Data and Safety Monitoring (DSM) Plans

The MSK Policy document to ensure the highest quality clinical research and safety of participants in our Clinical Research and Population Science Research Programs.

Date Original Document created: July 2001, NCI Approved: September 2001
Date Revised: February 2007, NCI Approved: March 2007
Date Revised: March 2011, NCI Approved: September 2011
Date Revised: October 2015, NCI Approved: April 2016
Date Revised: May 2018, NCI Approved: August 2018

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DATA AND SAFETY MONITORING (DSM) OF CLINICAL RESEARCH

Introduction

The following document outlines the policies established by Memorial Sloan Kettering (MSK) for the appropriate oversight and monitoring of the conduct of clinical trials supported by NIH, NCI/NCTN, Industry or MSK investigator-initiated research. MSK's DSM Plan was originally developed to comply with the NIH/NCI policy guidance entitled *"NCI's Essential Elements of Data and Safety Monitoring Plan for Clinical Trials funded by the NCI."* The institutional DSM Plans were first approved by the NCI in September 2001, and have been modified over time to ensure consistency with the national standards, new guidances and revisions to the institutional policies and procedures. Throughout the document there are hyperlinks to MSK's Clinical Research Portal providing easy access to relevant documents, forms, processes and Standard Operating Procedures (SOP).

These policies ensure the safety of human participants in our clinical and population science research (referred to as patient-oriented research) programs, the validity and integrity of the data, and the appropriate termination or suspension of trials. The policies and procedures for DSM at MSK maintain the same operational definition of a clinical trial as noted in the NCI policies with the additions noted below. The definition of a clinical trial is:

- A prospective study involving human subjects designed to answer specific questions about the effects or impact of a particular biomedical or behavioral intervention; these may include (but are not limited to) drugs, treatments, devices, or behavioral and nutritional strategies. Participants in these trials may be people with cancer or without a diagnosis of cancer but at risk for it.
- In the area of molecular or imaging diagnostics, a study is considered to be a clinical trial if it uses the information from the diagnostic test in a manner that somehow affects medical-decision making for the subjects. In this way the information from the diagnostic test may have an impact on some aspect of outcome, and assessment of this impact may be a key goal of the trial.
- Behavioral clinical trials include interventions whose goals are to increase behavior (e.g., cancer screening, physical activity, fruits and vegetable intake, etc.) eliminate or reduce behaviors (e.g., smoking, sun exposure) and/or improve coping and quality of life (e.g., among cancer survivors) and reduce the negative sequelae of treatment. Interventions may pertain to prevention, early detection, treatment, and survivorship. Observational studies are not considered clinical trials for this document.

- In addition to the areas defined above, human subjects participating in any study where (1) a dye is injected or (2) a blood specimen is drawn or a biopsy performed (not studies for specimen banking only) will qualify for review via the DSM mechanism as clinical trials.

The policies and procedures for DSM of the patient-oriented research programs at MSK are established and monitored by Clinical Research Administration (CRA). The CRA is a function of Memorial Hospital and the Memorial Sloan Kettering Cancer Center, and reports directly to the Deputy Physician-in-Chief, Clinical Research [Paul Sabbatini, MD] and the Senior Vice President, Research Technology Management [Eric Cottington, PhD]. A description of the protocol monitoring process, including before protocol approval to activation, and throughout the protocol life cycle is defined.

INSTITUTIONAL OVERSIGHT

The Clinical Research (CR) and Population Science Research (PSR) Programs, which make up MSK's patient-oriented research programs, grew significantly since the last competitive renewal. This growth was based on current scientific and research related advances in cancer care. This is demonstrated by the overall increase to our clinical research protocol portfolio, therapeutic participant accruals and research staffing numbers. Figures 1 and 2 illustrate the change between 2010 and 2016 in the number of accruals to therapeutic clinical trials.

Figure 1

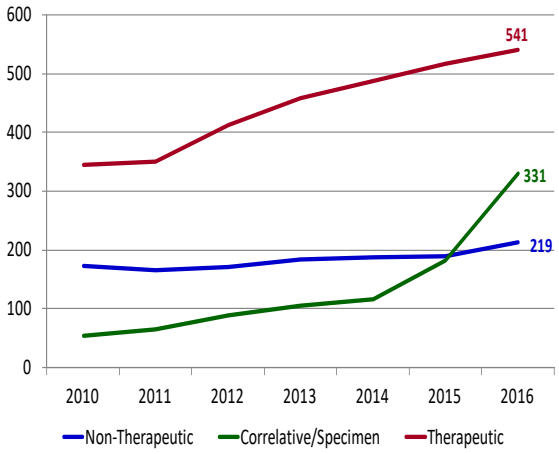
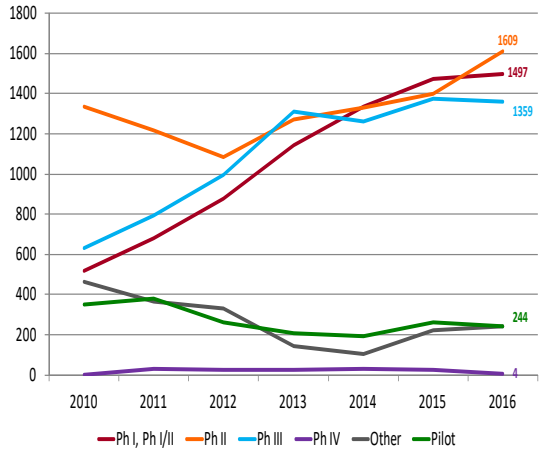


Figure 2



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The result of this rapid growth in the clinical research portfolio and accruals required an increase and demand for additional research staff to support the patient-oriented research enterprise as reflected in Table 1.

Table 1:

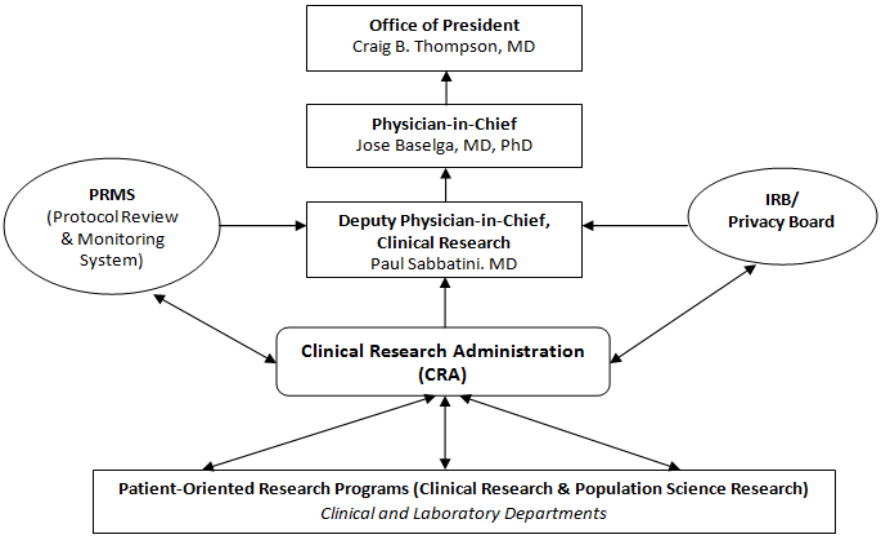
2010 Research Position	# of Staff	2016 Research Position	# of Staff
Research Assistants	250	Research Assistants	478
Research Coordinators	68	Research Coordinators	196
Research Managers	26	Research Managers	43
Program Managers	8	Program Managers	11

In response to this need for additional support, we systematically evaluated in early 2016 the various components of the patient-oriented research programs. This included the pre-existing Office of Clinical Research (OCR) and the clinical departments. The evaluation included identification of stakeholders [patients, researchers and sponsors] with the goal of equalizing the opportunities for trial participation at all stages and across all of MSK's facilities, increasing awareness and availability of trials to physicians and patients, enhancing our capacity to conduct transformative research, and improving the overall quality management of the clinical trials portfolio. This review required a comprehensive evaluation of all areas involved in CR and PSR trial support. This analysis showed areas of redundancy, inefficiency in standards and workflows, need for technology enhancements in daily operational tasks, and opportunities to centralize more key services across the patient-oriented research programs. The overall intent was to rebuild a lean infrastructure to support the growing needs of the patient-oriented research programs.

The reorganization created a new entity referred to as Clinical Research Administration (CRA) which takes advantage of economies of scale while ensuring effective support for clinical research. CRA collaborates with department administration and center divisions in the development and delivery of services that are responsive to the needs of the principal investigators (PIs) and respective programs. The overall mission of CRA is to oversee the research involving human subjects at MSK ensuring that the efficient and effective conduct of the research is in full compliance with requisite federal regulations, institutional policies and the CCSG requirements for Clinical Protocol and Data Management (CPDM). The CRA is an institutional office that reports to the Deputy Physician-in-Chief, Clinical Research, Dr. Paul Sabbatini and works in conjunction with Institutional Leaders, the Protocol Review and Monitoring System (Research Council), the IRB/Privacy Board, and the Clinical and Laboratory Departments that make up the

patient-oriented research programs. Dr. Sabbatini reports to José Baselga MD, PhD, who in addition to being Physician-in-Chief of Memorial Hospital, is the Deputy Director, Memorial Hospital of the Cancer Center. The placement of the CRA within the institutional organizational structure can be found in Figure 3.

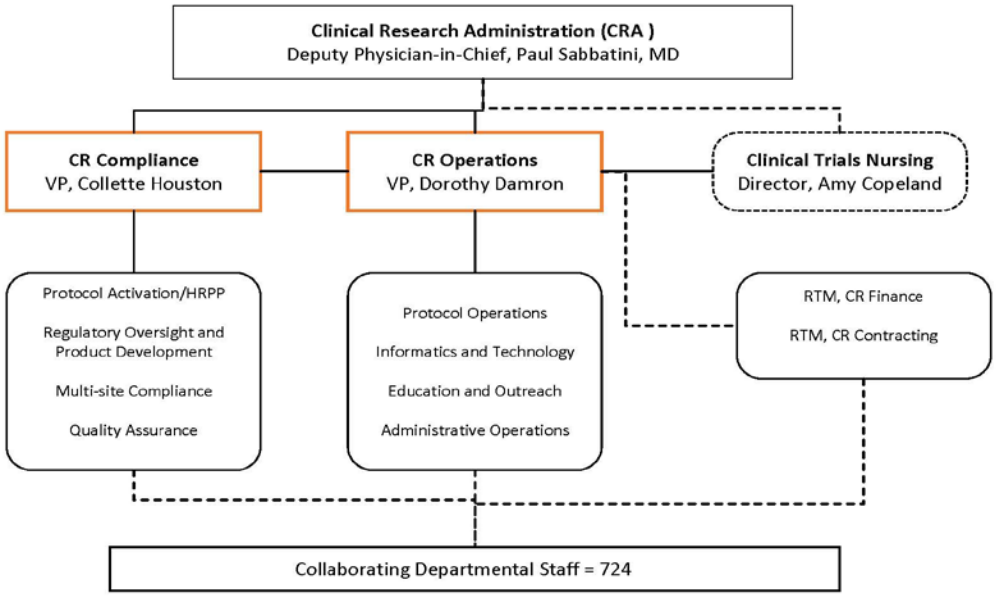
Figure 3:



CRA is an institutional level entity comprised of two primary divisions, Clinical Research Operations (CRO) and Clinical Research Compliance (CRC), each with distinct functions and responsibilities. The Clinical Trials Nursing Department has a matrix report into the CRA to provide increased integration of Clinical Trial Nurses (CTN) with the patient-oriented research teams.

The divisions (CRO and CRC) within CRA are divided into 10 units with specific core responsibilities, functions, and oversight. The units in CRO are: Protocol Operations, Clinical Research Informatics and Technology, Clinical Research Education and Outreach, and Administrative Operations. Two units within Research and Technology Management have matrix reporting into CRO, Clinical Research Finance and Clinical Research Contracting. The units in CRC are: Protocol Activation and Human Research Protection Program, Regulatory Oversight and Product Development, Multi-Site Compliance, and Quality Assurance. The organizational structure of CRA and the core responsibilities of each unit are referenced in Figure 4, described below and available on the Clinical Research Portal: Clinical Research Administration

Figure 4



Clinical Research Operations

Protocol Operations**:** *Stephanie Terzulli, Ph.D., Director*
The core responsibility of this unit is to manage the co[illegible] of clinical research by providing services including: clinical research practice standards, oversight of clinical research data collection/data management, analysis and reporting, regulatory coordination, and guidance to investigators in planning and conducting clinical research protocols. Protocol Operations works collaboratively with MSK's ambulatory care program and provides organizational and research management services to all of our facilities where investigational activities are conducted. Protocol Operations works cohesively with Clinical Trials Nursing and the Clinical Departments involved in the patient-oriented research programs. Protocol Operations is also responsible for the management and oversight of Protocol Core Services (PCS), a centralized core service that provides institutional resources to support the institutional biospecimen collection, management and processing of samples.

Clinical Research Informatics and Technology (CRIT): *Joseph Lengfellner, Senior Manager*
The reorganization of the clinical research infrastructure has resulted in an expanded CRIT unit with the core responsibility of deploying technology to improve clinical research practice across the patient-oriented research programs. CRIT develops and implements new technology initiatives to enhance efficiencies in workflows for the clinical research community. This unit is also responsible for all institutional initiatives relating to clinical

research informatics. CRIT manages the centralized databases utilized by the CR and PSR Programs including but not limited to PIMS (Protocol Information Management System) which is the institutional protocol repository and used by PRMS and CPDM, the CRDB (Clinical Research Database), Medidata Rave, REDCap, and OnCore's CTMS (Clinical Trials Management System) for active research protocol management and reporting.

Clinical Research Education and Outreach: *Mayra Nicola, Manager*
This unit's core responsibility is to provide interactive education with post-education assessments for all levels of staff involved in clinical research to ensure safe, efficient, and informative clinical research via awareness and knowledge of relevant procedures, processes, and regulations. This group also tracks certification dates on required Human Subjects Protection and Good Clinical Practice training. All new clinical research staff are required to attend an intensive multi-day orientation which includes an overview of clinical research methodology and an introduction to various research-related processes at MSK. The Education and Outreach unit is in the process of revising and/or developing new trainings focused on particular research concepts and processes which will be open to all staff across CR and PSR including, an introduction to the RSA role, consenting principles (basic to complex), and Serious Adverse Event (SAE) reporting.

Administrative Operations: *Lawrence Lupkin, Senior Manager*
This unit's core responsibilities include the financial management and revenue tracking of CRA services, managing the day-to-day administrative and operational management of CRA, working across MSK as needed in areas like Human Resources, Facility Management, Business and Disaster Recovery, and other such administrative duties that are essential in a large division like CRA.

Clinical Research Finance: *Barry Zakrzewski, Director*
The core responsibility of this unit is to provide centralized oversight for the fiscal management of clinical research studies, ensuring an efficient, compliant, and transparent process. A dedicated team within this unit has been established to develop budgets in collaboration with appropriate study team members, and to ensure protocol recovery. This until will reconcile variances between the protocol budget and expense.

Clinical Research Contracting: *Lee Stetson, Assistant General Counsel*
The core responsibility of the CR Contracting unit is to provide contracting and legal services focused on the timely negotiation and execution of clinical trial agreements (and associated amendments) in support of the CR and PSR Programs. The Clinical Research Contracting unit has embarked on several key initiatives: 1) developing master clinical trial

agreements where possible with pre-negotiated language to accelerate time to protocol activation, 2) adopting uniform standard operating procedures with the goal of streamlining negotiations.

Clinical Research Compliance

Protocol Activation/Human Research Protection Program (HRPP): *Ann Rodavitch, Director*
The Protocol Activation and HRPP unit has the dual responsibilities of providing guidance, standardized processes and assistance with regards to protocol development including review and approval and provides leadership oversight of the HRPP. There are three sub-groups within this unit, each focused on a specific aspect of trial activation: Protocol Activation Core, Protocol Review Core and the HRPP Office.

Regulatory Oversight and Product Development: *Richard Ellis, Manager*
The Regulatory Oversight and Product Development unit has the core responsibility for ensuring Investigators and research staff across the patient-oriented research programs adhere to institutional standards and federal regulatory requirements of the FDA, NIH, and OHRP with respect to investigational drugs, devices and biologics for all MSK-sponsored IND trials and MSK-manufactured products. This unit also oversees the management of MSK's Investigational New Drug and Device (IND/IDE) Program, providing guidance to MSK Investigators on product development strategy and preclinical requirements for MSK's IND/IDEs including preparation of IND applications and technical documents for regulatory agencies.

Multi-Site Compliance: *Mary Warren, Director*
The Multisite Compliance unit is responsible for regulatory and quality oversight of MSK's patient-oriented research being conducted at sites and centers in addition to MSK. MSK has expanded our CR and PSR opportunities in the community through the MSK Alliance Program, operation of our multisite clinical trials portfolio including the POETIC (Pediatric Oncology Experimental Therapeutics Investigators Consortium), and oversight of the NCI-supported portfolio including the NCTN U10 Grant and the NCI-supported clinical trials portfolio. The unit is increasingly taking on direct oversight of protocol activation, regulatory compliance and quality performance of the above to allow research staff to focus on protocol oversight and data management.

Clinical Research Quality Assurance (CR QA): *Karima Yataghene, M.D., Director*
The core responsibility of QA is to provide leadership in quality and regulatory oversight to minimize risk and to ensure reliable, quality management services to support the overall

success of CR and PSR programs. The QA unit ensures that the Institution is in compliance with Good Clinical Practice and Good Manufacturing Practice guidelines and adheres to all federal regulatory requirements. Since the last Competitive Renewal this unit has been reorganized into three teams organized by functional responsibility: Audits, Monitoring Visits, and Investigational Product QA. The QA programs were reevaluated and new QA processes for protocol selection, databases/systems, eligibility verification and investigational drug pharmacy were implemented. QA is also responsible for the oversight and management of MSK's Data and Safety Monitoring (DSM) plans in collaboration with the Protocol Activation and HRPP unit.

The CRA has a total of 219 staff on its table of organization. The division reports to Paul Sabbatini, MD, Deputy Physician-in-Chief, Clinical Research and the Senior Vice President, Research Technology Management, and is led by Dorothy Damron (CRO) and Collette Houston (CRC). The CRA has a senior management team led by Ms. Damron and Ms. Houston. The qualifications, experience and responsibilities of the leadership team are described below.

Dorothy Damron, VP, Clinical Research Operations, has been involved in research for 35 years. Prior to coming to MSK, she spent 13 years as Director of the Clinical Research Office at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. Ms. Damron has been involved in clinical research operations at MSK since 2015.

Collette Houston, VP, Clinical Research Compliance, has been involved in clinical research activities and management at MSK for the last 30 years. Ms. Houston oversees the overall compliance of the patient-oriented research programs.

PROTOCOL REVIEW AND ACTIVATION

In order to improve efficiency, maximize experience, and enhance the throughput we have centralized the staffing resources involved in protocol review and activation. This includes a team of experts who shepherd the protocol through the review process including quality review, writing consent forms, responding to review committees and facilitating the communications between the PI, Study Team and the Review Committees. This effort has significantly aided in improving the overall time to protocol activation. To compliment this effort, we have also centralized the administrative management team that supports all of the protocol review committees. The protocol activation workflows can be found in **Appendix A** and on the CR Portal: Protocol Review Flows. The protocol sponsor will determine the appropriate committee reviews that are required, with MSK investigator

initiated research protocols requiring the most steps in the review process including but not limited to: Primary/Participating Department Review, Research Council (Scientific Peer Review) and IRB/Privacy Board. Depending on the protocol intervention and the regulatory requirements of the protocol, additional review committees may be required (e.g., Committee on Radiation, Investigational New Drug/Device Committee, etc).
The primary steps in the MSK Investigator-Initiated studies are described below and demonstrated in Figure 5.

Primary Department/Participating Department: The primary department will review the protocol for scientific merit, quality, programmatic fit within the disease/service portfolio, and resource allocation. If the Co-Principal Investigator is from a different clinical department, that department must evaluate the impact of the protocol on the department (e.g., patient referrals, involvement in the intervention, etc) and either provides a full review similar to the primary department, or an expedited review and sign-off which equates to a commitment to participate in the study.

Committee on Radiation (COR): This committee is a committee mandated by the federal, state and city regulations and is charged with developing policy for and monitoring the use of radioactive materials and exposure in the Center. COR is required to review all protocols investigating the use of radioactive materials in humans including radiolabeled antibodies. COR evaluates the safety of the protocols related to the radioactive materials and radiation exposure.

Regulatory Committees: Protocols that involve the use of non-FDA approved drugs, devices and/or radionuclides are required to be reviewed by either the Investigational New Drug/Device Committee or the Radioactive Drug Research Committee prior to the IRB/Privacy Board review.

- The **Investigational New Drug/Device Committee** is required for any MSK investigator initiated protocol that is utilizing a non-FDA approved drug or device or one being used for an unapproved indication in a manner that would require the filing of an IND/IDE.
- The **Radioactive Drug Research Committee** is mandated by the FDA and is required for any study that uses radionuclides to probe biological processes including physiology, pharmacology or biochemistry in humans. These protocols almost always involve the administration of tracer doses and are not focused on therapeutic endpoints or demonstrating safety or efficacy.

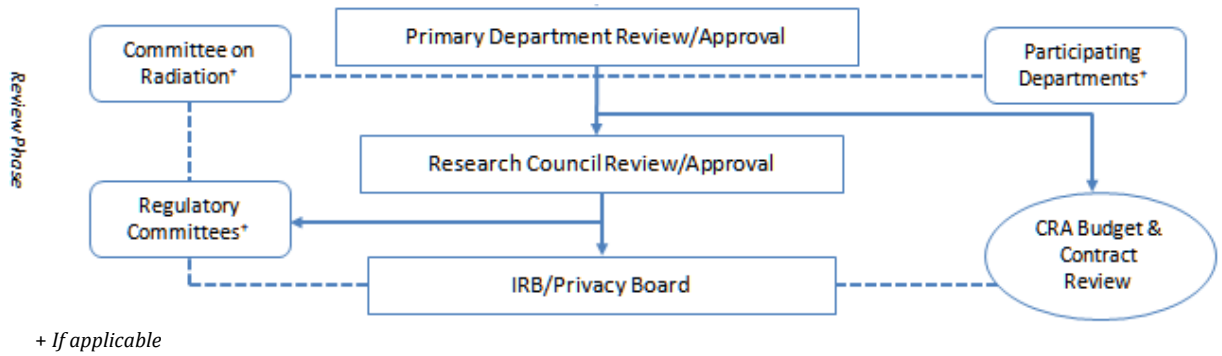
Research Council: Oversees the protocol review and approval process at MSK and is the scientific review committee mandated by the NCI. It is a multidisciplinary institutional committee whose charge is to review proposed research protocols for quality, scientific merit, institutional priority, programmatic fit, and resource allocation while promoting timely protocol activation. The Research Council Membership can be found in **Appendix B** and on the CR Portal: Research Council.

The Research Council also reviews studies that are not meeting the Center's Core Grant (CCSG) expectations on accrual performance. The expected time to complete a clinical study is less than 5 years. The clinical study portfolio is reviewed twice a year. A Principal Investigator who has a clinical study that is not meeting accrual expectations will be asked to provide an action plan to improve study performance. The Research Council will review the plan and determine if it is sound and should be pursued or if the study should be closed with the IRB/PB.

All protocols reviewed and monitored by MSK Research Council and that are open for accrual will be reviewed for scientific progress every six (6) months. Protocols identified as non-performing must be addressed as outlined the Research Council Non-Performing Protocol Review NP Protocol SOP.

IRB/Privacy Board: Oversees the protection, rights and welfare of the human subjects who participate in our clinical research portfolio, evaluating the overall risk versus benefit ratio to the participant. The IRB/Privacy Board reviews all protocols, informed consent documents, grants involving human subjects, protocol amendments, annual reviews, safety profiles, adverse events, and unanticipated problems. A list of Standard Operating Procedures that govern the IRB/Privacy Board can be found in **Appendix C** and on the CR Portal: IRB/Privacy Board SOPs.

Figure 5



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NCI and/or NCTN Protocol Activation

All NCI approved protocols go through an extensive protocol development and review process through the NCI's different mechanisms (i.e., Cooperative Group, Clinical Trials Evaluation Program, Experimental Clinical Trials Network, etc.) which include NCI approval and submission to the NCI's Central IRB. The protocol then passes through the MSK IRB/Privacy Board for local privacy review and approval.

PROTOCOL RISK DETERMINATION

Risk determination is a critical part of the evaluation process. The protocol risk category is defined by the Principal Investigator and reviewed and approved by the IRB/PB. This determination is made by utilizing the following criteria: Risk Category Definitions

Low	**Probability of harm/discomfort not greater than daily life or routine physical/psychological exams** 45 CFR 46.102(i) **Examples**: Survey research, venipuncture, taste and observation studies, non-contrast MRI studies, non-invasive procedure
Moderate	**Intervention commensurate with those inherent in their expected medical, social, or education situations. Risks are reasonable in relation to anticipated benefits and the importance of knowledge expected to result** 45 CFR 46.111(a)(2) 21 CRF 50.3k **Examples**: Investigations drug/device, therapeutic research including but not limited to surgery, radiation therapy, chemotherapy, vaccines, biologics.
High	**Greater than minimal risk which may or may not have direct benefit to the subject. Risks are high in relation to anticipated benefits.** **Examples**: Gene transfer, First in human Phase 1, Studies of new articles having high/severe pre-clinical toxicity but may be commensurate to the potential benefit.

There are additional risk categories for clinical trials involving children and investigational devices. Please refer to the following links on the Clinical Research Portal for more information: Children Risk Level and IDE Risk Level. The protocol specific risk determination is taking into consideration when assigning the Data and Safety Monitoring (DSM) review cycle.

PROCEDURES FOR MONITORING CLINICAL TRIALS AT MSK

There are several different mechanisms by which clinical research studies are monitored for accrual performance, data, safety and quality at MSK. The Principal Investigator (PI) is ultimately responsible for the conduct and monitoring all aspects of a trial on an on-going basis. In addition to the PI, there are institutional processes in place for quality oversight through the Research Council, Data and Safety Monitoring Committee and Board, and the Quality Assurance Unit in CRA.

Data and Safety Monitoring Committees

MSK has established two distinct monitoring oversight committees that have responsibility to provide data and safety monitoring over our clinical trials program focused primarily on MSK sponsored, investigator-initiated research, but as necessary will review protocols from other sponsor types (Industrial, External Peer Reviewed, NCI/NCTN), as needed. The two committees, **Data and Safety Monitoring Committee** (DSMC) and **Data and Safety Monitoring Board** (DSMB) report up to the Deputy Physician-in-Chief, Clinical Research.

Data and Safety Monitoring Committee (DSMC), Chair: Eileen O'Reilly, MD

The DSMC provides oversight for nearly 600 active clinical trials at any given time. The committee monitors the risk participants are exposed to, the progress of the study, the adequacy of data collection and management, and confirms that the trial is proceeding as expected.

The DSMC is responsible for monitoring all Phase I, I/II, II, Pilot, and non-phase based clinical trials, including but not limited to therapeutic, investigational device, nutritional, diagnostic, prevention, behavioral, quality of life and some correlative science trials, when deemed appropriate. At the time of study activation it is determined whether the trial will be monitored by DSMC, and at what frequency (quarterly, bi-annually or once a year). This determination takes into consideration the following:

- Adherence to the NCI definition of a clinical trial (defined on page 3)
- Protocol sponsor/funding source
- Protocol Risk
- Accrual rate and estimated time to accrue
- External oversight or monitoring provided through another source

The DSMC consists of twenty-two members from throughout the Center with various areas of expertise including a Biostatistician. There is one external member who is critical to evaluating DSM for studies with Institutional Conflicts. The external member is important to the review process, ensuring and protecting against any potential conflicts. The list of DSMC membership can be found in **Appendix D**.

The DSMC members receive all relevant materials for each of their assigned trials prior to the committee meeting. Review assignments are determined by the member's clinical expertise, study modality, and patient population. Review assignments are vetted to ensure there are no conflicts of interest between reviewers and their assignments. If DSMC members have conflicts during the meeting, they are asked to recuse themselves from the discussion and vote.

Each study is reviewed with the following questions in mind:

1. Are patients being exposed to unanticipated or excessive toxicity?
2. Is enrollment proceeding according to projections; has accrual target been met?
3. Are the protocol specific rules being followed as per protocol (e.g., dose escalation in a Phase I, response assessment, etc.)?
4. Are early stopping rules being enforced?
5. Are sufficient data being collected/entered to effectively assess study progress?

Each study is evaluated prior to the meeting by the assigned reviewer. Protocols with any issues and/or concerns are discussed. Approval actions are determined, and communicated to the PI and the Research Team in an official memorandum. Committee meeting actions/outcomes are stored in electronically in PIMS (Protocol Information Management System) along with all other review committee and monitoring activities in the Protocol Activation and HRPP Unit. Should a study not be approved, the PI has 14 days to provide a written response to the DSMC's concerns; if the response is not satisfactory to the reviewer, it will return to the committee for discussion and possible escalation to the Deputy Physician-in-Chief, Clinical Research (Institutional Official).

Data and Safety Monitoring Board (DSMB), Chair: Colin Begg, Ph.D.

The DSMB provides monitoring oversight to MSK investigator-initiated (IIT) Phase III randomized clinical trials, or any Phase III trial that is not reviewed by an independent review board. The DSMB conducts a comprehensive review of the trials focusing on study endpoints and outcome data, as well as study accrual, toxicities, unexpected adverse events, risks to participants, the overall progress of the study, and the adequacy of data collection and management. This review process provides the PI with guidance and

recommendations throughout the life of the study, ensuring the PIs ability to carry out the study as designed.

The DSMB meets annually (typically in June) and is comprised of six voting members, four of whom are unaffiliated with MSK. The DSMB Chair is one of the two MSK voting members. The DSMB Membership list can be found in **Appendix E**. The majority of the DSMB members are external, and therefore eliminates the potential for study reviewer conflicts and/or bias. The area of expertise represented across the DSMB reflects the diversity of proficiency necessary to review the various aspects of the MSK IIT Phase III portfolio. If a given study has Investigator and/or Institutional Conflict, the reviewers are aware of the conflict, and their responsibility to consider the conflict when evaluating the study quality and outcomes. The DSMB Chair asks members to recuse themselves from a discussion and voting based on their own personal conflicts.

Prior to the annual DSMB Meeting, individual PIs must submit a summary report including the following information:

- Accrual information, including planned accrual goals and timelines
- Participant eligibility and compliance
- Comprehensive summary of side effects/toxicities experienced
- Comprehensive statistical analysis of the study endpoints including blinded outcome data
- Any actions the PI has taken based on prior DSMB review and recommendations

The DSMB Members receive a complete packet of all protocols to be discussed several weeks prior to the meeting; if a protocol was reviewed in prior years the previous year's recommendations are also included in the packet. Board members review these packets prior to the annual meeting and come with questions and concerns for discussion. At the meeting the PI and study statistician are present, and given an opportunity to discuss the progress of the study and to answer any additional questions the board members may have. Following the dialogue, the PI will leave and the board members have time to further discuss the study and vote. In the case of blinded trials, the interim analysis is submitted separately by the protocol Biostatistician, and is discussed at the meeting only with the statistician present.

Each PI will receive official notification from the DSMB with their overall feedback on the study progress, any recommendations they have to improve the study, and the final voting outcome. The PI's sponsoring department and study statistician will be copied on the PI correspondence. Minutes of the DSMB's proceedings are produced summarizing the

discussions for each study, and the board's recommendations. The comprehensive minutes and outcomes are shared with the Deputy Physician-in-Chief for Clinical Research and the Board Members. The IRB Chair and the Human Research Protection Program Office receives all recommendations made by the board. The meeting minutes are maintained in the Protocol Activation and HRPP Unit.

CLINICAL RESEARCH QUALITY ASSURANCE PROGRAM: CR QA

Audit Program

Another mechanism in place for the data and safety monitoring of human subjects participating in clinical trials is through the auditing program. All active MSK protocols and databases are eligible for auditing, including investigator initiated, NCI, and pharmaceutically sponsored. In addition, studies may be audited by external groups such as: pharmaceutical companies, cooperative groups, or the NCI. Audits are conducted to ensure compliance with federal regulations (21 CRF 50, 21 CRF 56, 21 CFR 312, 45 CRF 46), Good Clinical Practice (GCP) guidelines and MSKCC Clinical Research Audit Guidelines.

Protocol Compliance Auditing

There are two levels of protocol compliance auditing. Each level of auditing covers the same quality review of both protocol compliance verification and source data quality accuracy. The first level of auditing is institutional, and conducted by Clinical Research Quality Assurance (CR QA). The second level of review is a quality control review conducted by the research staff in the clinical department of the Principal Investigator.

Institutional Audits Conducted by CR QA

CR QA conducts audits on trials for consent, eligibility, protocol compliance, regulatory document completeness and verification that database data entry is accurate and complete. The following procedure is used to ensure adherence to all policies:

- Protocols are chosen randomly across all MSK clinical departments and/or can be performed at the request of any institutional department, CRA leader or PI.

- The PI, department leaders and research staff are notified of the upcoming audit, the study being audited and the audit start date. All audits are projected to be completed within 1-2 weeks.

- Protocol specific audit forms are created focusing on adherence for all areas under review in the audit (e.g. consent, eligibility, treatment, baseline and on-study testing evaluations, guidelines for assessment of toxicity and outcome and data entry verification).

- Approximately four to six participants are audited on each trial and are randomly chosen over the entire course of the study. Additional cases can be selected if deemed appropriate.

- Protocol regulatory binders and participant electronic medical records, office research files and database printouts are reviewed to evaluate compliance and data verification.

- It is the responsibility of the department staff to retrieve any records on selected participants who are registered at outside sites who have been selected for audit.

- The compliance part of the review consists of 100% verification of the protocol specific requirements in the areas under review, for all selected participants.

- A standardized audit report which summarizes the audit findings and resulting recommendations is compiled by CR QA and reviewed by the Manager, Clinical Research Audits and the Director, CR QA.

- The PI is given an appropriate timeframe to respond to any major deficiencies noted in the report with a corrective and preventative action plan to be implemented within his/her service/department. Acknowledgment of the receipt and adequacy of the plan is sent to the protocol PI and research staff.

- CR QA can choose to re-audit any trial where major deficiencies were found. This is done after sufficient time has allowed for accrual of new participants and is done via the routine procedure already outlined.

External Site Audit/Inspection Preparation

CR QA is responsible for the oversight and coordination of research teams that prepare for MSK audits by external groups (e.g. cooperative groups, federal agencies, and industrial sponsors). CR QA leads and facilitates the audit planning, day of audit activities and post audit activities when the audit involves a federal agency or multiple clinical departments or at the request of the PI.

The following procedure is used to ensure that the institution is organized and well prepared for these audits:

- Upon receiving notification of an upcoming audit, the appropriate personnel from the departmental research team, CR QA, IRB/PB, Clinical Information Center, Pharmacy, Radiology, Clinical Lab Department and the Conference Planning Department are notified.

- The external auditor is contacted to confirm logistics of the audit/inspection in order to plan appropriately (e.g., number of auditors, meetings to occur, etc.).

- CR QA staff in collaboration with the PI(s) and Research Study Teams ensures that all pre audit preparations are completed in a timely manner, these include but are not limited to: identify appropriate space with computer/EMR, printer and phone access, identify research staff to assist auditor, ensure availability of PI, and create any necessary key staff contact lists.

- The Pharmacy Department conducts the review of participant drug doses and drug accountability. All source documents are prepared and reviewed prior to the audit.

- CR QA pre audits Regulatory Binders to ensure completeness and accuracy in regard to: protocol/consent versions, IRB/PB documents/approvals/ SAEs/safety reports, protocol violations, any correspondence between MSK and sponsor or IRB/PB or FDA, Lab certifications/NL ranges, federal forms (1571, if applicable and 1572), investigator CVs and investigator's brochure.

- A pre audit of participant cases is also conducted for protocol compliance, source documentation (EMR chart completeness), and verification of data accuracy on CRFs or electronic data submissions and compliance with data submission timetables.

- The designated audit lead prepares a summary of pre audit findings to inform the PI and CRA leadership of any noted deficiencies.

- During the audit, a CR QA audit team representative is available to ensure logistics of the audit/inspection are managed appropriately.

- It is the responsibility of the PI and Research Team to draft the initial audit response from MSK. If multiple PIs/departments are involved, CR QA will help facilitate the institutional response. The Manager, CR Audits and Director, CR QA will review and approve any response to an external audit/inspection before finalized and distributed.

Documentation of all institutional, departmental and external site audits (e.g., audit notification, audit reports and corrective action plans) is maintained in the Protocol Information Management System.

Clinical Research Monitoring Program

The Clinical Research Monitoring Program developed in 2010 is another mechanism for the data and safety monitoring of human subjects participating in clinical trials. Monitoring is an ongoing process for overseeing the progress of a research study, and of ensuring that it is conducted according to the protocol, institutional SOPs, Good Clinical Practice (GCP) and

applicable regulatory requirements. The MSK CR Monitoring Program focuses on trials where MSK is the sponsor, and places priority on MSK-held IND/IDE trials and/or Multi-Center Trials.

Monitoring priority is determined by study risk, protocol status (percent complete), rate of accrual, trial complexity and serious adverse event reporting. A series of monitoring forms, tools and templates including a Monitoring Checklist, MSK Clinical Research Monitoring Guide for Major Protocol Deficiencies and Sample Summary Monitoring Letter are utilized to ensure standard and consistent monitoring practice across CR QA. These tools are available on the CR Portal under QA, linked above. Monitoring focuses on the study-specific primary objective and the data required to answer these objectives. Monitoring visits are scheduled every 4-6 weeks based on current rate of accrual. Monitoring findings are reported to the PI and study team. Recommendations are made to the study team on methods to improve protocol compliance, data accuracy and regulatory reporting. The Deputy Physician-in-Chief of Clinical Research is alerted to any ongoing unresolved issues or unacceptable visit findings.

The Clinical Research Monitoring Program uses the following enhancements to improve review:

Eligibility Verification

Throughout the year CR QA ensures real-time participant/patient eligibility through a verification process.

The CR QA Monitoring Program selects a randomized sample of clinical trial patient registrations completed in the Clinical Trial Management System (CTMS) to review the eligibility checklist for quality assurance compliance. The eligibility checklist verification review ensures both that participants are eligible when registered to the protocol and that the eligibility checklist captures the protocol's eligibility criteria accurately and appropriately. The program prioritizes eligibility verification based on MSK clinical trial risk level, complexity and any known historical issues. Eligibility checklist verification findings are immediately communicated with the study team's Clinical Research Manager (CRM), Program Manager (PM), Clinical Trial Nurse (CTN), and Principal Investigator (PI) for instant resolution.

Monitoring and Auditing Tracking System (MATS)

MATS is an automated, online feedback system that is used, under the oversight of CR QA, to collect feedback from industrial monitors, share feedback with MSK study teams in real-time, request auditor access, and store relevant tracking data in a database.

Using this system, the CR QA Monitoring Program evaluates real-time feedback from Industrial Sponsors, monitors trends, evaluates data, and implements changes to improve the efficiency of the CR Monitoring Program and process. CR QA escalates emergent protocol compliance, data quality or process concerns to the PI and CRA Leadership. PIs are expected to rectify issues and concerns in a timely fashion, and the CR QA Team tracks their responses for completeness and Monitor oversight.

Pharmacy Review Program

Another mechanism in place for safety monitoring of human subjects participating in therapeutic clinical trials is through the pharmacy auditing and monitoring program. CR QA is responsible for conducting pharmacy QA review as part of the protocol audit, a monitoring visit and pharmacy investigational product (IP) operational audit similar to that of our industrial sponsors and external federal agencies. Review involves preparing QA review reports of observation/findings and evaluating the implementation of the agreed upon corrective and preventive action plan (CAPA).

Types of QA Reviews:

- Pharmacy QA review as part of protocol audit: Pharmacy protocol audits are conducted as required (when a protocol is selected for audit) to assess whether pharmacy is compliant with internal standards and regulatory requirements (i.e., U.S. Food and Drug Administration (FDA), Good Clinical Practice (GCP), etc).
- Pharmacy QA review as part of Monitoring visit: Pharmacy monitoring visits are conducted based on accruals or at least every six months to access whether pharmacy complies with internal standards and regulatory requirements (i.e., FDA, GCP, etc).
- Pharmacy IP Operational Audit: Pharmacy operation audits are conducted annually to assess whether pharmacy operations comply with internal standards and regulatory requirements (i.e., FDA, GCP, etc) and to provide an opportunity for continuous improvement.
- "For Cause" Audits: Following the identification of a serious issue related to the pharmacy QA review and pharmacy IP operations, CR QA may determine additional monitoring or auditing of the pharmacy is required. The goal will be to impart renewed structure or control, and thus ensure the quality of the pharmacy operation. The findings of a "For Cause" audit will be reported within 60 days to the Management Review Committee (MRC). The remediation of audit findings will be fully documented & reported to the MRC at the next scheduled meeting. Following a "For Cause" audit, the

pharmacy will be monitored by CRQA until demonstrating the risk of reoccurrence is acceptable.

With all type of QA review, CR QA issues a report listing any findings and/or observations found during the review. All findings are communicated with the study team, pharmacy and CR QA for resolution.

MULTI-SITE COMPLIANCE COORDINATION Multi-Site Compliance

Multi-Site Compliance Unit comprises of four clinical research sub-units: the Multicenter Office (MCT Office), Clinical Research Strategic Partnerships, NCI Network Program, and the POETIC Consortium.

- The MCT Office is charged with the oversight and management of multicenter trials (MCTs) where MSK serves as the Data Coordinating Center and external sites accrue participants. The MCT Office establishes and monitors compliance with multicenter policies, conducts staff training, and coordinates regulatory, protocol operations activities, and data monitoring of external participating sites.
- The Clinical Research Strategic Partnerships oversees and manages a team of dedicated research staff who liaise between Alliance Members, CR Strategic Partners, MSK, and the Industrial Sponsor as needed to identify appropriate studies, facilitate study activation, oversees and ensures regulatory compliance and data quality as well as payment for clinical trial activity.
- The NCI Network Program provides efficient and effective regulatory and quality management of NCI sponsored trials. In the Department of Medicine, these studies have been centralized under the NCI Network Program. In 2018, we'll be incorporating studies from all other departments to ensure consistent portfolio management by creating standardization, and providing resources to all study teams.
- The POETIC Consortium is comprised of a network of leading academic medical centers. Our members serve a geographically and ethnically diverse patient population, with an emphasis on comprehensive cancer care and research.

INCIDENT REPORTING

MSK is obligated to report certain types of incidents in human subject's research to the Office for Human Research Protection (OHRP). The following is the regulatory background on this reporting obligation, excerpted from the May 27, 2005 Guidance on Reporting Incidents to the OHRP.

HHS regulations at 45 CFR 46.103(a) and (b)(5) require that institutions have written procedures to ensure that the following incidents related to research conducted under an OHRP-approved assurance are promptly reported to OHRP:

- Any unanticipated problems involving risks to subjects or others;
- Any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB/PB; and
- Any suspension or termination of IRB/PB approval.

The HRPP (Human Research Protection Program) Office handles the reporting of incidents to the OHRP. Clinical research staff can report information relating to potentially reportable incidents to the HRPP Office via SAE report, deviation report, or memo. In addition, any potentially reportable incidents identified via any of the other monitoring procedures described in the MSKCC DSM plan will utilize the same mechanism. The IRB Chairman, HRPP Director, and HRPP Office staff will review all potentially reportable incidents. If it is determined that an incident may constitute a reportable event, the event and a proposed management plan is drafted using the OHRP Incident Report Form, **Appendix F**. The report is reviewed at a full board IRB meeting, and the board votes on 1) whether or not the event constitutes a reportable incident and 2) to either accept the proposed management plan or to require additional actions that might be required to protect the safety, welfare, or rights of research participants. The HRPP Office handles all reporting and follow-up correspondence with the OHRP. The IRB/PB SOP for Unanticipated Problems can be found: UP SOP.

Adverse Event Reporting

An adverse event can occur on any clinical trial. It is the responsibility of the Principal Investigator and his/her research team to identify, review and report all necessary adverse events to the institutional IRB/PB, the sponsor, and participating institutions, as appropriate. The SAE Manager will report to governmental agencies (i.e., FDA), if necessary. Adverse events should be identified through standard, routine protocol review and clinical assessment of each subject participating in the clinical trial. This review should be timely in order to meet the requirements for adverse event reporting defined below.

Procedures for Assuring Compliance for Adverse Event (AE) Reporting

Federal guidelines require the timely reporting of any unanticipated toxicities/events/side effects while a participant is on a research protocol. Investigators must follow the guidelines for timely reporting of adverse events as outlined in the protocol by the institution, sponsor, or cooperative group. All serious adverse events (SAEs), regardless of

the type of research study, phase or sponsor must be reported to the MSKCC IRB/PB. SAE reporting is required from the time the participant/LAR signs the informed consent through 30 days after the last date of treatment or intervention, unless otherwise specified in the protocol. Appendix R is specifically designed for an AE experienced on a NCI sponsored clinical trial supported by a grant or contract funding. The investigator/ researcher must be familiar with the specific reporting requirements of their sponsor.

Adverse Event (AE)

An adverse event is defined by the GCP as an undesirable experience occurring to a participant during a clinical trial, whether or not considered related to the investigational product(s).

Serious Adverse Event (SAE) SAE Reporting

A serious adverse event is an adverse event that results in ANY of the following outcomes:

- Death
- A life-threatening adverse event
- An adverse event that results in inpatient hospitalization or prolongation of existing
- hospitalization (Note: a hospital admission for a planned procedure/disease treatment is not considered an SAE)
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon 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

Unexpected Adverse Event

An unexpected AE is an experience not previously reported (in nature, severity or incidence) in the current Investigator's Brochure or general investigational plan or protocol document.

Outside Safety Report

A report of an SAE experienced by a subject not enrolled on trial through MSK

Institutional Serious Adverse Event Manager

MSKCC has identified the need for an Institutional SAE Manager who will work with the IRB/PB Chairman, HRPP Office staff, and Clinical Research Administration. The SAE Manager will be responsible for providing expertise in the area of adverse events and serious adverse event reporting. The SAE Manager will facilitate the AE and SAE activities, monitoring and reporting to the IRB/PB, regulatory agencies (e.g., NCI, NIH, and FDA) and industrial sponsors. All reported SAEs related to clinical trials conducted at MSKCC are entered into CRDB.

The SAE Manager generates queries from PIMS as needed on incomplete and outstanding SAE reports that have not been submitted to the SAE office and sends them to the clinical department's Research Manager and Research Data Coordinators for resolution.

Lastly, the SAE Manager will assist the IRB/PB Chairman and IRB/PB Office staff on the necessary education, training and practice of adverse event reporting as per the federal regulatory guidelines.

NOTIFICATION PROCEDURES FOR CLINICAL TRIALS SPONSORS

If, through any of the internal data and safety monitoring procedures or clinical trials auditing/monitoring mechanisms, a decision is made to temporarily close or suspend a trial based on the information identified, then it is the responsibility of the individual reporting body (i.e., Principal Investigator, Clinical Research Administration, DSMC, DSMB, QA Office, Clinical Department, etc.) to notify the VP, Clinical Research Operations and VP, Clinical Research Compliance, of the temporary closure or suspension. The official closure and/or suspension information should be described in detail, and a procedure for corrective action should also be identified. The PI will review the information and report it appropriately to the sponsoring federal agency or study sponsor.

Simultaneously, a similar report of information and corrective action should be forwarded to the Deputy Physician-in-Chief for Clinical Research, and the IRB/Privacy Board Chairman. The other federal regulatory agencies will be contacted, as appropriate (e.g., OHRP and FDA).

RESEARCH MISCONDUCT Research Misconduct SOP

MSK is committed to the responsible conduct of research, and has policies and procedures in place for responding to allegations of misconduct in science. Allegations of research misconduct will be reviewed promptly, thoroughly, and objectively, with concern for the rights, reputations, and privacy of all those involved.

MSK policies and procedures that guide the manner in which all allegations of misconduct in science are handled, regardless of the funding source. It is written to conform to federal regulations (see 42 CFR Part 93 "Public Health Service Policies on Research Misconduct" or ORI DHHS Policy), as is required for managing misconduct proceedings that involve research support from agencies of the U.S. Public Health Service (PHS), including the National Institutes of Health. If the source of funding for the work in question is not an agency of the U.S. Public Health Service, these policies and procedures will be followed, but reporting to the Office of Research Integrity (ORI), PHS, is not required.

Definition of Research Misconduct

Misconduct in science is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

Research misconduct does not include honest error, differences in opinion, or authorship or collaboration disputes.

The Principals Responsible for Managing Misconduct Proceedings

Research at MSK is conducted under the auspices of either the Sloan Kettering Institute (SKI) or Memorial Hospital (MH), or both, and is overseen by Program Chairs (in SKI) or Department Chairs (in Memorial Hospital) and by subordinate laboratory heads and service chiefs.

When allegations of misconduct arise, a number of individuals with oversight of research may become involved, but the person with primary responsibility is the Senior Vice President, Research and Technology Management, who is the Research Integrity Officer (RIO). The RIO is responsible for assessing allegations of research misconduct, overseeing inquiries and investigations and other matters described in this policy.

CONFLICT OF INTEREST MANAGEMENT COI SOP

The Conflict of Interest Advisory Committee (COIAC) is a standing body appointed by the President of the Center; it is responsible to review and adjudicate situations in which a Covered Person is engaged in an Outside Activity that may be in conflict with any of his or her job duties, as set forth in the Policy on Conflict of Interest and Conflict of Commitment. Collaborations between academic health professionals and the private sector provide many societal, institutional and individual benefits. At the same time, these relationships can give rise to conflicts of interest or conflicts of commitment. Such conflicts may compromise - or appear to compromise - the integrity and objective of research, education and patient care, which in turn undermines public trust in our work. MSKCC's policy is designed to assist the investigator and the Center in identifying and managing situations that can give rise to conflicts. The COIAC membership can be found in **Appendix G**.

Any investigator, who is determined to have an individual Conflict defined by the COIAC, requires a Management Plan describing the permitted activities for that individual related to the human subjects' research. Each Management Plan is specific to the research the individual is involved in, taking into consideration the study design, risk level, study management in relation to the conflict. All Management Plans are reviewed and approved by the MSK IRB. All studies with a Management Plan include external members on the monitoring committees who are designated as the primary reviewer for the trial.

APPENDIX:

A. Protocol Review and Approval Flow Diagrams

B. Research Council Membership (Council A and B)

C. IRB/Privacy Board SOP List

D. DSM Committee Membership

E. DSMB Membership

F. OHRP Incident Report Form

G. Conflict of Interest Advisory Committee Membership

Date Original Document created: July 2001, NCI Approved: September 2001
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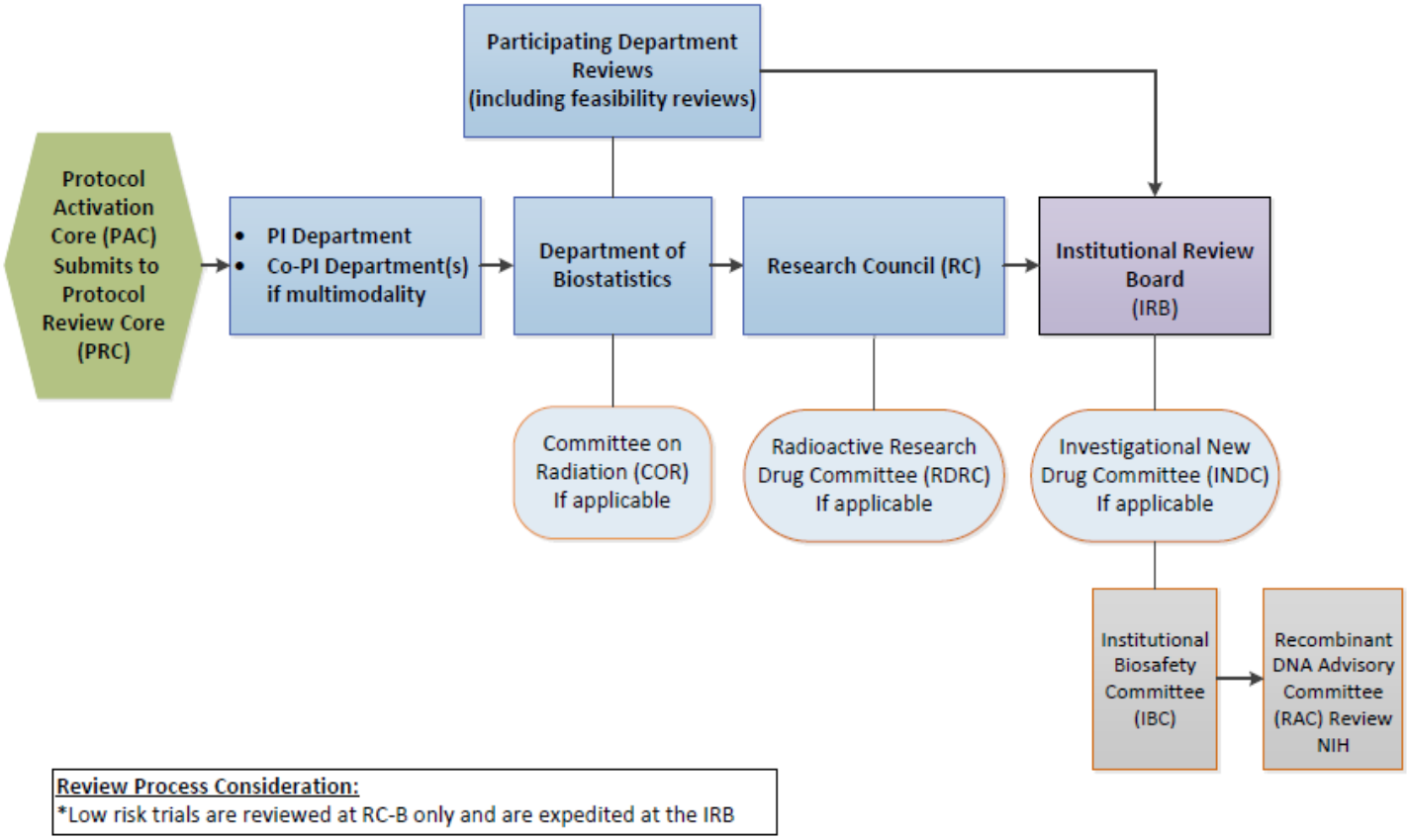
Date Revised: October 2015, NCI Approved: April 2016
Date Revised: May 2018, NCI Approved: August 2018

Appendix A: Protocol Review and Approval Flow Diagrams

MSK Investigator Initiated Trial (IIT) Committee Review Flow



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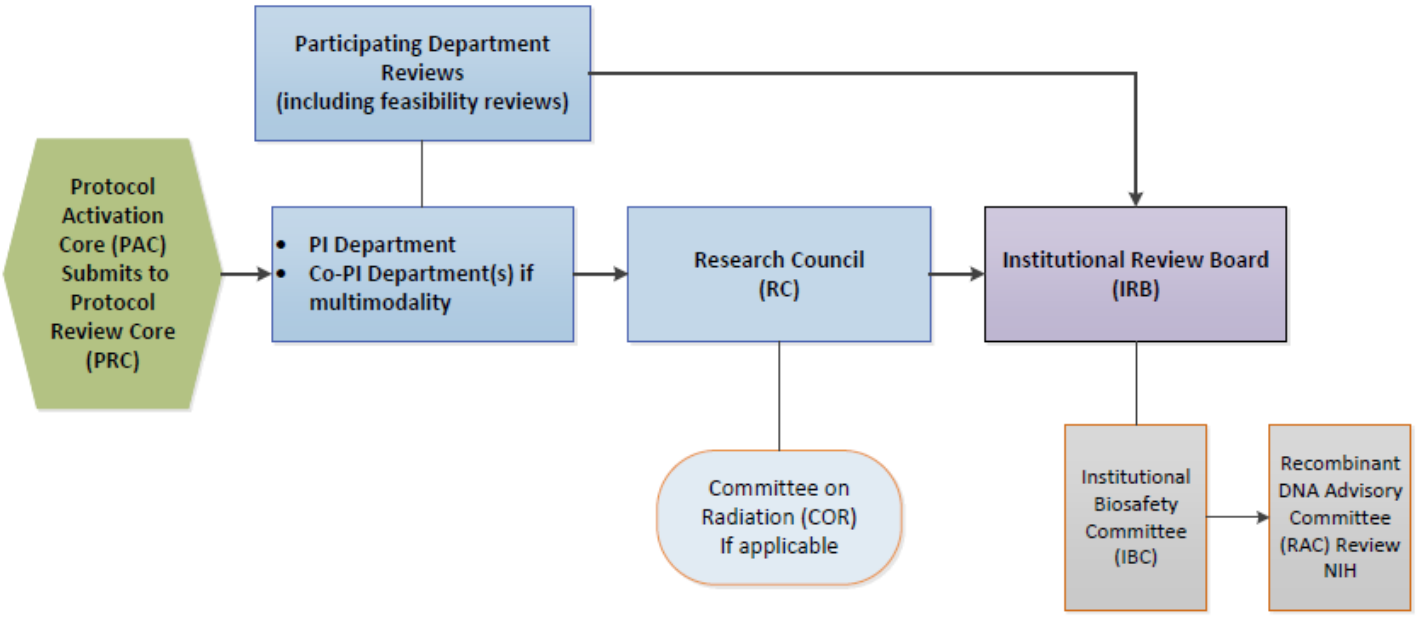
External Protocol Committee Review Flow



Review Process Considerations:
*Low risk trials are reviewed at RC-B only and are expedited at the IRB
*NCI Cooperative Group Protocols skip RC

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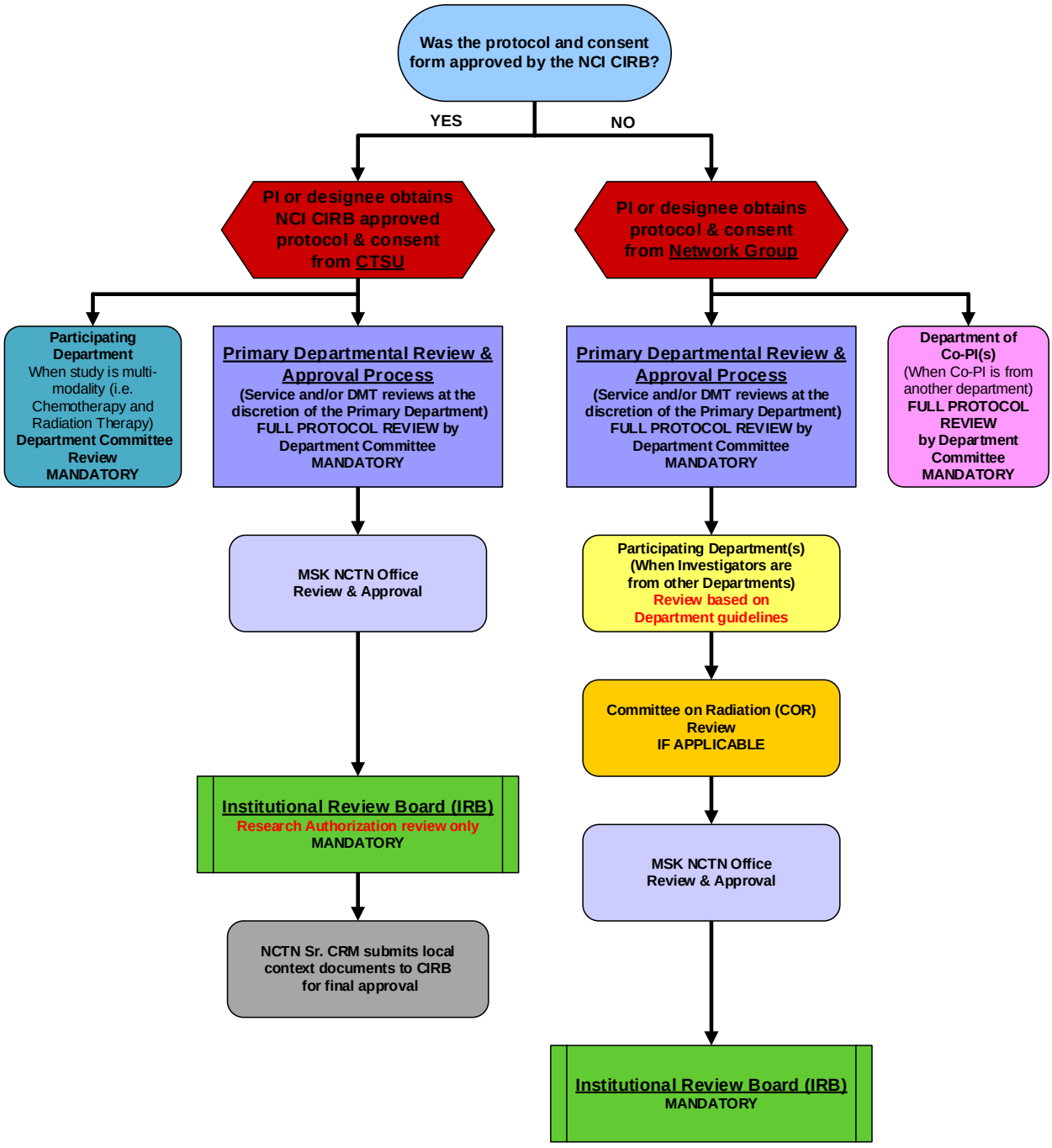
Protocol Review Process for NCTN (Cooperative Group) Protocols



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Appendix B: Research Council Membership (Council A and B)

Research Council A

David H Ilson, MD, PhD, Co-Chair	Department of Medicine, Gastrointestinal Oncology Service
Valerie Rusch, MD, Co-Chair	Department of Surgery, Thoracic Service
Eric J Sherman, MD, Co-Chair	Department of Medicine, Head and Neck Oncology Service
Oguz Akin, MD	Department of Radiology, Body Imaging Service
Margaret Callahan, MD, PhD	Department of Medicine, Melanoma and Immunotherapeutics
Marinela Capanu, PhD	Department of Epidemiology and Biostatistics, Biostatistics Service
Daniel G Coit, MD	Department of Surgery, Gastric & Mixed Tumor Service
Anne Covey, MD	Department of Radiology, Interventional Radiology Service
Christopher Crane, MD	Department of Radiation Oncology
Sandra D'Angelo, MD	Department of Medicine, Sarcoma Medical Oncology Service
Gary Deng, MD	Department of Medicine, Integrative Medicine Service
Eli Louis Diamond, MD	Department of Neurology
Ira J Dunkel, MD	Department of Pediatrics
Ronald Ghossein, MD	Department of Pathology, Surgical Pathology Service
Alexia Iasonos, PhD	Department of Epidemiology and Biostatistics, Biostatistics Service
David P. Kelsen, MD	Department of Medicine, Gastrointestinal Oncology Service
Atif Khan, MD	Department of Radiation Oncology
Ola Landgren, MD, PhD	Department of Medicine, Myeloma Service
Robert Motzer, MD	Department of Medicine, Genitourinary Oncology Service
Garrett Nash, MD	Department of Surgery, Colorectal Service
Esperanza B Papadopoulos, MD	Department of Medicine, Bone Marrow Transplant Service
Raajit Rampal, MD, PhD	Department of Medicine, Hematology Service
Ann Rodavitch, MA	Clinical Research Administration
Jonathan E Rosenberg, MD	Department of Medicine, Genitourinary Oncology Service
Charles Michael Rudin, MD, PhD	Department of Medicine. Thoracic Oncology Service
Paul J Sabbatini, MD (Ex officio)	Office of Physician-in-Chief
Eytan Stein, MD	Department of Medicine, Leukemia Service
Tanya Trippett, MD	Department of Pediatrics
Robert Veselis, MD	Department of Anesthesiology & Critical Care Medicine
Hannah Wen, MD, PhD	Department of Pathology, Surgical Pathology Service
Roger S. Wilson, MD	Department of Anesthesiology and Critical Care Medicine
Anas Younes, MD	Department of Medicine, Lymphoma Service
Anthony Yu, MD	Department of Medicine, Cardiology Service

Research Council B

Kim Kramer, MD, Co-Chair	Department of Pediatrics
Christian Nelson, PhD, Co-Chair	Department of Psychiatry and Behavioral Sciences, Psychiatry
Dana Rathkopf, MD, Co-Chair	Department of Medicine, Genitourinary Oncology Service
Karen Autio, MD	Department of Medicine, Genitourinary Oncology Service
Margaret Barton-Burke, PhD, RN	Department of Nursing
Denise Correa, PhD	Department of Neurology
Aimee Crago, MD, PhD	Department of Surgery, Gastric & Mixed Tumor Service
Mark Dickson, MD	Department of Medicine, Sarcoma Medical Oncology Service
Pamela Drullinsky, MD	Department of Medicine, Breast Medicine (Regional Networks)
Lara Dunn, MD	Department of Medicine, Head & Neck Oncology Service
Elena Elkin, PhD	Department of Epidemiology and Biostatistics
Daphna Gelblum, MD	Department of Radiation Oncology (Regional Networks)
Jada Hamilton, MPH, PhD	Department of Psychiatry & Behavioral Sciences, Behavioral Sciences
Collette Houston	Clinical Research Administration
Geoffrey Ku, MD	Department of Medicine, Gastrointestinal Oncology Service
Mario Lacouture, MD	Department of Medicine, Dermatology Service
Michael LaQuaglia, MD	Department of Surgery, Pediatric Surgical Service
Peter Maslak, MD	Department of Laboratory Medicine
Sean McBride, MD	Department of Radiation Oncology
Shakeel Modak, MBBS, MD	Department of Pediatrics
Alison Moskowitz, MD	Department of Medicine, Lymphoma Service
Chaya Moskowitz, PhD	Department of Epidemiology and Biostatistics, Biostatistics Service
Sara Olson, PhD	Department of Epidemiology and Biostatistics, Epidemiology Service
Neeta Pandit-Taskar, MD	Department of Radiology, Molecular Imaging & Therapy Service
Sujata Patil, PhD	Department of Epidemiology and Biostatistics, Biostatistics Service
Michael A Postow, MD	Department of Medicine, Melanoma & Immunotherapeutics Service
Melissa Pulitzer, MD	Department of Pathology
James Root, PhD	Department of Psychiatry & Behavioral Sciences, Psychiatry Service
Paul J Sabbatini, MD (Ex officio)	Office of Physician-in-Chief
Talya Salz, PhD	Department of Epidemiology & Biostatistics, Biostatistics Service
Emily Tonorezos, MPH, MD	Department of Medicine, General Internal Medicine Service
Tiffany Traina, MD	Department of Medicine, Breast Medicine Service
Brian Untch, MD	Department of Surgery, Head and Neck Service
Herbert A. Vargas Alvarez, MD	Department of Radiology

Appendix C: IRB/Privacy Board SOP List

IRB/PB SOPs		
GENERAL ADMINISTRATION		
IRB/PB	GA 101	Policies and Procedures Maintenance
IRB/PB	GA 102	Training and Education
IRB/PB	GA 103	Management of HRPP Office Staff
IRB/PB	GA 104	IRB Member and Consultant Conflict of Interest
IRB/PB	GA 105	IRB Signatory Authority
IRB/PB	GA 106	IRB of Record
IRB/PB	GA 107	Responsibilities of the IO
IRB/PB ORGANIZATION		
IRB/PB	OP 201	Composition of IRB
IRB/PB	OP 202	Management of IRB
IRB/PB	OP 203	Duties of IRB Members
IRB/PB	OP 204	Undue Influence of IRB members and HRPP Office Staff
FUNCTION AND OPERATION		
IRB/PB	FO 301	Authority and Purpose of the HRPP
IRB/PB	FO 302	Activities Requiring IRB Review
IRB/PB	FO 303	Research Exempt from IRB Review
IRB/PB	FO 304	Research Submission Requirements for Non-Exempt Research
IRB/PB	FO 305	IRB Meeting Administration
IRB/PB	FO 306	Administrative Review and Distribution of Materials
IRB/PB	FO 307	Documentation and Document Management
IRB/PB	FO 308	HIPAA and Research
IRB/PB	FO 309	Noncompliance in Human Research
IRB/PB	FO 310	Suspensions and Terminations of IRB Approval
REVIEW OF RESEARCH		
IRB/PB	RR 401	Initial Review - Criteria for IRB Approval
IRB/PB	RR 402	Categories of Action
IRB/PB	RR 403	Reviews Utilizing the Expedited Procedure
IRB/PB	RR 404	Amendments to IRB Approved Research
IRB/PB	RR 405	Continuing Review - Criteria for Renewal
IRB/PB	RR 406	Advertisements and Recruitment Incentives
IRB/PB	RR 407	Deviations to IRB Approved Research and IRB SOPs
IRB/PB	RR 408	Reporting of Serious Adverse Events (ongoing continuing review)
IRB/PB	RR 409	Unanticipated Problems involving Risk to Participant or Others
IRB/PB	RR 410	Study Completion

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REVIEWS REQUIRING SPECIAL CONSIDERATION		
IRB/PB	SC 501	Vulnerable Populations
IRB/PB	SC 502	Gene Transfer Research
IRB/PB	SC 503	Genome-Wide Association Studies (GWAS)
IRB/PB	SC 504	Use of Germline DNA in MSK Sponsored Research
IRB/PB	SC 505	Genomic Advisory Panel Authority
IRB/PB	SC 506	Genomic Advisory Panel Administration
IRB/PB	SC 507	Genomic Advisory Panel - Member Composition
IRB/PB	SC 508	Genomic Advisory Panel - Member Duties
IRB/PB	SC 509	Emergency Use of a Test Article
IRB/PB	SC 510	Use of Investigational Drugs or Biologics in Human Research
IRB/PB	SC 511	Use of Investigational Devices in Human Research
IRB/PB	SC 512	Humanitarian Use Devices
IRB/PB	SC 513	Research Subject to DoD Regulations
IRB/PB	SC 514	Genomic Data Sharing (GDS)
IRB/PB COMMUNICATION		
IRB/PB	CO 601	Communication with Investigative Staff
IRB/PB	CO 602	Communication with Other Entities
INFORMED CONSENT		
IRB/PB	IC 701	General Requirements for Informed Consent and HIPAA Research Authorization
IRB/PB	IC 702	Waivers and Alterations of Informed Consent
IRB/PB	IC 703	Assent
IRB/PB	IC 704	Consenting Participants Who Do Not Read or Speak English
IRB/PB	IC 705	Consenting Professionals
IRB/PB	IC 706	Documentation of Informed Consent and Research Authorization
RESPONSIBILITIES OF INVESTIGATORS		
IRB/PB	RI 801	Principal Investigators/Co-Principal Investigator Qualifications
IRB/PB	RI 802	Requirements for the Coordination of Multicenter Research Projects
IRB/PB	RI 803	Investigator Responsibilities
QUALITY ASSURANCE		
IRB/PB	QA 901	QA/QC Program
IRB/PB	QA 902	Audits by Regulatory Agencies

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Appendix D: DSM Committee Membership

Eileen O'Reilly, M.D.	Chair, DSMC Attending Physician Department of Medicine, Gastrointestinal Oncology
Virginia Klimek, M.D.	Associate Chair, DSMC Associate Attending Physician Department of Medicine, Leukemia
Ronald Blum, M.D.*	Professor of Medicine Director, Cancer Centers and Programs Beth Israel Medical Center and St. Luke's Roosevelt Hospital
Jamie Chaft, M.D.	Assistant Attending Physician Department of Medicine, Thoracic
Guido Dalbagni, M.D.	Attending Surgeon Department of Surgery, Urology
Nicola Fabbri, M.D.	Attending Surgeon Department of Surgery, Orthopedic
Josef Fox, M.D.	Assistant Attending Radiologist Department of Radiology, Molecular Imaging & Therapy
Igor Gavrilovic, M.D.	Associate Attending Neurologist Department of Neurology
Paul Hamlin, M.D.	Associate Attending Physician Department of Medicine, Lymphoma
Komal Jhaveri, M.D.	Assistant Attending Physician Department of Medicine, Breast
Mary Keohan, M.D.	Associate Attending Physician Department of Medicine, Melanoma and Sarcoma
Meredith E. MacGregor, M.D.	Instructor Department of Psychiatry & Behavioral Sciences, Psychiatry
Vicky Makker, MD	Assistant Attending Physician Department of Medicine, Gynecologic Medical Oncology

John Mulhall, MD	Attending Surgeon Department of Surgery, Urology
Irina Ostrovnaya, Ph.D.	Associate Attending Biostatistician Department of Epidemiology & Biostatistics
M. Lia Palomba, M.D.	Associate Attending Physician Department of Medicine, Lymphoma
Genovefa Papanicolaou, M.D.	Attending Physician Department of Medicine, Infectious Disease
Miguel Perales, M.D.	Associate Attending Physician Department of Medicine, Bone Marrow Transplant
Nitya Raj, M.D.	Assistant Attending Physician Department of Medicine, Gastrointestinal
Tanya Trippett, M.D.	Associate Attending Pediatrician Department of Pediatrics
Anna Varghese, M.D.	Assistant Attending Physician Department of Medicine, Gastrointestinal
Yoshiya Yamada, M.D.	Attending Radiation Oncologist Department of Radiation Oncology, Brachytherapy

* Consulting Member

Appendix E: DSMB Membership

Colin B. Begg, Ph.D.	Attending Biostatistician Chair - DSMB Chair, Department of Epidemiology and Biostatistics Memorial Sloan Kettering Cancer Center New York, NY
Eileen O'Reilly, M.D.	Attending Physician Gastrointestinal Oncology Service Department of Medicine Memorial Sloan Kettering Cancer Center New York, NY
Richard Gralla, M.D.	Director of Oncology Research Jacobi Medical Center Professor of Medicine Albert Einstein College of Medicine Bronx, NY
David Harrington, Ph.D.	Chair, Department of Biostatistical Science Dana-Farber Cancer Institute Boston, MA
Franco Muggia, M.D.	Professor of Oncology (Medicine) NYU Cancer Institute New York University Medical Center New York, NY
Suzanne Miller-Halegoua, Ph.D.	Professor, Cancer Prevention and Control Director, Psychosocial and Behavioral Medicine Program and Behavioral Research Core Facility Fox Chase Cancer Center Philadelphia, PA

Appendix F: OHRP Incident Report Form

Memorial Sloan-Kettering Cancer Center

OHRP Incident Report Form Date of Report:

Category of Incident (Check One):	☐ Unanticipated problem with risks to subjects or others	☐ Serious or continuing noncompliance	☐ Suspension or termination of IRB approval

Institution:
Memorial Sloan Kettering Cancer Center
1275 York Avenue
New York, NY 10065

Contact:
Laura Godfrey
HRPP Office
646-888-0923
godfreyl@mskcc.org

Title of research project and/or grant proposal

Protocol PI

IRB No.

Nos. of federal awards

Description of problem

Actions to address the problem

Status of Incident Report: ☐ Interim ☐ Final

MSKCC Approval:

Collette Houston _____
Vice President, Clinical Research Compliance Date

Reported by Clinical Research Administration, OHRP Reporting Workgroup

Date Original Document created: July 2001, NCI Approved: September 2001
Date Revised: February 2007, NCI Approved: March 2007
Date Revised: March 2011, NCI Approved: September 2011
Date Revised: October 2015, NCI Approved: April 2016
Date Revised: May 2018, NCI Approved: August 2018

Appendix G: Conflict of Interest Advisory Committee Membership

	Member	Title	Current Status
1	Peter Scardino, MD	Attending Physician, Urology Service	Chairman/Voting Member
2	Jose Baselga, M.D.	Physician-in-Chief	Voting Member
3	Deborah Berns, Esq	SVP and Chief Risk Officer	Voting Member
4	Ned Groves	Senior Vice President and Chief Hospital Administrator	Voting Member
5	Eric Cottington, PhD	Senior Vice President, Research & Technology Management	Voting Member
6	Cliff Hudis, MD	Consultant, Breast Medicine Service	Voting Member
7	Jason Lewis, PhD	Chief, Radiochemistry and Imaging Service, Radiology and Director, Radiochemistry and Molecular Imaging Probe Core	Voting Member
8	Joan Massague, PhD	Director, SKI	Voting Member
9	Greg Raskin, M.D.	Executive Director, Office of Technology Development	Voting Member
10	Marilyn Resh, PhD	SKI Member & Lab Head	Voting Member
11	Greg Riely, MD	Division Head Dept. of Medicine	Voting Member
12	Vacant – Surgeon	Department of Surgery	Voting Member
	Yashodhara Dash, PhD	Senior Manager, Technology Management and Commercialization, OTD	Non-Voting Member/Advisory
	Carolyn Levine, Esq	Deputy General Counsel and Corporate Secretary	Non-Voting Member/Advisory
	Mercedes Gorre	Director, Office of the President	Non-Voting Member/President Representative
	Kristen Ahearn	Associate General Counsel, Director, Compliance & Privacy Officer	Non-Voting Member/Advisory
	Malikah Fulton	Institutional Compliance Manager, Conflict of Interest	Non-Voting Member/Advisory
	Marie Diaz	Institutional Compliance Manager	Non-Voting Member/Administrative