized below:

- Assembles all documents needed to open a study
- Initiates confidentiality and Disclosure Agreements
- Coordinates IRB applications and correspondence
- Processes adverse events
- Tracks study contract
- Coordinates protocol continuing review and reports
- Coordinates protocol amendments
- Implements study terminations
- Retains training logs, CLIA certificates and curriculum vitae
- Retains document storage, conflict of interest records and communication with all Emory, Winship Affiliates, NCTN groups, NCI, sponsors, and FDA regulatory committees or spokespersons
- Arranges site initiation meetings

Investigational Pharmacy

The IDS is an integral part of the research enterprise at Emory University. Since January 1, 2008, University policy has required that investigators who conduct drug studies use IDS for the management and dispensing of research drugs. The policy applies to all investigational drugs and drugs provided free of charge and used in clinical trials. IDS provide research pharmacy services to Emory and Winship patients, investigators, and sponsors, and in the process ensure that research drugs are handled safely, accurately, and effectively. IDS strives to provide quality and efficiency in research drug management, enhance patient care in research and always ensure audit-readiness.

The Investigational Pharmacy (NOT within the CTO) activities related to data and safety monitoring summarized below:

- Reviews protocol for study drug concerns
- Receives investigational and/or study drugs
- Maintains drug accountability
- Verifies ordering physician is on the Form FDA 1572, if applicable
- Stores, prepares, and dispenses study drugs

Quality Management

Winship has made it a priority to continuously strengthen our internal quality management program. Quality management is an independent office within Winship CTO, reporting administratively to the Director of the Winship CTO. To ensure adequate quality controls at all levels of clinical research has required the

interaction of a number of Winship CTO employees, oversight by the DSMC and Emory Clinical Trials Audit and Compliance (CTAC). Currently there are two procedures in place for quality oversight: routine quality assurance monitoring review by the CTO Quality Management Department for NCTN, ETCTN, and NCI trials (DSMC for IITs) and internal audits by CTAC. Emory CTAC works to ensure compliance in clinical trials at Emory University by quality assurance reviews, training/education, providing tools for compliance, and quality improvement. The CTAC team has experience in the roles of investigators, bench scientist, clinical research coordinators/nurses, clinical trial monitors, regulatory, research and development, and quality assurance.

Recognizing the benefits of identification of protocol implementation or regulatory compliance problems in real time, the CTO has implemented an internal quality management (QM) program. The QM team uses a multidisciplinary approach to continued monitoring of clinical trials activated in Winship. The QM team ensure protocol compliance with all Winship policies and procedures, FDA regulations, IRB policies, ICH-GCP and adherence to the protocol through monitoring activities throughout the year. The QM team track and evaluate adherence to performance standards and requirements from monitoring, working with the training and education team to for continuous education of research staff and investigators. The QM, DSMC, Education/Training/Outreach team, ADs of clinical operations and ADs of regulatory meet monthly to evaluate quality trends to revise training curriculum and competency trainings for CTO staff. The QM team will audit the first patient enrolled on an institutional or NCTN trial, and the first patient enrolled by new clinical research staff members. Frequency of audits depends on the type of protocol (institutional studies are given the highest priority), protocol risk, and rate of accrual per the DSMP. Key quality indicators audited against standard operating procedures include informed consent process; eligibility criteria/screening; interim medical history, concomitant medications, identification, and reporting of adverse events, and serious adverse events; lab test/procedures; deviations/violations; case report form completion; pharmacy/investigational agents; and regulatory compliance. Based upon audits, the QM Coordinator identifies areas in need of corrective action and educates the research staff and investigators. The QM team is responsible for providing CAPAs from audit findings, SOP development and annual reviews or renewals. Audit findings are reported to IRB and DSMC as per institutional policies and procedures. Quarterly audit reports are prepared and submitted to the CTO Director, CTO Medical Director, and Associate Director for Clinical Research for review, approval, and input on further corrective action. The CTO Director presents audit findings quarterly to the CTLC. The QM Coordinator reviews audit findings and corrective action plans with the TMWG.

The CTO quality management activities related to data and safety monitoring summarized below:

- Compiles data for monitoring as defined by the DSMP and reports the results to the DSMC.
- Completes second review of eligibility for off-site (affiliate) enrollments to IITs and NCTN protocols.
- Conducts ongoing retrospective and focused audits on selected protocols
- Reviews all unexpected deaths on study for IITs and submits to DSMC for action
- Serves as the point of contact for external audits (NCTN, ECTCN, and NCI)
- Receives and reviews results of external audits (NCTN, ECTCN, and NCI) and works with PI and CTO Director to take appropriate action
- Prepares or coordinates formal external triennial audit responses with cooperative groups
- Provides education based on audit results
- Provides quarterly report of auditing activity to the Winship Executive Director, AD of Clinical Research, CTO Director and Medical Director, and the Chairs of the PRMC and DSMC.

Institutional Review Board (IRB)
Winship clinical trials are overseen by the Institutional Review Boards (IRBs) and operate under their respective Federal-Wide Assurances and their IRBs are registered with the Office for Human Research Protections. Moreover, Human Subject Protection Programs at both IRBs are accredited with the Association for the Accreditation of Human Research Protection Programs, Inc.

IRBs adhere to federal, state, and local regulations and guidelines for Human Subjects Research Protection and ensure that research meets ethical standards as per these regulations. The IRBs require certification of the PI and anyone who obtains written consent for the protocol in human subject protection. This requirement also applies to Winship staff. The initial review of a cancer-related trial by the IRB can only take place after PRMC review and approval. As per IRB policies and procedures, the IRBs review protocols, consent forms, amendments, continuing reviews, SAEs and IND safety reports, protocol violations and deviations, and other study-related actions, as appropriate. As part of the continuing review process, the IRBs review study progress including accrual. IRB members are expected to objectively evaluate all protocols presented to the IRB to ensure adequate protection of human subjects. Any member with an actual or perceived conflict of interest must excuse himself/herself from voting on a protocol with which he/she has a conflict. All IRB members are required to complete a core educational program, a new member orientation and educational programs, as well as continuing education and training, as appropriate.

AUDITS
External Audits Requested by the Winship Executive Director
The Winship Executive Director may request an external audit of a study by non-Winship or non-Emory faculty in exceptional circumstances, such as overwhelming conflict of interest by the members of the DSMC that would preclude sufficient members for an impartial review. If the Winship Executive Director determines that an external audit of the study should be conducted, he/she will appoint external auditors (who may be members of the Emory faculty who are not involved with the study or outside, non-Emory experts) to conduct such an audit. The Winship Executive Director will determine if monitoring is needed for trials that are outside of the scope of DSMP (e.g., COVID, NCTN, industry). The Winship Executive Director will establish the scope and conduct of the audit and allocate staff support for the audit including procedures for obtaining charts, facilitating access to the electronic medical record, etc.

Independent Audits
Audits beyond the scope of internal monitoring, as described in this document, can be done “For Cause” at the discretion of the DSMC. If such an audit is required, a qualified independent auditor who may be a member of the Winship, Emory faculty who are not involved with the study, or outside experts will be identified and engaged to conduct the audit. The report of such an independent audit will be delivered directly to the DSMC and reported to the IRB if appropriate.

Appendices

Appendix A: Abbreviations
Appendix B: Operational Definitions
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Appendix R: DSMC Toxicity Review Letter
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Appendix T: DSMC Patient Review Form
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Appendix X: DSMC Study Monitoring Disposition Letter
Appendix Y: Interim Analysis Report
Appendix Z: DSMC Corrective Action Follow-up
Appendix AA: DSMC Appeal Letter
Appendix BB: DSMC Notice of Review of Primary Institution’s Monitoring Plan

APPENDIX A.

ABBREVIATIONS

AE	Adverse Event
AER	Adverse Event Reporting
COI	Conflict of Interest
CAPA	Corrective and Preventive Action
CFR	Code of Federal Regulations
CR	Continuing Review
CRA	Clinical Research Administrator
CRC	Clinical Research Coordinator
CRF/eCRF	Case Report Form/electronic Case Report Form
CRN	Clinical Research Nurse
CTAC	Clinical Trials Audit and Compliance
CTO	Clinical Trials Office
CTRP	Clinical Trials Reporting Program
DLT	Dose Limiting Toxicity
DSM	Data and Safety Monitoring
DSMB	Data and Safety Monitoring Board
DSMC	Data Safety Monitoring Committee
DSMP	Data and Safety Monitoring Plan
FDA	Food and Drug Administration
ICH-GCP	International Conference on Harmonization-Good Clinical Practice
IDE	Investigational Device Exemption
IIT	Investigator Initiated Trial
IND	Investigational New Drug Application
IRB	Institutional Review Board
MSC	Multi-Site Coordinator
NCI	National Cancer Institute
NCTN	National Clinical Trials Network
NIH	National Institutes of Health
ORC	Office of Research Compliance
OHRP	Office for Human Research Protections
PI	Principal Investigator
PRMC	Protocol Review and Monitoring Committee
PRMS	Protocol Review and Monitoring System
QA/QC	Quality Assurance/Quality Control
QM	Quality Management
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TMWG	Treatment Modality Working Group
UP	Unanticipated Problem

APPENDIX B.

OPERATIONAL DEFINITIONS:

To guide the reader of the Data and Safety Monitoring Plan (DSMP) the following operational definitions of the components of the Winship Cancer Institute clinical trials operations are provided.

Clinical Studies: The National Cancer Institute (NCI) defines a clinical trial operationally as "a prospective study involving human subjects designed to answer specific questions about the effects or impact of particular biomedical or behavioral interventions; these may include drugs, treatments, devices, or behavioral or nutritional strategies. Participants in these trials may be patients with cancer or people without a diagnosis of cancer but at risk for it."

Definitions used here are from the P30 Cancer Center Support Grant Data Table Guide 2017. The DSMP of the Winship Cancer Institute governs cancer clinical trials, i.e., interventional clinical research, defined as: individuals are assigned prospectively by an investigator based on a protocol to receive specific interventions. The participants may receive diagnostic, treatment, behavioral, or other types of interventions. The assignment of the intervention may or may not be random. The participants are followed and biomedical and/or health outcomes are assessed.

Diagnostic Research Studies: Diagnostic studies (such as molecular or imaging diagnostics) are considered to be clinical studies if they use the information from the diagnostic test in a manner that in some way affects medical decision-making for the study participant. In this way, the information from the diagnostic test may have an impact on some aspect of outcome, and the assessment of this impact may be a key goal of the study. By contrast, studies that do not use information from the diagnostic test in any manner that can affect the outcome of study participants, but whose objective is only the gathering of data on the characteristics of a new diagnostic approach are not clinical studies and are not covered by this plan, unless performing the diagnostic test itself imposes some risk on study participants.

Institutional Studies: Institutional studies include both Winship Cancer Institute investigator-initiated studies (IITs) and multi-site studies that include Winship Cancer Institute investigators that are initiated by an institutional investigator at another academic center.

Interventional Studies: There are two kinds of interventional studies, therapeutic and prevention. The primary purpose of an interventional trial may be:

- Diagnostic: protocol designed to assess one or more interventions aimed at identifying a disease or health condition.
- Prevention: protocol designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition.
- Supportive Care: protocol designed to evaluate one or more interventions where the primary intent is to maximize comfort, minimize side effects, or mitigate against a decline in the participant's health or function. In general, supportive care interventions are not intended to cure a disease.
- Treatment: protocol designed to evaluate one or more interventions for treating a disease, syndrome, or condition.

Investigator-Initiated Trials (IITs): IITs are those authored by a member of the Winship Cancer Institute faculty or staff. IITs are internally monitored according to this plan.

Multi-Site trial: Clinical trial conducted at more than one medical center or clinic. Most large clinical trials, particularly Phase II and Phase III trials, are conducted at several clinical research centers. The benefits of multicenter trials include a larger number of participants, different geographic locations, the possibility of inclusion of a wider range of population groups, and the ability to compare results among centers, all of which increase the generalizability of the study. In many cases, efficacy will vary significantly between population groups with different genetic, environmental, and ethnic or cultural backgrounds ("demographic" factors); normally only geographically dispersed trials can properly evaluate this.

Non-interventional Studies: Studies in which there are no interventions with the intent to treat or prevent cancer.

Phase I trials: Clinical trials are designed to test new therapeutics, often in a dose escalation manner, seeking evidence of maximum tolerated dose, dose limiting toxicity (DLT), safety of administration, and identification of novel toxicities.

Phase II trials: Clinical trials are designed to test treatment regimens for efficacy in a limited number of diseases or molecularly characterized populations and to provide evidence of tolerance and response. Early phase clinical trials of molecularly- targeted agents may blur the distinction between phase I and II, and new study designs may explore clinical activity in phase I studies.

Phase III trials: Clinical trials are expanded controlled trials, typically conducted after preliminary evidence suggesting effectiveness of the drug has been obtained and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide adequate basis for drug licensing.

Prevention interventional: Clinical trials for the modulation of cancer risk and inhibition of cancer progression using nutrition, dietary or chemoprevention interventions.[1]

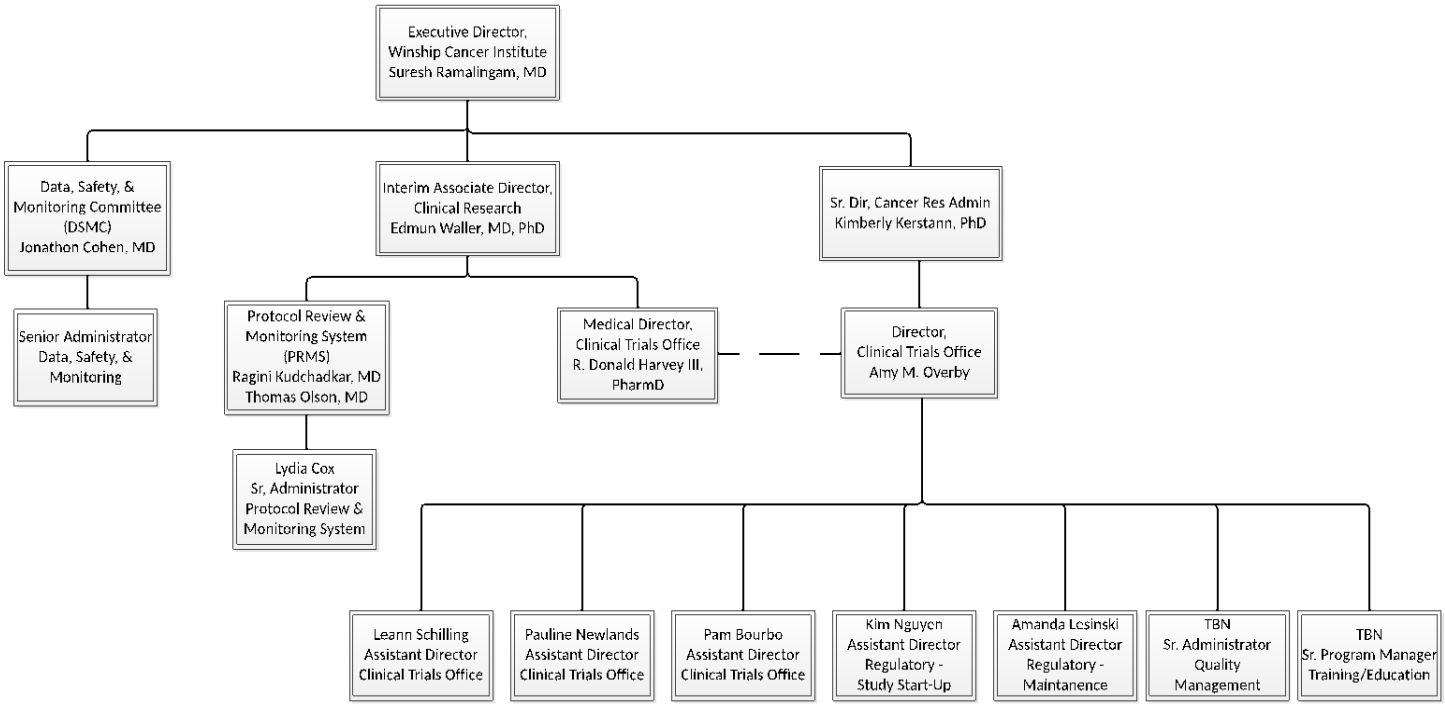
Therapeutic interventional: Clinical trials with therapeutic intent using drugs, radiation, surgery, and/or biological agents.

[1] 2004 Guidance for Cancer Centers (http://www3.cancer.gov/cancercenters/CCSG_Guide12_04.pdf).

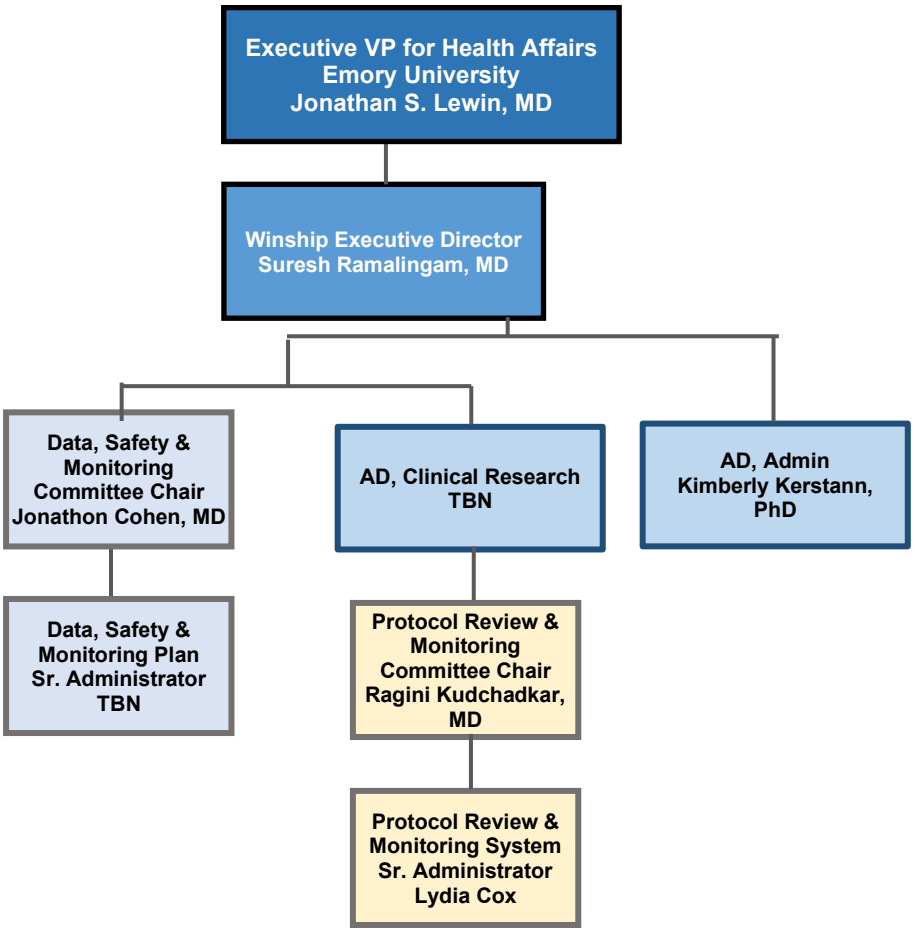
APPENDIX C.
Winship Satellite, Affiliate and Network Sites

Winship Satellite, Affiliate and Network Sites		
Institution	Site Type	Oversight
Emory Johns Creek Hospital (EJCH)	Satellite Site	Integrated into Emory System, Winship CTO provides management and oversight. 1.0 FTE, 11 active trials
Emory Proton Therapy Center (EPTC)	Satellite Site	Integrated into Emory System, Winship CTO provides management and oversight. 3.0 FTE, 35 accruals & 19 active trials
Emory Saint Joseph's Hospital (ESJH)	Satellite Site	Integrated into Emory System, Winship CTO provides management and oversight 9.0 FTE, 75 accruals & 84 active trials
Emory Midtown Hospital (EUMH)	Satellite Site	Integrated into Emory System, Winship CTO provides management and oversight Multidisciplinary: 9.0 FTE, 66 accruals & 153 trials Head/Neck: 8.0 FTE, 53 accruals & active trials
Emory Decatur Hospital (EDH)	Satellite Site – Future Site	Integrated into Emory System, developing Winship CTO services to support clinical research program, provide management and oversight
Grady Memorial Hospital (GMH)	Affiliate Site – Future (AIDS/Malignancy and Sickle Cell WG)	Not within Emory System, Winship CTO provides management and oversight 6.0 FTE, 14 accruals & 40 active trials
Atlanta Veterans Administration Medical Center (VA)	Affiliate Site	Not within Emory System, Winship CTO provides management and oversight 2.0 FTE, 7 accruals & 18 active trials
Archbold Memorial Hospital	Network Site	Not within Emory System, Winship CTO provides training/education to clinicians and staff, Winship does not own or operate organization
Hamilton Medical Center	Network Site	Not within Emory System, Winship CTO provides training/education to clinicians and staff, Winship does not own or operate organization
Northeast Georgia Health System	Network Site	Not within Emory System, Winship CTO provides training/education to clinicians and staff, Winship does not own or operate organization

APPENDIX D.
CPDM Organizational Chart



APPENDIX E.
Winship PRMC and DSMC Organizational Chart



APPENDIX F.
Treatment Modality Working Group (TMWG)

Winship Treatment Modality Working Group Leaders		
Team Name	**Leader**	**Meeting Schedule**
Breast Cancers	Kevin Kalinsky, MD, MS Associate Professor, Depart of Hematology & Medical Oncology	Every Wednesday; 4 PM – 5 PM
BMT	Edmund Waller, MD, PhD, FACP Professor, Departments of Medicine, Pathology, and Hematology and Medical Oncology	Every 3rd Thursday; 8 AM – 9 AM
Cellular Therapy	Jean Koff, MD Assistant Professor, Depart of Hematology & Medical Oncology	Every Tuesday; 9 AM – 10 AM
Gastrointestinal Cancers	TBN	Every Tuesday; 11 AM – 12:30 PM
Genitourinary Cancers	Mehmet Asim Bilen, MD Associate Professor, Depart of Hematology & Medical Oncology	Every Friday; 10 AM – 11 AM
Head & Neck Cancers	Nabil Saba, MD, FACP Professor, Depart of Hematology & Medical Oncology	Every Thursday; 7:45 AM – 9 AM
Leukemia Cancers	William Blum, MD Professor, Depart of Hematology & Medical Oncology	Every Thursday; 9 AM – 10 AM
Lymphoma Cancers	Jonathon Cohen, MD, MS Associate Professor, Depart of Hematology & Medical Oncology	Every Wednesday; 11:30 AM – 12:30 PM
Melanoma Cancers	Ragini Kudchadkar, MD Associate Professor, Depart of Hematology & Medical Oncology	Every Monday; 3:30 PM – 4:30 PM
Multiple Myeloma Cancers	Ajay Nooka, MD, MPH, FACP Associate Professor, Depart of Hematology & Medical Oncology	Every Monday; 12:30 PM – 2 PM
Neurological Oncology	Jeffery Olson, MD Professor, Depart of Hematology, Medical Oncology, and Neurosurgery	Every 1st Wednesday 12 PM – 1 PM

Phase I Therapies	R. Donald Harvey III, PharmD, BCOP, FCCP, FHOPA Professor, Department of Hematology and Medical Oncology and Pharmacology and Chemical Biology	Every Tuesday; 8 AM – 9 AM
Pediatric Oncology	Ann Mertens, MD Professor, Department of Pediatrics	Every Month
Radiation Oncology	Kristin Higgins, MD Associate Professor, Department of Radiation Oncology	Every Tuesday; 10 AM – 11 AM
Thoracic Cancers	Ticiana Leal, MD Acting Associate Professor, Depart of Hematology & Medical Oncology	Every Thursday; 8 AM – 9 AM

APPENDIX G.
Protocol Review and Monitoring Committee

Table 2. 2022 PRMC Membership

Name	Department/Division	Disease Specialty/ Expertise	Academic Rank
Ragini Kudchadkar, MD (Chair)	Hematology/ Medical Oncology	Cutaneous Oncology, phase I clinical trials	Associate Professor
Thomas A. Olson, MD (Co-Chair)	Pediatrics Hematology/ Oncology	Pediatric solid tumors; early phase clinical trials	Professor
Jacqueline Brown, MD*	Hematology/ Medical Oncology	GU malignancies, phase I clinical trials unit, health disparities	Assistant Professor
Mehmet Asim Bilen, MD*	Hematology/ Medical Oncology	Genitourinary cancers, phase I clinical trial unit	Associate Professor
Keerthi Gogineni, MD, MSHP	Hematology/ Medical Oncology	Breast oncology; clinical trial design; quality of life and outcomes research	Associate Professor
L. Thompson Heffner, Jr., MD	Hematology/ Medical Oncology	Leukemia; phase II/III clinical trials	Professor
Nisha Joseph, MD*	Hematology/ Medical Oncology	Multiple Myeloma; amyloidosis & other plasma cell disorders; bone marrow and stem cell transplant	Assistant Professor
Jane Meisel, MD	Hematology/ Medical Oncology	Breast and gynecologic cancers; phase I clinical trial unit	Associate Professor
Jason Romancik, MD*	Hematology/ Medical Oncology	Lymphoma; bone marrow transplant	Instructor
Rein Saral, MD	Hematology/ Medical Oncology	Leukemia; bone marrow transplant; outcomes research	Professor
Malathy Shanmugam, PhD, MS*	Hematology/ Medical Oncology	Cell and molecular biology	Associate Professor
Conor Steuer, MD*	Hematology/ Medical Oncology	Thoracic oncology, head and neck oncology, phase I clinical trials unit	Assistant Professor
Duc Quang Tran, Jr., MD, MSc	Hematology/ Medical Oncology	Benign hematology; hemophilia	Assistant Professor

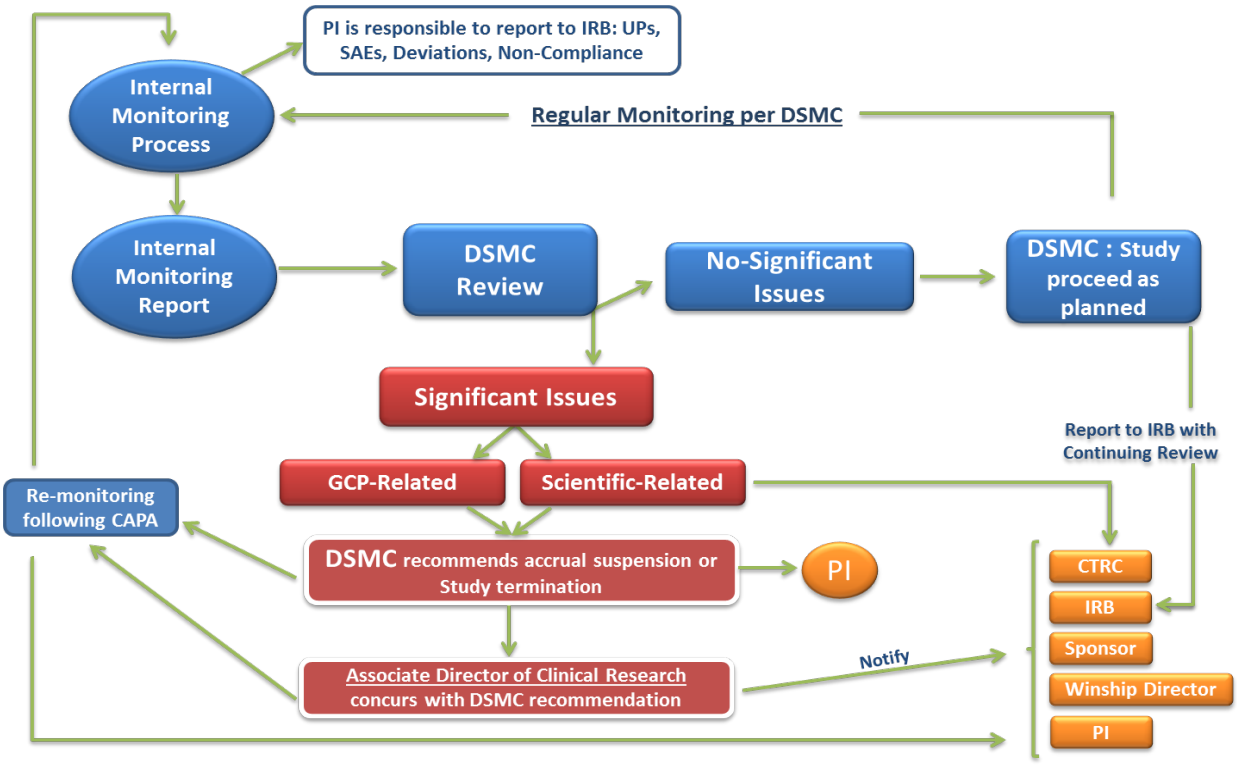
Melinda Yushak, MD, MPH*	Hematology/ Medical Oncology	Melanoma, sarcoma, phase I clinical trials unit	Assistant Professor
Frank Keller, MD	Pediatric Hematology/ Oncology	Pediatric hematologic malignancies; early phase study design	Professor
Himalee Sabnis, MD, MSc	Pediatric Hematology/ Oncology	Pediatric hematologic malignancies	Assistant Professor
James Bates, MD*	Radiation Oncology	Radiation oncology, head and neck cancer, lymphoma, Emory Proton Therapy Center	Assistant Professor
Zachary Buchwald, MD, PhD*	Radiation Oncology	Radiation oncology, melanoma	Assistant Professor
Rebecca D. Pentz, PhD	Bioethics and Patient Advocacy: Hematology/ Medical Oncology	Informed consent process; human subject protection; study design; population science; Diversity Committee Liaison	Professor/ Ethicist
Jinbing Bai, PhD, RN	Nursing/ Public Health	Nursing science; randomized phase II/III trials; population science	Associate Professor
Colleen Lewis, RN, NP	Winship Nursing	Infusion Center Nursing Director Nursing science; early phase clinical trials	Nurse Practitioner
Namita Khanna, MD	Gynecologic Oncology	Gynecologic oncology; surgical sciences	Associate Professor
Michael Lowe, MD	Surgical Oncology	Surgical Oncology	Associate Professor
Toncred Styblo, MD	Surgical Oncology	Breast Oncology	Associate Professor
Yuan Liu, PhD	Biostatistics	Biostatistics and database analysis	Associate Professor
Jeffery Switchenko, PhD	Biostatistics	Biostatistics and bioinformatics	Assistant Professor

APPENDIX H.
Data and Safety Monitoring Committee

2022 Members of the Data Safety and Monitoring Committee		
Name	**Academic Title**	**Expertise**
Jonathon Cohen, MD, MS	Chair, DSMC; Associate Professor	Hematology and Medical Oncology
Manali Bhave, MD	Vice-Chair, DSMC Assistant Professor	Hematology and Medical Oncology
Kristie Blum, MD	Professor	Hematology and Medical Oncology
Kevin Hall, PharmD, BCOP	BMT Clinical Pharmacy	Hematology and Medical Oncology
Robert Lyles, PhD	Professor	Biostatistics and Bioinformatics
Tamara Miller, MD	Assistant Professor	Pediatric Oncology
Stephanie Pouch, MD, MS	Assistant Professor	Infectious Disease
Jill Remick, MD	Assistant Professor	Radiation Oncology
Emily Tiao, PharmD, BCOP	Clinical Pharmacy Specialist	Pharmacy
Jim Zhong, MD	Assistant Professor	Radiation Oncology
Stephanie DeRijke, RN, MSN, FNP, CIP*	Director	Clinical Trials Audit and Compliance
Amanda Lesinski, BS*	Assistant Director	Regulatory Affairs
Susan Rogers, RPh*	Registry Pharmacist	Investigational Drug Service

*non-voting members

APPENDIX I.
DSMC Process Workflow



APPENDIX J.
PRMC Scientific Review Form

Protocol Review and Monitoring Committee Scientific Review Form
The overall objective of a PRMC review is to promote and ensure the safe conduct of scientifically valid human subject research. Please carefully consider these key components in your review:

1. Risk and Benefits to participants
2. Science
3. Study Feasibility:
    a. Design
    b. Investigator
    c. Competing Studies
    d. Accrual Goal
4. Statistics (*changes to statistical plan allowed if Winship Investigator-Initiated Trial (IIT) or external IIT with significant flaw). For FDA-approved phase III trial or multicenter consortium studies with prior detailed statistical review, recommendation for improved statistical plan for planned study is allowed but may not be the sole ground for study disapproval).*

Principal Investigator:		Date of Review:	
Protocol Title:			
Reviewer:			
Review:	☐ Primary	☐ Secondary	
Protocol Type: (Refer to "Guidelines for PRMC Scientific Review by Study Type")	☐ Federally approved and funded – R01 or equivalent		
	☐ Federally supported Pilot Study		
	☐ Foundation, seed money, junior investigator, new investigator or investigator-initiated industry-funded		
	☐ Industry-initiated and funded		
Pilot Protocol:	☐ Yes	☐ No	
If Yes, select all applicable criteria met:	☐ Preliminary testing of a new hypothesis		
	☐ Investigator is performing experiments to learn a new technique (may be an established technique but unfamiliar to the investigator)		
	☐ Investigator will perform experiments exploiting newly developed technologies		
	☐ Multi-disciplinary teams working together to establish parameters for interactions between team members		

	☐ Investigator(s) will engage in activities to allow definition of requirements for larger scale studies

NIH-Defined Phase III Clinical Trial:	☐ Yes	☐ No

Protocol Involves:	☐ Gene transfer study (involving recombinant DNA)
	☐ Emergency research with a waiver of informed consent
	☐ Investigator-initiated trial for a drug that has no current FDA approval for any indication
	☐ Implantation of a device with an IDE designated by the IRB as a significant risk device
	☐ Phase I trial for which the trial is the very first trial in humans (no clinical data exists)
	☐ Study of a surgical intervention not in use at the Winship
	☐ Clinical trial requiring the withdrawal of subjects' own prescribed medication
	☐ Decisionally-impaired subjects
	☐ Medication administration to pregnant women
	☐ Fetuses and neonates

RISK LEVEL DETERMINATION

Risk Level	☐ High Risk • Phase I (toxicity/dose finding) or gene transfer therapeutic IIT with institution or PI as IND/IDE holder (Emory faculty as sponsor) and not routinely monitored by a CRO • Phase I (toxicity/dose finding) or gene transfer therapeutic Industry study that is routinely monitored by a CRO
	☐ Moderate Risk • Phase II interventional or therapeutic IIT with IND/IDE (sponsor is Emory faculty) • Phase I/II IIT of FDA approved agents and other Phase II trials (i.e., commercially available agents or devices; IND Exempt or Nonsignificant Risk IDE) • Phase I/II Industry studies of FDA approved agents and other Phase trials
	☐ Low Risk • Non-therapeutic trial that is non-interventional/non-invasive (i.e., chart review, behavioral, quality of life, etc.)

OVERALL EVALUATION		
Overall summary of review and general comment(s)	Response(s)	
SCIENTIFIC REVIEW COMMENTS		
Hypothesis and/or Aims		
Are the hypothesis and/or aims stated clearly?	☐ Yes	☐ No
Are the primary aims achievable?	☐ Yes	☐ No. If no, please explain.
Are the secondary aims achievable?	☐ Yes	☐ No. If no, please explain.
Comment(s)	Response(s)	
Scientific Critique		
Comment(s)	Response(s)	
STATISTICAL REVIEW COMMENTS		
Comment(s)	Response(s)	
SAFETY REVIEW COMMENTS		
Protection of Human Subjects from Research Risk		
☐ Acceptable	Comment	Response

☐ Unacceptable		
Data Safety and Monitoring Plan		
☐ Acceptable ☐ Unacceptable	Comment See below	Response
Data Safety and Monitoring Board (required for NIH-Defined Phase III Clinical Trials)		
Is a DSMB needed?	☐ Yes	☐ No
If Yes, is the description in the protocol:	☐ Acceptable	☐ Unacceptable

Comment	Response

Inclusion Plans			
Gender Inclusion	☐ Acceptable ☐ Unacceptable	Comment	Response
Minority Inclusion	☐ Acceptable ☐ Unacceptable	Comment	Response
Children Inclusion	☐ Acceptable ☐ Unacceptable	Comment	Response

Consent Forms		
☐ Acceptable ☐ Unacceptable ☐ Not Applicable	Comment	Response
IMPLEMENTATION		
Requested Utilization of Winshp/GCRC Resources		
☐ Acceptable ☐ Unacceptable ☐ Not Applicable	Comment	Response
Investigator		

☐ Acceptable ☐ Unacceptable ☐ Not Applicable	Comment	Response
Competing Studies		
☐ Acceptable ☐ Unacceptable ☐ Not Applicable	Comment	Response
Accrual Goal		
☐ Acceptable ☐ Unacceptable ☐ Not Applicable	Comment	Response
Requested Utilization of GCRC Resources Additional Comments		
Comment(s)		Response(s)
RECOMMENDATION		
☐ Approved as submitted		
☐ Approved pending response to noted concerns		
☐ Revise and re-submit for re-review		
☐ Disapproved		
SCORE		

Scoring Guidelines:

1.0 - 1.9 - Outstanding
2.0 - 2.9 - Excellent
3.0 - 3.9 - Average
4.0 - 4.9 - Fair
5.0 - 5.9 - Unacceptable

APPENDIX K.
DSMC Training Attestation Form

Winship Cancer Institute: Data Safety and Monitoring Plan Training Attestation Form

DSMP Version: _____

By signing below, I acknowledge that I have fully read and understood the Winship Cancer Institute's Data Safety and Monitoring Plan (DMSP). I understand that if I have any questions or concerns about this plan, it is my responsibility to discuss this with the Data Safety and Monitoring Committee (DSMC) Chair or designee.

_____ _____

Name Date
Title
Institution/Department

APPENDIX L.
DSMC Study Review Letter

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Study Review Letter

Date:
Protocol Title/Study Number.
IRB #:
Phase:
Principal Investigator: , MD

The Data and Safety Monitoring Committee (DSMC) of the Winship Cancer Institute discussed the monitoring report for this trial at the _____meeting. Upon review of the monitor findings, overall trial summary and PI responses, the DSMC voted that study conduct for this trial was deemed acceptable/acceptable needs follow up and may continue accrual.
Additional comments were generated during the meeting:
Add the form completion report (include monitoring report) if applicable

_____ _____
Chair, Data and Safety Monitoring Committee Date

APPENDIX M.
DSMC Study Approval Letter

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Study Approval Letter

Date:
Protocol Title/Study Number.
IRB #:
Phase:
Principal Investigator: , MD

The Winship Cancer Institute Data and Safety Monitoring Committee has reviewed and approved the data safety monitoring plan for the above-mentioned trial.

_____ _____
Chair, Data and Safety Monitoring Committee Date

APPENDIX N.
DSMC Study Follow-Up Response Letter

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Study Follow-Up Response Letter

Date:
Protocol Title/Study Number.
IRB #:
Phase:
Principal Investigator: , MD

The Data and Safety Monitoring Committee (DSMC) of the Winship Cancer Institute discussed the follow up responses to the DSMC review letter dated Month_Day_Year at the Month Day, Year meeting. The committee acknowledges and accepts the responses.

_____ _____
Chair, Data and Safety Monitoring Committee Date

APPENDIX O.
DSMC Notice of Discontinuing Reviews

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Notice of Discontinuing Reviews

Date:
Protocol Title/Study Number.
IRB #:
Phase:
Principal Investigator: , MD

The Data and Safety Monitoring Committee (DSMC) of the Winship Cancer Institute acknowledges that (Full title of study) has completed accrual and that there are no subjects on treatment. This study is closed to the IRB or has completed protocol required analysis. This study will no longer be reviewed by the Data and Safety Monitoring Committee.

_____ _____
Chair, Data and Safety Monitoring Committee Date

APPENDIX P.
DSMC Follow-Up Termination for Pending Items

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Follow-Up Termination for Major Pending Items

Date:
Protocol Title/Study Number.
IRB #:
Phase:
Principal Investigator: , MD

The Data and Safety Monitoring Committee (DSMC) of the Winship Cancer Institute has not received the completed response to the DSMC letter (date), despite (no. of reminders) reminders sent by us. These items are still pending:

We are happy to review the response if provided, but we will no longer make any attempts to follow up on this request. As a result of not responding to the pending items Winship CTO Leadership and the Emory IRB will be notified of non-compliance.

_____ _____
Chair, Data and Safety Monitoring Committee Date

Cc: Associate Director, Clinical Research
Cc: Emory IRB

APPENDIX Q.
DSMC Dose Escalation Approval Letter

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Dose Escalation Approval Letter

Date:
Protocol Title/Study Number.
IRB #:
Phase:
Principal Investigator: , MD

The Data and Safety Monitoring Committee (DSMC) of the Winship Cancer Institute has reviewed and approved to (what was requested) _____.
Please contact us if you have any questions or concerns.

_____ _____
Chair, Data and Safety Monitoring Committee Date

APPENDIX R.
DSMC Toxicity Review Letter

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Toxicity Review Letter

Date:
Protocol Title/Study Number.
IRB #:
Phase:
Principal Investigator: , MD

The Data and Safety Monitoring Committee (DSMC) of the Winship Cancer Institute discussed the toxicity data provided for the DSMC meeting dated Month_Day_Year. The committee acknowledges these data and may continue accrual.

_____ _____
Chair, Data and Safety Monitoring Committee Date

APPENDIX S.
Overall Trial Summary for DSMC Review
(Non-Winship Based Trials)

Study name:

PI:

Date of DSMC review:

Study Schema:

Primary endpoints:

Secondary endpoint:

Number of pts consented at Emory sites/ Number of patients enrolled at Emory sites:
_____/_____

Please describe any grade 5 toxicities occurring at Winship site, including toxicity type and attribution. Grade 5 toxicities deemed to be related to study therapy and/or unanticipated should be described in detail.

Please list all SAEs and unanticipated problems (UPs) that have occurred at Winship, including toxicity type, grade, and attribution. Provide details regarding SAEs/UPs at Winship that are deemed to be at least possibly related to study therapy.

PI signature_____ Date_____

APPENDIX S.
Overall Trial Summary for DSMC Review

Study name:

PI:

Date of DSMC review:

Study Schema:

Primary endpoints:

Secondary endpoint:

Number of patients consented/Number of Patients Treated:_____/_____

Short summary: (how the study is progressing including number of patients accrued out of planned, how many went on study, any withdrawals from the study, any unanticipated problems)

Results of any interim analysis if applicable (Example, please describe current status of dose escalation and/or incidence of DLT for phase 1 study and/or results of stage 1 analysis for 2-stage designs):

Please attach a table reporting type, grade, and attribution of all AEs since last DSMC review.

List all SAEs per study arms:

Please provide clinical details for any SAEs or unanticipated problems deemed to be at least possibly related to study therapy as well as all grade 5 toxicities.

PI signature_____ Date_____

APPENDIX T.

DSMC Patient Review Form

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

PATIENT REVIEW
Data and Safety Monitoring Committee

☐ **Phase I** ☐ **Phase II** ☐ **Phase III** ☐ **Other (Specify:_____)**

SECTION I – Study and Patient Information **Review Date:**

Study #: **PI:** **Study Opened:** **Current Status:**

Study Title:

Objectives/End Points:

Patient Number: **Age:** **Date of Enrollment:** **Cohort**:

Cycle Number	Date Cycle Started	Date Cycle Completed

Medical History:

SECTION II – General and Study Elements
CENTRAL ELEMENTS: Add comments and/or tables to each section as needed to facilitate review
Informed Consent

☐ **Compliant:** Consent complete and executed within regulations.

☐ **Non-Compliant** (see attached report)

Eligibility:

☐ **Compliant:** Double check eligibility performed, and enrollment approved.

☐ **Non-Compliant** (see attached report)

Data Quality- Accuracy and Timeliness

Data relevant to eligibility and Cycle ___ has been reviewed for accuracy.

☐ **Compliant**

☐ **Non-Compliant** (see attached report)

CONDUCT ELEMENTS:

Attached Reports:

☐ **H&P** ☐ **LABs** ☐ **Treatment Summary** ☐ **AE/SAE Summary** ☐ **ConMeds**

☐ **Response**

Tests and Observations

☐ **Compliant**: The patient received all required tests and observations for Cycle_____.

☐ **Non-Compliant** (see attached report)

☐ **N/A**

Treatment

☐ **Compliant**

☐ **Non-Compliant** (see attached report)

Toxicities

☐ **Compliant**

☐ **Non-Compliant** (see attached report)

Response

☐ **Compliant**

☐ **Non-Compliant** (see attached report)

☐ **N/A**

SAE and Protocol Deviation Reporting

☐ **Compliant**

☐ **Non-Compliant** (see attached report)

☐ **None**

Comments from the Senior Administrator; QM, Monitoring, and Training:

Select One:

☐ The PI has been given the opportunity to review this form and reports. No further information or comment was provided by the PI.

☐ The PI has been given the opportunity to review this form and reports. Further information/comments were provided below:

SECTION III – Reviewer Disposition and Action Item(s)

Notes from the DSMC Clinical Trials Monitor:

DSMC Study Disposition:

Check 1 safety disposition:

No safety concerns	
Safety concerns identified	

Check 1 status disposition:

No change in study status	
Change in study status	

Action Required:

Check all that apply if action required

Report Protocol Deviation	
Amendment Required	
Referral to PRMC (for scientific or accrual issues)	
PI Response Required (see comments)	
Temp Close to Accrual	
Data Accuracy/delinquency	

Perm Close to Accrual	
Close Study to IRB	
Analysis Due	
CAPA Required	
Early Re-review	

DSMC Reviewer Comments/Recommendations (if applicable):

APPENDIX U.

DSMC Study Review Form

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

STUDY REVIEW
Data and Safety Monitoring Committee

☐ **Phase I** ☐ **Phase II** ☐ **Phase III** ☐ **Other (Specify:_____)**

SECTION I – Study Information **Review Date:**

Sites:

Study #: **PI:** **Date Study Opened:** **Current Status:**

Study IRB Number: **IRB of Record:**

Study Title:

Objectives/End Points:

Stopping Rules:

Target Enrollment: ____ subjects over ____ years

Enrollment to date: _____ subjects

Review period: _____ months

Enrollment during this review period: _____ subjects

Informed Consent: ____ subjects consented during this review period were found to be appropriately consented prior to enrollment or registration. There have been ____ subjects withdrawn from the study to date.

Eligibility: ____ subjects enrolled during this review period met eligibility criteria

SECTION II – Study Conduct.
The information/documents (attachments) listed were reviewed. Add comments and/or tables to each section as needed to facilitate review.

A) IRB Compliance

1) Study progress report
2) Amendments this period

B) Investigational Drug Tracking and Accountability (if applicable)

1) Drug Accountability Logs

☐ Compliant ☐ Not Applicable

☐ Non-compliant

2) Drug Tracking and Disposition

☐ Compliant ☐ Not Applicable

☐ Non-compliant

C) Study Conduct and Safety

1) Has study been permanently closed to accrual?

☐ No, study is still enrolling patients

☐ Yes. – If Yes, please describe why study was closed to accrual: _____

2) Previous DSMC review results/action item(s) (if applicable):

- Date of last DSMC Review:
- Result of review:

3) Subject screening summary

_____ subjects screened but not enrolled / _____ total number subjects screened = _____% screen failure rate

4) Subject AEs

- _____ AEs have occurred in ___ subjects to date. ___ of these were Grade 3 or higher.
- _____ deaths have occurred on study within 30 days of enrollment or treatment.
- There were _____ unexpected AEs. (See attached report)
- There were _____ serious AEs (SAEs) (See attached)
- The AE summary and attribution data is provided below. <u>These are AEs only</u>. The SAEs are provided separately as described above.

AE Grade	Number of AEs
1	

AE Attribution	
Not related	

2	
3	
4	
5	
Total	

Unlikely	
Possible	
Probable	
Definite	
Total	

5) Reportable Protocol Deviation(s)

- ___ deviations occurred in ___ subjects. ____ of the deviations impacted subject safety.

6) Evaluable Status summary

Subject Status	**# of Subjects**
Evaluable	
Non Evaluable	
Patients pending threshold	
Total Enrolled	

7) Outcome/Response

- For this reporting period, ____ scans for ____ subjects were due for tumor measurement.
- Of this number of planned scans, ____ were non-compliant (no data). See attached report
- Overall Response to date is summarized below (Modify the table as necessary)

Overall Best Response	**# of Subjects**
Complete Response	
Partial Response	
Stable Disease	
Progressive Disease	
Total	

8) Re-consent / Patient Notifications
   - There were ____ reconsents and _____ patient notifications during this reporting period

Comments from the Senior Administrator; QM, Monitoring, and Training:

Select One:

☐ The PI has been given the opportunity to review this form and reports. No further information or comment was provided by the PI.

☐ The PI has been given the opportunity to review this form and reports. Further information/comments were provided below:

SECTION III – Reviewer Disposition and Action Item(s)

Notes from the DSMC Clinical Trials Monitor:

DSMC Study Disposition:

Check 1 safety disposition:

No safety concerns	
Safety concerns identified	

Check 1 status disposition:

No change in study status	
Change in study status	

Action Required:

Check all that apply if action required

Report Protocol Deviation	
Amendment Required	
Referral to PRMC (for scientific or accrual issues)	
PI Response Required (see comments)	
Temp Close to Accrual	

Perm Close to Accrual	
Close Study to IRB	
Analysis Due	
None	

DSMC Reviewer Comments/Recommendations (if applicable):

APPENDIX V.

DSMC Final Study Summary Form

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

FINAL STUDY SUMMARY

Data and Safety Monitoring Committee

☐ **Phase I** ☐ **Phase II** ☐ **Phase III** ☐ **Other (Specify:_____)**

SECTION I – Study Information **Review Date:** **Sites:**

Study #: **PI:**

Date Study Opened: **Date Closed to Accrual:**

Study IRB Number: **IRB of Record:**

Study Title:

Objectives/End Points:

SECTION II – Study Summary

Reason for Closure:

Please select the reason(s) why the study was closed to accrual:

- ☐ Study met target enrollment
- ☐ Slow / inadequate enrollment
- ☐ Inadequate funding
- ☐ New drug approvals or evolution of patient care led to trial obsolescence
- ☐ Other (please describe): _____

Accrual and Subjects Status

Target Enrollment: ____ subjects over ____ years

Final Enrollment: ____ subjects

Screen Failures: ____ subjects screened but not enrolled / ____ total number subjects screened = ____% screen failure rate

Status: ____ subjects are currently in long-term follow-up; ____ subjects are off-study

Central Elements

Informed Consent: ____ subjects consented during the study were appropriately consented prior to enrollment or registration.

There were ____ subjects withdrawn from the study.

Eligibility: _____subjects enrolled during the study fully met eligibility criteria

Prior Review

Previous DSMC review results/action item(s) (if applicable):

- Date of last DSMC Review:
- Result of review:

If there are deficiencies at the time of this final review, please list them beneath each of the following sections

Investigational Drug Tracking and Accountability (if applicable)

3) **Drug Accountability Logs**

☐ Compliant ☐ Not Applicable

☐ Non-compliant

4) **Drug Tracking and Disposition**

☐ Compliant ☐ Not Applicable

☐ Non-compliant

Subject Safety

9) Adverse Events (AEs)

- ____ AEs occurred in ___ subjects. ____ of these were Grade 3 or higher.
- ____ Deaths occurred on study. There were ____ deaths within 30 days of enrollment or treatment.
- There were ____ unexpected AEs. (Attach report if unexpected AEs occurred)
- There were _____ serious AEs (SAEs) (See attached)
- The AE summary and attribution data is provided below. These are AEs only. The SAEs are provided separately as described above.

AE Grade	Number of AEs
1	
2	
3	
4	
5	
Total	

AE Attribution	Number of AEs
Not related	
Unlikely	
Possible	
Probable	
Definite	
Total	

10) Protocol Deviation(s)

- ___ Deviations occurred in ___ patients. ____ of the deviations impacted subject safety
- If deviations occurred, please describe them briefly here and attach any documentation.

Evaluable Status Summary (if applicable)

Patient Status	# of pts
Evaluable	
Non Evaluable	
Patients pending threshold	
Total Enrolled	

Outcome/Response (if applicable)

- Of the number of planned scans, ____ were non-compliant (no data). (Attach report if necessary)
- Overall Response to date is summarized below (Modify the table as necessary)

Overall Best Response	# of pts
Complete Response	
Partial Response	
Stable Disease	
Progressive Disease	
Total	

Re-consent /Patient Notifications

- There were ____ reconsents and _____ patient notifications during the study.

Data Analysis:

If data for this study has been analyzed, please provide a brief summary of findings and/or manuscript or poster draft.

If data has not yet been analyzed, please briefly describe the current plan to report the data and provide an estimated timeframe for when this will occur.

Comments from the Senior Administrator; QM, Monitoring, and Training:

Select One:

☐ The PI has been given the opportunity to review this form and reports. No further information or comment was provided by the PI.

☐ The PI has been given the opportunity to review this form and reports. Further information/comments were provided below:

SECTION III – Reviewer Disposition and Action Item(s)

Notes from the DSMC Clinical Trials Monitor:

DSMC Study Disposition:

Check 1 safety disposition:

No safety concerns	
Safety concerns identified	

Action Required:

Check all that apply if action is required. If analysis is accepted, please check both "Analysis Accepted" AND "Close Study to IRB"

Report Protocol Deviation	
PI Response Required (see comments)	
Analysis Accepted	
Close Study to IRB	
Analysis Due	

DSMC Reviewer Comments/Recommendations (if applicable):

APPENDIX W.

Patient Monitoring DSMC Disposition Letter

Copy to: ☐ PI ☐ Medical Director ☐ CTO Director ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN
Date:

Data and Safety Monitoring Committee
Patient Monitoring Disposition Letter

A review was performed on the following patient and the committee has designated the following recommendation and corrective action (if applicable):

Date of Report:

Study #:	**PI:**	**Date Study Opened:**
Study Title:		
Patient:	**Date Enrolled:**	**Cohort:**
Cycle:	**Started:**	**Completed:**

Purpose of Review: Monitoring oversight for Patient

The Data and Safety Monitoring Committee made the following recommendation(s):

DSMC Study Disposition:

Check 1 safety disposition:

No safety concerns	
Safety concerns identified	

Check 1 status disposition:

No change in study status	
Change in study status	

Action Required:

Check all that apply if action required

Report Protocol Deviation	
Amendment Required	
Referral to PRMC (for scientific or accrual issues)	
PI Response Required (see comments)	
Temp Close to Accrual	

Perm Close to Accrual	
Close Study to IRB	
Analysis Due	
None	

Issues/Corrective Action (if applicable) / Summary:

Due Date for Actions Requested: _____

APPENDIX X.

DSMC Study Monitoring Disposition Letter

Copy to: ☐ PI ☐ Medical Director ☐ CTO Director ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN
Date:

Data and Safety Monitoring Committee
Disposition Letter

A review was performed on the following study and the committee has designated the following recommendation and corrective action (if applicable):

Date of Letter:
Study Information

Date of Report: **Sites:** **Study Status:**

PI: **Date Study Opened:** **Study IRB Number:** **IRB of Record:**

Study Title/#:
Date of Committee Review:
Purpose of Review:
☐ Interim /Annual Study Review ☐ Quarterly/Monthly Study Review

Type of Review: ☐ Full ☐ Expedited

The Data and Safety Monitoring Committee has evaluated your report and made the following recommendation:

DSMC Study Disposition:

Check 1 safety disposition:

No safety concerns	
Safety concerns identified	

Check 1 status disposition:

No change in study status	
Change in study status	

Action Required:

Check all that apply if action required

Report Protocol Deviation	
Amendment Required	
Referral to PRMC (for scientific or accrual issues)	
PI Response Required (see comments)	
Temp Close to Accrual	

Perm Close to Accrual	
Close Study to IRB	
Analysis Due	
None	

Issues/Corrective Action (if applicable)/Summary:

Due Date for Actions requested: _____

APPENDIX Y.
DSMC Interim Analysis Report

Data and Safety Monitoring Committee

☐ **Phase I** ☐ **Phase II** ☐ **Phase III** ☐ **Other (Specify:_____)**

SECTION I – Study Information **Review Date:** **Sites:**

Study #: **PI:**

Date Study Opened: **Date Closed to Accrual:**

Study IRB Number: **IRB of Record:**

Study Title:

Objectives/End Points:

SECTION II – Interim Analysis

Phase I Clinical Trials

Accrual to Date: _____ IRB approved accrual: annual _____ total _____

Current Accrual Status: (please mark one and provide requested information)

☐ Accruing to a Phase I dose level (please indicate dosage tier) _____

☐ Completed Phase I enrollment. Please indicate DLT that halted escalation:

_____

_____

☐ Have there been any changes to this protocol since last review? Please explain:

_____

_____

DATA AND SAFETY MONITORING INFORMATION

☐ Please attach a summary of all subjects that have been enrolled, and their current status (e.g., on treatment, off study, in follow-up, etc.).

☐ Please attach a toxicity summary that indicates the number and severity of toxicities observed. Please provide your overall impression of the toxicity observed to date (i.e. is it consistent with what you anticipated?)

☐ Please attach a summary of protocol deviations that have occurred and provide a justification.

Phase II or III Clinical Trials

Accrual to Date:_____ IRB approved accrual: annual _____ total _____

Current Accrual Status: (please mark one and provide requested information)

☐ Accruing to Phase II portion of study
Does this portion have an early stopping rule for toxicity? ☐Yes or ☐No

If Yes, please provide a summary of your assessment of the data that you used to either stop or continue the study:

_____

_____

Does this portion have an early stopping rule for efficacy? ☐Yes or ☐No

If Yes, please provide a summary of your assessment of the data that you used to either stop or continue the study:

_____

_____

☐ Have there been any changes to the protocol since the last review? Please explain:

_____

_____

DATA AND SAFETY MONITORING INFORMATION

☐ Please attach a summary of all subjects that have been enrolled, and their current status (e.g., on treatment, off study, in follow-up, etc.).

☐ Please attach a toxicity summary that indicates the number and severity of toxicities observed. Please provide your overall impression of the toxicity observed to date (i.e. is it consistent with what you anticipated?)

☐ Please attach a summary of protocol deviations that have occurred and provide a justification.

SECTION III – Reviewer Disposition and Action Item(s)

Notes from the DSMC Coordinator:

DSMC Study Disposition:	**Action Required:**
Check 1 safety disposition:	Check all that apply if action is required. If analysis is accepted,

please check “Analysis Accepted”

No safety concerns	
Safety concerns identified	

Report Protocol Deviation	
PI Response Required (see comments)	
Analysis Accepted	

DSMC Reviewer Comments/Recommendations (if applicable):

APPENDIX Z.
DSMC Corrective Action Follow-Up

Copy to: ☐ PI ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN Date:

Data and Safety Monitoring Committee
Corrective Action Follow Up

Date:
Protocol Title:
Protocol #: **IRB #:**
Principal Investigator:
Date of Disposition Letter and/or Request for Corrective Action:

Corrective Action Requested:

Corrective Action Completed: ☐ Yes ☐ No

Accepted ☐ - No further action

Delinquent ☐ - Due by _____

Delinquent ☐ - 2nd notice, temporarily close to accrual and forward to Medical Director

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Comments:

I certify that I do not have any conflict of interest in reviewing this study.

_____ _____
Chair, Data and Safety Monitoring Committee Date

Note: if this disposition addresses any sponsor or funding issues; please forward a copy to the Director of the Clinical Trials Office.

APPENDIX AA.
Appeal Letter

Copy to: ☐ PI ☐ Medical Director ☐ CTO Director ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN
Date:

Data and Safety Monitoring Committee
Appeal Request

Please complete the required study information. Address each issue listed in the study disposition letter. Those appeal requests not addressing each issue will not be considered for review and returned to the principal investigator. If you have any questions, please contact the Data Safety Monitoring Committee staff or the Chairman of the Committee.

Protocol Title:

Principal Investigator:

Date of DSMC Review: **Date of Appeal:**

Response:

APPENDIX BB.
DSMC Notice of Review of Primary Institution's Monitoring Plan

Copy to: ☐ PI ☐ Medical Director ☐ CTO Director ☐ AD CTO ☐ CROM ☐ TS ☐ CRC/CRN
Date:

Data and Safety Monitoring Committee
Notice of Review of Primary Institution's Monitoring Plan

Date:
Protocol Title/Study Number:
IRB #: **IRB:**
Phase:
Principal Investigator: **, MD Winship Cancer Institute**
Principal Investigator: **, MD Primary Institution**
Address:
Contact Person:

The Data and Safety Monitoring Plan or Monitoring as described in the Protocol from the above Institution has been reviewed and compared to Winship Cancer Institute's Data and Safety Monitoring Plan.

This study will be reviewed by Data and Safety Monitoring Committee at:

☐ **Emory University; Winship Cancer Institute**

☐ **Primary Institution as identified above**

_____ _____
Chair, Data and Safety Monitoring Committee Date

APPROVAL SIGNATURES

Amy Overby
Director, Clinical Trials Office
Winship Cancer Institute

Date

Jonathon Cohen, MD
Chair, Data and Safety Monitoring Committee
Winship Cancer Institute

Date

Suresh S. Ramalingam, MD, FACP, FASCO
Executive Director
Winship Cancer Institute

Date