

**University of Wisconsin Comprehensive Cancer Center  
(UWCCC)**

**DATA AND SAFETY MONITORING PLAN  
POLICY & PROCEDURES**

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## **I. Data and Safety Monitoring System**

### **A. Overview**

The Data and Safety Monitoring System (DSMS) of the UWCCC ensures that all clinical research being conducted under the auspices of the UWCCC is in compliance with federal and local requirements and most importantly that human subject safety is always optimized.

The DSMS is fundamental to the conduct of UWCCC clinical research according to UWCCC research policies and procedures. Quality assurance of good clinical research practices are enhanced in all groups within the UWCCC by the monthly Program Managers Committee meeting, continual development and updating of Standard Operating Procedures and advancements made to internal monitoring activities. Centralized clinical trial services such as the UWCCC database and overall data and safety monitoring assures consistency. In order to maintain an active, high quality clinical research program in the UWCCC, a high quality and efficient database management system is employed to track all clinical trials, including status and subject enrollment. The UWCCC database provides a tool for tracking documentation and reporting all clinical research trials ongoing in the UWCCC. Ongoing quality control reviews ensure accuracy of the information recorded in the database. The DSMS is assisted in its mission of safety and compliance by experienced UWCCC research staff, a Data and Safety Monitoring Committee (DSMC) comprised of experienced clinical researchers and staff, and the ongoing use of the UWCCC database which allows efficient tracking of protocols and research subjects. The DSMC reviews reports on quality assurance (internal audits, response reviews, protocol summary reports, compliance reviews), protocol deviations and serious adverse events. The DSMS also provides data review, data abstraction and entry, forms monitoring and final report generation for studies developed and solely monitored by the UWCCC.

### **B. Mission**

The mission of the DSMS is to provide a system that assures compliance with federal and local requirements for clinical research being conducted at the UWCCC. The DSMS works with the Clinical Research Offices (CRO) and the Protocol Review and Monitoring System (PRMS) to provide support to investigators. The DSMS ensures that all clinical research adheres to the UWCCC data and safety monitoring policy and procedures. The DSMS monitors the safety, toxicity and overall efforts of all UWCCC clinical research including the UWCCC Outreach Network, which includes UWCCC Regional Partners, members of the Wisconsin Oncology Network (WON), and cooperative group affiliates.

**C. The Clinical Research Committee (CRC)**

**1. Overview**

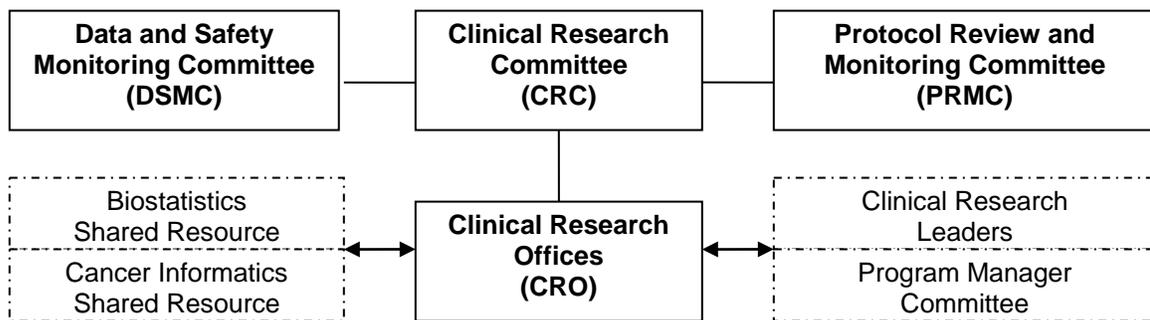
The Clinical Research Committee (CRC), composed of UWCCC senior leadership and Disease Oriented Working Group (DOWG) leaders, oversees all aspects of clinical research conducted at the UWCCC and makes final decisions on all issues related to clinical trials. The CRC ensures that all aspects of the clinical research process at the Cancer Center are conducted according to prescribed standard operating procedures. The committee:

- a) Reviews and approves all UWCCC policies and Standard Operating Procedures related to clinical research.
- b) Oversees all cancer clinical trials conducted at the UWCCC.
- c) Appoints membership and defines responsibility of the Protocol Review and Monitoring Committee (PRMC) and the Data and Safety Monitoring Committee (DSMC).
- d) Serves as review body for the PRMC and DSMC decisions.

**2. Clinical Research Committee (CRC) Membership**

Members of the Clinical Research Committee are key leaders of the UWCCC appointed by the Director. Their term is co-terminus with their leadership role. The committee meets monthly. Interim meetings to address specific issues that require immediate attention are scheduled to ensure subject safety. Members are listed in Appendix I.

**Table 1: UWCCC Clinical Research Infrastructure**



## **D. Data and Safety Monitoring Committee (DSMC)**

### **1. Overview**

The Clinical Research Committee delegates responsibility for continued review and monitoring of all clinical trials conducted by the UWCCC to the Data and Safety Monitoring Committee (DSMC). The DSMC is responsible for the regular review and monitoring of all on-going clinical research in the UWCCC. The Committee meets every other month to review reports on quality assurance including internal audits, quality assurance and response reviews, compliance reviews, as well as protocol violations, and Severe Adverse Events (SAE) and Protocol Summary Reports (PSR).

The Data and Safety Monitoring Committee activities are as follows:

- Review all clinical trials conducted at the UWCCC for data integrity and safety.
- Review all Serious Adverse Events (SAE) requiring expedited reporting as defined in the protocol.
- Review all reports generated by the UWCCC data quality control review process (internal audits, quality assurance reviews, response reviews, compliance reviews, and protocol summary reports) described in Section II of this document.
- Submit recommendations for corrective actions to the CRC.
- Notify the protocol Study Chair of the DSMC's recommended action.
- Work in conjunction with the UW Health Sciences IRB in the review of protocol deviations, violations and unanticipated problems reported by the UWCCC research staff.
- The committee ensures that notification is provided to external sites participating in multiple-institutional clinical trials coordinated by the UWCCC of AEs requiring expedited reporting.

### **2. DSMC Membership**

Members of the DSMC are appointed by the UWCCC Director. Membership duration is flexible to maintain required depth and breadth of expertise related to the spectrum of clinical research conducted at the Cancer Center. Interim meetings are scheduled to address specific issues that require immediate attention to ensure subject safety. Present membership is listed Appendix I.

### **3. DSMC Review of Quality Control Issues**

All Quality Control reports and/or issues from quality control audits and reviews are reported to the DSMC. Quality Control reviews are coordinated by the Compliance and Monitoring Specialist of the Clinical Research Compliance Office. Typically reports are received by the DSMC for Internal Audits, Quality Assurance Reviews, Response Reviews, Protocol Summary Reports and all other types of routine data monitoring reports. Subject confidentiality is upheld in all quality assurance reporting. These quality control reviews are described in the sections that follow. The DSMC reviews the quality control reports, ascertains if further information is required from the investigator and makes a recommendation for follow-up action if it is warranted. These decisions and recommendations are referred to the CRC. The DSMC ensures that the PI reports any temporary or permanent suspension of a clinical trial to the sponsor (e.g., NCI Program Director, Industry Sponsor Medical Monitor, Cooperative Group Study Chair, etc.) and other appropriate agencies.

### **4. DSMC Review of Serious Adverse Events (SAE) Reporting.**

The DSMC Chair reviews and evaluates all SAE reports in real time. The SAE review procedure was created to ensure that all SAEs occurring for all subjects treated on a protocol being conducted at the UWCCC and Affiliate Sites are adequately reviewed and that the appropriate action, if warranted, is taken. The research staff distributes SAE reports as directed by the protocol and UWCCC SOPs, which include submission to the UWCCC Data and Safety Monitoring Coordinator. The research group reporting the SAE must indicate if protocol/consent form changes are necessary in light of the SAE. The SAE information is forwarded immediately to the DSMC Chair for review in real time. The database allows cumulative SAE data and SAEs reported from the preceding two months for each DSMC meeting to be generated. It also includes information regarding the total number of SAEs over the lifetime of any given protocol, providing cumulative SAE data on a per-protocol basis. In addition to reviewing all SAE reports, the DSMC reviews all reports generated from quality assurance activities. Findings and required follow-up action, if any, will be recommended by the DSMC and submitted with the SAE report to the CRC.

## **E. Data and Safety Monitoring Plan**

### **1. Requirements**

All clinical trials conducted at the UWCCC must have information included in the protocol relating to data and safety monitoring commensurate with the level of risk to subjects. All intervention trials must have a satisfactory Data and Safety Monitoring Plan (DSMP) that is described in detail in the protocol (Appendix II includes a DSMP template for Institutional Trials). The Protocol Review and Monitoring Committee (PRMC) review ensures that subject safety and the degree

and frequency of data and safety monitoring for individual studies will be commensurate with the size, complexity and risks of the trial.

## **2. Trial Types**

### **Intervention Trials**

Intervention trials are those that produce an effect or alter the course of a disease in a patient population. Intervention trials include medical, social, behavioral, and environmental activities that are therapeutic, preventive, or supportive in nature. Intervention trials must have a detailed Data and Safety Monitoring Plan outlining the processes for the elements listed below. If the intervention trial is an Institutional Trial, investigators must utilize the DSMP template for institutional trials located in Appendix II. If the intervention trial is a cooperative group, consortium, or industry-sponsored trial, the complete DSMP must either be included in the protocol or on file with the UWCCC CRO.

### **Physical Non-Intervention Trials**

Physical Non-Intervention trials include those in which the study objectives are non-intervention in nature, but the study involves physical procedures performed by which data are gathered (e.g., venipuncture, external monitoring device, administering surveys, conducting interviews, etc.). Physical non-intervention trials must include a DSMP that is commensurate with the level of risk of the study and includes applicable elements listed below.

### **Non-Physical Non-Intervention Trials**

Non-Physical Non-Intervention trials include those in which the study objectives are non-intervention in nature and the study involves no physical procedures performed on subjects (e.g., registry studies, medical records research, laboratory studies using banked samples, etc.) Non-physical non-intervention trials must have data and safety monitoring language in the protocol commensurate with the level of risk.

## **3. Elements of a Data and Safety Monitoring Plan**

- Delineation of oversight responsibilities (either external DSMB or UWCCC Data and Safety Monitoring Committee).
- Description of data and safety review process.
- Time table for submission of data, safety, and progress information to the external DSMB or UWCCC Data and Safety Monitoring Committee, the IRB, and the sponsor.
- Process to implement temporary or permanent closure or suspension of studies when significant risks are identified.

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- Description of adverse event and Serious Adverse Event (SAE) reporting procedures.

A DSMP template to be used by investigators for Institutional Trials is found in Appendix II.

Guidelines for establishing and operating an external DSMB are presented in Appendix III.

## **II. Guidelines for Data and Safety Monitoring Implementation**

### **A. Requirements for Monitoring and Reporting**

UWCCC monitoring requirements for institutional trials without an acceptable DSMB are as follows:

#### **Phase I Trials**

Investigators will conduct continuous review of data and subject safety at their weekly Phase I/Disease Group meetings where the results of each subject's treatment are discussed and the discussion is documented in the minutes. The discussion will include for each dose level: the number of subjects, significant toxicities as described in the protocol, dose adjustments, and responses observed. Protocol Summary Reports must be submitted on a quarterly basis for review by the Data and Safety Monitoring Committee.

#### **Phase I/II and Phase II Trials**

Data related to these trials are discussed at regularly scheduled Disease Oriented Working Group meetings where the results of each subject's treatment are discussed and the discussion is documented in the minutes. The discussion will include for each treatment arm/dose level: the number of subjects, significant toxicities as described in the protocol, dose adjustments, and responses observed. Twice yearly, Protocol Summary Reports are required for submission to the Data and Safety Monitoring Committee for review.

#### **Phase III Trials and Trials Enrolling >300 Subjects**

All Phase III trials and trials enrolling >300 subjects will have an external Data and Safety Monitoring Board (DSMB) whose composition and review procedures are approved by the UWCCC Protocol Review and Monitoring Committee. Annually, Protocol Summary Reports are required for submission to the Data and Safety Monitoring Committee for review.

#### **Behavioral and Nutritional Studies**

These trials must have a DSMP commensurate with the level of risk to the participants and approved by the Protocol Review and Monitoring Committee.

### **Training Grant Trials**

Studies developed by an investigator in training who is supported on a training grant or mentored by a UWCCC investigator will be subject to the guidelines described above.

### **B. Requirements for Review and Oversight**

#### **Serious Adverse Events requiring expedited reporting – Reported Within 24 Hours**

Serious Adverse Events (SAE) requiring expedited reporting within 24 hours (as described in the protocol) will also be reported to the Data and Safety Monitoring Committee Chair within one business day. NCI ADEERS form or FDA Medwatch Form #3500 and/or any other documentation available at that time will also be reviewed by the DSMC Chair who will determine if immediate action is required. Within 10 working days all subsequent SAE documentation that is available will be submitted to the DSMC Chair, as well as others requiring documentation. The DSMC Chair will determine if further action is required. All information will be tracked in the UWCCC database.

If the SAE occurs on a multiple-institutional clinical trial coordinated by the UWCCC, the Outreach Coordinator will ensure that all participating sites are notified of the event and resulting action within one working day of the determination.

#### **Serious Adverse Event – Reported within 10 Days**

Serious Adverse Events requiring expedited reporting within 10 working days (as described in the protocol) will also be sent to the UWCCC DSMC Chair. NCI ADEERS form or FDA Medwatch Form #3500 and/or any other documentation available at that time will also be reviewed by the DSMC Chair who will determine if further action is required. All information will be tracked in the UWCCC database.

If the SAE occurs on a multiple-institutional clinical trial coordinated by the UWCCC, the Outreach Coordinator will ensure that all participating sites are notified of the event and resulting action within one working day of the determination.

The Study Chair will notify all investigators involved with the study at the UWCCC and external sites, the IRB, the sponsor and the funding agency and provide written documentation of these notifications to the DSMC.

### **Study Progress Review**

Protocol Summary Reports (PSR) are required to be submitted to the DSMC commensurate with the Phase of the study. The PSR provides a cumulative report of serious adverse events, as well as any protocol violations, deviations or unanticipated problems, toxicities and responses that have occurred on the protocol in the timeframe specified. PSRs are reviewed at each DSMC meeting.

Protocol Summary Reports enable DSMC committee members to assess whether significant benefits or risks are occurring that would warrant study closure. This information is also provided by Disease Oriented Working Group meeting minutes,

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internal audit and/or response review reports. In addition, the DSMC requires the DOWG or protocol Study Chair to submit external DSMB reports or any other significant study-related information.

In the event that there is significant risk warranting study suspension or closure, the DSMC will notify the PI of the DSMC findings. The DSMC ensures that the PI reports any temporary or permanent suspension of a clinical trial to the sponsor (e.g., NCI Program Director, Industry Sponsor Medical Monitor, Cooperative Group Study Chair, etc.) and other appropriate agencies. DSMC findings and recommended follow-up action will be submitted to the CRC.

**C. Conflict of interest**

Inherent in any institutional data and monitoring system is the potential for Conflict of Interest (COI) as a consequence of utilizing its own faculty and research staff members to conduct the monitoring activities. Therefore, all faculty and research staff are prohibited from serving on a monitoring team if they have any involvement in or relationship with the protocol under review. Examples would include any physician who is a sub-investigator on the study, or any study coordinator or research nurse involved in the conduct or data management of the study.

**D. Requirements for Data Quality Control**

All formal quality assurance activities and reports, as described in detail below, are submitted to and discussed by the DSMC and then submitted to the CRC if action is required. The CRC provides recommendations for follow-up action, if necessary, to the UWCCC Director.

The DSMS quality control elements are described in detail below.

**1. Internal Audit**

The Internal Audit (IA) procedure is a formal, comprehensive, source document review of all institutional studies not otherwise audited by an external agency. Annually, each DOWG is subject to an IA that examines a percentage of cases on all active Institutional Trials for that group. The Compliance Monitoring Specialist generates the appropriate list of studies and cases. A goal of 10% of cases is given as a general guideline, but will be tailored to the specifics of each study (i.e., level of experience of the investigator or enrolling clinical research coordinator, complexity of the protocol, etc.) The Compliance and Monitoring Specialist (CMS) serves as the lead auditor and oversees the audit process. The CMS notifies the PIs and research staff of the upcoming audit and provides them with a case list four weeks prior to the audit. The CMS recruits the audit team consisting of a physician and varying number of independent research support staff, depending on the number of protocols and subject cases scheduled for the audit. In addition, the CMS provides the audit team with audit materials for preparation in advance of the audit, coordinates the exit interview, and generates the final audit report. If the audit requires follow-up to address audit findings, the

DOWG is notified in the audit report that a Corrective Action Plan (CAP) is warranted. Upon submission of the CAP by the PI, the CAP is reviewed by the DSMC.

The NCI Clinical Trials Monitoring Branch (CTMB) Guidelines for Monitoring are followed for the following elements:

- Case review (Informed consent, eligibility, response, toxicity)
- Source document review
- Regulatory review
- Drug accountability/pharmacy
- Overall data quality/submission timeliness

## **2. Quality Assurance Review**

This review ensures that the UWCCC maintains the same high quality of data collection and monitoring for all studies, regardless of sponsor. Quality Assurance Reviews (QAR) are conducted on all intervention Institutional trials, Cooperative Group (CG) trials, Consortium trials, and NCI-Sponsored trials after the first two subjects are accrued to a given trial. Aspects of study conduct reviewed during a QAR include the informed consent process, subject eligibility, overall adherence to the protocol by the study team, and all regulatory documents. These reviews are conducted on a quarterly basis by the Compliance and Monitoring Specialist (CMS) and research staff from within the UWCCC who have no connection to the study under review. If the QAR requires follow-up to address findings, the DOWG is notified in the QAR report that a Corrective Action Plan (CAP) is warranted. Upon submission of the CAP by the PI and/or research staff, the CAP is reviewed by the DSMC. DSMC findings and any further required follow-up action is communicated by the DSMC to the Principal Investigator. If the PI appeals the DSMC findings, the appeal is brought to the CRC. The UWCCC Director has final authority in the appeal process.

## **3. Response Review**

This independent response confirmation complements the ongoing Quality Assurance Review and Internal Audit procedures at the UWCCC, as described above. A Response Review (RR) may be performed on confirmed partial responses (PR) or complete responses (CR) on any therapeutic clinical trial, regardless of sponsor. Response Reviews are mandatory for studies without an external data and safety monitoring entity. On a quarterly basis, the CRCO solicits from the DOWGs all subject cases in which a CR or a PR was recorded. The CRCO recruits physician reviewers with no connection to the case under review, obtains radiological films and any other necessary documents, and schedules a location and time for the first response review to occur. Measurements and/or assessments made by the independent reviewer are documented on the Response

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Review form. The RR findings are reported to the DSMC. If the independent review does not concur with the reported response from the investigator, the treating physician is notified. If the treating physician does not accept the RR findings he or she may request that a second response review be performed. If the PI wishes to appeal the second review finding, the appeal is brought to the CRC. The UWCCC Director has final authority in the appeal process.

**4. Compliance Review**

Research protocols that do not meet the criteria for an internal audit, quality assurance review or response review may be subject to a Compliance Review by the Compliance and Monitoring Specialist (CMS). This includes industry-sponsored trials. Compliance Reviews will be performed on as-needed basis based upon information provided to the DSMC related to study conduct, protocol adherence, and general compliance to research regulations. The Compliance Review findings are reported to the DSMC for review at the subsequent meeting.

**5. Subject Data**

On a monthly basis, OnCore subject registration reports are sent to the Program Manager of each DOWG with a listing of all the subjects enrolled to intervention protocols the prior month. Subject demographic and registration information is reviewed to ensure the information corresponds to source documents. The OnCore Support Office performs an additional data review on each subject record. Subject status reports are run by the OnCore Support Office quarterly to ensure subject treatment and follow up data are entered in the database. These reports are then sent to the Program Manager of each DOWG for a validation check against source documentation. Subject status information is also checked by the DOWGs prior to each submission of the Protocol Summary Report to the DSMC.

**6. Protocol Data**

New protocols entered into the OnCore database undergo a data review by the PRMC Coordinator to ensure all mandatory fields are completed and the data entered corresponds to the protocol documents. The study is opened to accrual only after this validation check is passed. Once the study is opened to accrual, the OnCore Support Office performs an additional data review on the new protocol record. Protocol status reports are run quarterly and sent to the Program Manager of each DOWG to ensure the most current protocol status is reflected in the database.

**7. Serious Adverse Events Data**

Data from Serious Adverse Events (SAEs) are reviewed by the SAE Coordinator within 24 hours of receiving the SAE notification to ensure all mandatory fields are completed. Source documentation validation is performed by the DOWGs prior to each submission of the Protocol Summary Report to the DSMC.

### **III. Data and Safety Management and Monitoring for Institutionally Developed Studies**

The following additional services are provided for institutionally developed studies that are monitored by the UWCCC DSMC.

#### **A. Subject Data**

In addition to the subject registration and subject status data entered in the OnCore database for all intervention trials, the DOWG research staff also enter the subject study data into electronic case report forms (eCRFs) for UW institutional studies. Data items required for the eCRFs and study analysis are specified during protocol development by the PI and Statistician.

#### **B. Forms Monitoring**

eCRF data are monitored on a monthly basis utilizing the OnCore database Data Monitoring Console to ensure all mandatory fields are entered completely, accurately, and within time requirements. This process can often identify a misunderstanding or deficiency in protocol requirements early in the study and can improve data quality. When a query uncovers an issue which cannot be resolved among the DOWG research staff, statistician, and PI, arbitration is achieved through the UWCCC CRC.

#### **C. Final Reports**

A summary of each subject's data record is continually available to the PI, research staff, and DSMC from the OnCore database Biostat Console. The availability of this information is a valuable tool for the preparation of final reports and manuscripts as well as ongoing deficiency reports.

### **IV. Conflict of Interest**

During their scientific review the Protocol Review and Monitoring Committee (PRMC) is responsible for identifying potential conflicts of interest (COI) involved in any UWCCC clinical trial. Investigators must indicate on the protocol submission form any potential COI resulting from their involvement in the trial. If a potential conflict is identified by the PRMC, the investigator must work with his/her department chair and the UW Conflict of Interest Committee to create a plan to eliminate or manage the conflict of interest. The University of Wisconsin Policies and Procedures for Conflict of Interest govern this process.

During their review of data and safety monitoring issues the DSMC is responsible for identifying potential conflicts of interest (COI) involved with any of the protocols that are being reviewed. DSMC members identified as having a COI will leave the room during discussion of the protocol and recuse themselves from a vote on any recommended action for that protocol.

**APPENDIX I**

**Clinical Research Committee Membership (11/2011)**

<i>Name</i>	<i>Leadership Role</i>
Brad Kahl, MD, Chair	Associate Professor of Medicine, Hematology/Oncology Associate Director, UWCCC Clinical Research Programs Hematology DOWG Leader
Rhoda Arzoomanian, BSN, MSM	Associate Director of Administration, UWCCC
Sarah Marcotte, MS, CCRP	Assistant Director, UWCCC Clinical Research Programs Manager, UWCCC Clinical Research Services Office
Dan Mulkerin, MD	Associate Professor of Medicine, Hematology/Oncology Medical Director, UW Health Cancer Services Committee Chair, UWCCC PRMC
Anne Traynor, MD	Associate Professor of Medicine, Hematology/Oncology Director, Wisconsin Oncology Network (WON) Committee Chair, UWCC DSMC Thoracic Oncology DOWG Leader
Rebecca Marnocha, Pharm. D.	Associate Professor of Pharmacy Director of Clinical Research, UW School of Medicine and Public Health and UW Hospital and Clinics Associate Executive Director of UW Institute of Clinical and Translational Research
KyungMann Kim, Ph.D.	Professor, Biostatistics and Medical Informatics Committee Co-Chair, UWCCC PRMC & DSMC
Kenneth DeSantes, MD	Associate Professor of Medicine, Pediatrics Section Head, Pediatric Oncology Pediatric Oncology DOWG Leader
Paul Harari, M.D.	Professor of Medicine, Human Oncology Department Chair, Human Oncology Head & Neck Oncology DOWG Leader
James F. Cleary, MD	Associate Professor of Medicine, Hematology/Oncology Palliative & Supportive Care DOWG Leader

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Howard Bailey, MD	Professor of Medicine, Hematology/Oncology Chemoprevention Scientific Program Co Leader Chemoprevention DOWG Leader
Herbert Chen, MD	Professor of Surgery Endocrine DOWG Leader
Glenn Liu, MD	Associate Professor of Medicine, Hematology/Oncology GU DOWG Leader Phase I Program Leader
Gary Wood, MD	Professor of Medicine, Dermatology Department Chair, Dermatology Skin/Non-Melanoma DOWG Leader
John Kuo, MD	Assistant Professor, Neurological Surgery Brain Cancer DOWG Leader
Mark Albertini, MD	Associate Professor of Medicine, Hematology/Oncology Melanoma DOWG Leader
Mark Burkard, MD	Assistant Professor of Medicine, Hematology/Oncology Breast DOWG Leader

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**Data and Safety Monitoring Committee Members (11/2011)**

<i>Name</i>	<i>Leadership Role</i>
Anne Traynor, M.D., Chair	Associate Professor of Medicine, Hematology/Oncology Director, Wisconsin Oncology Network Thoracic Oncology DOWG Leader
KyungMann Kim, Ph.D., Co-Chair	Professor, Biostatistics and Medical Informatics  Committee Co-Chair, UWCCC PRMC
Douglas McNeel, M.D., Ph.D.	Associate Professor of Medicine, Hematology/Oncology
Kevin Kozak, M.D.	Assistant Professor, Radiation Oncology
Kenneth DeSantes, M.D.	Associate Professor of Medicine, Pediatrics Section Head, Pediatric Oncology Pediatric Oncology DOWG Leader
Eliot Williams, M.D.	Professor of Medicine, Hematology Oncology
Shari Zeldin, B.S., CCRC	Manager, UWCCC Clinical Research Compliance Office

**APPENDIX II**

**I. PROTOCOL TEMPLATE FOR A DATA AND SAFETY MONITORING PLAN FOR CLINICAL TRIALS THAT DO *NOT* HAVE EXTERNAL DATA AND SAFETY MONITORING BOARD**

*Investigator: Insert information into protocol document.*

**Oversight And Monitoring Plan**

*(Investigator: Insert entire section into your protocol)*

The UWCCC Data and Safety Monitoring Committee (DSMC) is responsible for monitoring data quality and subject safety for all UWCCC clinical studies. A summary of DSMC activities follows:

- Review of all clinical trials conducted at the UWCCC for data integrity and safety
- Review of all serious adverse events requiring expedited reporting as defined in the protocol
- Review of reports generated by the UWCCC data quality control review process
- Submit recommendations for corrective action to the CRC
- Notify the Study Chair of the DSMC's recommendation to the CRC
- Work in conjunction with the Health Sciences IRB in the review of protocol deviations, violations and unanticipated problems reported by the UWCCC DOWGs.
- The committee ensures that notification is provided to all external sites participating in multiple-institutional clinical trials coordinated by the UWCCC of serious adverse events requiring expedited reporting.

**Monitoring And Reporting Guidelines**

*(Investigator: Insert the appropriate section that applies to your clinical trial into your document and delete all others)*

**Phase I Trials**

Investigators will conduct continuous review of data and subject safety at their weekly Phase I/Disease Group meetings where the results of each subject's treatment are discussed and the discussion is documented in the minutes. The discussion will include for each dose level: the number of subjects, significant toxicities as described in the protocol, doses adjustments, and responses observed. Quarterly, Protocol Summary Reports (PRS) are required for submission to the Data and Safety Monitoring Committee for review.

**Phase I/II and Phase II Trials**

Data related to these trials are discussed at regularly scheduled Disease Oriented Working Group meetings where the result of each subject's treatment is discussed and the discussion is documented in the minutes. The discussion will include for each treatment arm/dose level,

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the number of subjects, significant toxicities as described in the protocol, dose adjustments, and responses observed. Twice yearly, Protocol Summary Reports are required for submission to the Data and Safety Monitoring Committee for review.

**Behavioral and Nutritional Studies**

These trials must have a Data and Safety Monitoring Plan commensurate with the level of risk to the participants and approved by the Protocol Review and Monitoring Committee. Frequency of Protocol Summary Reports to be submitted to the UWCCC DSMC for review is stated in the UWCCC Protocol Review and Monitoring (PRMC) protocol approval letter.

**I. REVIEW AND OVERSIGHT REQUIREMENTS**

*(Investigator: Insert entire section into your protocol)*

**a) Serious Adverse Event – Reported Within 24 Hours**

Serious Adverse Events requiring reporting within 24 hours (as described in the protocol) must also be reported to the Data and Safety Monitoring Committee (DSMC) Chair via an email to [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu) within one business day. A 24 hr. initial “SAE Details” Report, generated in the UWCCC database, must be attached to the email along with any pertinent information available at the time of initial reporting. The DSMC Chair will review the information and determine if immediate action is required. Within 10 working days, all subsequent SAE documentation must be submitted electronically along with a 24 hour follow-up “SAE Details” Report and a completed UWCCC SAE Routing Form to [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu). All information is entered and tracked in the UWCCC database.

If the SAE occurs on a multiple-institutional clinical trial coordinated by the UWCCC, the Outreach Coordinator will ensure that all participating sites are notified of the event and resulting action within one working day of the determination.

See Section [III] for detailed instructions on SAE reporting.

**b) Serious Adverse Event – Reported within 10 Days**

Serious Adverse Events requiring reporting within 10 working days (as described in the protocol) will also be sent to the UWCCC DSMC Chair via email to [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu). A 10 day “SAE Details” report, generated in the UWCCC database must be attached to the email along with pertinent information regarding the SAE and the UWCCC SAE Routing Form. The Committee Chair will review the information and determine if further action is required. This information is entered and tracked in the UWCCC database.

If the SAE occurs on a multiple-institutional clinical trial coordinated by the UWCCC, the Outreach Coordinator will ensure that all participating sites are notified of the event and resulting action within one working day of the determination.

See Section [III] for detailed instructions on SAE reporting.

c) **Study Progress Review**

**Study Progress Review- Protocol Summary Reports**

Protocol Summary Reports (PSR) are required to be submitted to the DSMC commensurate with the Phase of the study. The PSR provides a cumulative report of serious adverse events, as well as any protocol violations, deviations or unanticipated problems, toxicities and responses that have occurred on the protocol in the timeframe specified. PSRs are reviewed at each DSMC meeting.

Protocol Summary Reports enable DSMC committee members to assess whether significant benefits or risks are occurring that would warrant study closure. This information is also provided by Disease Oriented Working Group meeting minutes, internal audit and/or response review reports. In addition, the DSMC requires the DOWG or protocol Study Chair to submit external DSMB reports or any other significant study-related information.

In the event that there is significant risk warranting study suspension or closure, the DSMC will notify the PI of the DSMC findings. The DSMC ensures that the PI reports any temporary or permanent suspension of a clinical trial to the sponsor (e.g., NCI Program Director, Industry Sponsor Medical Monitor, Cooperative Group Study Chair, etc.) and other appropriate agencies.

**II. EXPEDITED REPORTING OF SERIOUS ADVERSE EVENTS**

*(Investigator: Insert entire section into your protocol)*

Depending on the nature, severity, and attribution of the serious adverse event an SAE report will be phoned in, submitted in writing, or both according to Table [A, B, C, D, etc] below. All serious adverse events must also be reported to the UWCCC Data and Safety Monitoring Committee Chair. All serious adverse events must also be reported to the UW IRB (if applicable), and any sponsor/funding agency not already included in the list.

Determine the reporting time line for the SAE in question by using the following table. Then refer to sections A and B below if the SAE occurred at the UWCCC or sections C and D if the SAE occurred at 1 South Park, Johnson Creek, or a WON Site.

*[Investigator: Insert appropriate Expedited Reporting Table here. These tables are located at the end of this Appendix II of the DSMP]*

**A. SAE Requiring 24 Hour Reporting Occurs at UWCCC:**

**a. To the [FDA or NCI]:**

*[Select appropriate reporting requirement below and remove bracketed language and remaining requirements]*

Report the SAE using the online FDA Med Watch form available at

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<https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>. Also print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for voluntary reporting to the FDA, when no IND is involved]*

Report the SAE using the FDA Med Watch form available at

<http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM082728.pdf> .

Print the completed Med Watch form and fax it to (800) 332-0178.

*[for mandatory reporting to the FDA when an IND is involved]*

Report the SAE using the online AdEERS form available at

[https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers\\_main\\$.startup](https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers_main$.startup). Also print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for reporting to the NCI]*

**b. To the Sponsor:**

*[Insert specific sponsor reporting instructions, if applicable. Can remove section b if sponsor notification is not required]*

**c. To the IRB:**

Consult the UW-IRB website for reporting guidelines.

**d. To the UWCCC:**

Reference the **SAE SOP** (Standard Operating Procedure) and the **SAE Reporting Workflow for DOWGs** on the UWCCC website (<http://www.uwccc.wisc.edu>) for specific instructions on how and what to report to the UWCCC for [24] hour initial and follow-up reports. **A follow-up report is required to be submitted within 10 days of the initial [24] hour report.**

For this protocol, the following entities are required to be notified:

1. [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu)
2. Any other appropriate parties listed on the SAE Routing Form (for follow-up reports only)
3. *[optional: other entities or individuals, as needed]*

**B. SAE Requiring [10] Day Reporting Occurs at UWCCC:**

**a. To the [FDA or NCI]:**

*[Select appropriate reporting requirement below and remove bracketed language and remaining requirements]*

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Report the SAE using the online FDA Med Watch form available at <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>. Also print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for voluntary reporting to the FDA, when no IND is involved]*

Report the SAE using the FDA Med Watch form available at <http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM082728.pdf>.

Print the completed Med Watch form and fax it to (800) 332-0178.

*[for mandatory reporting to the FDA when an IND is involved]*

Report the SAE using the online ADEERS form available at [https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers\\_main\\$.startup](https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers_main$.startup). Also print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for reporting to the NCI]*

**b. To the Sponsor:**

*[DOWG insert specific sponsor reporting instructions, if applicable. Can remove section b if sponsor notification is not required]*

**c. To the IRB:**

Consult the UW-IRB website for reporting guidelines.

**d. To the UWCCC:**

Reference the **SAE SOP** and the **SAE Reporting Workflow for DOWGs** on the UWCCC website (<http://www.uwccc.wisc.edu>) for specific instructions on how and what to report to the UWCCC for [10] day reports.

For this protocol, the following entities are required to be notified:

1. [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu)
2. Any appropriate parties listed on SAE Routing Form
3. *[optional: other entities or individuals, as needed]*

**C. SAE Requiring 24 hour reporting Occurs at 1 South Park (1SP), Johnson Creek (JC), or a WON Site:**

**a. To the [FDA or NCI]:**

*[Select appropriate reporting requirement below and remove bracketed language and remaining requirements]*

Report the SAE using the online [FDA Med Watch, ADEERS] form available at

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<https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>. Print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for voluntary reporting to the FDA, when no IND is involved]*

Report the SAE using the FDA Med Watch form available at

<http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM082728.pdf> .

Print the completed Med Watch form and fax it to (800) 332-0178.

*[for mandatory reporting to the FDA when an IND is involved]*

Report the SAE using the online AdEERS form available at

[https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers\\_main\\$.startup](https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers_main$.startup). Print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for reporting to the NCI]*

**b. To the Sponsor:**

*[Insert specific sponsor reporting instructions, if applicable. Can remove section b if sponsor notification is not required]*

**c. To the IRB:**

WON sites should follow their local IRB reporting guidelines for SAE submission. The UWCCC is responsible for the submission of the SAE to the UW IRB.

**d. To the UWCCC:**

Reference the **SAE SOP** and the **SAE Reporting Workflow for ISP, JC, and other Affiliates** on the UWCCC website (<http://www.uwccc.wisc.edu>) for specific instructions on how and what to report to the UWCCC for [24] hour initial and follow-up reports. **A follow-up report is required to be submitted within 10 days of the initial [24] hour report.**

For this protocol, the following entities are required to be notified:

1. [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu) (for initial reports only)
2. [affiliatecoordinators@uwcarbone.wisc.edu](mailto:affiliatecoordinators@uwcarbone.wisc.edu)
3. *[required: UWCCC Program Manager's email address]*
4. *[required: UWCCC Study PI's email address]*
5. *[optional: other entities or individuals, as needed]*

**NOTE:** After ISP, JC, or a WON site has submitted the [24] hour SAE follow-up report, the UWCCC Program Manager is responsible for completing the UWCCC SAE Routing Form

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(available on the UWCCC website) and forwarding the Routing Form and submitted SAE report to [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu), [affiliatecoordinators@uwcarbone.wisc.edu](mailto:affiliatecoordinators@uwcarbone.wisc.edu), and any appropriate parties identified on the SAE Routing Form. The Program Manager also submits the SAE to the UW-IRB if required.

**D. SAE Requiring [10] Day Reporting Occurs at 1 South Park (1SP), Johnson Creek (JC), or a WON Site:**

**a. To the [FDA or NCI]:**

*[Select appropriate reporting requirement below and remove bracketed language and remaining requirements]*

Report the SAE using the online [FDA Med Watch, ADEERS] form available at <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>. Print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for voluntary reporting to the FDA, when no IND is involved]*

Report the SAE using the FDA Med Watch form available at <http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM082728.pdf>.

Print the completed Med Watch form and fax it to (800) 332-0178.

*[for mandatory reporting to the FDA when an IND is involved]*

Report the SAE using the online ADEERS form available at [https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers\\_main\\$.startup](https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers_main$.startup). Print the report or save it as a pdf for reporting to the [sponsor (see section B) and] UWCCC (see section d).

*[for reporting to the NCI]*

**b. To the Sponsor:**

*[Insert specific sponsor reporting instructions, if applicable. Can remove section b if sponsor notification is not required]*

**c. To the IRB:**

The UWCCC is responsible for the submission of the SAE to the UW IRB. WON sites should follow their local IRB reporting guidelines for SAE submission.

**d. To the UWCCC:**

Reference the **SAE SOP** and the **SAE Reporting Workflow for 1SP, JC, and other Affiliates** on the UWCCC website (<http://www.uwccc.wisc.edu>) for specific instructions on how and what to report to the UWCCC for [10] day reports. For this protocol, the following entities are required to be notified:

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1. [affiliatecoordinators@uwcarbone.wisc.edu](mailto:affiliatecoordinators@uwcarbone.wisc.edu)
2. *[required: UWCCC Program Manager's email address]*
3. *[required: UWCCC Study PI's email address]*
4. *[optional: other entities or individuals, as needed]*

**NOTE:** After 1SP, JC, or a WON site has submitted the [10] day SAE report, The UWCCC Program Manager is responsible for completing the UWCCC SAE Routing Form and forwarding the Routing Form and submitted SAE report to [saenotify@uwcarbone.wisc.edu](mailto:saenotify@uwcarbone.wisc.edu), [affiliatecoordinators@uwcarbone.wisc.edu](mailto:affiliatecoordinators@uwcarbone.wisc.edu), and any appropriate parties identified on the SAE Routing Form. The Program Manager also submits the SAE to the UW-IRB if required.

**EXPEDITED REPORTING TABLES**

**Legacy tables for studies activated prior to March 28, 2011**

*(Investigator: As indicated above, choose the appropriate Reporting Table from the following tables and insert into your protocol document)*

<i>Category</i>	<i>Applicable Table</i>
NCI Holds IND	Tables A-I – A-III
Other Holds IND	Tables B-I – B-II
No IND	Table C
Cancer Vaccine Trials	Table D

**Pending revised reporting tables, per 3/28/11 FDA ruling**

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<b>TABLE A-I-1</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Supported By Grant Or Contract Where NCI Holds IND (See Table A-II for DNA Molecules – Gene Transfer)			
<b>EXPEDITED REPORTING FOR PHASE I STUDIES</b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 – 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>
<p><i>Grade 2</i> - Expedited report within 10 working days to IDB.</p> <p><i>Grade 3</i> - Report by phone to IDB within 24 hrs. Expedited report to follow within 10 working days.</p> <p>(<i>Grade 1</i> - Adverse Event Expedited Reporting NOT required.)</p>	<p>Report by phone to IDB within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p>	<p>Adverse Event Expedited Reporting NOT required.</p>	<p>Report by phone to IDB within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p>

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

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<b>TABLE A-I-2</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Supported By Grant Or Contract Where NCI Holds IND (See Table A-II for DNA Molecules – Gene Transfer)			
<b><i>EXPEDITED REPORTING FOR PHASE II AND PHASE III STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
Expedited report within 10 working days to IDB.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)	Report by phone to IDB within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.	Adverse Event Expedited Reporting NOT required.	Expedited report, including grade 5 Aplasia in leukemia subjects, within 10 working days.  Report by phone to IDB within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.  Grade 4 Myelosuppression or other Grade 4 events that do not require expedited reporting will be specified in the protocol.

**IDB = Investigational Drug Branch**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

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<b>TABLE A-II-1</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Involving DNA Molecules Or Gene Transfer Supported By Grant Or Contract Where NCI Holds IND			
<i>EXPEDITED REPORTING FOR PHASE I STUDIES</i>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
Grade 2 - Expedited report within 10 working days to IDB/OBA.  Grade 3 - Report by phone to IDB/OBA within 24 hrs. Expedited report to follow within 10 working days.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)	Report by phone to IDB/OBA within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.	Adverse Event Expedited Reporting NOT required.	Report by phone to IDB/OBA within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.

**IDB = Investigational Drug Branch    OBA = Office of Biotechnology Activities**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

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<b>TABLE A-II-2</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Involving DNA Molecules Or Gene Transfer Supported By Grant Or Contract Where NCI Holds IND			
<i><b>EXPEDITED REPORTING FOR PHASE II AND PHASE III STUDIES</b></i>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
<p>Expedited report within 10 working days to IDB/OBA.</p> <p>(Grade 1 - Adverse Event Expedited Reporting NOT required.)</p>	<p>Report by phone to IDB/OBA within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p>	<p>Adverse Event Expedited Reporting NOT required.</p>	<p>Expedited report, including grade 5 Aplasia in leukemia subjects, within 10 working days.</p> <p>Report by phone to IDB/OBA within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p> <p>Grade 4 Myelosuppression or other Grade 4 events that do not require expedited reporting will be specified in the protocol.</p>

**IDB = Investigational Drug Branch    OBA = Office of Biotechnology Activities**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

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<b>TABLE A-III-1</b>			
Summary Of Reporting Requirements For Adverse Events On Cooperative Group Trials Where NCI Holds IND			
<b><i>EXPEDITED REPORTING FOR PHASE I STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
Grade 2 - Expedited report within 10 working days to IDB/CG.  Grade 3 - Report by phone to IDB/CG within 24 hrs. Expedited report to follow within 10 working days.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)	Report by phone to IDB/CG within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.	Adverse Event Expedited Reporting NOT required.	Report by phone to IDB/CG within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.

**IDB = Investigational Drug Branch CG= Cooperative Group**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

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<b>TABLE A-III-2</b>			
Summary Of Reporting Requirements For Adverse Events On Cooperative Group Trials Where NCI Holds IND			
<b><i>EXPEDITED REPORTING FOR PHASE II AND PHASE III STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
<p>Expedited report within 10 working days to IDB/CG.</p> <p>(Grade 1 - Adverse Event Expedited Reporting NOT required.)</p>	<p>Report by phone to IDB/CG within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p>	<p>Adverse Event Expedited Reporting NOT required.</p>	<p>Expedited report, including grade 5 Aplasia in leukemia subjects, within 10 working days.</p> <p>Report by phone to IDB/CG within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p> <p>Grade 4 Myelosuppression or other Grade 4 events that do not require expedited reporting will be specified in the protocol.</p>

**IDB = Investigational Drug Branch    CG = Cooperative Group**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade

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3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

<b>TABLE B-I-1</b>			
Summary Of Reporting Requirements For Adverse Events On Industry Trials Where A Corporate Sponsor Holds IND			
<b><i>EXPEDITED REPORTING FOR PHASE I STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
Grade 2 - Expedited report within 10 working days to CS.  Grade 3 - Report by phone to CS within 24 hrs. Expedited report to follow within 10 working days.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)	Report by phone to CS within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.	Adverse Event Expedited Reporting NOT required.	Report by phone to CS within 24 hrs. Expedited report to follow within 10 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.

**CS = Corporate Sponsor**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

**POLICY & PROCEDURES FOR DATA AND SAFETY MONITORING**

<b>TABLE B-I-2</b>			
Summary Of Reporting Requirements For Adverse Events On Industry Trials Where A Corporate Sponsor Holds IND			
<b><i>EXPEDITED REPORTING FOR PHASE II AND PHASE III STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
<p>Expedited report within 10 working days to CS.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)</p>	<p>Report by phone to CS within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p>	<p>Adverse Event Expedited Reporting NOT required.</p>	<p>Expedited report, including grade 5 Aplasia in leukemia subjects, within 10 working days.</p> <p>Report by phone to CS within 24 hrs. Expedited report to follow within 10 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.</p> <p>Grade 4 Myelosuppression or other Grade 4 events that do not require expedited reporting will be specified in the protocol.</p>

**CS = Corporate Sponsor**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

POLICY & PROCEDURES FOR DATA AND SAFETY MONITORING

<b>TABLE B-II-1</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Where The Investigator Holds IND			
<b><i>EXPEDITED REPORTING FOR PHASE I STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
Grade 2 - Expedited report within 15 working days to FDA.  Grade 3 - Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)	Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.	Adverse Event Expedited Reporting NOT required.	Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

POLICY & PROCEDURES FOR DATA AND SAFETY MONITORING

<b>TABLE B-II-2</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Where The Investigator Holds IND			
<b><i>EXPEDITED REPORTING FOR PHASE II AND PHASE III STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
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**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

**POLICY & PROCEDURES FOR DATA AND SAFETY MONITORING**

<b>TABLE C-1</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Involving Commercial Agents With No IND Is Voluntary (Med Watch Form)			
<b><i>EXPEDITED REPORTING FOR PHASE I STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
Grade 2 - Expedited report within 15 working days to FDA.  Grade 3 - Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)	Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.	Adverse Event Expedited Reporting NOT required.	Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.

**NOTE: Use Med Watch Form**

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

**POLICY & PROCEDURES FOR DATA AND SAFETY MONITORING**

<b>TABLE C-2</b>			
Summary Of Reporting Requirements For Adverse Events On Trials Involving Commercial Agents With No IND Is Voluntary (Med Watch Form)			
<b><i>EXPEDITED REPORTING FOR PHASE II AND PHASE III STUDIES</i></b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
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**Note: Use Med Watch Form**

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Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

**POLICY & PROCEDURES FOR DATA AND SAFETY MONITORING**

<b>TABLE D-1</b>			
Summary Of Reporting Requirements For Adverse Events On Cancer Vaccine Trials			
<i>NOTE: Until further guidelines are established, any AE occurring subsequent to administration of a cancer vaccine will be reported to the FDA using the VADERS system according to the tables below.</i>			
<b>EXPEDITED REPORTING FOR PHASE I STUDIES</b>			
<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
Grade 2 - Expedited report within 15 working days to FDA.  Grade 3 - Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  (Grade 1 - Adverse Event Expedited Reporting NOT required.)	Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.	Adverse Event Expedited Reporting NOT required.	Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.  This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.  Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.

**For Hospitalization Only** – Any medical event equivalent to the CTC Grade 3,4,5 which precipitated hospitalization (or prolongation of existing hospitalization) must be reported regardless of requirements for phase of study, expected or unexpected and attribution.

Expedited reporting may not be appropriate for specific expected adverse events for certain later phase 2 and phase 3 protocols. In those situations the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. An expected Grade 3 event that is using the generic reporting criteria, for instance. In a trial of investigational agents where grade 3 diarrhea requiring hospitalization is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

**POLICY & PROCEDURES FOR DATA AND SAFETY MONITORING**

**TABLE D-2**

**Summary Of Reporting Requirements For Adverse Events On Cancer Vaccine Trials**

*NOTE: Until further guidelines are established, any AE occurring subsequent to administration of a cancer vaccine will be reported to the FDA using the VADERS system according to the tables below.*

**EXPEDITED REPORTING FOR PHASE II AND PHASE III STUDIES**

<b>Unexpected Event</b>		<b>Expected Event</b>	
<b>GRADES 2 - 3 Attribution of Possible, Probable, or Definite</b>	<b>GRADES 4 and 5 Regardless of Attribution</b>	<b>GRADES 1 - 3</b>	<b>GRADES 4 and 5, Regardless of Attribution</b>
<p>Expedited report within 15 working days to FDA.</p> <p>(Grade 1 - Adverse Event Expedited Reporting NOT required.)</p>	<p>Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.</p>	<p>Adverse Event Expedited Reporting NOT required.</p>	<p>Expedited report, including grade 5 Aplasia in leukemia subjects, within 10 working days.</p> <p>Report by phone to FDA within 24 hrs. Expedited report to follow within 15 working days.</p> <p>This includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution.</p> <p>Any late death attributed to the agent (possible, probable, or definite) should be reported within 15 working days.</p> <p>Grade 4 Myelosuppression or other Grade 4 events that do not require expedited reporting will be specified in the protocol.</p>

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**APPENDIX III**

**GUIDELINES FOR ESTABLISHING AND OPERATING AN EXTERNAL DSMB**

**1. Membership**

- a) Monitoring activities should be conducted by experts in all scientific disciplines needed to interpret the data and ensure subject safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted.
- b) Voting members may be from within or outside the institution, but the majority should not be affiliated with the institution. Members should view themselves as representing the interest of subjects and not that of the institutions. Investigators directly involved with the conceptual design or analysis of the particular trial are not eligible to serve on the DSMB.

**2. Meeting Procedures**

- a) Frequency
  - (1) DSMB meetings will be held at least annually and more often depending on the nature and progress of the trial being monitored.
- b) Elements for Review
  - (1) A written summary of status, toxicity and outcome of the clinical trial will be prepared by the clinical trial statistician. The summary will be submitted to DSMB members allowing sufficient review time prior to meeting.
  - (2) This summary will also address specific toxicity concerns as well as concerns about the conduct of the trial. It may contain recommendations for consideration by the DSMB concerning whether to close the trial, report the results, or continue accrual or follow-up.
- c) Meeting Structure DSMB

Meetings will be divided into three sessions as follows:

- (1) **Open Session** – members of the clinical trial team present review of the trial conduct and answer questions from DSMB members. Focus is on accrual, protocol compliance, and general toxicity.
- (2) **Closed Session** – Includes DSMB members and the clinical trial statistician(s). The statistician presents and discusses outcome results with DSMB.

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- (3) **Executive Session** – DSMB members only discuss the general conduct of trial, all outcome results including toxicities as described in the protocol, all adverse events and develop recommendations.

**3. Recommendations**

- a) It is the responsibility of the Study Chair, the clinical trial statistician(s), and individual DSMB members to ensure that the DSMB is kept apprised of non-confidential results from other related studies that became available, and any programmatic concerns related to the clinical trial being monitored. It is the responsibility of the DSMB to determine the extent to which this information is relevant to its decisions related to the specific trial.
- b) DSMB recommendations will be given to the Study Chair and the sponsor. The DSMB must provide an adequate rationale for recommendation made to change the trial for other than safety or efficacy reasons or for slow accrual.
- c) The Study Chair is responsible to implement the change recommended by the DSMB as expeditiously as possible.
- d) The sponsor must be informed of the reason for disagreement in the unlikely situation that the Study Chair does not agree with the DSMB recommendation.
- e) The sponsor, DSMB Chair, and Study Chair will be responsible for reaching a mutually acceptable decision about the study.

**4. Release of Outcome Data**

- a) In general, outcome data should not be made available to individuals outside of the DSMB until accrual has been completed and all subjects have completed their treatment.
- b) The DSMB may approve the release of outcome data on confidential basis to the Study Chair for planning the preparation of manuscripts and/or to a small number of others for future trial planning purposes.
- c) Any release of outcome data prior to the DSMB recommendation for general dissemination of results must be reviewed and approved by the DSMB

**5. Confidentiality**

- a) No communication, either written or verbal, of the deliberations or recommendations of the DSMB will be made outside of the DSMB.
- b) Outcome results are strictly confidential and must not be divulged to any non-member, except as indicated above in Recommendations, until the recommendation to release the results are accepted and implemented.

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- c) Each member of the DSMB, including non-voting members, must sign a statement of confidentiality.

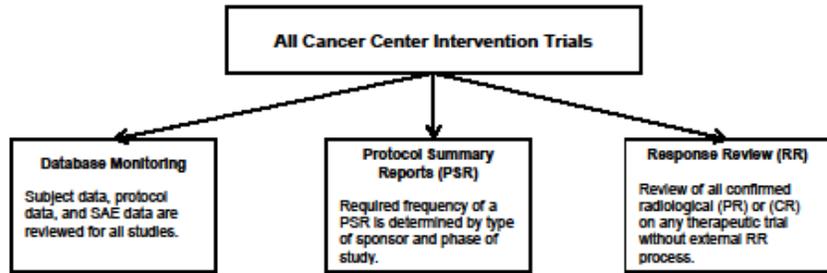
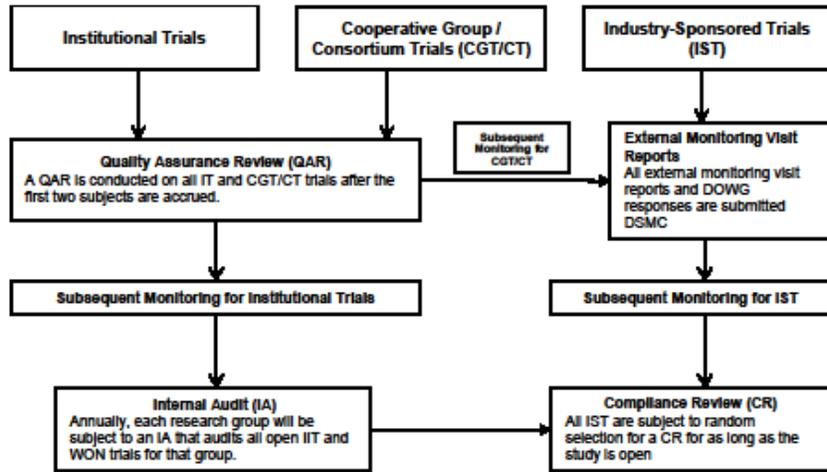
**6. Conflict of Interest**

- a) DSMB members are subject to the UW policies regarding standards of conduct.
- b) Individuals invited to serve on the DSMB (voting or non-voting) will disclose any potential conflicts of interest, whether real or perceived, to the Study Chair and the appropriate institutional officials, in accordance with the UW Conflict of Interest Policies. Conflict of interest can include professional interest, proprietary interest, and miscellaneous interest as described in the NIH Grants Policy Statement, Page II-12, and 45 CFR Part 94.
- c) Decision concerning whether individuals with potential conflicts of interest or the appearance of conflicts of interest may participate in the DSMB will be made in accordance with the UW Conflict of Interest Policies.
- d) Potential conflicts, which develop during a member's tenure on a DSMB, must also be disclosed and addressed in accordance with the UW Conflict of Interest Policies.

**APPENDIX IV**

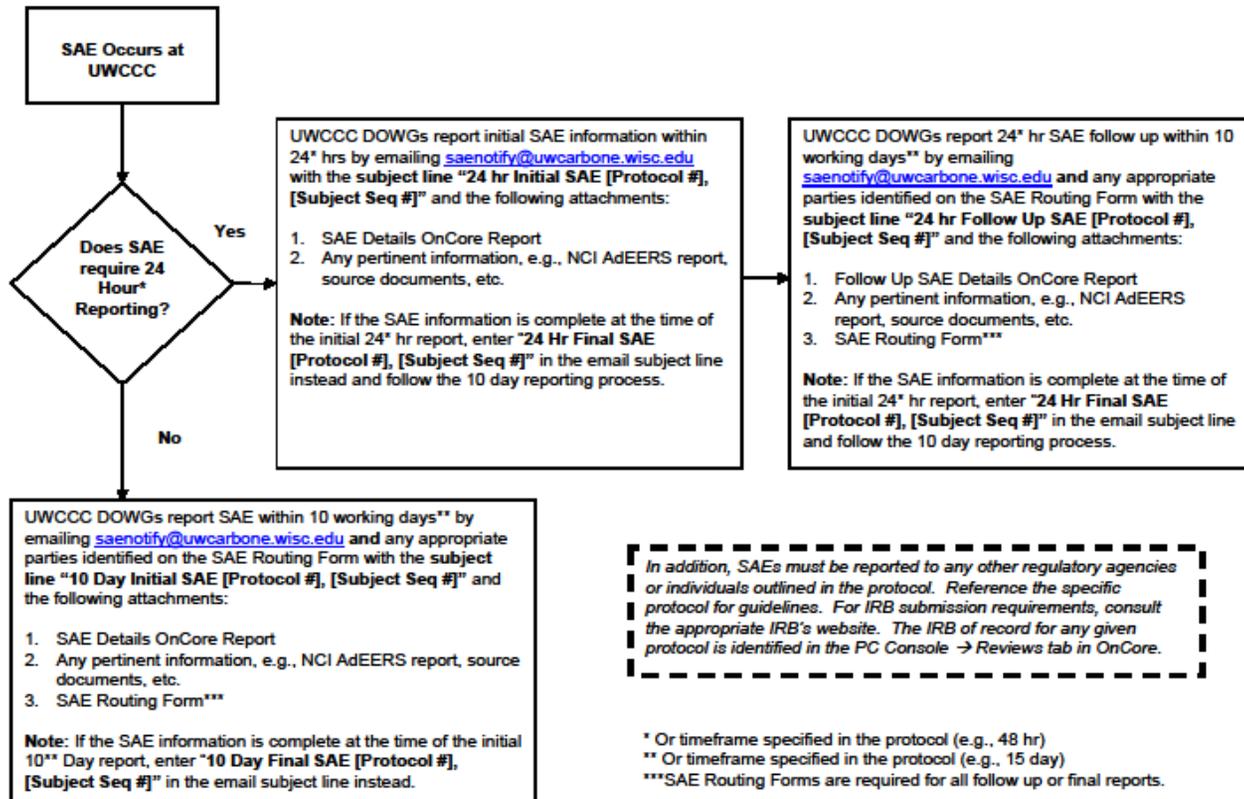
**UWCCC Monitoring Flow Chart**

**UWCCC Quality Assurance and Monitoring for Intervention Trials**



**APPENDIX V**

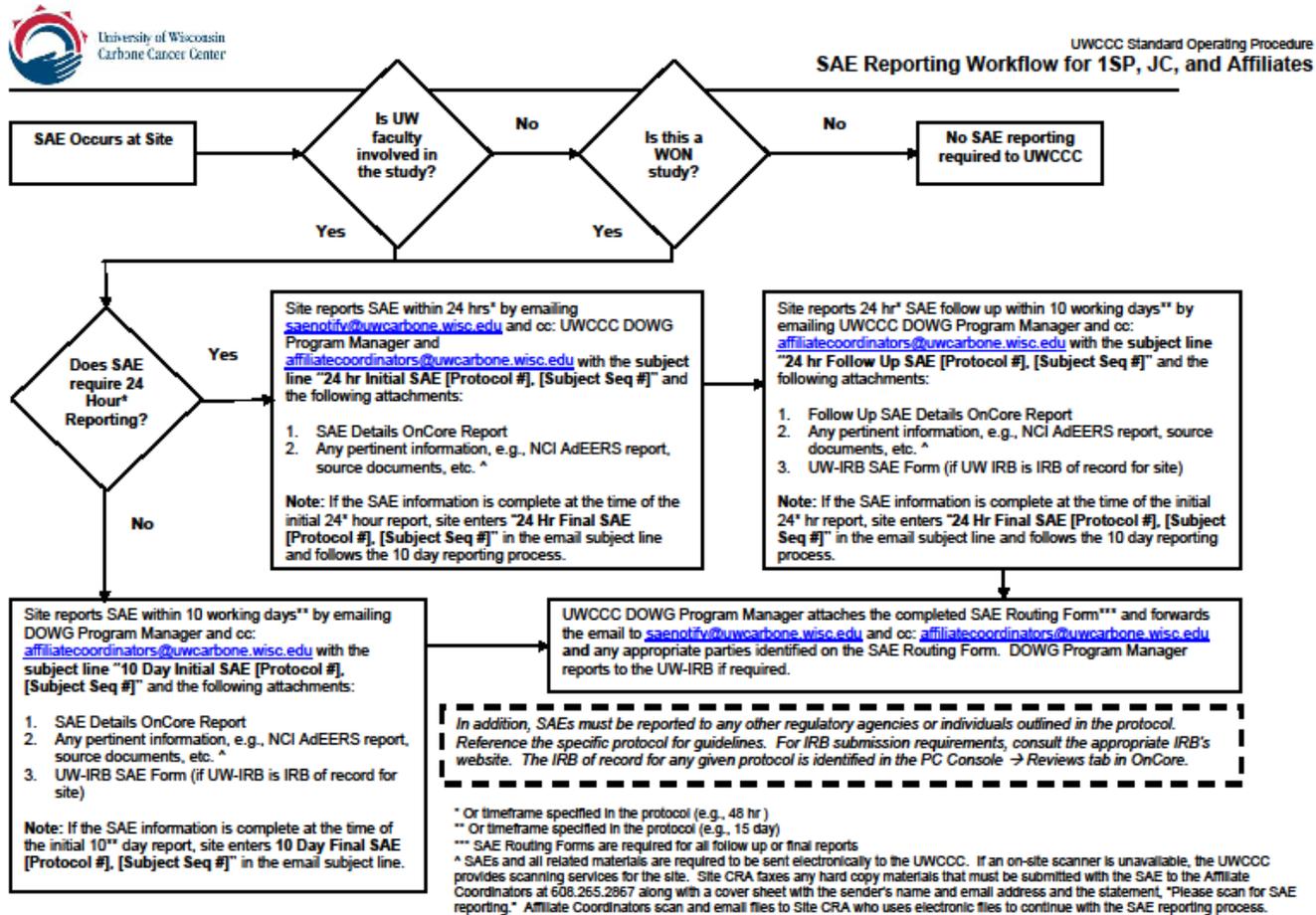
**SAE Reporting Work Flow for UWCCC Disease Oriented Working Groups (DOWGs)**



University of Wisconsin Comprehensive Cancer Center (UWCCC)  
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**APPENDIX VI**

**SAE Reporting Work Flow for UWCCC Affiliate Sites**



6.7.10 SAE Reporting Workflow\_1SP\_JC\_Affiliates.doc  
 Implementation Date: 6.8.10

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**APPENDIX VII**

**UWCCC Data and Safety Monitoring System Elements**

Sponsor Type	Intervention Trials			Non-Intervention Trials	
	Therapeutic, Supportive Care, Prevention Protocols			Physical Procedures	Non-Physical Procedures
	Institutional	Federal	Industry	All Sponsors	All Sponsors
<b>DSMS Monitoring Functions</b>					
Internal Audit (IA)	X				
Quality Assurance Review (QAR)	X	X			
Response Review (RR)	X				
Compliance Review (CR)			X	X	X
<b>Reports for DSMC Review</b>					
IA, QAR, RR Reports	X	X			
CR Reports			X	X	X
Protocol Summary Report (PSR)	X	X	X		
Serious Adverse Events (SAEs)	X	X	X	X	
Deviations, Non-Compliance, Unanticipated Problems	X	X	X	X	X
External Monitor/Audit Reports		X	X		
External DSMB/DSMC Reports		X	X		
<b>Database Quality Control Measures</b>					
Subject Data	X	X	X		
Protocol Data	X	X	X	X	X
SAE Data	X	X	X		