DATA AND SAFETY MONITORING PLAN

Ensuring Patient Safety and the Validity and Integrity of Clinical Research Data

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Table of Contents

Data and Safety Monitoring Plan for Clinical Trials

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Summary

The University of Hawai‘i Cancer Center (UH Cancer Center) places the highest priority on ensuring the safety of human subjects participating in clinical trials. A **clinical trial** is defined as a prospective study involving human subjects designed to answer questions about the effects of biomedical or behavioral **interventions**; this may include drugs, other treatments, devices, and nutritional and behavioral strategies. Participants in clinical trials may be cancer patients, persons without a diagnosis of cancer but at an increased risk of developing it, or healthy volunteers. Studies in human subjects where there is **no intervention**, such as observational studies, are not considered within the definition of a clinical trial and are not reviewed under the Data and Safety Monitoring Plan (DSMP).

All cancer clinical trials conducted by the UH Cancer Center including its hospital partners of the State of Hawai‘i Cancer Consortium (HCC) - together referred to as the Center, must include a plan for safety and data monitoring. This includes trials where a Center faculty member is the Principal Investigator (PI) or where Center (including HCC hospital) resources are utilized. As a participating institution in multi-institution trials generated and coordinated by another organization such as an NCI cooperative group, the UH Cancer Center will comply with all data and safety monitoring requirements of the coordinating organization.

The Data and Safety Monitoring Committee (DSMC) is the dedicated data and safety monitoring committee for the Center. It communicates with the **Protocol Review and Monitoring Committee (PRMC),** which oversees the Center’s protocol review and monitoring system, and is responsible for the **scientific quality** of all clinical trials conducted through the Center. The DSMC also communicates with the **Institutional Review Board (IRB)** who protects the rights and welfare of the research subjects. The DSMC is comprised of practicing oncology physicians and research faculty representing partner institutions, at least one of whom is a biostatistician, a quality assurance compliance officer, and a clinical research nurse. The DSMC Chair and all committee members are appointed by the Director of the UH Cancer Center, in consultation with the HCC Advisory Board. Appointments to the committee will be made for one year and reviewed annually. Consecutive reappointments will be permitted. Members must recuse themselves from review where they are seen to have a conflict of interest and/or perceived to personally gain from the research.

The DSMC oversees the monitoring described in this Plan and assures compliance with procedures. The Compliance Office will conduct study audits and forward their audit findings to the DSMC for review to assure compliance with protocol and data and safety monitoring procedures.

At the initiation of a study, the PI is required to send to the DSMC chair the proposed data and safety monitoring plan of the clinical trial. This review is part of the overall approval process of the protocol by the PRMC. The DSMC meets every quarter to review Data and Safety Monitoring (DSM) reports, new DSM plans, local serious adverse events (SAE) summaries, new policies or developments related to safety monitoring, and completed audits. In addition, the DSMC Chair reviews DSMP’s of new protocols upon receipt and all SAE and protocol violations reported. The Chair can convene ad hoc meetings or request that select members review DSMP’s and local SAE reports at any time.

All local, investigator-generated and coordinated clinical trials are required to have specific data and

safety monitoring procedures. The development of protocol monitoring procedures and reporting requirements are dependent upon the study sponsor, the nature of the investigational agent, and the phase of trial. In general, the **frequency** of monitoring and audits depends upon the degree of risk to subjects, size and complexity of the clinical trial, the nature of the study, the progress of enrollment, and any special considerations described by the protocol.

Local, investigator-generated **Phase I & II** protocols will require monitoring by the PI of the study with reports submitted to the Center's DSMC which closely monitors all reported adverse events to identify intervention-related toxicities and emerging patterns.

Local, investigator-generated randomized Phase III clinical trials will be monitored by protocol-specific **Data and Safety Monitoring Boards (DSMB's)**. The PI will submit annual data and safety monitoring reports which have been generated by the study DSMB to the DSMC, the designated IRB, and the study sponsor (e.g., National Cancer Institute (NCI)/National Institutes of Health (NIH) Program Director responsible for the grant). Reports will summarize study safety experience and efficacy over the past year. Note that NIH no longer requires low-risk nutritional and behavioral interventions to have a DSMB. However, all clinical trials are required to have a data and safety monitoring plan.

The **components** of data and safety monitoring reports generally include the number of patients entered, number of patients treated, dose level of agent[s] involved, summary of all adverse events reported to date using the current Common Toxicity Criteria Adverse Events (CTCAE) grading, a specific list of adverse events requiring expedited reporting to include **ALL** SAE's, and, on an annual basis or as it arises, significant literature reporting developments that may affect the safety of participants or the ethics of the study.

Although NCI-sponsored cooperative group and Industry-sponsored multi-center clinical trials are monitored for data and safety through cooperative group and Industry mechanisms, all SAE's experienced by Hawai'i subjects on these studies will be reviewed by the DSMC chair to assess risks to protocol participants and assure compliance with reporting requirements, as outlined in the expedited reporting guidelines of the NCI. If, for some reason, a trial is not being centrally monitored or the institution feels that additional monitoring is required, it will be conducted as to the policies for local investigator-generated studies.

All SAE's experienced by patients who are registered on all clinical trials being conducted through the Center will be reported, as outlined in the expedited reporting guidelines of the NCI, by the PI to the study-specific DSMB (**for local, investigator-generated protocols)** and to the DSMC, the study sponsor, the designated IRB and the Food and Drug Administration (FDA), (if applicable). SAE's of externally coordinated protocols will be reported to the monitoring committee of the coordinating site.

A recommendation to **suspend or close** any study because of patient safety concerns due to SAE's attributed to the intervention or an inferior efficacy (of a Phase III study arm) may be made by the PI, the study DSMB or the DSMC. The DSMC may also recommend study closure or suspension for lack of compliance with data and safety monitoring procedures. If there is disagreement, the final authority to suspend or close a study rests with the Director of the UH Cancer Center. Notification of study suspension or closure will be made by the DSMC to the designated IRB, the PRMC and appropriate sponsoring and regulatory agencies. For NCI-funded clinical trials the NCI Program Director responsible for funding the trial will be included in this communication along with , FDA and other sponsor Program Directors, if appropriate. Data and Safety Monitoring activities for each study will continue until all patients have completed their treatment or as stated in the original application.

Acknowledgments

The UH Cancer Center's Data and Safety Monitoring Plan (DSMP) is greatly indebted to efforts of the National Institute of Health, particularly the National Cancer Institute, the National Institute on Aging, and the National Institute of Allergy and Infectious Diseases, whose data and safety monitoring policies and plans formed the basis of this plan. In some cases, text from NCI/NIH policies was directly copied. Additional gratitude is extended to the Ohio State University Comprehensive Cancer Center, the University of Pennsylvania Cancer Center, and the Norris Cotton Cancer Center for sharing their plans with the University of Hawai'i. Nevertheless, we assume all responsibility for the consolidation of plans and its implementation at the UH Cancer Center.

Data and Safety Monitoring Plan for Clinical Trials

Introduction

A clinical trial is defined as a prospective study involving human subjects designed to answer questions about the effects of biomedical or behavioral interventions; this may include drugs, other treatments, devices, and nutritional, psychosocial and behavioral strategies. Participants in clinical trials may be cancer patients and persons without a diagnosis of cancer but at risk for it, or healthy volunteers.

A clinical trial in the area of molecular and imaging diagnostics is a study that uses information from a diagnostic test in a manner that affects medical decision-making and hence the clinical outcome. Imaging studies collecting data on the characteristics of a new diagnostic approach are not considered to be clinical trials and are not reviewed under the DSMP.

Behavioral clinical trials include interventions whose goals are to increase, decrease or eliminate behaviors, improve coping or quality of life among survivors, and reduce the negative effects of treatment.

Studies in human subjects where there is **no intervention**, such as observational studies and surveys that utilize questionnaires, and the collection of physical measurements and specimens, are not considered to be clinical trials and are not reviewed under the DSMP.

The UH Cancer Center places the highest priority on ensuring the safety of human subjects participating in clinical trials. Since the first patient was entered on a cancer center clinical trial on March 22, 1976, studies have undergone cancer center-sponsored data and safety monitoring. All cancer clinical trials conducted by the UH Cancer Center including its hospital partners of the HCC must include a plan for safety and data monitoring. This includes trials where a Center faculty member is the Principal Investigator (PI) or where Center (including HCC hospital) resources are utilized. The extent of monitoring varies by the degree of risk encountered by human subjects on the study, the study sponsor, the type of agent or agents involved, and the phase of the clinical trial.

The Center's DSMP has been developed to coordinate and provide oversight for data and safety monitoring for all clinical trials consistent with the National Institutes of Health Policy for Data and Safety Monitoring dated June 10, 1998 [http://grants.nih.gov/grants/guide/notice-files/not98-084.html], with further guidance issued on June 5, 2000 [http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html], and the NCI policy issued on June 22, 1999 for data and safety monitoring of all trials with special emphasis on randomized Phase III trials by DSMBs [http://deainfo.nci.nih.gov/grantspolicies/datasafety.htm]. The NCI website clarifies that low-risk behavioral and nutritional interventions require a Data and Safety Monitoring plan but do not require a DSMB [http://cancertrials.nci.nih.gov/clinicaltrials/conducting/dsm-guidelines/page2].

All Center trials receive data and safety monitoring through the mechanisms described below. The UH Cancer Center's DSMC oversees this process. The DSMC Chair reviews all data and safety monitoring reports, including SAEs, protocol violations and DSMPs of new protocols upon receipt. The Chair can call a full meeting of DSMC to address any issues or concerns at any time. In addition, every quarter the DSMC meets to review DSM reports and plans, as well as the data and safety

monitoring process at the Center. The DSMC communicates to the PRMC any actions taken as a result of patient safety issues and compliance with data and safety monitoring procedures.

Infrastructure support for clinical trials comes largely from the Center's Clinical Trials Unit (CTU). The Center's CTU provides a team of clinical research associates for monitoring clinical trials of drugs and other interventions that are conducted through a network of our consortium hospitals, community hospitals, private physician offices, and the UH Cancer Center outpatient clinic. Principal Investigators of locally generated and coordinated clinical trials use the CTU for study support as appropriate for the study type. Studies of behavioral and nutritional interventions may use specialized staff rather than the CTU for trial support.

For local investigator-generated and coordinated trials, the study PI is responsible for submitting a DSMP and SAE reports to the DSMC, or to the protocol-specific DSMB. The PI ensures that copies of these reports are also sent to the designated IRB, the study sponsor (NCI/NIH Program Director responsible for the grant), and the FDA (if applicable).

LOW-RISK BEHAVIORAL AND NUTRITIONAL INTERVENTIONS

As noted previously, the NIH no longer requires low-risk nutritional and behavioral interventions to have a DSMB. However, all clinical trials are required to have a Data and Safety Monitoring plan. For low-risk nutritional and behavioral interventions, the DSMC Chair may review protocols before the PRMC, and can seek consultation with another DSMC member, e.g., a behavioral researcher. These studies will not need auditing.

The NCI provides general guidelines for Data and Safety Monitoring. However, the NCI advises institutions and individual investigators to employ "wide discretion" in carrying out Data and Safety Monitoring in an effective and reasonable manner. A sensible DSMP must be based on the context of the particular study, and in particular, the actual level of risk that participants in the study are exposed to. For more information, see: http://www.cancer.gov/clinicaltrials/conducting/dsm-guidelines/page2.

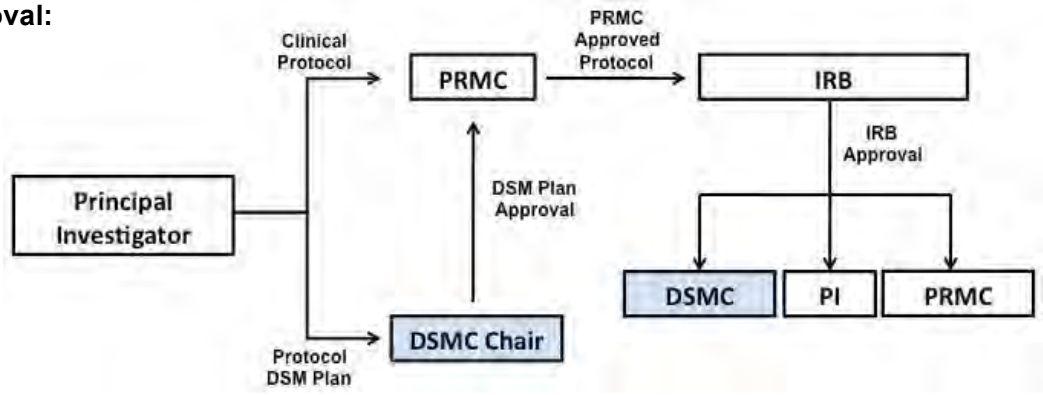
Organization and Administration

As the specific types of monitoring and reporting vary by the nature of the individual trial, the responsibilities to ensure that monitoring is timely and effective include a number of UH Cancer Center offices and committees. The Director of the UH Cancer Center is ultimately responsible for all of the Center's clinical trials, including data and safety monitoring. The DSMC specifically focuses on Data and Safety Monitoring and communicates to the PRMC, which is responsible for scientific quality and progress. Both in turn report through the UH Cancer Center Associate Director of Clinical Sciences and Translational Research to the UH Cancer Center Director.

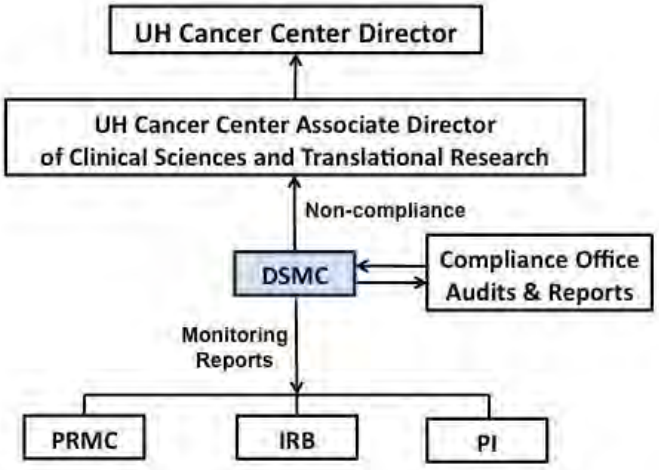
Study principal investigators and additional committees directly oversee the progress of all Center generated and coordinated clinical trials in respect to human subject protection through regular data and safety monitoring. **Phase I & II** protocols are directly monitored by the DSMC while most Phase III protocols have additional monitoring by study-specific DSMB's. Local PIs of externally generated and coordinated trials such as cooperative group studies are obligated to report all serious adverse events directly to the DSMC, the designated IRB, all involved local hospital IRBs, the study sponsor (e.g., NCI) and the FDA (if applicable).

<u>Communication Flow of the Data & Safety Monitoring System</u>:

For Trial Approval:



During Trial Conduct:



For locally-generated and coordinated studies, annual reports and serious human safety concerns will be sent to the designated IRB and to **study sponsors**. Notification of study suspension or closure and serious human subject safety concerns made by the **DSMC** will be reported to the Associate Director of Clinical Sciences and Translational Research, the PRMC, the designated IRB and the PI. Study accrual suspension will occur immediately following notification to PI of a study suspension or closure and will be followed with communication to the PRMC and IRB at their next scheduled meeting. For NCI-funded clinical trials the NCI Program Director responsible for funding the trial will be included in this communication, along with FDA and other sponsor Program Directors, if appropriate.

DATA AND SAFETY MONITORING COMMITTEE (DSMC)

The **DSMC** is the dedicated data and safety monitoring committee for the UH Cancer Center. The DSMC has the primary responsibility for monitoring described in this Plan and assures compliance with procedures. DSMC reviews study **audits** as necessary to assure compliance with protocol and data and safety monitoring procedures. DSMC reviews and approves protocol specific data and safety monitoring plans on all Center-initiated and coordinated clinical trials after DSMC Chair review and approval. No study receives DSMC approval without a data and safety monitoring plan.

Membership of DSMC includes members with expertise relevant for monitoring the safety and outcomes of the types of studies initiated and coordinated by Center investigators. In particular, membership will include representatives from clinical oncology, psychology/behavioral science, nursing, biostatistics and quality assurance. All DSMC members will need to sign a DSMC Conflict of Interest form and Confidentiality Pledge form. To avoid conflict of interest, a PI of a study who is a DSMC member will be included in any DSMC discussion of the study, but will recuse himself or herself from voting on the study. The PRMC Chair will be a non-voting, ex officio member of the DSMC. The DSMC Chair and all committee members are appointed by the President of the Hawai‘i Cancer Consortium, who is the Director of the University of Hawai‘i Cancer Center, in consultation with the HCC Advisory Board. A quorum of 50% of members, including an oncologist, must be present at DSMC meetings in order for the DSMC to make any decisions requiring a vote.

The DSMC meets quarterly to review all DSM reports, plans and SAE summaries, as well as the data and safety monitoring process at the UH Cancer Center, and to make recommendations to address concerns about patient safety issues and compliance with data and safety monitoring procedures. In addition, the DSMC Chair reviews DSMPs of new protocols upon receipt and all SAE reports as they occur. The DSMC Chair can call ad hoc meetings or request that select members review DSMPs and SAE reports at any time.

The DSMC reviews all SAE’s experienced by patients on therapeutic trials conducted through the UH Cancer Center, regardless of the phase of the study, sponsor, or nature of agent/regimen. Following SAE review, the DSMC will either recommend that the study continues with no modifications or that a revision is required to ensure patient safety. In the event that the Committee feels that a revision is warranted, the Committee will immediately notify the principal investigator of the study. The DSMC may close a trial to patient accrual should the risk to patients be excessive or outweigh the potential benefits of the study. The PI has the right to appeal the closure decisions to the DSMB Chair and

through the UH Cancer Center Associate Director for Clinical Science & Translational Research to the UH Cancer Center Director who has the final authority to close or suspend a clinical trial.

DATA AND SAFETY MONITORING FOR PHASE I & II PROTOCOLS

The DSMC monitors the safety and verifies the evaluation of clinical response of local investigator-generated Phase I and Phase II clinical trials. Quarterly reports will include the current accrual, drug and dose level administered, and a summary of SAEs. Should an unexpected severe toxicity be identified, this committee will also review these on an emergency basis. Trials viewed as excessively toxic by the review team will be appropriately modified, suspended pending further investigation or closed to further accrual. Based on evaluation and verification of objective clinical responses in the Phase II setting, the DSMC will recommend that a study continue or be closed based on first stage results if the study incorporates the usual multi-stage Phase II design.

The report will be sent to the PI, the PRMC, designated IRB and when appropriate, the local hospital IRB's, the study sponsor, and/or FDA.

DATA AND SAFETY MONITORING BOARDS (DSMBs) FOR PHASE III PROTOCOLS

Requirements for a DSMB

A DSMB must be established if the proposed study meets the following criteria:

- The study is a randomized, Phase III clinical trial.

***Note*:** Principal investigators for studies that do not meet the above criteria may still propose to have a DSMB if they feel it would be useful for their study. Note that DSMB's are no longer required by NCI for low-risk behavioral and nutritional interventions.

Forming a DSMB

The formation of a DSMB is the responsibility of the study PI at the UH Cancer Center including the HCC partners for investigator-initiated trials and of the coordinating center for cooperative group trials. Prospective DSMB members will be appointed by the study PI and approved by the sponsor if required. The following information will be provided to the DSMC chair for each DSMB member: a curriculum vitae (CV); a list of their current affiliations with pharmaceutical and biotechnology companies, including the name of the company and the type of affiliation (e.g., stockholder, consultant); and any relationships that could be perceived as a conflict of interest related to the study and associated with commercial interests. The Chair of the DSMC reviews the nominations and discusses any concerns with the PI. [DSMB members should have no direct involvement with the study or conflict of interest with investigators conducting the study.] The DSMC Chair may serve as a non-voting, ex officio member of the protocol DSMB.

Formal DSMBs will consist of clinical investigators, biostatisticians, clinical trial experts, and lay patient advocates independent of investigators involved in the design and conduct of the trial. Some randomized Phase II and Phase III studies of nutritional interventions/feeding studies or behavioral interventions may also have DSMBs with a different composition, incorporating nutritional and behavioral expertise.

The study's Data and Safety Monitoring plan should indicate the proposed frequency of meetings for the DSMB, and include a proposed list of data items to be provided to the DSMB and if appropriate, estimates for DSMB-related expenses (e.g., for travel) in the proposed protocol budget. All masked studies should describe the specific criteria and procedures for unmasking the randomization.

If the PI has not proposed a DSMB, but the DSMC believes an independent DSMB is required, the PI will make arrangements for a DSMB as described above.

The Nature of Clinical Trials and Monitoring Required

The extent of the monitoring and reporting period varies by the degree of risk encountered by patients on the study, the study sponsor, the type of agent or agents involved, and the phase of the clinical trial.

Given the great diversity of clinical trials at the UH Cancer Center, trial data and safety monitoring, by necessity, reflects that diversity. The Center's Data and Safety Monitoring System is tailored to:

1. Ensure monitoring of all clinical trials,
2. Meet the reporting requirements of individual trial sponsors,
3. Eliminate redundant monitoring and reporting.

The individual trial sponsor or sponsoring group generally dictates minimal standards for data and safety monitoring and reporting. Trial sponsors include the National Cancer Institute or other units of the National Institutes of Health, other national granting agencies, pharmaceutical companies, and local sponsors.

EXTERNALLY COORDINATED STUDIES

National Institutes of Health and other National Peer Reviewed Studies

The UH Cancer Center participates in a large number of clinical trials from NCI supported Community Clinical Oncology Program (CCOP) research bases / cooperative groups such as: Southwest Oncology Group [SWOG], National Surgical Adjuvant Breast and Bowel Project [NSABP], American College of Surgeons Oncology Group [ACOSOG], Radiation Therapy Oncology Group [RTOG], Gynecologic Oncology Group [GOG], University of Rochester Cancer Center CCOP Research Base [URCC], Children's Oncology Group [COG], North Central Clinical Trials Group [NCCTG], and CTEP's Cancer Trials Support Unit [CTSU]. Each of these national groups conducts a range of therapeutic [Phase II, III] and prevention clinical trials. These studies are monitored by long-standing and established systems for cooperative group data submission, reporting, review, and monitoring. Other externally coordinated clinical trials may be with a limited number of institutions and funded through R01, U01, R21 or similar peer-review mechanisms. The NIH may or may not be the Investigational New Drug (IND) holder.

Each externally coordinated study will clearly specify the minimal data and safety monitoring requirements. Since these trials are multi-institutional, specific data management systems using a variety of computer and communications technology allow safety and efficacy data to be closely monitored for each study by site and for the group as a whole. We will not place additional reporting requirements on staff supporting these trials, but will rely on mandated reporting mechanisms to monitor patients.

Although NCI sponsored cooperative group clinical trials are monitored for data and safety through cooperative group and Industry mechanisms, all SAEs experienced by Hawai‘i subjects on these studies will be reviewed by the DSMC chair to assess risks to protocol participants and assure compliance with reporting requirements, as outlined in the expedited reporting guidelines of the NCI.

If, for some reason, a trial is not being centrally monitored or the institution feels that additional monitoring is required, it will be conducted as to the policies for local investigator-generated studies.

All SAEs from all cooperative group trials are required to be reported within the time parameters of the current CTCAE guidelines. Based on local or national/external SAEs reported, the designated IRB has the authority to close any active study to further accrual and can require more detailed reporting of SAE's observed and steps taken to minimize patient risk and maximize the safety of participating patients.

Pharmaceutical Company Sponsored Trials

All clinical trials generated and coordinated by pharmaceutical industry sponsors with subsequent Center participation are monitored for data and safety by the industry mechanism. If, for some reason, a trial is not being monitored or the institution feels that additional monitoring is required, it will be conducted as to the policies stated herein for local, investigator-generated studies.

SAE's are reported to the DSMC, the designated IRB and the involved local hospital IRB's using either industry-specified report formats or the FDA Med Watch SAE reporting form.

DSMC will review annual data and safety monitoring reports and make recommendations on whether the study should continue unchanged, require modification/amendment, or be closed based on unacceptable risk to participants.

LOCAL, INVESTIGATOR-GENERATED AND COORDINATED STUDIES

Local, investigator-generated studies may include studies with NIH or other peer-reviewed sponsorship through R01, R21, UO1, or similar mechanisms. These grant-supported clinical trials are required to have specific data and safety monitoring plans prior to receipt of funding. Multi-center, limited-institution randomized Phase III trials coordinated by the UH Cancer Center will be held to the same standards as local, investigator-generated Phase III trials conducted by the UH Cancer Center.

Local, investigator-generated and coordinated trials may also include studies that are supported by local funding such as Center developmental funds, pharmaceutical companies, or other private funding. Such studies receive the highest level of oversight and will be reviewed by the DSMC to determine if data and safety monitoring plans are complete and appropriate before they are approved. The study PI will be required to develop a DSMP.

In multi-site studies coordinated at the UH Cancer Center, the study PI is responsible for sending DSMB reports to the DSMC, collaborating site PIs, who in turn are required to distribute these reports to their local IRB's.

Phase I

These studies are small, with limited numbers [usually fewer than 30], and intend to determine a safe and tolerable dose of the drug/regimen and evaluate adverse events/toxicity. They may include correlative biologic or pharmacologic studies. Occasionally, Phase I trials will evaluate feasibility endpoints in the case of medical devices and procedures. Nevertheless, due to the unknown safety and relatively high risk to the patient of the agent, regimen, or device/procedure under study, these trials require particular attention in monitoring patient safety.

For Phase I studies, the study PI must provide continuous monitoring of patient safety, with quarterly reporting to the DSMC for oversight of monitoring. The data to be reported will include summary data similar to that submitted by investigators using the NCI/NIH Adverse Event Expedited Reporting System (AdEERS).

For early Phase I trials of agents or regimens with little existing data on toxicity that pose a high risk to patients, the DSMC may require the investigator to provide more frequent data [i.e. monthly] and safety monitoring reports. The frequency of reporting will be determined on a protocol-by-protocol basis.

The report schedule of individual trials may be modified over the course of the study based on the safety experience of patients treated. Studies may be required to initiate more frequent reporting should the frequency or severity of adverse events so warrant.

In the event of a SAE experienced by a patient on a local, investigator-generated Phase I trial, the study PI is required to report the SAE to the DSMC chair, designated IRB(s), study sponsor and FDA [if applicable] using appropriate reporting forms.

By federal regulations, a SAE is defined as any adverse event that:

1) Results in death, is life-threatening, or places the participant at immediate risk of death from the event as it occurred,
2) Requires or prolongs hospitalization
3) Causes persistent or significant disability or incapacity,
4) Results in congenital anomalies or birth defects, or
5) Is another condition which investigators judge to represent significant hazards. (Dec 28, 2007 from http://www.nia.nih.gov/NR/rdonlyres/98BE08AF-E107-4833-AB3E-73CF97328EC6/0/NIAAEandSAEGuidelinesFINAL12_28_07.doc).

Adverse events which do not meet the definition of a SAE also require timely reporting, as defined in the PRMC, dependent upon the grade of adverse event using the current CTCAE criteria, attribution, and whether the event is expected or unexpected. Local Phase I safety monitoring will use the same matrix of reporting requirements and schedules as does CTEP and which is available at the CTEP website at http://ctep.cancer.gov/guidelines/index.html; NCI Guidelines: Expedited Adverse Event Reporting Requirements for NCI Investigational Agents dated January 2005, page 13.

All expedited adverse event reports must be sent to the DSMC chair, and the designated IRB. Nutritional interventions may use reporting criteria outside the CTCAE grading to better reflect specific effects more relevant to these types of studies.

Phase II

Phase II studies are also small, with relatively limited numbers of patients [usually fewer than 50], and intend to determine the efficacy of an agent, regimen, device, or procedure and may include correlative biologic or pharmacologic studies. While more is known concerning the risks and benefits of the study treatment as compared to Phase I studies, more patients are exposed to the study regimen. Toxicity and outcomes are often confounded by the disease process.

While some variation may exist in monitoring, PIs of local, investigator-generated Phase II studies are required to provide monitoring of patient safety on a monthly basis to the DSMC Chair with quarterly reporting of summary data to the DSMC for oversight of monitoring. As with reports for late Phase I trials, the summary data will be similar to that submitted by investigators using the NCI /NIH AdEERS. However, the actual data to be reported and report format will be determined by the DSMC in collaboration with the study PI.

On the anniversary date of the original IRB approval of each local Phase II trial at the designated IRB, the study PI will be required to report to the DSMC the number of patients entered on the trial, the number of patients treated, a summary of all adverse events reported to date using the current CTCAE grading, a specific list of serious adverse events requiring immediate reporting, and significant literature reporting developments that may affect the safety of participants or the ethics of the study.

In the event of a SAE experienced by a patient on a Phase II trial, the study PI is required to report the SAE to the DSMC chair, designated IRBs, study sponsor and FDA [if applicable] using appropriate reporting forms.

The DSMC will review annual data and safety monitoring reports and make recommendations whether the study should continue unchanged, require modification or amendment, or be closed based on unacceptable risk to participants. Local Phase II safety monitoring will use the same matrix of reporting requirements and schedules as does Cancer Therapy Evaluation Program (CTEP) and which is available at the CTEP website at http://ctep.cancer.gov/guidelines/index.html; NCI Guidelines: Expedited Adverse Event Reporting Requirements for NCI Investigational Agents dated January 2005, page 14.

Phase III

Randomized Phase III studies require large patient populations with lengthy patient follow-up. The large number of patients required for comparative randomized Phase III trials dictates special concerns in ensuring patient safety. While the risk to individual patients may be less than that encountered in Phase I and II trials, the longer period of treatment and exposure to investigational regimens may pose significant risks to patients.

PIs should clearly state in the protocol for an intervention whether the proposed study meets NIH's criteria for an NIH-defined Phase III trial and the basis for that opinion. NIH defines a Phase III clinical trial as a broadly based prospective Phase III clinical investigation (usually involving several hundred or more human subjects) to evaluate an experimental intervention in comparison with a standard or control intervention or to compare two or more existing treatments. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials also are included. (From; http://grants.nih.gov/grants/glossary.htm.) The DSMC will review the information provided by the PI. If the protocol deemed by the DSMC to be a Phase III trial, the study will need to provide the required information for such studies prior to activation.

Commensurate with risk and NIH guidelines, all local Phase III clinical trials will require the establishment of an independent DSMB. Note that low-risk behavioral and nutritional interventions no longer require DSMB's, but do require DSMP's.

Independent DSMB's must be established prior to the initiation of the trial. While DSMB's may vary in size and composition, at a minimum they will require no less than two persons. No members of a DSMB will be associated with the trial. See details under the section on "Forming a DSMB".

For non-cooperative group, limited-institution Phase III studies without NCI/NIH monitoring, the PI at the lead institution will be responsible for monitoring the study and establishing a DSMB. The DSMC chair will be required to review and approve data and safety monitoring plans and the membership of the DSMB prior to activation of the study.

The following policies describe the UH Cancer Center's requirements for local, investigator-generated Phase III trials. They do not replace existing regulations on protection of human subjects, policies and guidelines for conduct of clinical research, inclusion of women and minorities, research project administration, reporting, and financial management, or requirements of local IRB's. Department of Health and Human Services (DHHS) regulations for the protection of human subjects are described in 45 CFR46. The implementation of these regulations for Public Health Service (PHS) research grants involving human subjects is found in the PHS 398 form (rev. 6/2009), available on the NIH home page (http://www.nih.gov/grants/forms.htm). This UH Cancer Center Data and Safety Monitoring Plan document describes further steps to be taken to ensure the protection of human subjects. In individual cases, the UH Cancer Center may find it beneficial to have additional levels of involvement or oversight beyond those described in the PHS policies.

PIs are responsible for generating and providing reports to the study-specific DSMB under NIH policy criteria, including annual reports on the anniversary date of the original IRB approval of the trial. This annual report will include the number of patients entered on the trial, the number of patients treated, a summary of all adverse events reported to date using the current CTCAE grading, a specific list of serious adverse events that required immediate reporting, and significant literature reporting developments that may affect the safety of participants or the ethics of the study. The PI will provide the DSMB reports to the DSMC.

In the event of a SAE experienced by a patient on a Phase III trial, the study PI is required to report the SAE to the DSMB, the DSMC chair, designated IRB, and PIs at participating institutions, study sponsor and FDA [if applicable] using appropriate reporting forms. Local Phase III safety monitoring will use the same matrix of reporting requirements and schedules as does CTEP and which is available at the CTEP website at http://ctep.cancer.gov/guidelines/index.html; NCI Guidelines: Expedited Adverse Event Reporting Requirements for NCI Investigational Agents dated January 2005, page 14.

In summary, Phase III protocols must include:

- Plans for establishment of an independent DSMB (if not a low-risk behavioral or nutritional intervention).

- Plans for securing support, resources, and funding appropriate for the DSMB to meet its requirements as listed below.

- A data processing and analysis unit administered by a designated individual other than the PI(s) of the trial (e.g., the study statistical group). This individual may report to the PI. In all cases, all data from this unit must be directly available to the DSMC.

- Procedures for quality assurance/quality control, data management, and analysis.

- Plans for notifying subjects of trial results after the conclusion of the trial and providing the subjects' health care providers with the appropriate information from the trial, as needed, concerning the individual subject (e.g., cessation of drugs, changes in dosage, etc.).

Investigator Requirements and Responsibilities

The principal investigator (PI) of each study is ultimately responsible for every aspect of the design, conduct, and final analysis of the protocol. The study PI is responsible to insure that:

- All protocols must include a **Data and Safety Monitoring Plan** and procedures for its implementation.

- All protocols will have data and safety monitoring by the Center's DSMC or by an independent DSMB (Phase III) as above.

- All studies must have a structured adverse event determination, monitoring and reporting system.

- The proposed schedule for reporting adverse events to the DSMC for local investigator-generated Phase I & II trials, a DSMB [if one is established], the CHS [and/or hospital IRBs in the case of multi-site studies], the study sponsor (NCI, NIH Program Director) and the FDA [if applicable]. The proposed schedule should include a system for the DSMB to send reports regarding safety issues [see section "Requirements of Data and Safety Monitoring Boards"] to the study PI. In multi-site studies, the study PI is responsible for sending these DSMB reports to collaborating site PIs, who in turn are required to distribute these reports to their local IRBs if applicable.

- Protocols must include the proposed human subjects consent form and describe procedures for protection of human subjects.

- All masked studies should describe the randomization scheme, and specific criteria and procedures for unmasking. If a DSMB is not proposed, the application should also designate individuals with access to unmasked data.

- If the PI believes that an independent DSMB is required for adequate subject safety, the protocol should indicate the proposed frequency of meetings for the DSMB, and include a proposed list of data items to be provided to the DSMB and estimates for DSMB-related expenses in the proposed protocol budget. Prospective DSMB members will be appointed by the study PI and approved by the sponsor if required. The following information will be provided to the DSMC chair for each DSMB member: a CV; a list of their current affiliations with pharmaceutical and biotechnology companies, including the name of the company and the type of affiliation (e.g., stockholder, consultant); and any relationships that could be perceived as a conflict of interest related to the study and associated with commercial interests. The Chair of the DSMC reviews the membership and discusses any concerns with the PI. [DSMB members should have no direct involvement with the study or conflict of interest with investigators conducting the study.]

- If the PI has not proposed a DSMB, but prior to activation of the proposed project the DSMC Chair believes an independent DSMB is required, the PI will make arrangements for a DSMB as described under “Forming a DSMB”.

- If the proposed protocol has additional clinical sites besides the UH Cancer Center, the protocol should describe procedures by which the PI will notify sites of any problems as identified by the DSMB if one is established.

- In specific cases where an outside agency is the sponsor of the test agent (i.e., holder of the Investigational New Drug [IND] application), PIs must submit individual adverse event reports to the funding agency (as sponsor) in accordance with agency and FDA regulations.

- The PI is responsible for adhering to all reporting requirements outlined in the protocol’s data and safety monitoring plan. This includes:

    - Arranging for timely meetings of the DSMB to review data or providing timely reports to the DSMC.

    - Ensuring that the DSMB reports are submitted to the DSMC.

    - Adhering to annual reporting requirements to the DSMC, IRBs, and study sponsor.

    - Immediately reporting to the DSMC, IRB’s, study sponsor (NCI/NIH Program Director) and FDA (if applicable) when there is concern about a serious patient safety issue, efficacy difference in Phase III study arms, or the study is suspended or closed.

All principal investigators will need to complete a human research subject’s protection training course [such as the NIH “Protecting Human Research Participants” course or the Collaborative IRB Training (CITI) “Protection of Human Research Subjects” course].

Investigators should also be aware of NIH policy "Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials" (NIH Guide for Grants and Contracts, June 11, 1999), "NIH Policy on Data and Safety Monitoring" (NIH Guide for Grants and Contracts, June 10, 1998), and "Further Guidance on a Data and Safety Monitoring for Phase I and Phase II Trials" (NIH Guide for Grants and Contracts, June 5, 2000). In addition, the NCI website provides further clarification of Data and Safety Monitoring requirements [http://cancertrials.nci.nih.gov/clinicaltrials/conducting/dsm-guidelines].

UH Cancer Center Responsibilities

DATA AND SAFETY MONITORING COMMITTEE (DSMC) RESPONSIBILITIES

Prior to activation of any local, investigator-generated trial, the DSMC Chair will review the risks of the intervention proposed in the protocol. If the information required in protocols having potentially harmful interventions is not included in the protocol, the DSMC Chair (or full DSMC, if the Chair deems it necessary) will notify the PI of what items are missing and indicate that the UH Cancer Center will not activate the study until this information is received, reviewed, and approved by the DSMC.

The study will not be approved by the PRMC unless a Data and Safety Monitoring Plan is included and approved by DSMC Chair. The DSMC will determine if an external DSMB is required and whether the Center's DSMC can function as the study's DSMB. If an external DSMB is required, the DSMC Chair will request the PI to indicate the proposed frequency of meetings for a DSMB; to submit a proposed list of data items to be provided to the DSMB; and to nominate a DSMB of no less than two persons and provide the information listed under "Forming a DSMB". The proposed membership will be reviewed by the DSMC chair who will communicate any concerns to the PI.

If appropriate, PIs should also submit a proposed budget for travel and administrative expenses for the DSMB. The DSMC will reserve the right to require appointment of additional members to the DSMB to include scientific expertise in topic areas relevant to the trial such as biostatistics, ethics, or patient advocacy.

Prior to protocol approval and activation, the DSMC will:

- Review and approve the protocol data and safety monitoring plan
- Verify that the investigator has sent a detailed monitoring plan to the designated IRB.
- Institute any other appropriate conditions needed for subject safety (e.g. data reporting formats and schedules, restrictions on expenditure of funds pending completion of particular activities, etc.).

Following protocol activation, the DSMC will:

- Review all SAE's and protocol violations.
- For studies with DSMB's, review regular reports from these boards (including unmasked data if needed) on adverse events.
- Request additional data from investigators as needed on safety issues arising over the course of the study.
- At least annually (and more frequently if necessary), review rationale for continuation of study, and terminate the study if appropriate (e.g., excessive adverse events). Any recommendations of the DSMB for closure or suspension will be communicated to the PRMC, the designated IRB and the PI.
- For Phase III trials, review regular reports of relevant masked group data on treatment effects.

- Provide advice, or request that the DSMB provide advice, to the study PI on trial protocol and safety issues; data management, quality, and analysis; recruitment, retention, and protocol adherence issues arising over the course of the study; and continuation or termination of the study.
- Facilitate implementation of any DSMC or DSMB recommendations.
- Acknowledge reports of serious data discrepancies found by the DSMB or other sources within two weeks of the receipt of this information by the DSMC. This acknowledgment should be in writing and shall request a plan from the PI describing what steps will be taken next, with a copy of the communication from the PI sent to the chair of the DSMB, the chair of the PRMS, and the UH Cancer Center Director through UH Cancer Center Associate Director for Clinical Science & Translational Research Depending upon the nature of the discrepancies, the DSMC may suspend the study until an adequate response plan is received from the PI.
- Assure preparation and dissemination of a clinical alert in the event of a clinically significant finding. This dissemination should also include informing the subjects of this clinical alert and providing them and their health care provider with as complete information as possible that may affect the subjects' well-being.
- Reserve the option, at any point in the trial, to obtain an independent audit of a sample of primary subject records for comparison with the trial's regular audit reports. Auditors so engaged will report directly to the DSMC chair.
- Have the authority to recommend the study be suspended or closed. The PI may appeal this decision through the Chair of the DSMB and through the UH Cancer Center Associate Director for Clinical Science & Translational Research to the Center Director who has the final authority (during the appeal process) in respect to closing or suspending a clinical trial.

UH CANCER CENTER OFFICE OF COMPLIANCE

Supervised by the UH Cancer Center's Compliance Officer who reports directly to the UH Cancer Center Director, the Office of Compliance receives notification of all clinical trials that are recommended for activation by the Protocol Review Monitoring System (PRMS) and conducted through the Center. The Center's designated IRB automatically forwards all trials submitted from the Center to the Office of Compliance as a measure of oversight and to ensure that the initiation of oversight by the Office of Compliance begins.

Oversight includes collection of the trials DSMP, regulatory documents, quarterly trial updates (accruals), notification of serious adverse events (to include external safety reports), protocol violations, and audit and monitoring reports. The Office of Compliance is responsible for ensuring that the DSMC Chair is aware of any patient safety or compliance issues that need immediate attention and facilitates the quarterly reporting of this information to the DSMC. The Office of Compliance also ensures that any recommendations made are communicated to the appropriate personnel and/or committee and facilitated in a timely manner.

AUDITS

To ensure quality assurance, the Compliance Officer of the UH Cancer Center will conduct annual audits on a minimum of 10% of the institutionally generated protocols and 5% of cooperative studies that the DSMC is monitoring. A minimum of 10% of subjects entered on each selected clinical trial will be audited. If there are less than 20 subjects on a study, a minimum of 2 subjects will be audited.

Audit Process

Cases will be selected at random by the Audit Function from active clinical trials, and trials following closure. Cases may also be audited for cause. For Committee-selected audits, Principal Investigators will be notified in writing at least 30 days before a planned audit. PIs will be notified of the randomly selected patient(s) no less than two weeks in advance of the audit date.

For the audit, the Principal Investigator is expected to present all the study records to the audit team. Records for review include the source documents, study files that include any case report forms, flow sheets, and adverse event report forms. During the audit, the auditors will review regulatory compliance, including IRB documentation and content of the informed consent document. Pharmacy records will be reviewed when appropriate. Each patient case will be reviewed for protocol compliance, patient eligibility, data collection and verification of case report forms as compared to source documentation. Patient follow-up procedures per protocol as well as reporting of adverse events will also be reviewed for timeliness, completeness and accuracy. The investigator and staff will be given the opportunity to clarify any questions the audit team has and provide explanations for any concerns.

After the audit, auditors will report their findings at the next meeting of the DSMC. A final Quality Assurance Audit Report with the Committee's recommendations will be generated for the PI. The DSMC may make recommendations for improvement. The PI will be asked to provide written explanation of the identified problems, and a plan to prevent future occurrences. If the audit results are serious, the audit team could decide to conduct further audits of other research conducted by the same investigator and/or make recommendations for closure or suspension of the audited trial. The PI is responsible for providing the DSMC with copies of the audit report and responses.

RESPONSIBILITIES OF DATA AND SAFETY MONITORING BOARD (DSMB) FOR PHASE III PROTOCOLS

Once a DSMB is established, its initial tasks are to review the entire study protocol and the informed consent form with regard to recruitment, randomization, intervention, subject safety, data management, plan's for auditing of subject records, quality control and analysis. Recommendations for modifications will be provided to the PI. The DSMB shall then identify the relevant data parameters and the format of the information to be regularly reported. If the need for modifications to the protocol or consent form is indicated, the DSMB shall postpone its recommendation for the initiation of subject recruitment to the PI until after the receipt of a satisfactorily revised protocol.

The DSMB will meet every six months. This may not be less than twice a year for interventions requiring an IND Application or using prescription medications, but may be extended to once a year for low risk psychosocial and nutritional interventions with additional meetings as needed.

Purpose of the DSMB meeting:

- Review data (including masked data) over the course of the trial relating to efficacy, recruitment, randomization, compliance, retention, protocol adherence, trials operating procedures, form completion, intervention effects, gender and minority inclusion, and subject safety.
- Identify problems relating to safety over the course of the study. Inform study PI via written report, who in turn will ensure that all clinical site PIs receive this report.
- Identify needs for additional data relevant to safety issues and request these data from the study investigators.
- Propose appropriate analyses and periodically review developing data on safety and endpoints.
- At each meeting, consider the rationale for continuation of the study, with respect to recruitment, progress of randomization, retention, protocol adherence and compliance, data management, safety issues, and outcome data, if relevant, and make a recommendation for or against continuation of the trial.
- Provide the PI and DSMC written reports following each DSMB meeting. The PI will then forward the report to the designated IRB.
- Provide advice on issues regarding data discrepancies found by the data auditing system or other sources. If the DSMC requests this advice, it should be provided by the DSMB in writing within two weeks of the date of the request.
- If there is more than one clinical site, the study PI is responsible for sending the reports to individual site PIs, who in turn are required to distribute the report to their local IRB's, as detailed in the NIH "Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials" (NIH Guide for Grants and Contracts, June 11, 1999).

DSMB Meetings

DSMB meetings will be divided into three parts: First, an open session in which members of the clinical trial team may be present, at the request of the DSMB, to review the conduct of the trial and to answer questions from members of the DSMB. Issues discussed may include accrual, protocol compliance, and general toxicity. Outcome results must not be discussed during this session. Following the open session, a closed session involving the DSMB and statistical staff will be held. The statistician[s] should present and discuss the outcome results with the DSMB. A final executive session involving only DSMB members should be held to allow the DSMB opportunity to discuss the general conduct of the trial and all outcome results, including toxicities and adverse events, develop recommendations, and take votes as necessary.

DSMB Recommendations

DSMB recommendations should be based on results for the trial being monitored as well as on data available to the DSMB from other studies. It is the responsibility of the PI to ensure that the DSMB is kept apprised of non-confidential results from other related studies that become available. 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 being monitored.

A written copy of DSMB recommendation(s) will be given to the clinical trial PI and the DSMC. If the DSMB recommends a study change for patient safety or efficacy reasons, or that a study be closed early due to slow accrual, the PI must act to implement the change as expeditiously as possible. In the unlikely situation that the PI does not concur with the DSMB, then the DSMC must be informed of the reason for disagreement. The Principal Investigator, DSMB chair, and DSMC chair will be responsible for reaching a mutually acceptable decision about the study. Confidentiality must be maintained during these discussions. However, in some cases, relevant data may be shared with other clinical trial investigators at the UH Cancer Center or seek advice to assist in reaching a mutually acceptable decision.

If a recommendation is made to change a trial for other than patient safety or efficacy reasons or for slow accrual, the DSMB will provide an adequate rationale for its decision. If no mutually acceptable decision can be reached, the ultimate decision rests with the Center Director.

Release of Outcome Data

In general, outcome data should not be made available to individuals outside of the DSMB until accrual has been completed and all patients have completed their treatment. Any early release of outcome for general dissemination of results must be reviewed and approved by the DSMB.

Confidentiality Procedures

No communication, either written or oral, of the deliberations or recommendations of the DSMB will be made outside of the DSMB except as provided for in this policy. Outcome results are strictly confidential and must not be divulged to any non-member of the DSMB, except as indicated above in the Recommendations section.

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

For Confidentiality Pledge form please see Appendix A

Conflict of Interest

DSMB members must adhere to the UH Cancer Center policies regarding standards of conduct. Individuals invited to serve on the DSMB as either voting or non-voting members will disclose any potential conflicts of interest, whether real or perceived, to the PI and the DSMC chair. 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. Potential conflicts which develop during a member's tenure on a DSMB must also be disclosed. Decisions concerning whether individuals with potential conflicts of interest or the appearance of conflicts of interest may participate in a DSMB will be made by the DSMC Chair.

For Conflict of Interest Disclosure Form please see Appendix B

Review and Approval of Data and Safety Monitoring Plans

According to NIH policy, the UH Cancer Center Data and Safety Monitoring Plan and individual protocol data and safety monitoring plans require UH Cancer Center DSMC and IRB approval. In addition, the UH Cancer Center Data and Safety Monitoring Plan requires approval by NCI.

APPENDIX A

University of Hawai'i Cancer Center
Data and Safety Monitoring Committee
2011 Confidentiality Pledge Form

PLEDGE

- I understand that all materials, discussions, and proceedings of the University of Hawai'i Cancer Center's Data and Safety Monitoring Committee (DSMC) are completely confidential and will not be disclosed outside of the DSMC except as provided for in the UH Cancer Center Data and Safety Monitoring Plan.
- I recognize the importance of maintaining the confidentiality of data discussed within this committee, and of assuring the right of privacy of persons cooperating in clinical trials.
- I also understand that my employer has agreed to protect the privacy of these persons.
- I therefore pledge that I will not divulge to anyone who is not a member of the UH Cancer Center DSMC the identity of individuals included in the program, nor will I discuss any individual responses with any person not on the UH Cancer Center DSMC.
- I understand that in some cases, relevant data may be shared with other clinical trial investigators at the UH Cancer Center to seek advice to assist in reaching a mutually acceptable decision.

PRINT NAME: _____

SIGNATURE: _____

DATE: _____

APPENDIX B

University of Hawai'i Cancer Center
Data and Safety Monitoring Committee
2011 Conflict of Interest Disclosure Form for DSMB, DSMC & PRMC Members and Staff

I agree to disclose any economic or professional research interest that may be perceived as a conflict of interest for me in respect to any research proposal that I will be asked to consider as a member of the University of Hawai'i Cancer Center's DSMB, DSMC and/or PRMC.
With respect to a research sponsor or any entity that would benefit from the results of a protocol under review and which I or an immediate family member has any of the following relationships with, I will check all that apply and provide the names of companies in the space provided.
I also agree to disclose whether I could be perceived to benefit professionally from a decision for or against any protocol being reviewed by the Committee.

NAME: _____ **DATE: _____**

With respect to a sponsor or any entity known to be doing business with the UH Cancer Center that could benefit from a favorable review of a study, either I or an immediate family member:

Acts as a Consultant: ☐Yes ☐No

Holds sole proprietary or partnership interests: ☐Yes ☐No

Holds private or public stock ownership (>5% of company value): ☐Yes ☐No

Holds intellectual property rights: ☐Yes ☐No

Holds inventor patent or royalty rights: ☐Yes ☐No

Holds a contractual, governance or administrative/scientific affiliation: ☐Yes ☐No

Has a substantive past of present research funding with the sponsor (excluding involvement as a single site in large multicenter trials): ☐Yes ☐No

Has either a research or economic interest (ownership or compensation) in a competitor of the sponsor or of the UH Cancer Center or its affiliated entities: ☐Yes ☐No

Explain any items checked "Yes" above and disclose financial interests that exceed $10,000:
_____

Describe any other situation that might constitute a conflict of interest or the appearance of a conflict of interest:
_____
_____

To the best of my knowledge, I have disclosed any and all relationships between my family and any sponsors that constitute or might to appear to constitute a conflict of interest. If, as studies come under review, I recognize potential conflicts of interest, whether disclosed here or not, I will excuse myself from the discussion and vote for that study.

DATE: _____ **SIGNATURE: _____**

APPENDIX C

Acronyms

ACOSOG – American College of Surgeons Oncology Group

AdEERS – Adverse Event Expedited Reporting System

CCOP – Community Clinical Oncology Program

CFR – Code of Federal Regulations

CTCAE – Common Terminology Criteria for Adverse Events

CTEP – Cancer Therapy Evaluation Program

CTSU – Cancer Trials Support Unit

CTU – Clinical Trials Unit

DHHS – Department of Health and Human Services

DSMB – Data and Safety Monitoring Board

DSMC – Data and Safety Monitoring Committee

DSMP – Data and Safety Monitoring Plan

FDA – Food and Drug Administration

GOG – Gynecologic Oncology Group

HCC – State of Hawai‘i Cancer Consortium

IND – Investigational New Drug

IRB – Institutional Review Board

NCI – National Cancer Institute

NIH – National Institutes of Health

NSABP – National Surgical Adjuvant Breast and Bowel Project

RTOG – Radiation Therapy Oncology Group

PHS – Public Health Service

PI – Principal Investigator

PRMC – Protocol Review and Monitoring Committee

SAE – Serious Adverse Event

SWOG – Southwest Oncology Group

UH – University of Hawai‘i

UH CANCER CENTER – University of Hawai‘i Cancer Center

URCC – University of Rochester Cancer Center