YALE CANCER CENTER

DATA AND SAFETY MONITORING PLAN

I. Background and Summary

II. Overview

III. Objectives

IV. Organization and Administration
   A) Steering Committee (SC)
   B) Protocol Review Committee (PRC)
   b) Quality Assurance, Compliance & Safety Committee (QUACS)
   c) Executive Committee
   d) Office of Protocol Review & Monitoring (OPRM)
   e) Clinical Trials Office (CTO)

V. Investigator Requirements and Responsibilities

VI. Reporting Serious Adverse Events

VII. Monitoring Guidelines According to Type of Protocol

VIII. Data and Safety Monitoring Boards

IX. Conflict of Interest

X. Appendices
I. BACKGROUND AND SUMMARY

The Yale Cancer Center is committed to ensuring the safety of patients participating in clinical trials and requires all clinical trials conducted at the YCC to include provisions for data and safety monitoring. The development of protocol monitoring plans and reporting requirements are dependent upon the overall risk to patients, the nature of the agent, the phase of the trial and prior safety data with the proposed treatment regimen, the role of the Yale principal investigator and the institution, and the study sponsor. In addition, the plan must be integrated into the overall structure of Clinical Trial Data and Safety Monitoring covered by other policies within the Yale School of Medicine.

In July, 2001 the NCI approved the Yale Cancer Center (YCC) Data and Safety Monitoring Plan. In the spring of 2005, the Protocol Review and Monitoring System of the Yale Cancer Center was reorganized to provide a more intensive scientific review and to establish new committees to monitor and oversee the conduct of the clinical trials. This reorganization required a revision of the Data and Safety Monitoring Plan and approved by NCI in May of 2006. The new committee structure provided a comprehensive mechanism for review of both the scientific merit of the research protocols and an ongoing review of the safety and general conduct of the trials. In the spring of 2011 several improvements in the both the committee structure and functions were implemented.. In addition certain areas of the plan were re-written for clarification.

II. OVERVIEW

The Data and Safety Monitoring Plan (DSMP) for all YCC trials recognizes three essential components of responsibility:

- Study investigator’s responsibility for continually reviewing the conduct of the study, the prompt assessment and reporting of adverse events, and requirements for compliance with Federal regulations, University policies, and sponsor requirements.
- YCC intermittent review of audit reports, safety and other study data.
- YCC and/or study sponsor audits and monitoring of source records and study data to assure compliance with the protocol, appropriate conduct of the study, compliance with federal and institutional regulations, prompt and complete reporting of adverse events to appropriate oversight groups, and accuracy of the database.

As the specific types of monitoring and reporting vary by the nature of the individual trial, the responsibilities to ensure that the monitoring is timely and effective include a number of YCC committees and offices. While the YCC Director holds the primary responsibility for data and safety monitoring, the Principal Investigator (PI) and other individuals, along with the disease teams, have responsibilities for data and safety monitoring, including:

Committees:
- YCC Steering Committee (SC)
- YCC Protocol Review Committee (PRC)
- YCC Quality Assurance, Compliance and Safety (QUACS) Committee
III. OBJECTIVES

The objectives of the YCC DSMP are to:

- Ensure a commitment to safety and the protection of human subjects
- Provide mechanisms that are well integrated with existing data and safety monitoring policies at the School of Medicine
- Correlate the risks of a particular clinical trial with the extent of monitoring and the involvement of various oversight committees or groups. Particular attention is paid to investigator-initiated studies without any external monitoring mechanisms in place.

IV. ORGANIZATION AND ADMINISTRATION

Steering Committee (SC) reviews all study concepts prior to scientific review to identify competing studies, assesses feasibility as it relates to accrual perspectives, evaluate resource availability, and ensure the study is consistent with larger aims of Cancer Center. In addition the Steering Committee monitors accrual and has the authority to close studies with low accrual or poor performance.

The Protocol Review Committee (PRC) reviews studies for scientific merit, sets a priority score and establishes a protocol specific data and safety monitoring plan. The frequency of YCC auditing and data safety review that comprises the institutional component of the DSMP for each clinical trial is assigned during the initial review of the trial by the YCC PRC.

The Quality Assurance, Compliance and Safety Committee (QUACS) has responsibility for the oversight of the safety and compliance of trials, and reviews internal and external audit and monitoring reports. The QUACS Committee has the authority to suspend accrual and close trials for safety or compliance concerns.

To assure the integrity and independence of the YCC scientific review and study monitoring process, the independent Office of Protocol Review and Monitoring oversees protocols from the point of submission to completion of the study. The OPRM is independent of the Clinical Trials Office (CTO), which manages the submission and conduct of the trials, including data collection and reporting, as well as adverse event reporting.

To further enhance the data and safety monitoring process, the YCC Executive Committee, comprised of members of YCC leadership, provides a mechanism for adjudicating issues not resolvable within the scope of the PRC or the QUACS Committees.

The YCC DSMP for all trials is subject to review and oversight by Yale’s IRB. The individual parameters for the DSMP for each trial are provided to the Yale IRB at the time of initial YALE IRB review of the study. Minutes and actions of the QUACS Committee are communicated immediately to
the Yale IRB. To ensure adequate communication between Yale IRB and the YCC, members of the Yale IRB sit on both the PRC and the QUACS Committees. In addition, several members of the PRC and QUACS Committees sit on the Yale IRB.

A. Clinical Research Steering Committee (Sc)

The Steering Committee (SC) was created in 2006 to review concepts for proposed clinical trials prior to submission to PRC. The SC meets every two weeks and determines the following:

- Is this study consistent with the mission of the YCC?
- Is there sufficient patient population to accrue and complete the study in a timely manner?
- Are there adequate resources to manage the study in a safe and complaint manner?
- Does the study compete with any other active or pending studies?
- Are there other studies within the disease unit that are not accruing at an acceptable rate?

If the study has less than 30% of the projected accrual for a one-year period, the Committee will recommend closure and has the authority to close a study for inadequate accrual, changes in scientific findings, safety concerns, or priorities based on competing studies. Accrual reviews of all protocols are conducted at least annually.

Steering Committee Membership (See Appendix I)

B. Protocol Review Committee (PRC)

The Protocol Review Committee was established in the early 1990’s and conducts a review of all therapeutic and non-therapeutic clinical trials conducted at the Yale Cancer Center, based on specific criteria, prior to approval and study initiation. The Yale IRB requires PRC approval prior to IRB approval.

Objectives

- To evaluate the scientific rationale for the protocol
- To assure that the patient population is appropriate; that the risk/benefit ratio is appropriate; and that the study provide maximum protection for patient safety
- To assess the adequacy of the endpoints, and to determine that high quality and appropriate clinical trials and statistical design have been incorporated into the protocol
- To prioritize the protocol, based on scientific merit, and with consideration of other protocols available within the institution
- To assure the protocol will be conducted according to applicable institutional and Federal regulations, and the relevant lead investigators have the experience and training to conduct the trial safely and in compliance with all regulations
- To ensure the Informed Consent Form accurately reflects the scientific content of the protocol

In addition:

- At the time of the initial review, the PRC evaluates the study to determine an adequate Data and Safety Monitoring Plan. The DSMP includes the protocol-specified investigator responsibility for reporting adverse events and monitoring safety data; monitoring that may be provided by an external sponsor, cooperative group, or consortium; an internal audit schedule for studies that do
not have appropriate external monitoring; and reporting requirements for the QUACS Committee regarding safety and accrual data and external monitoring reports, where applicable.

• To determine if a DSMB should be required.
• Any study in which a Yale investigator holds an IND is evaluated to ensure that adequate resources are available for the additional responsibilities of the investigator/sponsor.
• Any study in which a Yale investigator is the study chair for a multi-center study is evaluated to ensure that adequate resources are available for the additional responsibilities of the investigator and the institution, including the responsibilities for data reporting, adverse event reporting, and compliance with protocol and local IRB submissions and approvals at external sites.

Specific criteria for PRC review:

Under the guidelines of the NCI in conjunction with the Cancer Center Core Grant, clinical research that must be reviewed by the PRC is defined as follows:

• Interventions for the treatment, staging, or diagnosis of cancer or cancer-related problems
• Interventions to obtain specimens from cancer patients for the sole purpose of performing basic laboratory studies related to cancer
• Interventions to obtain specimens from normal subjects for the sole purpose of performing basic laboratory research studies related to cancer
• Use of stored specimens from cancer patients or normal subjects for basic laboratory research related to cancer
• Interventions for the prevention of cancer
• Interventions for the determination, management, and study of cancer risk in normal subjects
• Interventions for the detection of cancer in normal subjects

Overview of Protocol Review Process

The PRC meets twice a month. The review process is initiated by the submission of the required protocol information to the PRC by the Principal Investigator. The protocol must receive at least conditional approval by the PRC, prior to submission to the Yale IRB. Cancer Center studies cannot be activated until both the Yale IRB and PRC provide approval.

New Protocol Review:

Protocol reviewers are usually members of the PRC, although ad hoc reviewers may be recruited to provide special expertise, at the discretion of the Chair. A full copy of the protocol and the consent form are distributed to each committee member prior to the meeting.

Protocols are presented at the PRC meeting by the reviewers, and are discussed by the full Committee, followed by a Committee vote. The primary reviewer for a therapeutic protocol must be a physician with clinical experience. Investigator-initiated studies must have two independent reviewers, not including the statistical review. A guide for systematic review of the protocol is provided to reviewers. Based upon the reviewer’s comments, and those of other members, one of the following decisions is made:

• approve
• approve with comments requiring a response
• approve with recommendations to the protocol and/or the consent form (recommendations do not require a response)
• disapprove
PI’s may attend the PRC meeting to respond to members’ questions, in order to expedite the review process. PI’s are excused during the committee discussion, nor are they present for the vote on their protocol.

At the time of the initial review, the PRC evaluates the protocol for study-specific factors before assigning the institutional portion of the Data and Safety Monitoring Plan. The PRC determines the need for a Data and Safety Monitoring Board (DSMB), the appointment of a medical monitor, or of an ad hoc safety committee. At Yale, the QUACS serves as the independent medical monitor, or ad hoc safety committee, for almost all therapeutic trials. A completely independent DSMB would be required for any institutional (or institution-led) Phase III trials.

**Biostatistics Review:**

In 2009 The Yale Center for Analytical Sciences (YCAS) was established jointly by YCCI and the School of Public Health to integrate biostatistical and epidemiological support for clinical and translational research and the YCC Biostatistics Shared Resource now resides within YCAS. The group consists of both PhD and Master’s level biostatisticians available to consult and review studies throughout the medical school. They have one dedicated biostatistician to cancer studies with the Director and Assistant Director and other biostatistical staff available for consults as the need arises. Members of YCAS serve on the SC, the PRC and the QUACS.

**Format and Content of Committee Comments to Investigator:**
Reviewer:
Committee Decision:
Vote:
Priority Score:
Schedule for Data Safety and Monitoring Review by QUACS:
Internal Audit Schedule:
Competing Trials:
Expected Yearly Accrual at Yale:
Expected Total Accrual at Yale:
National Accrual:
General Comments Regarding the Trial:
Comments Requiring a Response:
Comments Regarding the Data and Safety Monitoring Plan:
General Recommendations
Recommendations Regarding the Informed Consent:

**Amendment Review:**
All amendments must be submitted to the PRC and Yale IRB. Amendments will be initially reviewed by the Chair of the PRC. Changes to the protocol can be approved by one of the Chairs. Any amendment representing substantial change, or a conflict of interest for the Committee Chairs, will be referred to the PRC committee for full review. The PRC may require a change to the DSMP based on the amendment. Administrative changes and changes to CIRB studies are acknowledged by the office of OPRM. Translations to already approved consents and local personnel changes do not require review.

**Appeal Process:**
All decisions made by the PRC may be appealed to the YCC Executive Committee.

**Evaluation Criteria for Protocol Specific Data and Safety Monitoring Plans**
The DSMP for each study will be assigned according to the degree of risk associated with participation in the trial, the complexity and nature of the study, and other special circumstances that the committee feels will impact on the safety of the participants. All studies, regardless of risk, will be reviewed by the QUACS Committee at least annually.

The DSMP for each protocol should address the following:

- Protocol specified reporting of serious adverse events
- Protocol-specified frequency of investigator and/or sponsor safety data review
- Protocol specified procedures and responsibilities for conduct of multicenter trials, if applicable
- Responsibility for, and frequency of, monitoring/auditing the trial for compliance, accuracy of data, adverse event reporting, and appropriate submissions to and approvals from FDA/YALE IRB and other oversight bodies
- Frequency of sponsor and/or institutional review of safety data, accrual rate, and other trial data
- Need for a DSMB: A DSMB is established for all randomized Phase III studies, and other studies involving high risk interventions which warrant more vigilant oversight, as identified by the Principal Investigator or the PRC
- Adequate management of COI concerns
- Monitoring, auditing, and safety reviews commensurate with the risk of the study
- Requirements for other institutional committee oversight, if appropriate

The DSMP submitted with each protocol is written by the investigator, and should address the following questions:

- How is the study monitored for patient safety (physical and psychological)?
- What procedures are in place to report adverse events or unanticipated problems?

Protocol Review Committee (PRC) Membership (See Appendix II)

C. QUALITY ASSURANCE, COMPLIANCE AND SAFETY COMMITTEE (QUACS)

This committee was established in 2005 and provides the essential mechanism for the ongoing monitoring of activated studies, as defined in the DSMP. QUACS provides oversight for safety, compliance, through self reporting and through internal or external audits. Internal audits are conducted by the OPRM on all studies that are not monitored externally by a sponsor. OPRM tracks safety data reports, submitted by the PI’s from all studies, for review by the QUACS. QUACS also reviews the monitoring reports or audits conducted by external agencies, such as industrial sponsors, CTEP, Cooperative Groups, DSMBs, or any other external oversight committees.

The QUACS Committee meets ten times a year and on an ad hoc basis. All submissions to the Committee, such as data and safety reports, audit reports, and monitoring reports, are made to the OPRM. Copies of the meeting agendas, minutes, and all correspondence are kept on file in the YCC Office of Protocol Review and Monitoring.

Overview of QUACS Process

Once a protocol is approved by the PRC, the Data and Safety Monitoring Plan is forwarded to the OPRM for coordination of internal audits and the establishment of a review schedule for all external and/or internal auditing/monitoring reports, and internal and/or external safety data reports. OPRM forwards all reports to the QUACS Committee Chair, and coordinates the QUACS Committee meetings.
The Committee reviews all reports and votes to:

- Approve
- Approve with recommendations
- Place study on administrative hold pending the resolution of outstanding issues
- Terminate

The Committee has the right to terminate a study, or to suspend accrual, by placing it on administrative hold pending the resolution of an unacceptable audit or a safety review that reveals situations considered to be unacceptable. PI’s of studies which are suspended or terminated will be required to submit a response within a given timeframe set by the Committee. If a corrective action plan is necessary, a timeframe will be set and a follow up schedule will be put into place to evaluate the corrective action plan.

The QUACS Committee has the authority to amend the initial DSMP, require additional monitoring or more frequent reporting on study progress and serious adverse events, require the establishment of a DSMB, or require the appointment of a medical monitor or an ad hoc safety committee, external to the QUACS, during the course of the study.

Serious issues concerning safety, compliance, or scientific misconduct are referred to the YCC Executive Committee. Decisions made by QUACS may be appealed by the PI to the Executive Committee. All QUACS actions are communicated to the Yale IRB.

Safety:

In addition to the regular reporting requirements outlined in the DSMP for specific studies, the PI’s are responsible for notifying the QUACS Committee of any serious safety or compliance problems.

Serious unexpected adverse events that are possibly related to study drug treatment must be reported to the Yale IRB and other oversight agencies, as designated in the protocol. Cumulative safety reports are submitted to the QUACS Committee either by the investigator or his/her designee. The QUACS Committee must be informed of treatment-related SAEs if the SAEs would significantly alter the risk/benefit ratio of the trial.

Compliance:

All studies are monitored for compliance, either by internal or external audits, or sponsor monitoring visits. The frequency of these audits is determined by the PRC at the initial review. All reports are submitted to the QUACS Committee through the OPRM. Internal audits are coordinated by the OPRM.

Criteria for Termination of Protocol:

Protocols may be closed for the following indications:

- Serious unexpected adverse event(s) that significantly alter the risk/benefit ratio
- Serious or multiple deficiencies in study conduct (e.g., lack of informed consent, violation of patient eligibility criteria, failure to report an adverse event(s) in a timely fashion, etc.)
- Lack of compliance with IND obligations
• New data suggesting the active protocol cannot achieve study objectives, or significantly altering the risk/benefit ratio
• Inadequate accrual (<30% below projected accrual for a one-year period) with little or no likelihood that the study's target will be met
• Excessive accrual (>10% above the total projected accrual)
• Target accrual and/or study objectives are met
• Principal Investigator leaves institution
• Multiple major deficiencies in an internal or external audit or monitoring report
• Evidence of serious scientific misconduct or unsafe practices

Data & Safety Monitoring Reports:

Data & Safety Monitoring Reports are required on a schedule using a standardized reporting format and determined by the initial PRC review and should include:

• Total number of patients entered on each trial
• Total number of patients treated
• Safety data should be provided by patient, dose levels administered, arms of study, and agent(s) involved
• A summary of all adverse events reported to date using CTC grading criteria as defined in the protocol
• A specific list of adverse events requiring expedited reporting – to include ALL serious adverse events (SAE’s)
• Significant literature reporting developments that may affect the safety of participants or the ethics of the study

The QUACS Committee can request additional data from the investigators, as needed, on safety issues arising over the course of the study.

The QUACS Committee will review data and safety monitoring reports, and recommend whether the study should continue unchanged, require modification/amendment, or be closed. In the event the committee feels a revision is warranted, the QUACS Committee will immediately notify the principal investigator of the study. The QUACS Committee has the authority to close trials to patient accrual, should the risk to patients be excessive or outweigh the potential benefits of the study. Should this occur, the QUACS Committee would be responsible for reporting the termination to the Yale IRB, the NCI, and other sponsors and regulatory agencies. The QUACS Committee has authority to stop a study for non-compliance with a DSMP.

Quality Assurance, Compliance & Safety Committee (QUACS) Membership (See Appendix III)

D. Executive Committee

The Executive Committee is comprised of members of the YCC leadership and provides a mechanism for adjudicating issues not resolvable within the scope of the PRC or the QUACS Committees. PI’s may appeal decisions made by the PRC or QUACS Committees to the Executive Committee.

Yale Cancer Center Executive Committee Membership (See Appendix IV)
E. Office of Protocol Review & Monitoring (OPRM)

This Office was established in 2005 and is the coordinating center for the SC, PRC, and QUACS Committees, the internal audit program, and the training program for clinical trial staff. Copies of the meeting agendas, minutes, and all correspondence related to these activities are kept on file at this office. Training records are maintained in the office and tracked in the University’s TMS (Training Management System).

Internal Audit Program: An internal audit schedule is determined by the PRC at the time of initial study approval. The audits are conducted by the OPRM and reviewed by the QUACS Committee.

The purpose of the audit program is:
- To assure patient safety by monitoring compliance
- To assure regulatory compliance by reviewing consent and adverse event reporting
- To assure scientific integrity by monitoring accuracy and completeness of data collection.

The results of the audit are reported to the investigator and to the QUACS Committee, with comments and recommendations for a corrective action plan, if appropriate. Non-therapeutic studies may also be audited to assess the completeness of records and to review consent procedures, ensuring regulatory compliance.

Items audited may include:
- Consent form for signatures, dates, and validity of form
- Protocol compliance and patient safety
- Eligibility Criteria
- Adherence to treatment plan as written in the protocol
- Adverse event grading, documentation, and reporting
- Response evaluations

Regulatory Compliance:
- Compliance with all regulations, Yale University policies, and Yale IRB guidelines.

Accuracy of data:
- Data collection will be evaluated to ensure the information needed to test the hypothesis will be available for analysis
- Accuracy of data will be determined by comparing data collection with source documents
- Clinical responses will be subjected to independent confirmation when appropriate

Drug Accountability:
- Drug accountability forms will be audited whenever an investigational agent is involved.

OnCore Database: In July of 2011 the OnCore database was implemented for the tracking and management of all clinical trials conducted at YCC. OnCore allows for tracking of all committee activity as well as providing reports on individual protocol or disease unit activity. Serious adverse events, protocol deviations, internal audits and findings, accruals and regulatory history are tracked. OnCore also provides electronic case report forms for investigator initiated studies. This replaces two databases maintained by the OPRM and the CTO. Historical data from these databases has been migrated into OnCore.

Training Program: The OPRM coordinates a training program for all staff involved with oncology clinical trials. In addition to encompassing many standard topics, including Good Clinical Practices, IRB Basics,
Research Ethics and Misconduct, specific topics indispensable to the understanding of compliance and safety are identified and addressed as required. Education sessions and training programs are done in coordination and collaboration with Yale’s Human Research Protection Program and the Yale Center for Clinical Investigations.

F. YCC Clinical Trials Office (CTO)

The YCC Clinical Trials Office provides study coordination, data management, and administrative assistance and support to Yale investigators.

The Clinical Trials Office, in correlation with the YCC DSMP, also:

- Provides information and assists in the review and monitoring of clinical studies reviewed by the SC, PRC and QUACS Committees
- Designs case report forms for investigator-initiated studies
- Maintains a database (OnCore) for tracking specific protocol activity.

The CTO collects data for the Investigator’s Data and Safety Monitoring Reports according to the timeline established by the initial PRC review. These reports go beyond the SAE report, listing all adverse events, regardless of severity or attribution, and convey cumulative study-wide experience. In addition, annual data and safety monitoring reports are submitted by the principal investigators of all studies to the QUACS Committee, for review at least annually.

V. CONFLICT OF INTEREST

COI procedures for all YCC Committee Members and Staff:

- Once a conflict of interest has been identified, the YCC Committee Chair shall evaluate the conflict and discuss it with the committee member or staff person to evaluate the individual’s ability to take part in protocol review and approval activities that may be influenced by the individual’s interest. The individual will be directed to recuse him/herself from deliberations or decisions when considering any research project or report for which a real or potential conflict has been identified. The Committee Chair shall consult with the Provost’s Office or the Yale IRB regarding further actions when appropriate.

- In the event the Chair has a conflict the Vice Chair shall evaluate the conflict and make a recommendation for the Chair to recuse him/herself. In the event that both the Chair and the Vice-Chair have a conflict a non-conflicted member shall serve in this capacity.

- The minutes shall include any identification of conflict or appearance of conflict and the Committee’s decision or action taken related to that conflict.

- At the start of each meeting the Committee Chair shall ask members and staff to identify any conflict of interest they may have with a protocol scheduled for review on the meeting agenda. Committee members and staff must recuse themselves from deliberations or decisions concerning protocols in which they have, or appear to have, a conflict of interest. This includes any actual or anticipated direct involvement in the design, conduct, or reporting of a study that is being reviewed, or other interests that might affect or appear to affect their objectivity in reviewing the study. However, at the discretion of the Chair, members/staff may provide information and answer questions regarding the research prior to the recusal.

- Committee members and staff may choose to recuse themselves from the Committee discussion and/or vote, even if no actual conflict exists, if it will avoid the appearance of a conflict of interest.
If conflicts are identified or recognized during the course of a meeting or review the member shall recuse themselves at that time and this action shall be noted in the minutes.

The University policy on conflict of interest can be found at [http://provost.yale.edu/conflict-policy](http://provost.yale.edu/conflict-policy) All investigators must report potential conflicts to the office annually.

VI. **INVESTIGATOR REQUIREMENTS AND RESPONSIBILITIES**

The Principal Investigator of each study is ultimately responsible for every aspect of the design, conduct, and final analysis of their protocol. The study PI is responsible for ensuring:

- Adherence to the DSMP
- Assessment and reporting of adverse events, per approved protocol specific guidelines
- Establishing a DSMB if the proposed study meets any of the following criteria:
  - The study is a randomized, Phase III, investigator-initiated, clinical trial
  - The study includes a high-risk intervention
  - The study is a blinded and/or high risk intervention Phase II multicenter study
  - The study involves a conflict of interest

Note: The QUACS Committee, or a subcommittee, can serve as the DSMB for high-risk interventions, studies involving conflict of interest, or high risk intervention multi-center phase II trials. The QUACS may choose to appoint an external DSMB for a particular trial.

VII REPORTING OF ADVERSE EVENTS:

All studies must have a structured adverse event determination, monitoring and reporting system, and procedures for referring and/or treating subjects experiencing adverse events.

*By regulation (21 CFR Part 312.32), an SAE is defined as one that:*

- is fatal or life-threatening (i.e., results in an immediate risk of death)
- is permanently or substantially disabling
- requires or prolongs hospitalization
- is a congenital anomaly

*This definition also includes any other event the investigator judges to be serious, or which would suggest a significant hazard, contraindication, side effect, or precaution.*

Studies must include a proposed schedule for reporting adverse events to the DSMB (if one is established), the Yale IRB (or additional IRBs, in the case of multi-site studies), study sponsors, and/or the NIH/FDA.

- If the proposed protocol has additional clinical sites besides the Yale Cancer Center, the protocol should describe procedures by which the PI will notify all sites regarding SAE’s, as identified by the investigator, the DSMP or DSMB, if one is established. Furthermore, the protocol must specify procedures for individual sites to report SAEs either directly to the appropriate oversight authorities, or through the study PI. In all cases, the study PI must be informed of all SAEs, and will be responsible for the overall safety of the trial.
• In cases where the IND is held by a Yale investigator, the Yale investigator will be responsible for reporting all SAEs in timeframes consistent with 21 CFR Part 312.32.

• In specific cases where an outside agency is the sponsor of an investigational agent, i.e., holder of an Investigational New Drug [IND] application, the PI’s must submit individual Adverse Event Reports to the IND holder, in accordance with agency and FDA regulations.


*The Yale Cancer Center follows the guidelines provided by NCI for reporting adverse events for drugs.*
Trials for which NCI is also the IND sponsor (for details, see NCI's *Investigator's Handbook*, available online at


**TABLE A: Expedited Reporting for Phase I Studies (including hospitalization*)**

<table>
<thead>
<tr>
<th>UNEXPECTED EVENT</th>
<th>EXPECTED EVENT</th>
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</thead>
<tbody>
<tr>
<td>GRADES 2 - 3 Attribution of Possible, Probable or Definite</td>
<td>GRADES 4 - 5 Regardless of Attribution</td>
</tr>
<tr>
<td><strong>Grade 2 -</strong> Expedited report within 10 working days</td>
<td><strong>GRADE 1 - 3</strong> Regardless of Attribution</td>
</tr>
<tr>
<td><strong>Grade 3 -</strong> Report by phone to IDB within 24 hrs. Expedited report to follow within 10 working days.</td>
<td><strong>GRADE 4 - 5 Regardless of Attribution</strong></td>
</tr>
<tr>
<td><em>(Grade 1 - Adverse Event Expedited Reporting NOT required.)</em></td>
<td></td>
</tr>
<tr>
<td>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.</td>
<td>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.</td>
</tr>
</tbody>
</table>
### TABLE B: Expedited Reporting for Phase II and III Studies (including hospitalization*)

<table>
<thead>
<tr>
<th>UNEXPECTED EVENT</th>
<th>EXPECTED EVENT</th>
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</thead>
<tbody>
<tr>
<td>GRADES 2 - 3 Attribution of Possible, Probable or Definite</td>
<td>GRADES 4 - 5 Regardless of Attribution</td>
</tr>
<tr>
<td>Expedited report within 10 working days</td>
<td>Report by phone to IDB within 24 hrs. Expedited report to follow within 10 working days.</td>
</tr>
</tbody>
</table>

**Grade 1 - Adverse Event Expedited Reporting NOT required.**

Expedited reporting may not be appropriate for specific expected adverse events for certain later Phase II and Phase III protocols. In those situations, the adverse events that will not have expedited reporting must be specified in the text of the approved protocol. For instance, an expected Grade 3 event that is definitely related to the investigational agent is only to be reported if the patient is hospitalized using the

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* For Hospitalization Only — Any medical event equivalent to 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.
generic reporting criteria. In a trial of an investigational agent where Grade 3 diarrhea, requiring hospitalization, is expected, only diarrhea requiring ICU care (Grade 4) might be designated for expedited reporting.

**IND Trials for which NCI is NOT the IND sponsor** have reporting requirements that are specific to the study. The regulations governing these requirements can be found at


### Serious Adverse Event Reporting

<table>
<thead>
<tr>
<th>UNEXPECTED EVENT</th>
<th>EXPECTED EVENT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade 1</strong> – Adverse event reporting not required.</td>
<td><strong>Grade 1</strong> – Adverse event reporting not required.</td>
</tr>
<tr>
<td><strong>Grades 2-3</strong> Attributed as Possible, Probable or Definite</td>
<td><strong>Grades 4 and 5</strong> Regardess of Attribution</td>
</tr>
<tr>
<td>Grade 2 – Expedited report within 10 working days</td>
<td>Adverse Event Expedited Reporting is NOT required</td>
</tr>
<tr>
<td>Grade 3 – Report by phone/fax within 24 hrs. Expedited report to follow within 10 working days.</td>
<td>Report within 24 hrs. Expedited report to follow within 10 working days. This includes deaths within 30 days of the last dose of treatment.</td>
</tr>
</tbody>
</table>

**NOTE:** The death of any patient on a clinical trial is considered a Serious Adverse Event, regardless of attribution and is required to be reported to the Yale IRB and study sponsor.

**Trials involving commercial agents only (no INDs involved):**

Adverse events which do not meet the definition of an SAE also require timely reporting, dependent upon the grade of adverse event, using CTC criteria, attribution, and whether the event is expected or unexpected. Reporting requirements are available at the CTEP website at [http://ctep.info.nih.gov](http://ctep.info.nih.gov); under the NCI Guidelines:

**Expedited Adverse Event Reporting Requirements for NCI Investigational Agents.**

All expedited adverse event reports must be reported to the Yale IRB.

**Trials involving recombinant DNA molecules (gene transfer):**

Investigators should refer to NIH guidelines for Research Involving Recombinant DNA Molecules.
Yale Investigator-Initiated Multi-Center Studies:

The protocol must define a mechanism for all sites to centrally report all SAEs to the PI at Yale. In addition to complying with all regulations for reporting the SAEs occurring at Yale, the investigator is responsible for informing all sites of all SAE’s occurring on the study, and for insuring all IRBs are informed.

Data and Safety Monitoring Boards:

If an independent DSMB is required for adequate subject safety, the PI will make arrangements for a DSMB to review the serious adverse events within that specific study, as described in Section VI of this document, pertaining to phase III trials and DSMB.

VIII. MONITORING GUIDELINES ACCORDING TO TYPE OF PROTOCOL

According to Sponsor:

National Institutes of Health:

The National Institutes of Health sponsors therapeutic and non-therapeutic trials at the Yale Cancer Center using a number of mechanisms, each with their particular data and safety monitoring requirements.

National Cooperative Oncology Group Contracts:

The YCC conducts clinical trials with several of the National Cooperative Oncology Groups sponsored by the NCI.

Each contract with the principal investigator clearly specifies the data and safety monitoring requirements for each study. 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. There are no additional reporting requirements. However, all SAE’s are required to be reported to the Yale IRB, and will be included in annual summary reports to the Yale IRB and QUACS.

Other NCI Contracts:

In the event a Yale PI conducts a clinical trial under the auspices of a grant from the NCI, the following would be applicable. In these grants, the NCI may or may not hold the IND for agents administered in these programs. Each protocol includes specific plans for data and safety monitoring using established NCI data monitoring systems. Local monitoring will be determined on a study-by-study basis by the PRC Committee.

In addition, any action taken by the QUACS Committee, Yale IRB, sponsor, or the investigator, resulting in a temporary or permanent suspension of an NCI-funded clinical trial, will be reported to the NCI grant program director responsible for the grant. These actions include, for example, any FDA actions that affect NCI-funded trials.

Pharmaceutical Industries:
All clinical trials conceived and initiated by pharmaceutical industry sponsors, with subsequent YCC participation, will require data and safety monitoring plans that have been reviewed and approved by both the PRC and Yale IRB. These protocol-specific plans will adhere to industry and FDA-specified guidelines. Local reporting for Data and Safety Monitoring for industry-sponsored trials will require SAE’s to be reported to the Yale IRB, using the applicable Yale IRB form, and either industry-specified report formats, or the FDA MEDWATCH SAE reporting form. All serious and unexpected adverse events at least possibly related to protocol treatment will be reported to the Yale IRB and will be included in annual summary reports to the Yale IRB and QUACS.

**Investigator-Initiated Studies:**

Investigator-Initiated Studies – Local

Local, investigator-initiated studies frequently have no external requirements for data and safety monitoring, and therefore require particular attention for local monitoring. These studies receive the highest priority for local oversight. Each such study will be reviewed by the PRC to determine if data and safety monitoring plans are complete and appropriate. In the event that no monitoring is specified by external agencies, in addition to requiring appropriate investigator reporting of adverse events to be specified in the protocol, the PRC will assign a schedule for internal audits and data reporting to the QUACS Committee that adheres to the following guidelines according to the phase of trial. The QUACS may in addition require the investigator to create a DSMB. The membership and charter of the DSMB is subject to QUACS review.

Investigator-Initiated – Multi-Institution Trials

Yale investigator-initiated trials conducted in a multi-institution setting may not have been subjected to the rigorous review and reporting requirements imposed by NIH funding. All investigator-initiated multi-center studies must be approved by the PRC. Depending upon the risk level, a DSMB may be required. The protocol document must include a detailed plan for the investigator to inform all sites of SAEs, or individual sites to report SAEs to the PI and the sponsor (directly or through the study PI). The DSMP will establish a schedule for the overall monitoring of toxicity and efficacy, as well as the fulfillment of all regulatory requirements, at all sites, in a timely manner. Additionally, the investigator must provide evidence of adequate funding to support the proposed monitoring plan. If Yale is a participant in an investigator-initiated multi-center trial but is not the lead institution, the investigator will be required to show that the DSMP for the trial meets institutional and NIH standards. The DSMP for the trial at Yale may include an institutional component in which the PRC assigns internal auditing and safety data reporting for patients accrued at Yale.

The QUACS Committee requires a comprehensive summary of the study status, including the number of patients enrolled, and serious adverse events, from all participating sites, once enrollment begins. The QUACS Committee may revise the DSM requirements at anytime and may consider the appointment of a medical monitor or an ad hoc safety committee, based on the DSM reports and consultation with the PI.

**According to Phase of Therapeutic Study:**

**Phase I**

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 to monitoring patient safety. The PRC will require the study PI to provide continuous monitoring of patient safety, with formal reports to the QUACS Committee for monitoring oversight. The frequency of reporting will be determined on a
protocol-by-protocol basis, such as after each cohort or semi-annually, and by other factors such as the sponsor and the number of sites involved. For regimens that pose a particularly high risk to patients, such as those with little existing toxicity data, the PRC may require that the investigator provide more frequent data, e.g., monthly. The report schedule may be modified over the course of the study based on the safety experience of patients treated. The study PI is required to promptly report all serious adverse events (SAE) experienced by a patient on a local, investigator-initiated Phase I trial to the HIC and FDA (if applicable) using appropriate reporting forms.

**Phase II**

While some variation may exist in monitoring, the PRC will normally require PI’s of local, investigator-initiated Phase II studies to provide periodic monitoring of patient safety, with formal reporting to the QUACS Committee. High risk studies will be evaluated on a protocol-by-protocol basis to ensure the monitoring plan is commensurate with the patient risk.

**Phase III**

Any Phase III investigator-initiated protocols must include the establishment of an independent DSMB. Procedures for quality assurance/quality control, data management, and analysis must be included in text of the protocol. Evidence for securing support, resources, and funding appropriate for the DSMB to meet its requirements is required. All data must be directly available to the DSMB upon request.

**According to Non-Therapeutic Studies:**

**Epidemiology Studies (Case Control Studies):**

Population-based case control studies that propose to use the Rapid Case Ascertainment Shared Resource (RCA), must be approved by the Shared Resource Utilization Review Committee (SRURC) prior to PRC review and approval. These studies will be considered in the category of minimal risk. Therefore, a yearly annual report will be required listing the number of patients enrolled, a summary of adverse events or unanticipated problems, withdrawals, recent pertinent literature that may alter the previously stated risk to the study participants, and any changes in the protocol.

**Other**

Other non-therapeutic studies (not RCA studies) will be required to submit a DSMP plan to the PRC prior to Yale IRB approval. These studies will be considered in the category of minimal risk. Therefore, a yearly annual report will be required with the number of patients enrolled, summary of adverse events or unanticipated problems, withdrawals, recent pertinent literature that may alter the previously stated risk to the study participants, and any changes in the protocol.

**IX. DATA AND SAFETY MONITORING BOARDS**

If the study is approved by the PRC on scientific grounds, and the PI has not proposed a DSMB, the PRC Committee will determine whether or not a DSMB is required for adequate subject safety. If a DSMB is required, the PRC will request the following from the PI:

- proposed frequency of meetings for the DSMB
- proposed list of data items to be provided to the DSMB
- nominate as members no less than three persons, providing information on the nominated DSMB members, including:
CV
- list of current affiliations with pharmaceutical and biotechnology companies
- name of the company
- type of affiliation (e.g., stockholder, consultant)
- any other relationship that could be perceived as a conflict of interest, related to the study and associated with commercial interests.

These nominations are subject to approval by the Yale Cancer Center QUACS Committee. The PRC will reserve the right to appoint additional members to the DSMB to include scientific expertise in topic areas relevant to the trial, such as biostatistics, ethics, or patient advocacy.

**DSMB responsibilities will include the following:**

- Review the entire study protocol, the data and safety monitoring plan, and the informed consent, recommending changes to these, as appropriate.
- Recommend the initiation of subject recruitment only after final acceptance of the above documents.
- Identify the format, timing, and specific data parameters to be provided by study personnel for review by the DSMB during the course of the study.
- At specified intervals over the course of the trial (at least twice yearly throughout the conduct of study with additional meetings as needed), review data on patient safety, efficacy, and accrual, including gender and minority inclusion, randomization, protocol compliance, retention, and data collection.
- Identify patient safety issues raised by ongoing review, informing the PI of these issues by written report. The PI will be responsible for expeditious distribution to all site PI’s.
- Propose appropriate analyses, and identify and request from study investigators, any additional data required to fully evaluate safety issues and efficacy endpoints.
- At each meeting, reconsider the rationale for continuation of the study, based on all available information on accrual, progress of randomization, retention, protocol compliance, data management, safety and efficacy outcomes, as well as new information from other clinical trials, and make a recommendation for or against continuation of the trial.
- Provide the PI with written reports following each DSMB meeting. The study PI is responsible for sending reports to the QUACS Committee and the Yale IRB, and to individual site PI’s, who are required to distribute the report to their local IRBs.
- Review and approve any release of outcome data.
- Review manuscripts of trial results prior to submission for publication or public presentation.

The content and structure of DSMB meetings are determined by each DSMB for a particular study, but should generally include three parts:

- An open session in which investigators and personnel involved with the clinical trial 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 toxicity.
- A closed session involving the DSMB and study statistical staff at which the statisticians should present and discuss the outcome results with the DSMB.
- A final closed session involving only DSMB members for discussion of the general conduct of the trial and all safety and efficacy results, and in order to come to a consensus about further recommendations or actions required, including recommendation for or against continuation of the trial.
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 until the recommendation to release the results are accepted and implemented. Each member of the DSMB must sign a statement of confidentiality.

Conflict of Interest:

DSMB members are subject to the YCC policies regarding standards of conduct. Individuals invited to serve on the DSMB will disclose any potential conflicts of interest to the trial principal investigator and to appropriate Yale Cancer Center officials, in accordance with institution policies. Potential conflicts which develop during a member's tenure on a DSMB must also be disclosed. Conflict of interest can include professional interests, proprietary interests, and miscellaneous interests, as described in the NIH Grants Policy Statement, Page II-12, and 45 CFR Part 94. Decisions concerning DSMB membership for individuals with potential conflicts of interest will be made in accordance with institution policies.

Institutional Approval of Data and Safety Monitoring Plans:

Individual protocol data and safety monitoring plans also require Yale IRB approval.
Acknowledgements

The YCC Data and Safety Monitoring Plan is greatly indebted to efforts of the National Institutes of Health, particularly the National Cancer Institute. Data and Safety Monitoring plans or policies from the University of Pennsylvania Cancer Center, Stanford University, the Ohio State University Comprehensive Cancer Center, Norris Cotton Cancer Center, Duke University, University of Wisconsin, Yale School of Medicine, and Policies of the Yale School of Medicine Yale IRB formed the basis of our plan. In a few cases, text from these sources was copied in part or in total from these sources. Nevertheless, we assume complete responsibility for the consolidation and integration of plans and its implementation at the Yale Cancer Center.
### APPENDIX I

**Clinical Research Steering COMMITTEE (CRSC)**

<table>
<thead>
<tr>
<th>Members</th>
<th>Expertise / Program</th>
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</thead>
<tbody>
<tr>
<td>Howard Hochster, M.D., Chair</td>
<td>Gastroenterology</td>
</tr>
<tr>
<td>Joachim Baehring, M.D.</td>
<td>Neuro-Oncology</td>
</tr>
<tr>
<td>Anees Chagpar, M.D.</td>
<td>Breast / Surgery</td>
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<tr>
<td>Roy Decker, M.D.</td>
<td>Therapeutic Radiology</td>
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<tr>
<td>Hari Deshpande, M.D.</td>
<td>Head &amp; Neck</td>
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<td>Frank Detterbeck, M.D.</td>
<td>Thoracic</td>
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<tr>
<td>Madhav Dhodapkar, M.D.</td>
<td>Hematology / Myeloma</td>
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<tr>
<td>Francine Foss, M.D.</td>
<td>Lymphoma</td>
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<tr>
<td>Lyndsay Harris, M.D.</td>
<td>Breast</td>
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<td>Roy Herbst, M.D.</td>
<td>Professor, Chief, Medical Oncology</td>
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<td>Gary Kupfer, M.D.</td>
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<tr>
<td>Ruth McCorkle, R.N., Ph.D.</td>
<td>Nursing</td>
</tr>
<tr>
<td>Peter Schwartz, M.D.</td>
<td>Obstetrics/Gynecology</td>
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<tr>
<td>Mario Szol, M.D.</td>
<td>Melanoma</td>
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<tr>
<td>Xiaopan Yao, Ph.D.</td>
<td>Biostatistics</td>
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**Ex-officio**

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<tbody>
<tr>
<td>Henry Durivage, Pharm.D.</td>
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<td>Chad Ellis, Ph.D.</td>
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## APPENDIX II

### Protocol Review Committee

<table>
<thead>
<tr>
<th><strong>Members</strong></th>
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</thead>
<tbody>
<tr>
<td>Mario Sznol, M.D., Chair</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Peter Marks, M.D., Vice Chair</td>
<td>Hematology</td>
</tr>
<tr>
<td>Osama Abdelghany, Pharm.D.</td>
<td>Pharmacy</td>
</tr>
<tr>
<td>Joachim Baehring, M.D.</td>
<td>Neuro-Oncology</td>
</tr>
<tr>
<td>Roy Decker, M.D.</td>
<td>Therapeutic Radiology</td>
</tr>
<tr>
<td>Hari Deshpande, M.D.</td>
<td>Head &amp; Neck Cancer</td>
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<tr>
<td>Michael DiGiovanna, M.D.</td>
<td>Breast Cancer</td>
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<tr>
<td>James Dziura, Ph.D.</td>
<td>Biostatistics</td>
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<tr>
<td>Mark Faries, M.D.</td>
<td>Melanoma</td>
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<tr>
<td>Scott Gettinger, M.D.</td>
<td>Head &amp; Neck Cancer</td>
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<td>Roy Herbst, M.D.</td>
<td>Lung Cancer</td>
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<td>Howard Hochster, M.D.</td>
<td>Gastroenterology</td>
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<tr>
<td>Benjamin Judson, M.D.</td>
<td>Otolaryngology</td>
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<tr>
<td>Maurice J. Mahoney, M.D., J.D.</td>
<td>Genetics</td>
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<tr>
<td>Daniel Morgensztern, M.D.</td>
<td>Thoracic, Head &amp; Neck Cancer</td>
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<tr>
<td>Peter Peduzzi, Ph.D.</td>
<td>Biostatistics</td>
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<tr>
<td>David Rimm, M.D.</td>
<td>Pathology</td>
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<tr>
<td>Alessandro Santin, M.D.</td>
<td>Obstetrics/Gynecology</td>
</tr>
<tr>
<td>Stuart Seropian, M.D.</td>
<td>Lymphoma/Transplant</td>
</tr>
<tr>
<td>Xiaopan Yao, Ph.D.</td>
<td>Biostatistics</td>
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**Ex. Officio – Non Voting:**

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<thead>
<tr>
<th><strong>Members</strong></th>
<th><strong>Expertise</strong></th>
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<tbody>
<tr>
<td>Nancy Beaulieu, R.Ph.</td>
<td>Investigational Pharmacy</td>
</tr>
<tr>
<td>Henry Durivage, Pharm.D.</td>
<td>Associate Director, Clinical Trials</td>
</tr>
<tr>
<td>Chad A. Ellis, Ph.D.</td>
<td>Deputy Director for Research, Yale Cancer Center</td>
</tr>
<tr>
<td>Thomas Lynch, M.D.</td>
<td>Director, Yale Cancer Center</td>
</tr>
<tr>
<td>Susan Mayne, Ph.D.</td>
<td>Nutritional Epidemiology</td>
</tr>
<tr>
<td>Kathleen Uscinski, M.B.A., CIP</td>
<td>Associate Director, Clinical Trials Operations</td>
</tr>
<tr>
<td>Daniel Zelterman, Ph.D.</td>
<td>Biostatistics</td>
</tr>
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</table>
APPENDIX III

Quality Assurance, Compliance & Safety Committee

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<th>Members</th>
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<tbody>
<tr>
<td>Michal Rose, M.D., Chair</td>
<td>VAMC, Oncology</td>
</tr>
<tr>
<td>Edward Snyder, M.D., Vice Chair</td>
<td>Transfusion Medicine</td>
</tr>
<tr>
<td>Sandra Alfano, Pharm.D., FASHP</td>
<td>Yale IRB Chair, Associate Research Scientist</td>
</tr>
<tr>
<td>Susan Anderson, R.N.</td>
<td>Quality Assurance</td>
</tr>
<tr>
<td>Lisa Baker, R.N.</td>
<td>OB/GYN</td>
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<tr>
<td>Daniel Boffa, M.D.</td>
<td>Thoracic Surgery</td>
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<tr>
<td>James Dziura, Ph.D.</td>
<td>Biostatistician</td>
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<tr>
<td>Michael Glasgow</td>
<td>Grants &amp; Contracts</td>
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<tr>
<td>Roy Herbst, M.D.</td>
<td>Professor, Chief of Medical Oncology</td>
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<tr>
<td>Jill Lacy, M.D.</td>
<td>Oncology</td>
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<tr>
<td>Peter Peduzzi, Ph.D.</td>
<td>Biostatistician</td>
</tr>
<tr>
<td>Timothy Shannon, M.D.</td>
<td>Drug Development</td>
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<tr>
<td>Mario Sznol, M.D.</td>
<td>Melanoma</td>
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<tr>
<td>Lynn Wilson, M.D.</td>
<td>Therapeutic Radiology</td>
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<td>Fred Wright, M.D.</td>
<td>VAMC, Nephrology</td>
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<td>Xiaopan Yao, PhD</td>
<td>Biostatistician</td>
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<tr>
<td>Thomas Lynch, M.D.</td>
<td>Ex-Officio</td>
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<tr>
<td>Henry Durivage, Pharm.D.</td>
<td>Ex-Officio</td>
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<tr>
<td>Chad Ellis, Ph.D.</td>
<td>Ex-Officio</td>
</tr>
<tr>
<td>Kathleen Uscinski, M.B.A., CIP</td>
<td>Ex-Officio</td>
</tr>
<tr>
<td>Stuart Warner, J.D.</td>
<td>Legal Consultant</td>
</tr>
</tbody>
</table>

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APPENDIX IV

Executive Committee

Karen Anderson, PhD  Co-Program Director, Developmental Therapeutics
Lieping Chen, MD, PhD  Co-Program Director, Cancer Immunology
Frank Dettterbeck, MD  Assistant Director, Surgical Oncology
                  Deputy Director, Yale Cancer Center; Associate Director, Basic Sciences; Program Director, Molecular Virology
Daniel DiMaio, MD, PhD  Program Director, Radiobiology and Radiotherapy
Henry Durivage, PhD  Associate Director, Clinical Trials Office
Chad Ellis, PhD  Deputy Director, Research Administration
Renee Gaudette  Director, Public Affairs and Marketing
Peter Glazer, MD, PhD  Program Director, Cancer Genetics and Genomics
Lyndsay Harris, MD  Co-Program Director, Cancer Genetics and Genomics
Roy Herbst, MD, PhD  Director, Developmental Therapeutics
Howard Hochster, MD  Associate Director, Clinical Sciences
Melinda Irwin, PhD, MPH  Co-Program Director, Cancer Prevention and Control
Gary Kupfer, MD  Assistant Director, Pediatric Oncology
Peter Lamothe  Director of Development
Abe Lopman, MBA  Vice President and Executive Director, Smilow Cancer Hospital
Thomas Lynch, MD  Director, Yale Cancer Center; Physician in Chief, Smilow Cancer Hospital
Susan Mayne, PhD  Associate Director, Population Sciences
Ruth McCorkle, PhD  Assistant Director, Psychosocial Oncology
Jennifer Mulligan, MBA  Associate Director, Business Office
Peter Peduzzi, PhD  Director, Biostatistics Shared Resource
Adam Roshka  Associate Administrator, Yale Cancer Center Finance
Warren Shlomchik, MD, PhD  Co-Program Director, Cancer Immunology
Jeffrey Sklar, MD, PhD  Assistant Director, Pathology and Tissue Acquisition Services
Frank Slack, PhD  Co-Program Director, Cancer Genetics and Genomics
Edward Snyder, MD  Assistant Director, Membership
David F Stern, PhD  Associate Director, Shared Resources; Program Director, Signal Transduction
Kevin Vest, PT, MBA, FACHE  Deputy Director, Administration and Clinical Affairs
Yong Zhu, PhD  Co-Program Director, Cancer Prevention and Control