Data and Safety Monitoring Plan

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### Abbreviations

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<th>Description</th>
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<tr>
<td>AER</td>
<td>Adverse Event Report</td>
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<td>CAPA</td>
<td>Corrective Action and Preventative Action Plan</td>
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<td>CFR</td>
<td>Code of Federal Regulations</td>
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<tr>
<td>COI</td>
<td>Conflict of Interest</td>
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<tr>
<td>CRO</td>
<td>Lurie Cancer Center Clinical Research Office</td>
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<td>CTAC</td>
<td>Clinical Trial Audit Committee</td>
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<td>CTEP</td>
<td>Cancer Therapy Evaluation Program</td>
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<td>CTEP AERS</td>
<td>CTEP Adverse Event Reporting System</td>
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<td>DCTD</td>
<td>Division of Cancer Treatment and Diagnosis</td>
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<td>DCP</td>
<td>Division of Cancer Prevention</td>
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<td>DLT</td>
<td>Dose-limiting Toxicity</td>
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<td>DSMC</td>
<td>Data and Safety Monitoring Committee</td>
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<td>DSMB</td>
<td>Data and Safety Monitoring Board</td>
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<td>DSMP</td>
<td>Data and Safety Monitoring Plan</td>
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<td>eCRF</td>
<td>Electronic Case Report Form</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FSM</td>
<td>Feinberg School of Medicine</td>
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<td>HIPAA</td>
<td>Health Insurance Portability and Accountability Act</td>
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<td>IDE</td>
<td>Investigational Device Exemption</td>
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<td>IIT</td>
<td>Investigator-Initiated Trial</td>
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<td>IND</td>
<td>Investigational New Drug</td>
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<td>IRB</td>
<td>Institutional Review Board</td>
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<td>LCC IIT</td>
<td>Lurie Cancer Center investigator-initiated trial</td>
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<td>NCI</td>
<td>National Cancer Institute</td>
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<td>NIH</td>
<td>National Institutes of Health</td>
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<td>NOTIS</td>
<td>Northwestern Oncology Trial Information System</td>
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<tr>
<td>NU</td>
<td>Northwestern University</td>
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<tr>
<td>PI</td>
<td>Principal Investigator</td>
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<td>QA</td>
<td>Quality Assurance</td>
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<td>Quality Assurance Monitor</td>
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<td>RNI</td>
<td>Reportable New Information</td>
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<td>SAE</td>
<td>Serious Adverse Event</td>
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<td>SIM</td>
<td>Study Implementation Meeting</td>
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<td>SITC</td>
<td>Site Initiation Telephone Conference</td>
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<td>SOP</td>
<td>Standard Operating Procedure</td>
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<td>SRAL</td>
<td>Shirley Ryan Ability Lab</td>
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<td>SRC</td>
<td>Scientific Review Committee</td>
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<td>SUSAR</td>
<td>Suspected Unexpected Serious Adverse Reaction</td>
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<tr>
<td>UPIRSO</td>
<td>Unanticipated Problems Involving Risks to Subjects or Others</td>
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<tr>
<td>VAERS</td>
<td>Vaccine Adverse Events Reporting System</td>
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* Please note: through this document, all references to online documents can be found on the Lurie Cancer Center website at [www.cancer.northwestern.edu/ROS](http://www.cancer.northwestern.edu/ROS).*
Data and Safety Monitoring Plan

1.0 Introduction

The Robert H. Lurie Comprehensive Cancer Center (Lurie Cancer Center) of Northwestern University (NU) has a diverse research program, including a large portfolio of protocols in the areas of primary cancer treatment and prevention, cancer control and other interventional trials, observational and outcomes studies, and lab-based research including correlative and ancillary studies. Therapeutic trials range from First in Human (FIH) and Phase I trials to multi-institutional randomized Phase III studies. The Lurie Cancer Center is dedicated to ensuring that all clinical trials are appropriately monitored to ensure research participant safety and that the validity and integrity of clinical trial data are maintained. Responsibility for this mission falls to the committees that comprise our Research Oversight System.

The Lurie Cancer Center’s Data and Safety Monitoring Plan (DSMP) has been developed to provide oversight for data and safety monitoring for clinical trials consistent with the following: the NIH Policy for Data and Safety Monitoring as of June 10, 1998; Policy of the NCI for Data and Safety Monitoring of Clinical Trials as of June 22, 1999; Further Guidelines on a Data and Safety Monitoring Plan for Phase I and II Trials from the NIH on June 5, 2000; Essential Elements of a Data and Safety Monitoring Plan for Clinical Trials Funded by the NCI as of April 2001; and The Cancer Centers Branch of the National Cancer Institute Parts I and II: Policies and Guidelines Relating to the Cancer Center Support Grant, dated September 2004. This document provides a description of the Lurie Cancer Center’s policies and procedures related to data and safety monitoring activities at the center.

2.0 Background

2.1 Definition of a Clinical Trial

This plan follows the NIH definition of a clinical trial, released October 23, 2014 that states a clinical trial is “A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.” Interventions may include drugs, treatments, devices, or behavioral or nutritional strategies. Participants in these trials may be patients with cancer or people without a present diagnosis of cancer, but who are considered cured from a prior cancer and/or people who are considered to be at risk for developing it in the future.

Diagnostic research utilizing molecular or imaging diagnostics is considered to be a clinical trial if the information from the diagnostic test is used in a manner that affects medical decision-making for the study participant. As such, the information from the diagnostic test may have an impact on some aspect of outcome, and assessment of this impact may be a key goal of the trial. Studies that do not use information from the diagnostic test in a manner that can affect the outcome of study participants, but whose objective is solely the gathering of data on the characteristics of a new diagnostic approach, are not clinical trials and are not covered by this policy (unless performing the diagnostic test itself imposes some risk on study participants).

Behavioral clinical trials include interventions whose goals are to increase behaviors (e.g., cancer screening, physical activity, etc.), eliminate or reduce behaviors (e.g., smoking, sun exposure) and/or improve coping and quality of life and reduce the morbidity associated with treatment. Interventions may pertain to cancer prevention, early detection, treatment, and survivorship.

Observational studies and those that do not test interventions are not considered clinical trials.
2.2 Applicability

This plan applies to investigators conducting cancer-relevant clinical research within Northwestern University, Northwestern Medicine, the Shirley Ryan Ability Lab (SRAL, formerly the Rehabilitation Institute of Chicago), the Jesse Brown VA Medical Center (JBVAMC) and at sites participating in Lurie Cancer Center investigator-initiated trials (LCC IITs).

For purposes of this plan, a LCC IIT is a trial authored by a Lurie Cancer Center member or by any NU faculty member conducting cancer-relevant research. LCC IITs covered by this plan include studies supported through various funding mechanisms, including competitive NCI/NIH grants, other agency/sponsor grants or gifts, and grant-in-aid support from pharmaceutical sponsors. These trials are required to comply with the minimum requirements as described in this DSMP, or to develop an alternate plan that must be reviewed and approved by the Lurie Cancer Center’s Scientific Review Committee (SRC). Multi-center trials originating at an outside institution are required to submit a DSMP to the SRC for approval. If the originating site does not have a plan, they will be required to comply with the plan outlined in this document for the Lurie Cancer Center to be a participating site. As required by the NCI, other grants and contracts from NCI/NIH (e.g. National Clinical Trial Network studies) and studies developed and funded by industry are excluded from this plan.

2.3 Conflict of Interest

Conflict of Interest (COI) can include professional interest, proprietary interest, and miscellaneous interest as described in the NIH Grants Policy Statement and 45 CFR Part 94. NU has the following COI policies: “Policy on Conflict of Interest and Conflict of Commitment”, “Conflict of Interest in Research”, and “Institutional Conflict of Interest in Research”. These documents outline rules and reporting requirements governing all types of conflicts, including financial conflicts and disclosures, and also outlines policy specifically related to clinical research. Importantly, the NU policy requires that an investigator disclose if the value of any remuneration received from the entity in the twelve months preceding the disclosure and, in the case of publically traded entities, the value of any equity interest in the entity as of the date of disclosure, when aggregated for the Investigator and members of his or her immediate family, exceeds $5,000. NU employs an online, electronic system for reporting COI, and faculty and staff must report all significant financial interests (SFI) prior to engaging in research and at least annually thereafter; any new SFIs must also be reported within 30 days. These are reviewed by NU COI office and may be referred to the faculty member’s respective school and/or the COI Oversight Committee if additional review is required. If any COIs exist, the Dean’s office of the respective school and NU COI office will work with NU personnel to develop a plan to manage, reduce or eliminate the COI.

In addition to this University-wide policy, the NU Feinberg School of Medicine (FSM) has adopted a complementary policy titled “Disclosure and Professional Integrity Policy” developed with the integrity of medical research in mind. This policy also requires faculty to report financial COI, but there is no de minimis threshold for disclosure. Instead, all outside professional activities related to the health care industry are to be reported, no matter the payment amounts and these are posted on the FSM website. Both the NU and FSM policies may be found online at NU COI Policies.

Lurie Children’s has a “Financial Conflicts of Interest in Research and Sponsored Programs” policy that is applicable throughout the Lurie Children’s organization and requires disclosure of significant financial interest annually, using an online reporting system. Per their policy, significant financial interest in a publicly or non-publicly traded entity exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. This policy is located online at Lurie Children’s COI Policy.
The Lurie Cancer Center’s research oversight committees abide by Lurie Children’s, NU and FSM COI policies. Any faculty member invited to serve on or to review items for any of the committees described in this DSMP must disclose any potential COI relevant to committee membership, whether real or perceived, to the appropriate Lurie Cancer Center officials (i.e., the cancer center Director and/or applicable committee leader). Potential conflicts that develop during a member’s tenure on a committee must also be disclosed. Decisions concerning whether individuals with potential conflicts of interest, or the appearance of conflicts of interest, may participate on a committee or in a particular meeting will be made by the committee chair and/or co-chair.

While the Lurie Children’s and NU policies outline general rules related to COI, the Lurie Cancer Center has established the following specific committee rules that govern the activity of members who have a conflict:

- A committee member may not vote on a protocol on which he or she serves as a Principal Investigator (PI) or sub-investigator. When a faculty member is present at an SRC meeting and a protocol on which he or she will be a PI or sub-I is being discussed in consideration for initial approval, he or she is required to leave the meeting during the discussion and committee vote on the project. The investigator is allowed to be present during discussion related to protocol revisions or data and safety monitoring issues; however, he or she may not vote on these items. He or she may also not serve as an auditor for his or her own trial.

- Any committee member who is not an investigator on a trial, but who has another identified conflict may or may not be allowed to vote on actions related to the protocol. This will be determined by the committee chair and/or co-chair. Those individuals found by the chair and/or co-chair to have a significant conflict related to a trial will not be allowed to vote on items related to that trial, as described above.

2.4 Confidentiality

All discussions that occur within any of the Lurie Cancer Center research oversight committees are confidential and are not disclosed except as outlined in this plan. Committee decisions are conveyed to the respective PI and other committees, as appropriate, on behalf of the entire committee via the meeting administrator, but no specifics are given related to the persons involved or details of the discussion that occurred. Any paper materials containing confidential information distributed during committee meetings are collected and destroyed after each meeting.

Further, the committees are especially aware of issues related to confidentiality of data. The committees abide by, and enforce, the design of each study; confidentiality of the data are maintained when data are presented (e.g., treatment assignment is not disclosed). Blinded studies remain so until they are to be un-blinded as per study design, or in response to a safety issue that requires knowledge of treatment received by a study participant.

3.0 Institutional Clinical Trial Risk Assessment and Monitoring Requirements

The Lurie Cancer Center expects that all LCC IITs will follow the data safety monitoring procedures and requirements outlined in this plan. This plan also applies to other (non-LCC IIT) clinical trials that do not have an acceptable external or alternate plan. This plan applies only to clinical trials, as defined in section 2.2 of this document and include studies supported through various funding mechanisms, including competitive NCI/NIH grants, other agency/sponsor grants or gifts, and grant-in-aid support from industry sponsors.
### 3.1 Definitions of Levels of Risk and Associated Monitoring Requirements:

The Lurie Cancer Center complies with federal regulations and guidelines, as well as the Lurie Children’s and NU IRB Office policies and procedures related to the assignment of trial risk. The “Northwestern Human Subject Protection Policy Manual” is found online at NU IRB Policies. The Lurie Children’s “IRB Policy and Procedures Manual” is found at Lurie Children’s IRB Policies.

The SRC defines three levels of risk for clinical trials, ranging from minimal to high risk. The level of risk is assigned irrespective of the type of intervention under consideration (e.g., therapeutic, prevention, supportive care, etc.), and all clinical trials that fall under the purview of this plan are assigned a level of risk. The level of monitoring required will correspond with the level of risk assigned. A variety of factors are taken into consideration in making this determination, such as the size, expected duration and complexity of a trial, the trial phase, safety measures included in the study design, study population, and the toxicity profile associated with the agent under investigation. In the event that a study may be reasonably assigned to two categories, the highest risk category will be selected. The levels of risk and associated monitoring are:

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<th>Level of Risk</th>
<th>Monitoring Level</th>
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<td><strong>Minimal Risk</strong> – The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical and psychological examinations or tests and where confidentiality is adequately protected. An example of this type of trial is a computer internet-based strategy aimed at increasing awareness of cancer issues, a dietary intervention, or exercise study aimed at symptom management</td>
<td><strong>Minimal Intensity Monitoring</strong> – Monitoring by the Data and Safety Monitoring Committee (DSMC) is not required for these studies.</td>
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<td><strong>Moderate Risk</strong> – There is a probability of a moderate-severity event occurring but there is adequate safety monitoring in the trial to identify events promptly and to minimize their effects.</td>
<td><strong>Moderate Intensity Monitoring</strong> – An example of this type of trial is a topical agent used to control a drug rash. For these trials, the PI is required to submit adverse event CRFs/eCRFs to the QAMs in real time. Requires prospective registration. DSMC monitors adverse events and accrual of these studies semi-annually through review of semi-annual reports.</td>
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<td><strong>High Risk</strong> - There is a high probability of the occurrence of a serious adverse event and/or study monitoring and reporting requirements of the trial are such that events or event trends may not be immediately recognized. AND/OR The NU or LCC investigator holds the IND/IDE.</td>
<td><strong>High Intensity Monitoring (Routine or Intense)</strong> – An example of this type of trial is a chemotherapy trial aimed at treating cancer. DSMC monitoring of these studies is rigorous as described in section 5.2 The DSMC conducts a comprehensive review of study progress and safety in real-time in addition to semi-annually through review of semi-annual reports.</td>
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3.2 Data and Safety Monitoring Boards

Clinical trials for drugs or devices that were developed from lab work done within the Lurie Cancer Center are subject to more extensive monitoring, to ensure that COI is avoided. All such trials are required to follow the DSMC requirements for High Intensity Monitoring. In addition, they have the further requirement of establishing an independent Data and Safety Monitoring Board (DSMB). Composition of this board must be proposed by the study PI and approved by the DSMC.

Phase III medical intervention trials are required to follow the DSMC requirements for High Intensity Monitoring. In addition, they have the further requirement of establishing an independent Data and Safety Monitoring Board (DSMB). Composition of this board must be proposed by the study PI and approved by the DSMC.

Clinical trials that do not involve a drug or device intervention may require the establishment of an independent DSMB if required by the funding sponsor. These studies may present low to moderate risk, but additional safeguards are deemed necessary to ensure the trial is progressing acceptably. For example, the study may be comprised of several phases, each requiring data analysis prior to movement into the next phase. In a case such as this, an independent board is required to ensure an unbiased review of the data.

Appendix D outlines DSMB requirements for medical and non-medical intervention studies.

4.0 Research Oversight System Organization and Administration

The Lurie Cancer Center has developed a comprehensive system of research oversight, comprised of distinct committees that work collaboratively to provide robust oversight of all aspects of clinical research conducted at the Lurie Cancer Center. The Scientific Review Committee (SRC) and the Disease Teams (DTs) comprise the Center’s Protocol Review and Monitoring System (PRMS). The Data Monitoring Committee (DSMC) and the Clinical Trial Audit Committee (CTAC) are responsible for data safety monitoring and protocol compliance. The committees are independent and report directly to the Lurie Cancer Center Deputy Director. The Deputy Director, in turn, reports to the Director of the Cancer Center. Each committee or team includes a leader and co-leader as outlined below. A diagram of this system can be found in Appendix A. Committee responsibilities related to data safety monitoring are described below.

4.1 Disease Teams

The primary objective of each DT is to guide in the selection and prioritization of high quality cancer research studies. Each DT includes a team leader and co-leader, responsible for proper functioning of the team. A listing of DTs and their associated leaders may be found online at Disease Team listing.

The DTs meet at least monthly to review all studies under the purview of their team. DTs must first endorse each newly proposed study before the protocol may be submitted to the SRC. In addition, DTs serve as the first level of review for Lurie Cancer Center investigator-initiated trials (LCC IITs); this is usually done at the concept or letter of intent (LOI) stage prior to full protocol development. The SRC, DSMC and CTAC communicate with the DT leaders as needed, and will inform them of any issues or concerns that impact the DTs research portfolio. DSMC will send semi-annual reports for monitored studies as needed when issues arise, and CTAC will provide copies of all audit reports as applicable to the DTs.
4.2 Scientific Review Committee (SRC)

The SRC is charged with the responsibility of evaluating new and enrolling clinical research protocols for scientific merit, institutional priority and ongoing progress, including review of accrual for all clinical trials. The SRC is an independent committee within the Lurie Cancer Center’s PRMS, chaired by Al B. Benson III, M.D. and co-chaired by both Masha Kocherginsky, Ph.D. and Jeffrey Sosman, MD. A full member listing is included online at [SRC membership](#).

The SRC is primarily focused on the scientific design and importance of new studies, as well as ensuring appropriate data and safety monitoring plans; SRC will not approve protocols that do not include an adequate DSMP. SRC review of LCC IITs includes assignment of risk level, which corresponds to the requirements for monitoring that are described in the final protocol. This decision is communicated to the DSMC. During ongoing progress review, SRC will notify the DSMC regarding any decisions that impact protocol status (e.g., suspension or closure) for those studies under DSMC purview.

The DSMC is responsible for informing the SRC of any findings that may impact the scientific integrity of a trial. In the event that the committee is notified of misconduct or other issues impacting study integrity the SRC will help ensure that all appropriate authorities are notified as needed (e.g., the IRB, FDA, NCI, funding sponsor, etc.). In the event that a suspension or closure occurs on an NCI funded trial, the SRC will ensure the PI reports to this the NCI Program Director.

4.3 Data and Safety Monitoring Committee (DSMC)

The DSMC plays an integral role in data and safety monitoring. This is a multidisciplinary committee that consists of a core group of individuals providing the necessary expertise in the principal disciplines of clinical hematology/oncology and radiation oncology with additional representation from biostatistics. Members are selected by area of expertise to form a diversified group of clinicians and other professionals able to provide rigorous monitoring of studies. Olga Frankfurt, M.D. serves as chair of the committee and Sonali Chaudhury, M.D. is the co-chair. A full member listing is found online at [DSMC membership](#).

The Deputy Director of the Lurie Cancer Center provides oversight of the administration of the committee and also acts as a liaison between other clinical research oversight committees, investigators, and the Lurie Cancer Center Clinical Trials Office (CTO). The Lurie Cancer Center’s Quality Assurance team provides administrative support for the committee, and each study monitor is responsible for reporting trials they monitor at semi-monthly DSMC meetings. Their review specifically focuses on participant safety and toxicity, outcomes/response, accrual updates, compliance issues, and overall data integrity (see sections 5.0 for more information related to monitoring activities).

The DSMC is an independent committee responsible for safety review and study progress monitoring for Lurie Cancer Center investigator-initiated clinical trials. While the DSMC is a distinct independent committee, DSMC shares its findings with the other committees of the Research Oversight System, as needed. In particular, DSMC will notify SRC of any issues they believe to be potentially relevant to the scientific integrity of the trial. The DSMC will also communicate with Disease Teams, informing them of any concerns, and sends the team leaders semi-annual reports as necessary for relevant LCC IITs.

The DSMC meets semi-monthly and provides the following:

- Safety review: DSMC conducts ongoing safety reviews of all LCC IITs requiring moderate and high intensity monitoring, and semi-annual safety reviews for those studies determined to require minimal, moderate or high intensity monitoring. Safety review includes a listing of all reportable adverse events, as specified in each protocol, that occur on the trial. The DSMC has the authority to suspend or close...
any study if serious safety concerns are identified. If the decision is made to suspend or close a study, this change is made by the study assigned Quality Assurance Monitor (QAM) within the Lurie Cancer Center’s clinical trials management system (NOTIS), and this generates an automatic notice of study status change to the PI and study team.

- Ongoing study monitoring: DSMC reviews the progress of all LCC IITs through review of semi-annual reports, required for all clinical trials monitored by the committee. The semi-annual reports include such information as accrual, reported adverse events, and compliance issues. If the DSMC finds that study progress is not meeting the requirements of the Lurie Cancer Center Low Accrual Policy (see Low Accrual Policy) or in the event there is an issue with regards to the scientific progress of the study, SRC will be notified of the concern.

- Review of audit findings: DSMC reviews audit reports submitted by CTAC. In particular, CTAC submits audit reports and corrective and preventative action plans (CAPAs) to the DSMC for any audit findings that relate to data integrity or patient safety. The DSMC has the authority to require further corrective action if the submitted plans are determined to be insufficient to address the findings. The DSMC further has the authority to suspend or close the trial in the event that major concerns are found during an audit. If the decision is made to suspend or close a study, this change is made by the study assigned QAM within the Lurie Cancer Center’s clinical trials management system (NOTIS), and this generates an automatic notice of study status change to the PI and study team.

- Serious adverse event (SAE) review: DSMC reviews all SAEs that occur on trials monitored by the committee. The study assigned QAM reports the individual events at the first DSMC meeting after receipt of the completed event report. These events are also incorporated into each protocol safety review/adverse event summary table, which is regularly reviewed by the DSMC (as described in the first bullet point, above).

- Dose Limiting Toxicity (DLT) review: DSMC reviews all potential DLTs for Phase I dose-escalation studies. The study assigned QAM reviews all toxicity during the dose-escalation phase of studies and presents this data to the DSMC. Protocol suspensions and re-opening of accrual to the next cohort, based on DLT evaluation, fall under the purview of DSMC. If the decision is made to suspend or re-open a study, this change is made by the study assigned QAM within the Lurie Cancer Center’s clinical trials management system (NOTIS), and this generates an automatic notice of study status change to the PI and study team.

- FDA report review: DSMC is responsible for the review of all FDA annual reports prior to submission to the FDA for those studies where the Lurie Cancer Center PI holds the IND or IDE. Study assigned QAMs work directly with PIs on preparation of all reports to the FDA.

- Protocol deviation review: QAMs review all protocol deviations, and those determined to potentially be reportable to the IRB are reviewed at a DSMC meeting (this form may be found at Protocol Deviation Form). If the DSMC determines a deviation is reportable to the IRB, the QAM communicates this information to the study’s assigned regulatory coordinator and study team, and they work together to submit this to the IRB. All other protocol deviations, not potentially reportable to the IRB, are reviewed semi-annually by the DSMC as part of the semi-annual report.

- Data set review: QAMs are responsible for reviewing all data for trials as defined by this plan, and for presenting this data to DSMC as described in this section. Data to be used for abstract and/or manuscript development must be reviewed and approved by the DSMC prior to release to the study PI and/or biostatistician. For more details, please review Data Release policy.
• Reportable New Information (RNIs): All RNIs requiring reporting to the Northwestern or Lurie Children’s IRB will also be reported to the DSMC at the next scheduled DSMC meeting. For more information on what constitutes an RNI, please see https://irb.northwestern.edu/process/reportable-new-information. The only caveat to this rule will be short form consents, which are approved through the RNI mechanism, but do not require DSMC review.

• In the event that any issues are identified with a trial, the DSMC notifies the PI of the issue(s) and may request a response or a more formal Corrective and Preventative Action Plan (CAPA).

4.4 Clinical Trial Audit Committee (CTAC)

The CTAC is responsible for overseeing the conduct of the Lurie Cancer Center’s auditing program. The committee consists of members providing expertise in clinical oncology and research compliance and forms a diversified group of professionals able to provide rigorous oversight of auditing activities. This committee is chaired by Jessica Altman, M.D. and co-chaired by Priya Kumthekar, MD. A full member listing is provided online at CTAC membership. CTAC responsibilities include:

• Audit scheduling and conduct: The CTAC administrator schedules audits, assigns auditors, and ensures audits are conducted as required by the Lurie Cancer Center SOP on auditing of IITs under the supervision of the CTAC. CTAC leaders are available to advise on audit activities, answer questions as needed, and attend key audits, as needed.

• Review of audit findings: CTAC reviews all audit findings on LCC IITs and makes the final determination on the seriousness of issues identified during the audit. Individual findings are categorized as “lesser” or “major”, following NCI CTEP definitions. The committee will determine if the PI must submit a Corrective and Preventative Action Plan (CAPA), assesses the final audit outcome, and recommends measures for the subsequent audits.

• Cause-specific review of audits with major violations: CTAC pays particular attention to major and recurrent audit findings and has the authority to suspend study accrual for continued non-compliance. If the decision is made to suspend a study, this change is made by the study assigned QAM within the Lurie Cancer Center’s clinical trials management system (NOTIS), and this generates an automatic notice of study status change to the PI and study team. Suspensions initiated by the CTAC will also be reported to the DSMC. The committee communicates findings to the DSMC and may:
  o Recommend that the DSMC close a study to further accrual;
  o Recommend membership termination for a site due to substandard performance; and
  o Recommend changes to policy, protocols, or procedures based on cumulative audit findings.

• Administrative activities: CTAC advises leadership on audit-related activities, outcomes, and policy issues. They also assist in the development of quality assurance tools, measures and SOPs. Audits are conducted following the NCI’s Clinical Trials Monitoring Branch Auditing Guidelines. Lurie Cancer Center audit categories include:

• Comprehensive Audits – These are annual audits of studies that require high intensity monitoring and that accrued at least one participant since the prior audit done on a rolling basis. At least one case, or 10% of all accrual, whichever is greater, accrued since the previous audit is chosen at random. Full audit reports are submitted and reviewed by CTAC. These are complete study audits that include, as applicable to the trial, a review of:
o Regulatory compliance (consent content and IRB submissions);

o Drug accountability and pharmacy inspection;

o Shared resource documentation (e.g., Pathology Core Facility, Pharmacokinetics Core, etc.);

o Case review, including a review of protocol compliance (participant consent, eligibility, treatment administration, monitoring for adverse events and outcomes). This review includes source document verification;

o Adverse event reporting, focusing on identification of serious adverse events; and

o Data quality review.

- First Participant Audits – These are done on both the first Lurie Cancer Center participant to enroll on a new trial and also the first participant enrolled on a new trial at each collaborating site if applicable. Single-Case Audit reports are batched and presented at the next CTAC meeting, unless major violations are found or if the next CTAC meeting is greater than 3 months away. In this case, the audit report is sent to the committee via email. The case audit occurs after the first participant has completed reaches the first response assessment, or goes off active treatment, whichever comes first. These audits may count towards the annual audit as applicable.

- For Cause Audits – Typically these audits are the result of suspected or reported non-compliance. Requests for this type of audit are reviewed and approved by the CTAC or the Director. These audits may occur at any time and advanced notice is not required. For Cause Audit reports are sent to CTAC and Lurie Cancer Center senior leadership via email upon completion of the audit.

CTAC meets as needed based on the current audit schedule. Unless the Committee chairs request additional meetings, review following other audits is done via email or audit reports are batched and presented at the next scheduled CTAC meeting. While CTAC oversees the audit process, the committee itself is not primarily responsible for the actual conduct of the audits. Instead, the Lurie Cancer Center’s Administrative Director, Clinical Research or designee, who is an administrative/non-voting member of CTAC, assembles an independent audit team for each audit, including faculty members, fellows, nursing staff and CRO. To avoid COI, the faculty and staff cannot be chosen to audit a trial for which they are listed on the IRB’s authorized personnel list.

After each audit is complete, audit worksheets are collected by the QCM who generates an Audit Report (available online at Internal Audit Report Template). CTAC reviews and finalizes the Audit Report and determines if a CAPA is required of any study team. All CAPAs are then reviewed by CTAC. The CTAC approved Audit Report is then sent to the DSMC for review, and any questions or concerns related to audit findings are discussed at the next scheduled DSMC meeting. The DSMC is responsible for reporting any findings that affect the scientific integrity of the trial to the SRC.

4.5 Lurie Cancer Center Research Oversight Committees and the IRB

NU and Lurie Children’s each have independent IRBs but also have a signed Authorization Agreement that allows collaboration for the review of studies impacting both institutions. The SRAL is contracted to use the NU IRB. NU IRB provides six IRB panels, including five that meet monthly and one that meets weekly (for continuing reviews and other time-sensitive submissions). The Lurie Children’s IRB Office provides support for two panels that meet bi-monthly. NU faculty may also use a central IRB for certain types of studies. The Jesse Brown VA Medical Center has an independent IRB that meets twice a month. All new cancer-relevant
protocols and revisions must receive the appropriate SRC, IRB, and other required institutional approvals prior to activation or implementation.

The SRC and IRB perform separate but complementary activities, which do not overlap or duplicate effort. The Lurie Cancer Center oversight committees are responsible for scientific review, monitoring and evaluation of trials for ongoing progress, data and safety monitoring, and auditing. The IRB is responsible for the overall ethical and safety considerations of clinical research with respect to protecting the rights and welfare of human subjects involved in research. Additionally, the IRB ensures that all consent forms adequately express the risks, benefits, alternatives, and financial costs of clinical research protocols. The IRB further ensures HIPAA regulations are followed. Appendix B provides a comprehensive diagram of the relationships among these committees and with the Institutional Review Board (IRB).

5.0 Quality Assurance Monitoring

The Lurie Cancer Center has made it a priority to continuously strengthen our internal quality assurance program. Quality assurance and quality control is an independent office within Lurie Cancer Center, reporting administratively to the Assistant Director of Administration of the Cancer Center. To ensure adequate quality controls at all levels of clinical research has required the interaction of a number of Lurie Cancer Center employees, oversight by the DSMC and CTAC, and the participation of the Biostatistics Core Facility. Currently there are two procedures in place for quality oversight: quality assurance review and internal audit, which is overseen by CTAC.

5.1 Quality Assurance Review

Quality assurance review is the responsibility of six Quality Assurance Monitors (QAMs) who report directly to the office’s Quality Assurance Operations Manager (QAOM). The QAMs are responsible for the ongoing review of all clinical trial data for LCC IITs, concentrating on data accuracy and completeness, protocol adherence, and safety review. This includes the review of studies that are supported by competitive federal funding mechanisms that do not have an alternate data management plan.

The QAMs review all data submitted for trials at scheduled monitoring visits every 8-12 weeks unless otherwise specified, and they interact directly with each study PI as issues arise. They also work directly with treating physicians and study coordinators, both at the Lurie Cancer Center and at participating sites, if there are issues related to study participants and/or data submission. The QAMs regularly report all findings directly to the DSMC during semi-monthly meetings and via email, when needed.

The QAMs are intimately involved in data capture and review from protocol implementation through trial completion. Trials opened prior to July 2009 use paper-based case report forms, created by the QAMs. All LCC IITs opened to accrual after July 2009 use electronic case report forms (eCRFs), built into NOTIS, the Lurie Cancer Center’s clinical trial management system. The study assigned QAM builds eCRFs for each new trial. To ensure appropriate forms are used for each study, the QAOM and QAMs thoroughly review each new project, and revisions to ongoing projects, to determine eCRF needs. This review includes discussion with the study PI, biostatistician, study coordinator, data manager and/or other study team members to review study objectives, eligibility requirements and registration process, trial design, treatment plan, adverse event reporting requirements, measurement of outcomes and study parameters. The developed forms are the only CRFs used to collect data, and are used by the QAMs to monitor the study. For more information on specific monitoring logistics, please see the RHLCCC Quality Assurance Monitoring Guidelines.

The intensity of monitoring activities varies by the study assigned risk. QAM monitoring intensity is as follows:
• **Moderate Intensity Monitoring** – This monitoring level is for studies that involve a moderate risk, and more intensive monitoring for adverse events is required. PIs are required to prospectively register participants and submit adverse event eCRFs to the QAMs in real time; other types eCRFs (e.g., response data) are not required. DSMC monitors study progress through review of DSMC Semi-Annual Reports, which are completed collaboratively by the PI and the assigned QAM.

• **High Intensity Monitoring** – This monitoring level is for studies that involve a high risk, that require extensive monitoring by QA. For these trials, study participants must be prospectively registered, and all eCRFs are submitted to and monitored in a risk-based approach by QA at least every 8-12 weeks, or more often as required. In addition, all SAEs are reported to QA in real time, as defined by each protocol. SAEs, safety data, DLT review, FDA annual reports, and serious non-compliance are prepared and presented by QA as indicated per protocol at the next scheduled DSMC meeting. The DSMC conducts a comprehensive review of study progress semi-annually through review of the Semi-Annual Report, which is completed collaboratively by the PI and the assigned QAM.

5.2 **Other Quality Assurance Activities for High Risk Studies**

The QAMs work closely with faculty and staff throughout the life cycle of each protocol, from initial protocol development through final data analysis and study termination. New LCC IITs require a Study Implementation Meeting (SIM), which is a meeting that brings together members of the study and extended care teams, to ensure the study is feasible and that the protocol document is clear and easy to follow. The QAMs are important participants in the SIM, providing valuable input on the protocol document, including such things as ensuring registration procedures and other QA activities are adequately described. The QA team additionally reviews the protocol again at SRC review, to ensure QA activities are adequately described, and ensure the trial is assigned an accurate risk level. It is during this early stage that the QAMs also work with the PI and study team to develop eCRFs for the study.

The Quality Assurance Team is also responsible for preparing all data for submission for publication and presenting to the DSMC for review and approval as described in DSMC Data Release Policies and Processes that was developed with our Quantitative Data Sciences Core.

5.3 **Adverse Event Reporting Requirements**

Adverse event reporting requirements and timing of reporting are dependent on the phase of the trial, as well as the grade and attribution of the event and is completed as outlined in the guidelines published in the NCI Investigator Handbook ([http://ctep.cancer.gov/investigatorResources/investigators_handbook.htm](http://ctep.cancer.gov/investigatorResources/investigators_handbook.htm)). It is the responsibility of the study PI, the treating physician, and clinical team to identify events as they occur. Federal guidelines require timely reporting of all unanticipated adverse events as outlined by the study sponsor.

All Serious Adverse Events (SAEs) must be reported as required by institutional policy and federal guidelines. In addition, adverse events which do not meet the definition of a SAE may also require expedited reporting dependent upon the grade of adverse event, attribution, and whether the event is expected or unexpected. Expedited reporting may not be required for protocols when the adverse event is expected. Any exceptions will be outlined in the text of the protocol. In the event that a participant experiences an event requiring expedited reporting, the report must be submitted to the QA team, IRB of record, and federal agency (as applicable) using appropriate reporting forms.

21 CFR 312.32, defines a SAE as an adverse drug experience that results in any of the following outcomes:

• Death;
• A life-threatening adverse drug experience;
• Inpatient hospitalization or prolongation of existing hospitalization (for > 24 hours);
• A persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions;
• A congenital anomaly or birth defect;
• Important Medical Events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

Whenever a serious adverse event occurs on an LCC IIT, either at the Lurie Cancer Center or a participating site, the event is submitted to the QAM and is reviewed by the DSMC. The DSMC will review the event and the PI's assessment. The DSMC may determine the event requires expedited reporting, and in this case, the QAM will follow-up with the PI to help ensure the event is reported to the IRB of record. If an event is determined to require expedited reporting to the IRB, it will also be sent to participating sites as a SUSAR report requiring IRB submission and consent and/or protocol modification will be sent to the sites as appropriate. See Appendix C for flow diagrams outlining procedures for handling of both internal and external adverse events.

The CTO regulatory team is responsible for processing external SUSARs, and ensuring these are reviewed by PIs who hold an IND/IDE for that drug or device. The QAMs then present SUSARs that qualify as RNIs to the DSMC. Any event determined by the DSMC to be a UPIRSO is routed to participating sites for local IRB submission and consent and/or protocol modification will be sent to the sites as appropriate.

For all NCI funded or sponsored clinical trials, investigators are required to submit events through the CTEP Adverse Event Reports System (CTEP AERS) as described in the “NCI Guidelines for Investigators: Adverse Event Reporting Requirements for DCTD (CTEP and CIP) and DCP INDs and IDEs” found at https://eapps-ctep.nci.nih.gov/ctepaers/pages/task?rand=1397583886412.

If NCI does not hold the IND, the FDA regulations apply as outlined in 21 CFR Part 312.32 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.32).

If the trial uses commercially available agents/devices SAEs are reported using a format as indicated in the trial, or are reported through MedWatch (http://www.fda.gov/medwatch/index.html).

If the trial involves recombinant or synthetic nucleic acid molecules, the reporting requirements described above must be followed. In addition, the “NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)” apply. This guideline may be found at http://osp.od.nih.gov/office-biotechnology-activities/biosafety/ NIH-guidelines.

If the trial is a post-marketing vaccine trial, the reporting requirements described above must be followed. In addition, adverse events may be submitted through the Vaccine Adverse Events Reporting System (VAERS). Further information regarding vaccine adverse event reporting is found at http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/VaccineAdverseEvents/default.htm.
The NU IRB requirements for events that may be considered Reportable New Information (RNI) can be found online at [http://irb.northwestern.edu/policies](http://irb.northwestern.edu/policies). Those events determined to be Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) be submitted within 5 working days of the event. A UPIRSO is an event that is unexpected, related or possibly related, and suggests greater risk. More information on this policy can be found at [http://irb.northwestern.edu/process/reportable-new-information](http://irb.northwestern.edu/process/reportable-new-information). The Lurie Children’s IRB and the Jesse Brown VA Medical center have similar reporting requirements. The Lurie Children’s policy is described in the “IRB Policy and Procedures Manual” located online at [https://www.luriechildrens.org/en-us/research/management/toolkit/irb/Pages/policies-procedures.aspx](https://www.luriechildrens.org/en-us/research/management/toolkit/irb/Pages/policies-procedures.aspx), and the VA Policy is outlined online at [http://www.va.gov/ORO/Docs/Guidance/1058_01_Decision_Chart_Rsch_Death_SAE_Problem_09_14_2015.pdf](http://www.va.gov/ORO/Docs/Guidance/1058_01_Decision_Chart_Rsch_Death_SAE_Problem_09_14_2015.pdf).

If the trial involves behavioral or nutritional interventions that do not use an investigational agent, there are no standard grading scales for adverse events. Therefore, defining suitable grades for adverse events is the responsibility of individual investigators for each protocol. Adverse events of a psychological nature can occur with behavioral trials and should be specified for the particular intervention in question.

### 6.0 Multi-Center Trial Administration

The Lurie Cancer Center has established Standard Operating Procedures (SOPs) that are used for the management of multi-center LCC IITs. These procedures include activities related to site qualification, pre-activation, protocol training, trial initiation, and clinical and regulatory communications. Activities related to the Lurie Cancer Center oversight committees are addressed in all these areas, and are described below.

#### 6.1 Site Qualification and Trial Initiation

The Lurie Cancer Center has a dedicated Project Manager who provides oversight for our affiliate network and works directly with the network and other sites participating on LCC IITs. Communications related to study start up and ongoing regulatory compliance are directed by this Program Manager.

When the Lurie Cancer Center is informed of a potential new site for an LCC IIT, the study start-up lead sends the site a packet of information, including the Participating Site Questionnaire and the Participating Site Data Compliance Policy). The Participating Site Questionnaire must be completed by each new participating site, and all completed forms are routed to and reviewed by the Administrative Director of Clinical Research, and the Clinical Trial Office Medical director, to determine if a site is a good candidate for the trial. The Project Manager reviews the PI’s data delinquency status on other studies, as applicable. If the PI is in good standing and a confidentiality disclosure agreement is in place, the site may be approved and allowed to submit the Lurie Cancer Center IRB approved version of the protocol to their local IRB. Each new site PI must sign and return the Data Compliance Policy before any activity related to a study may begin.

While a participating site is awaiting local IRB approval, other site pre-activation activities may begin. During this time, the study start-up team and multi-site regulatory coordinator collects required regulatory documents (e.g., signed 1572, financial disclosure forms, medical licenses, contracts, etc.). Site training also begins at this time. The site is provided with all relevant SOPs related to multi-center trials. In addition, a site initiation telephone conference (SITC) is required for all studies, and the site will receive training on eCRFs. The site will be activated once all required pre-activation requirements are complete and their documentation of IRB approval has been received.
6.2 Active Trial Communications

Unless an alternate monitoring plan has been approved by the SRC, all sites participating in LCC IITs are expected to comply with this DSMP. As such, all sites will use the Lurie Cancer Center created eCRFs designed for the study. All data are submitted to the assigned QAM, as described in each study. The data is monitored by the QAM and reviewed by DSMC as described in this plan.

Participating site clinical and regulatory data are included in the auditing program. When a participating site case is selected for audit, the site is informed of this and is expected to submit all source documents for inclusion in the audit. In addition, regulatory documents and pharmacy logs must also be submitted for inspection. Sites are expected to comply with all requests of the CTAC.

6.3 Consortium Trials

In the event that in LCC IIT is activated through a consortium, the consortium may elect to use the Lurie Cancer Center’s Data and Safety Monitoring Plan as the monitoring plan of record. In such cases, quality assurance activities usually performed by the Lurie Cancer Center Quality Assurance department may be delegated to a Contract Research Organization. Any organization that manages quality assurance activities on such trials must explicitly agree to adhere to the Lurie Cancer Center Data and Safety Monitoring Plan and must report regularly to the Data and Safety Monitoring Committee.

7.0 Investigator Responsibilities

While the Lurie Cancer Center research oversight committees hold a great deal of responsibility for trial monitoring, the PI of each study is ultimately responsible for every aspect of the design, conduct, and final analysis of the protocol. All PIs are required to complete all institutional training requirements, abide by federal policies and guidelines, and abide by those commitments outlined in FDA Form 1572. In addition, the study PI must ensure that:

- All protocols include a data and safety monitoring plan (either this plan or a plan developed by the PI and approved by the SRC).
- 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.
- The proposed schedule for reporting adverse events to the QAMs, IRB, and appropriate federal agencies is described in the protocol.
- In specific cases where an outside agency is the sponsor of the test agent, (i.e., holder of the IND), PIs must submit individual adverse event reports to the funding agency/sponsor in accordance with sponsor and FDA regulations.
- 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.
- Semi-annual reports are reviewed and per DSMC guidelines.
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).

With the assistance of the CTO regulatory staff (or other personnel if not managed by the CTO), DMC, SRC and CTAC reports are submitted to the IRB of record per their requirements.

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 SRC. In the event that a waiver of consent will be requested, a justification must be submitted to the IRB.

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

All data used for abstracts and publications of LCC IITs have been reviewed and approved by the DSMC prior to use.

In the case where the Lurie Cancer Center PI is an IND/IDE holder, all FDA reporting requirement to maintain the IND/IDE are followed. This is done with the assistance of the QAMs.

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.
Appendix A: Lurie Cancer Center Research Oversight System

Lurie Cancer Center Research Oversight System

Faculty Leadership
- Director
- Deputy Director
- PRMS
- DSM
- SRC
- DMC
- Disease Teams
- CTAC

Administrative Support
- Assistant Director, Cancer Center
- PRMS Coordinator
- QA Office
- SRC
- DMC
- Disease Teams
- CTAC

Committee Leadership and Responsibility

Responsibility:
- Initial independent scientific review, interventional trials
- Approval of prioritization, interventional trials
- Ongoing monitoring, interventional trials
  - Scientific changes
  - Accrual
- Administrative review, non-interventional research

Responsibility:
- Administer DSMP
- Release of approved data to PI for abstracts, publication

Responsibility:
- Oversight of audit process
- Review of audit reports
- Review and approve of CAPAs
Appendix B: Lurie Cancer Center Research Oversight System Activity Flow Diagram
Appendix C: Adverse Event Management

Internal Adverse Events

Internal Adverse Event: any adverse event that occurs to any subject at Northwestern University (NU) or any subject at an affiliate on a LCC IIT.

LCC IITs only – Participating Sites

- SAE occurs at participating site
- SC completes appropriate AE form: Quality Assurance Monitor (QAM) enters into NOTIS and forwards to LCC PI for UPIRSO consideration.
- If the event qualifies as a UPIRSO, QAM presents report to DMC. If DMC concurs it is a UPIRSO, QAM distributes report to participating sites.
- SC reports event to outside agencies and Sponsor as dictated per protocol.
- SC files all AE paperwork in the research file(s).

For LCC – All Study Types

- AE occurs at LCC
- PI and Study Coordinator (SC) determine event status (UPIRSO, SAE, neither)
- SC completes appropriate AE form, enters SAE info into NOTIS and forwards to PI for UPIRSO consideration.
- If the event qualifies as a UPIRSO, SC forwards to Regulatory Coordinator (RC). For NU IITs SC forwards UPIRSOs and SAEs to QAM.
- RC submits UPIRSOs to IRB and submits revised consents and amendments as necessary within required timeframes. RC updates IRB dates in NOTIS.
- RC will file all UPIRSOs appropriately.
Appendix D: Guidelines for the Establishment of Data and Safety Monitoring Boards (DSMBs)

Medical Intervention Clinical Trials

Membership

Phase III trials and trials of drugs or devices developed within a Lurie Cancer Center lab require the establishment of an independent DSMB. The PI of each Phase III study is required to recommend board members to the SRC, who will approve the final board composition. A DSMB is required to consist of six voting members, four of whom are not affiliated with the Lurie Cancer Center. Members should have expertise relevant to the trial and must include:

- Two external physicians.
- One external biostatistician.
- One external behavioral scientist.
- One internal physician.
- One internal biostatistician.

Meetings

DSMB meetings will be held annually, but may be held more frequently depending on the nature and progress of the trial. Each meeting will begin with an open session, where the study PI presents a summary of the trial including current status, toxicity and response. The study biostatistician will present statistical analysis when appropriate. After these presentations and discussions have concluded, the board will meet in closed session to discuss the trial, including blinded results, and make recommendations. All recommendations are provided to the PI and are also submitted to the IRB.

Release of Data

The DSMB may not release outcome data until accrual for the trial has been completed. In the event that data are needed for manuscript preparation or future trial planning, data may be released on a confidential basis.

Confidentiality

All communication of board deliberations is confidential and may not be made available to anyone outside of the board membership, except those public recommendations made by the board.
Non-Medical Intervention Clinical Trials

Membership

Outcomes studies that involve a patient intervention may require the establishment of an independent DSMB. The PI of each study is required to recommend board members to the appropriate disease section leader, who will approve the final board composition. A DSMB is required to consist of a minimum of 4 voting members, all of who are not involved with the study. Members should have expertise relevant to the trial and must include:

- One researcher.
- One biostatistician.
- One clinician.
- A minimum of one additional investigator.

Meetings

DSMB meetings will be held annually, but may be held more frequently depending on the nature and progress of the trial. Each meeting will begin with an open session, where the study PI presents a summary of the trial including current status, toxicity and response. The study biostatistician will present statistical analysis when appropriate. After these presentations and discussions have concluded, the board will meet in closed session to discuss the trial, including blinded results, and make recommendations. All recommendations are provided to the PI and are also submitted to the IRB.

Release of Data

The DSMB may not release outcome data until accrual for the trial has been completed. In the event that data are needed for manuscript preparation or future trial planning, data may be released on a confidential basis.

Confidentiality

All communication of board deliberations is confidential and may not be made available to anyone outside of the board membership, except those public recommendations made by the board.