

UAB Comprehensive Cancer Center

Maintaining a High Quality of Care for Research Participants

DATA AND SAFETY MONITORING PLAN



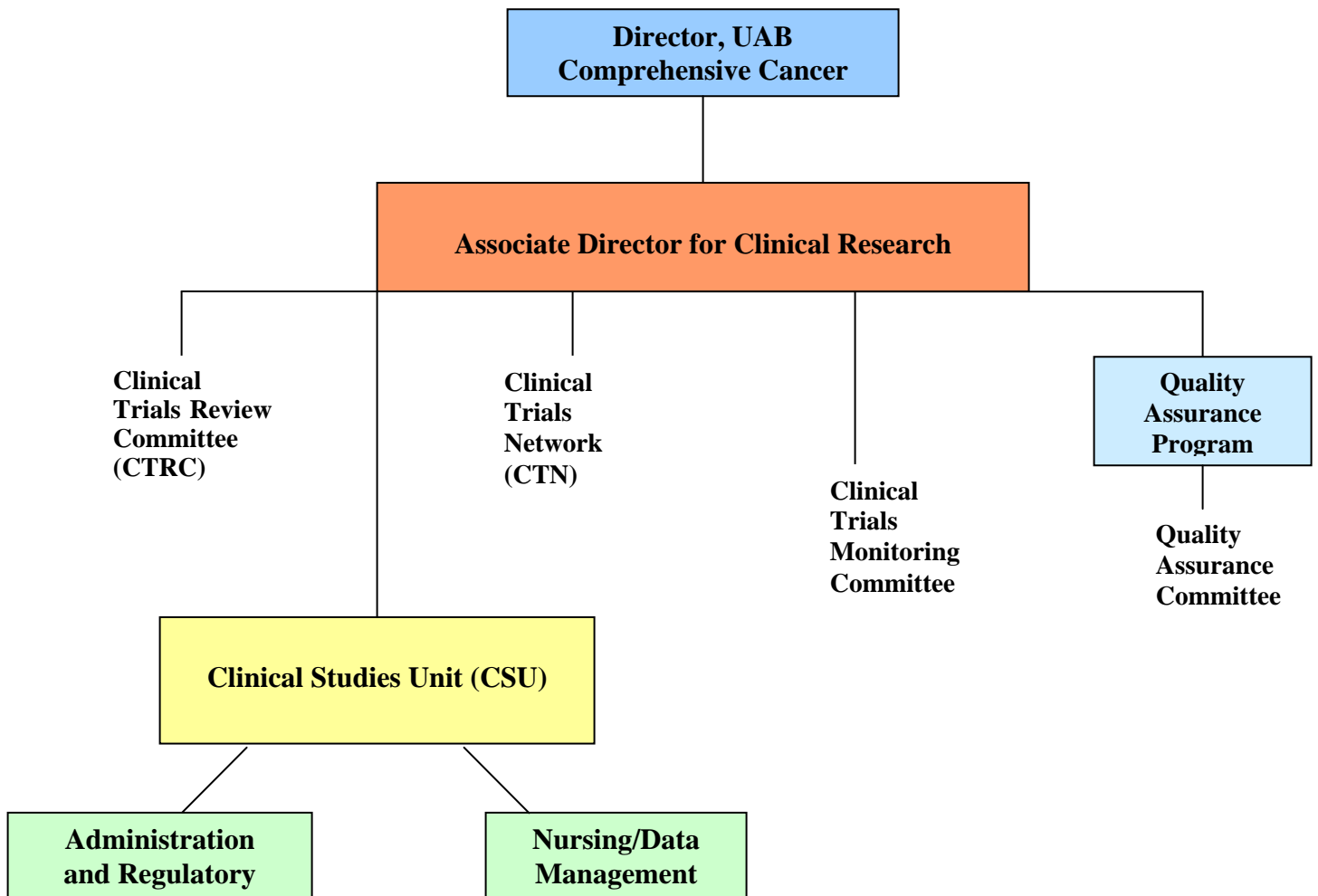
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The UAB Comprehensive Cancer Center (UAB CCC) is focused to provide optimal treatment options and to maintain the highest quality of care for research patients. Priority is given to patient safety, the integrity of the conduct of clinical trials and to the efficiency of the processes established to ensure this integrity is maintained.

1. OVERVIEW

ADMINISTRATIVE STRUCTURE OF CLINICAL RESEARCH AT THE UAB-CCC



1.2 CLINICAL TRIALS PROGRAM LEADERSHIP.

The Director of the UAB-CCC is responsible for the administration of all programs described. The Associate Director for Clinical Research has overall responsibility for the clinical research program including the Clinical Studies Unit (CSU), the Clinical Trials Review Committee (CTRC) the Clinical Trials Monitoring Committee, the Clinical Trials Network (CTN) and the Quality Assurance Program. The Director of the Comprehensive Cancer Center appoints the Director of the Quality Assurance Program which operates independent of the CSU.

1.3 CLINICAL TRIALS MANAGEMENT (See diagram next page):

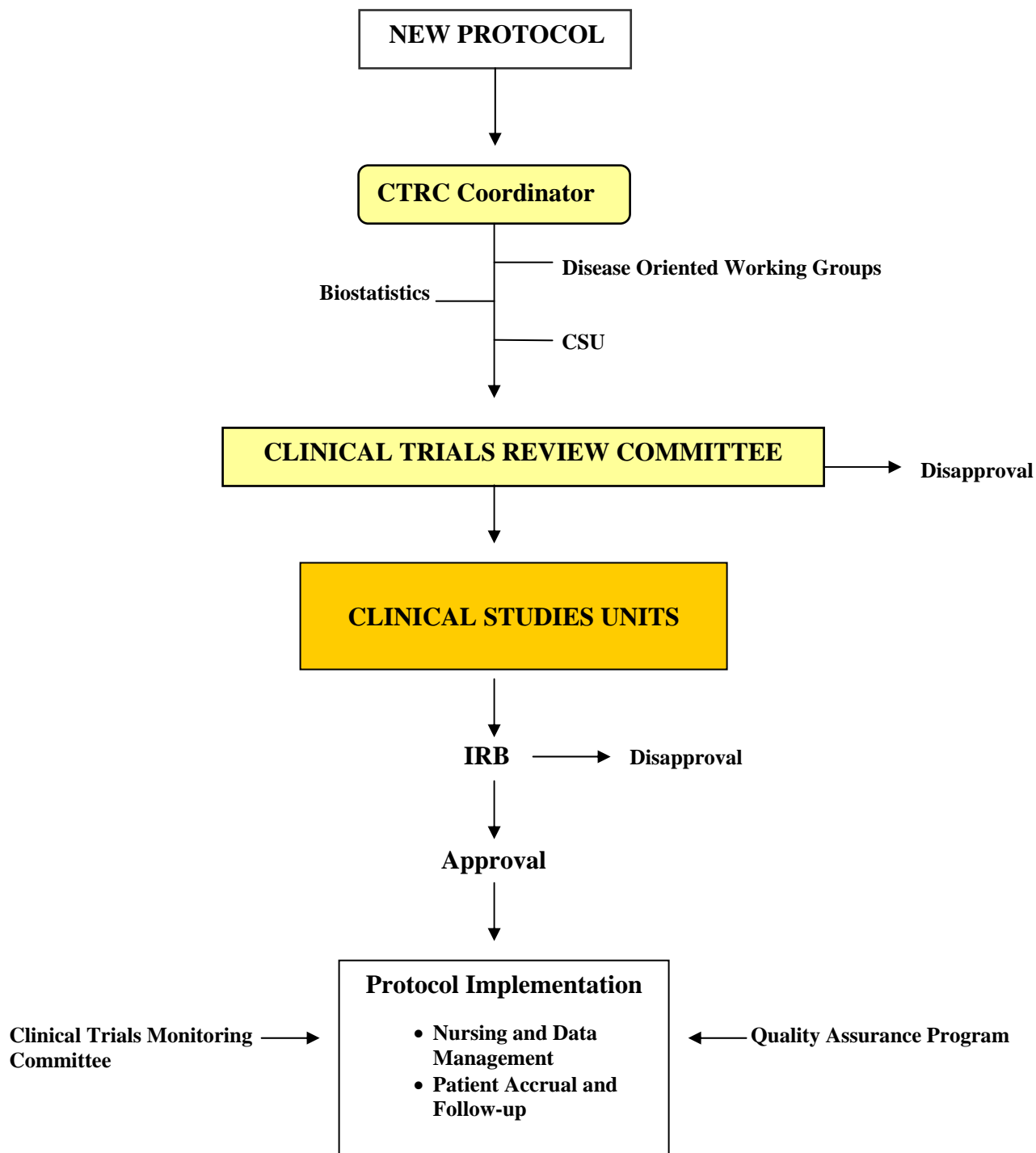
Initial Protocol Review: To conduct a new clinical trial involving cancer patients at the University of Alabama at Birmingham (UAB), a protocol must be submitted to the UAB Clinical Trials Review Committee (CTRC). The formal charge to the CTRC is to scientifically review, approve (or reject) protocols and to establish priorities for clinical protocols conducted within the Cancer Center, including protocols funded through NIH grants and Cooperative Group Trials. A cancer research protocol cannot receive University of Alabama at Birmingham–Institutional Review Board (IRB) approval until it has been approved by the CTRC.

Initiating the Study: Once a protocol is approved by the CTRC, it can undergo the activation process (IRB submission, budget negotiation, contract development, etc). The central CCC-Clinical Studies Unit is now located in a 13,000 square foot facility in the Liberty National Building and has off site offices including the Bone Marrow Transplantation Unit (BMT), Department of Surgery, Division of Gynecologic Oncology, Department of Neurology and Department of Radiation Therapy. The Department of Pediatrics maintains a separate CSU and its clinical trial activity has CCC-Quality Assurance Program oversight.

Study Management: Once the protocol is approved by the IRB and the contract has been signed, the protocol is assigned to a research nurse/ data manager. They are responsible for the scheduling of the initiation meetings, study enrollment, patient appointments, education of the patient and the family, handling of research samples, administration of the investigational drug, adverse events and serious adverse events collection and reporting, and quality control - including data, regulatory requirements, and drug accountability.

Monitoring of Clinical Trials: The Clinical Trials Monitoring Committee (CTMC) directly monitors the conduct of all the studies, except pediatric trials. (Information regarding the monitoring of pediatric trials can be found in Appendix E). The CTMC meets weekly and is responsible for the primary oversight of all active protocols (phase I, II and III – including Cooperative Group Trials). The CTMC weekly reports are sent to the Associate Director for Clinical Research and the Quality Assurance Program Director of the Comprehensive Cancer Center. Additionally, if a protocol is not monitored by an outside agency, an internal audit is performed annually by the Cancer Center. Reports from the internal audit are provided to the Associate Director for Clinical Research and the Quality Assurance Committee.

CLINICAL TRIALS MANAGEMENT



1.4 REQUIREMENTS FOR DATA AND SAFETY MONITORING PLAN

Every therapeutic interventional trial (Phase I, II, III) of UAB-CCC is covered by the institutional data and safety-monitoring plan. Modifications of a plan for some protocols may be developed based on the degree of risk involved in participation and difficulty of the clinical trial. The risk associated with the protocol is initially evaluated by the P.I. and subsequently by the CTRC. Additionally, if the CTRC determines that a clinical trial requires monitoring procedures in addition to those described in the CCC-DSMP; the investigator prior to the CTRC approval of the protocol must develop these extra procedures. The DSMP approved by the CTRC must be strictly followed. The CTMC is responsible for direct oversight and monitoring of the trials and adherence to the DSMP of the CCC or other protocol specific DSMPs. The CTMC provides weekly reports to the Associate Director for Clinical Research and the Quality Assurance (QA) Program. The QA Program operates independently from the CSU and is responsible for monitoring patient safety, AE reporting requirements, protocol compliance and DSMP compliance. The director of the QA Program will monthly review the CTMC reports, the internal audits/external audits and the annual investigator-initiated protocol IRB continuation (progress) reports. The Quality Assurance (QA) Committee will meet quarterly (minimum) and have additional meetings as determined by the QA Program director if potential problems or issues are identified. The QA Committee recommendations are provided to the Associate Director for Clinical Research with appropriate notification to the UAB-IRB. The Associate Director for Clinical Research will notify the sponsor and regulatory agencies as appropriate.

As discussed, oversight for participation in phase III trials is provided using this Master Plan. However, the sponsor/author of every Phase III trial must have its own Data and Safety Monitoring Plan, including protocol-specific Data and Safety Monitoring Board (composed by clinical investigators, biostatisticians, clinical trials experts and lay patient advocates independent of the investigators) to provide oversight of the entire trial. No members of a DSMB will be associated with the trial. Once the DSMB is established, its initial tasks are to review the protocol, the manual of procedures, and the informed consent form. The DSMB shall then identify the relevant data parameters and the format of the information to be regularly reported. The board must meet on a regular schedule - at least yearly over the course of the study. At each meeting the board must consider the rationale for continuation of the study after evaluation of recruitment, randomization, retention, protocol adherence and compliance, data management, safety issues and outcome data. Appropriate statistical stopping guidelines must be incorporated into the protocol for interim monitoring of efficacy endpoints. Recommendations are provided to the PI as well as the CTMC in which the protocol is followed. Reports are presented to the IRB as well as the respective sponsor agency (NCI, NIH, FDA, industry, etc.).

If a phase I or II multi-site trial is coordinated by the UAB-CCC, the institutional DSMP will provide oversight of all patient accrual or a separate DSMB may be formed depending on review/recommendations of the CTRC.

The phase I, II and III trials sponsored by the NCI Cooperative Group Program are excluded from this master data and safety monitoring plan. These trials are monitored by long-standing and well-established systems for cooperative group data submission, reporting, review and monitoring.

Special trials not managed in the CCC-CSU (behavioral trials, nutrition trials, dermatology trials, etc) must follow the same process: they must be presented to the CTRC for approval. The application must include the study protocol, the investigators brochure (if applicable), and a detailed Data and Safety Monitoring Plan including the DSMB (if applicable). These trials will be monitored for accrual and internally audited annually by the Cancer Center if the trial does not receive monitoring by an outside agency. The investigators of these trials have the option of forming a CTMC or may be monitored by the CCC-CTMC. The reporting intervals will be determined by the level of risk assigned to the protocol by the CTRC.

Monitoring of trials in which the physician member of UAB CCC holds the IND will follow the same DSMP; however, additional procedures have been designed for those protocols and can be seen in Appendix A.

2. CLINICAL RESEARCH PROGRAM:

2.1 PROTOCOL REVIEW:

All cancer-related protocols that are activated at the UAB-CCC undergo a rigorous scientific evaluation by the CTRC. The CTRC meets twice monthly and is divided into two boards (see members in appendix B); both are chaired by the Associate Director for Clinical Research or his designee. Prior to the CTRC meeting, protocols are assigned for review to two CTRC members: a primary and secondary reviewer, and two statistical reviewers. Also, prior to CTRC meeting, the appropriate Disease Oriented Working Group (DOWG) evaluates the study for scientific merit, consistency with their program and feasibility (See Appendix C – DOWGs and members). In the case of a gene therapy protocol, 3 additional gene therapy reviewers from our Gene Therapy Panel provide reviews (See Appendix D – Members of this panel). All reviews are presented at the CTRC meeting where the CTRC votes for rejection or approval (with or without changes) and assigns a priority score (1-5). Protocols with a priority score of > 3.0 will not be recommended for activation in the UAB-CCC. Studies with a priority score of ≤ 2.0 may be considered for CCC Core Grant support. Principal Investigators are not present at the time of the review of their own protocol. Sub-investigators involved in the conduct of the clinical trial may be present at the time of review of the protocol but may not be a reviewer or vote. If there are questions raised during a review, the Principal Investigator is contacted. At the time a new protocol is reviewed, the CTRC determines if a protocol requires additional monitoring procedures other than those provided in the CCC-DSMP or in the specific-DSMP provided by the PI (high risk protocols, multi-site trials, etc). Minutes of the CTRC meetings are maintained in the Office of Protocol Review and Monitoring. In addition to reviewing all new protocols, all active protocols are reviewed by the CTRC for accrual and scientific progress on an annual basis at the time of their IRB renewal.

Members of the CTRC are appointed to the committee based on their scientific expertise to provide representation across all disease categories, treatment modalities and clinical trials experience. Thus, the CTRC is composed of multidisciplinary representation (Medical Oncology, Hematology, Surgery, Pathology, Biostatistics, Radiation Oncology, Pediatric Oncology, Gyn-Oncology, Neuro-Oncology, research nurses, and others).

2.2 PROTOCOL ACTIVATION:

Upon approval of the new protocol by the CTTC, the protocol is transferred to the regulatory office of the CSU which is responsible for IRB submissions and also undertakes other critical regulatory functions: study budget development and negotiation, grants and contracts submission, conflict of interest, billing compliance, regulatory management, and ongoing study management including protocol amendments, exceptions, deviations and severe adverse events reports to the necessary regulatory agencies once they have been reviewed and approved by the PI.

Once the protocol is approved by the IRB and the contract has been signed, the protocol is transferred to the operative offices of the different CSUs where a research nurse and a data manager are assigned to each protocol as described in 2.3.

2.3 PROTOCOL MANAGEMENT:

2.3.1 Management of active studies: – Studies are managed by a team composed of the P.I., research nurse and data manager. The team formed by the assigned nurse and data manager is responsible for: scheduling of the initiation meetings, study enrollment (includes eligibility criteria verification, informed consent process with the P.I., registration), verification of inpatient and outpatient appointments and (in appropriate cases) admissions to and treatments in the General Clinical Research Center. In addition, the research nurse conducts education of the patient, family and staff. The research nurse is responsible for coordination of research samples, drug administration according to the protocol, adverse event and severe adverse event reporting, reporting with the P.I. according to the regulatory requirements as outlined by the appropriate governing agencies/offices (NIH, NCI, FDA, IRB and the Office of Radiation Safety), and quality control including data, regulatory requirements, and drug accountability. Nurses report data from protocols at the CTMC meetings. When radioactive agents are involved, the responsible research nurse is trained and certified by the Radiation Safety Office for the proper handling and disposal of radioactive materials. For such studies, the research nurse is responsible for coordinating the treatment of a given patient with the Radiolabeling Shared Facility.

2.3.2 Patient-specific Protocol Data

The research nurse and the data manager assigned to the protocol are responsible for maintaining the research file. The research file is housed in the CSU and is derived from and maintained separately from the UAB hospital and clinical medical record. All original documentation and physician records are maintained in the UAB hospital and clinical medical records. The research file is available only to research personnel to maintain confidentiality. The research file contains: copies of the eligibility checklist and supporting documentation; the individualized study calendar that ensures required data are collected at the time specified in the protocol; consent form (s); on- and off-protocol forms; data collection forms relevant to the study endpoints; survival forms; and study-specific flow sheets. The research nurse and the data manager compile all required information for interim and final study analyses.

2.4 INVESTIGATIONAL DRUG/AGENT MANAGEMENT, SAFETY AND ACCOUNTABILITY:

All investigational agents utilized by Cancer Center investigators (excluding Pediatrics) are used under the supervision of the Core Grant funded research pharmacy. The pharmacist, in conjunction with the research nurse, is responsible for preparing a drug information sheet for every investigational agent used in the Cancer Center. This serves as a resource for drug administration guidelines and potential side effects for Cancer Center and Hospital personnel. The pharmacist is responsible for ordering investigational drugs, formulating and dispensing investigational agents at the outpatient clinic, hospital and General Clinical Research Center, managing the drug inventory, submitting appropriate documentation, and disposal of all investigational agents used by Cancer Center faculty and affiliates. The research nurses and the research pharmacist are jointly responsible for communications and coordination regarding investigational drug supply, to ensure that the appropriate drug(s) is (are) available in the proper quantity and that all regulatory functions surrounding the use of the agent are fulfilled. The pharmacist confirms that written informed consent has been obtained from each patient entered onto a IRB-approved study before dispensing the agent for that patient's use. All records and documentation of drug dispensation and reagent stock is kept by the research pharmacist and available for audit.

2.5 CLINICAL TRIALS MONITORING COMMITTEE (CTMC):

The CTMC is part of the UAB CCC and is independent from the CTMC. The CTMC meets weekly and is responsible for data and safety monitoring of all active clinical trials conducted within the CCC (except pediatric trials). This includes compliance with regulatory requirements as outlined by the appropriate governing agencies/offices (NIH, NCI, FDA, IRB and the Office of Radiation Safety) for phase I, II, and III studies, including documentation and reporting of SAEs.

Off site operations report to the CTMC of the Cancer Center on a weekly to monthly basis based on the protocol risk and complexity of the clinical trial. (i.e., Gynecology Oncology, BMT, Surgical Oncology, Neuro-Oncology, and Radiation Oncology).

The membership of the CTMC is provided in Appendix E. In addition, the administrative personnel are present at every committee meeting to expedite the reporting process to the different sponsors and regulatory agencies as required. The operation of the CTMC is the responsibility of the Associate Director for Clinical Research. The reports and recommendations of the CTMC are provided to the Associate Director for Clinical Research and the Quality Assurance Program for review and appropriate actions.

Phase I and II trials. All pilot, phase I, and II protocols are presented in detail. Clinical investigators, research nurses and data managers are present for the review and present details regarding adequacy of patient accrual, patients treatments, dose levels of the agents, administration of the medication, adverse events, and serious adverse events. Additionally, literature pertinent to the trial is discussed. Minutes of the meetings are recorded and reviewed monthly by the Quality Assurance Program of the Comprehensive Cancer Center. They are maintained indefinitely for purposes of review. Documentation of the AEs, SAEs, accrual and drug administration is maintained in the administrative office of the CCC-CSU. Data safety and monitoring activities for each study continues until all patients have completed their treatment

and all patients are beyond the time point at which study related adverse events would likely to be encountered.

Phase III trials: Phase III studies are presented at the same meeting. However, for Phase III studies, discussion is limited to the following issues: SAEs, review of eligibility of patients entered on study, responses, evaluations of patients removed from study and adequacy of accrual.

The CTMC provides an independent monitoring system in addition to the Principal Investigator to prevent conflict of interest issues. Principal Investigators provide input in the monitoring of their protocols, but the Clinical Trials Monitoring Committee is responsible for supervision of the conduct of the study.

2.6 TOXICITY MONITORING AND REPORTING:

The Principal Investigator and the assigned research nurse are responsible for collecting and filing all patient toxicity data for the protocols to which he/she has been assigned. Generally, the research nurse will administer the investigational drug to patients and remain present to monitor and record toxicities.

Adverse Events: Adverse Event (AE) is defined as any unfavorable and unintended sign, symptom, clinically significant laboratory test abnormality or disease temporally associated with the use of a medical treatment or procedure regardless of whether it is considered related to the medical treatment or procedure. Any clinical study event that is judged to be an adverse event must be recorded on the case report forms during the course of the study. The collection of adverse events information will begin at the initiation of the investigational agent and will continue until the treatment period is completed (this includes AE within 30 days of the last dose of treatment, or 45 days for the radioimmunotherapy trials). Severity will be graded according to the current Common Toxicity Criteria. The Principal Investigator and the assigned nurse must evaluate severity, causal relationship, action taken and outcome. The Principal Investigator and the assigned nurse are responsible for documenting; filing and reporting through the administrative office of the CSU, in a timely fashion, all identified adverse events (see table below for reporting). However, all significant AEs are presented in each CTMC meeting. If known, the diagnosis of the underlying illness or disorder should be recorded, rather than the individual symptoms. Those AEs should be followed to resolution or stabilization, and reported as SAEs if they become serious.

ADVERSE EVENT REPORTING

EXPECTED EVENT	UNEXPECTED EVENT
GRADE 1, 2, 3 Reporting is not required	GRADE 1 Reporting is not required
GRADE 4, 5 Report by FAX, e-mail to the CSU, IRB and the respective sponsor (NCI, FDA, NIH, industry) within 24 hours. Written report to follow within 10 working days.	GRADE 2 (IF POSSIBLE, PROBABLE OR DEFINITE) Written report to the CSU, IRB and sponsor within 10 working days.
	GRADE 3, 4, 5 (REGARDLESS OF ATTRIBUTION) Report by FAX, e-mail to the CSU, IRB and sponsor within 24 hours. Written report to follow within 10 working days.

Severe Adverse Events: Severe Adverse Event SAE is defined, for our purposes, by the US Code of Federal Regulations, or by the sponsor if the sponsor’s definition is more stringent. The Code definition paraphrased: any adverse drug experience that results in death, is a life-threatening adverse drug experience, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a cancer, is a congenital abnormality/birth defect, results in overdose, and results in the development of drug dependency or drug abuse. Also, the occurrence of an unexpected toxicity, the specificity or severity of which is not consistent with current investigator brochure (or protocol) must be considered as a SAE.

The PI and the research nurse detecting the SAE will electronically (e-mail) or by fax, inform the IRB, the appropriate agency (NCI, NIH, FDA. Etc.) and the industry sponsor within 24 hours of knowledge of the event. This will be coordinated by the CSU administrative office. In some instances more than one sponsor or responsible review entity may need to be informed and the PI must explicitly outline these reporting lines. Written reports to the UAB IRB and the sponsor need to be provided within 24 hours, if at all possible, and no later than five working days. These reports will be written by the nurse clinical coordinators and the principal investigator and then reported to the UAB IRB and regulatory agencies. The Clinical Trials Monitoring Committee reviews severe adverse events every week.

2.7 EXTERNAL MONITORING

External monitoring will be coordinated by the CSU. Monitoring reports and CSU responses are provided to the UAB-IRB.

3.0 OVERSIGHT OF CLINICAL TRIALS

3.1 QUALITY ASSURANCE (QA) PROGRAM:

The Quality Assurance Program is the responsibility of the Associate Director for Clinical Research. The Associate Director for Clinical Research and the Cancer Center Director will appoint a director of the QA Program (2 year tenure and renewal) and the members of the QA Committee. The QA Program will operate independently from the CSU. A coordinator of the QA Program office will be appointed to coordinate the meetings of the QA Committee, attend and record the minutes of the meetings, receive appropriate reports and coordinate internal audits. The director of the QA Program will monthly review the CTMC meeting reports, external and internal audit reports and the copies of the annual investigator-initiated protocol IRB renewal documents, which include the number of patients entered, the number of patients treated, dose levels administered, summary of all adverse events requiring expedited reporting developments which may effect the safety of the participants or the ethics of the study. The QA Program director will review all internal audit reports and call a special QA Committee meeting for review, discussion and recommendations if serious issues were found in the audit. The QA Committee will meet quarterly to review the above data and to provide recommendations regarding safety issues, protocol modification or closure based on unacceptable risk to participants. These recommendations will be reported to the Associate Director for Clinical Research with appropriate notification to the UAB-IRB. The director of the QA Program may call meetings more frequently, depending on the monthly reviews of data reports or audit findings. The membership of the QA Committee is listed in Appendix F.

3.2 INTERNAL AUDIT PROGRAM

An internal auditing function will operate as a component of the QA Program. An internal audit team will be appointed by the director of the QA Program and include a lead physician and a data manager/nurse not involved with the protocol. Selection of protocols for audit will be carried out by the biostatistician representative in the QA Committee and will include: (1) all protocols which do not have external monitoring (includes "investigator initiated" and protocols whose IND is held by Cancer Center faculty) that have accrual of 5 or more patients. Protocols not meeting this accrual target will nonetheless be audited every other year at a minimum. Protocols will be evaluated to audit within 2 months of their IRB renewal anniversary; (2) For "cause" audits based on concerns received by faculty, staff, patients or based on issues raised by the Clinical Trials Monitoring Committee; (3) Selection of a representative protocol annually which do not fall into categories (1) or (2) above.

A biostatistician selects 10% of the protocol charts using a random number generator. Charts are reviewed for proper randomization, current consent form use and required signatures, regulatory compliance, eligibility, treatment compliance, toxicity documentation, response and follow-up. Additional charts may be audited when major deficiencies or important developments have occurred. Audit reports and CSU responses are sent to the Quality

Assurance Program, the Associate Director for Clinical Research and the UAB-IRB for review. Protocols with major deviations or that require changes/amendments by the Associate Director for Clinical Research and/or IRB may be put on hold until processes are in place to correct the problem or modify the protocol. If deficiencies are not resolved, the protocol may be subject to closure. The Quality Assurance Program will monitor internal audit reports and CSU responses to determine appropriateness of actions taken. Records of the audit are maintained indefinitely for purposes of review.

The responsibility of the QA Program and Committee are to (1) regularly review the CTMC reports; (2) review external audit reports; (3) review the internal audit reports; (4) review the annual IRB investigator-initiated protocol continuation reports; and (5) make recommendations to the UAB-IRB and Associate Director for Clinical Research regarding protocol modification or closure.

3.3 INVESTIGATOR REQUIREMENTS AND RESPONSIBILITIES:

The Principal Investigator of each study is ultimately responsible for every aspect of the design, conduct, and final analysis of the protocol. All protocols must include the DSMP (institutional plan or specific plan), and must have an adverse event determination, monitoring and reporting system, including standardized forms and procedures for reporting and treating subjects experiencing adverse events. If the protocol requires a DSM board, the protocol must include the proposed frequency of meetings and the list of the members. If the protocol requires evaluation by the Biologic Safety or Radiation Committee, the P.I. is responsible for obtaining the approval.

3.4 INSTITUTIONAL REVIEW BOARD:

The UAB IRB began meeting 4 times per month in January 2001 to review protocols of all categories, with two monthly submission deadlines strategically spaced. (See appendix G for members of the UAB IRB). Protocols initiated by pharmaceutical sponsors are reviewed by the Western IRB. Clinical Studies Unit administrative personnel have extensive experience with the preparation and handling of IRB submissions, as well as the drafting of informed consents and reporting AE's and SAE's. Protocol amendments, annual renewals, and study closures are also handled and monitored by the Clinical Studies Unit staff. This assures that all such interactions are conducted appropriately, well documented, and disseminated to the appropriate investigators, research personnel, and monitoring and regulatory organizations (NIH, NCI, FDA, cooperative groups, Industry sponsors, internal committees, etc.).

All key personnel responsible for the design and conduct of research involving human subjects must be trained in the protection of human research participants. UAB-IRB regularly offers the certification program that includes training and testing of Federal Regulations, University Policies and procedures applicable to human research, as well as the ethical use of human subjects and conflict of interest.

4.0 OFF-SITE CONDUCT OF INVESTIGATOR-INITIATED PHASE I, II, III STUDIES

The detailed description and guidelines of our Clinical Trials Network (CTN) is provided in Appendix H. In general, such protocols undergo identical review by the Clinical Trials Review Committee, identical monitoring by the Clinical Trials Monitoring Committee and identical participation in our Quality Assurance Program.

APPENDIX A

STANDARD OPERATING PROCEDURES (SOPs)

FOR

INVESTIGATOR INDs

HELD BY

PHYSICIAN MEMBERS OF THE

UAB COMPREHENSIVE CANCER CENTER

A. Introduction

Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the only means through which the sponsor technically obtains this exemption from the FDA.

During a new drug's early preclinical development, the sponsor's primary goal is to determine if the product is reasonably safe for initial use in humans, and if the compound exhibits pharmacological activity that justifies commercial development. When a product is identified as a viable candidate for further development, the sponsor then focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited early-stage clinical studies.

FDA's role in the development of a new drug begins when the drug's sponsor (usually the manufacturer or potential marketer) having screened the new molecule for pharmacological activity and acute toxicity potential in animals, wants to test its diagnostic or therapeutic potential in humans. At that point, the molecule changes legal status under the Federal Food, Drug and Cosmetic Act and becomes a new product subject to specific requirements of the drug regulator system.

There are three types of INDs:

- An Investigator IND is submitted by a physician who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. A physician might submit a research IND to propose studying an unapproved drug, or an approved product for new indication or in a new patient population. The obligations of an investigator-sponsor include both those of an investigator and those of a sponsor.
- Emergency Use IND allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND in accordance with 21CFR, Sec. 312.23 or Sec. 312.34. It is also used for patients who do not meet the criteria of an excising study protocol or if an approved study protocol does not exist.
- Treatment IND is submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while final clinical work is conducted and the FDA review takes place.

In rare instances, a UAB Comprehensive Cancer Center member will submit an Investigator IND. This decision will be made jointly by the member, the Cancer Center Director and the Associate Director for Clinical Research. After deciding to submit an Investigator IND, it is the member's responsibility to follow the relevant procedures outlined herein.

B. Filing the IND

To file an Investigator IND, a UAB Comprehensive Cancer Center member/physician must follow the following steps:

1. Have a clinical trial protocol that is approved by the Clinical Trial Review Committee of the Center.
2. Submit an IND application to the FDA per current and appropriate FDA submission guidelines. Delay initiation of the clinical trial for at least 30 days after submitting the IND, unless otherwise notified by the FDA.
3. Once the IND is submitted, an application for IRB approval of the clinical trial protocol can be submitted.
4. If an investigator IND is held by a faculty member, funding for “sponsor” responsibilities (i.e., monitoring, etc.) is necessary in addition to the costs of the clinical trial. If the investigator receives an exemption from an IND, “sponsor” funding will not be required.

C. Compliance with Principles of International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, Good Clinical Practice (ICH GCP). The investigator filing the IND must agree to comply with the following guidelines:

1. Clinical trials should be conducted in accordance with the ethical principals that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).
2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. The rights, safety and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
4. The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.
5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
6. A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favorable opinion.

7. The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial should be qualified by education, training and experience to perform his or her respective task(s).
9. Freely given informed consent should be obtained from every subject prior to clinical trial participation.
10. All clinical trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification.
11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
12. Investigational products should be manufactured, handled and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.
13. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

D. Training of Participants Conducting the Clinical Trial Using the IND

The investigator holding the IND is responsible for making certain that the following clinical trial participants receive training on the trial prior to its initiation:

- All physicians listed on Form 1572 for the clinical trial;
- At least one research nurse from each participating study location;
- Any pharmacist involved in preparing drug for the clinical trial;
- Any data manager/coordinator participating in the clinical trial.

All training sessions must include, at a minimum:

- An overview of the rationale for the IND and clinical trial;
- A description of the clinical trial;
- A review of the IRB and consent requirements for the trial;
- A review of drug development, transportation, storage, administration, and disposal requirements;
- A review of data collection, storage and security procedures;
- A review of serious adverse events procedures;
- An explanation of study oversight processes.

E. Oversight of the Clinical Trial by IND Holder

The investigator-sponsor is responsible for submitting all reports to the appropriate regulatory agencies (e.g., progress reports, safety reports, etc.). The Center member/physician who holds the IND is responsible for both the investigator and sponsor obligations relating to the study inclusive of monitoring the performance of each participant on the clinical trial, i.e., each physician listed on Form 1572. The IND holder is also responsible for assuring that only investigators listed on Form 1572 are enrolling patients on the trial. To provide necessary oversight, the IND holder must conduct an initiation visit and regular monitoring site visits. The initiation site visit is where the training of participants (described in Section D) occurs. The IND holder or designee must participate in all such initiation/training visits. Monitoring site visits may be conducted by a pharmaceutical company and approved by the IND holder. If monitoring site visits are conducted by someone other than the IND holder, the IND holder must review the data collected at such visits for accuracy, compliance and completeness within 30 days of these visits.

F. Essential Documents for the Conduct of the Clinical Trial Using the IND

1. **Essential Documents** – Essential Documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator-sponsor, subinvestigators and appropriate monitor with the standards of GCP and with all applicable regulatory requirements.

Essential Documents also serve a number of other important purposes. Filing essential documents at the investigator/institution-sponsor site(s) in a timely manner can greatly assist in the successful management of a trial by the investigator-sponsor, subinvestigators and appropriate monitor. These documents are also the ones that are usually audited by the investigator-sponsor's independent audit function and inspected by the regulatory authority(ies) as part of the process to confirm the validity of the trial conduct and the integrity of data collected.

The minimum list of essential documents that has been developed follows. The various documents are grouped in three sections according to the stage of the trial during which they will normally be generated (1) before the clinical phase of the trial commences, (2) during the clinical conduct of the trial, and (3) after completion or termination of the trial. A description is given of the purpose of each document, and whether it should be filed in either the investigator-sponsor files or at the ancillary study site. It is acceptable to combine some of the documents, provided the individual elements are readily identifiable.

Trial master files should be established at the beginning of the trial, both at the investigator-sponsor's site and office as well as at ancillary study sites, as is appropriate. A final close-out of a trial can only be done when the monitor has reviewed both investigator-sponsor and study site files and confirmed that all necessary documents are in the appropriate files.

Any or all of the documents addressed in this guidance may be subject to, and should be available for, audit by the investigator-sponsor's auditor and inspection by the regulatory authority(ies).

Essential Documents for a study must be retained for the appropriate period of time as required by applicable regulatory agencies.

2. **Before the Clinical Phase of the Trial Commences** – During this planning stage the following documents should be generated and should be on file before the trial formally starts.

Title of Document	Purpose	Located in Files of	
		Investigator-Sponsor (IND Holder)	Ancillary Study Site
Investigator's brochure	To document that relevant and current scientific information about the investigational product has been provided to the investigator	O	C
Signed protocol and amendments, if any, and sample case report form (CRF)	To document investigator and sponsor agreement to the protocol/amendment(s) and CRF	O	C
Information given to trial subject	To document the informed Consent	O	C
<ul style="list-style-type: none"> • Informed consent form (including all applicable translations) • Any other written information 	To document that subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent.	O	C
<ul style="list-style-type: none"> • Advertisement for subject recruitment (if used) 	To document that recruitment measures are appropriate and not coercive	O	C
Financial aspects of the trial	To document the financial agreement between the investigator/institution and the sponsor for the trial	O	N/A
Insurance statement (where required)	To document that compensation to subject(s) for trial-related injury will be available	O	C
Signed agreement between involved parties, e.g.:	To document agreements		
<ul style="list-style-type: none"> • Investigator/institution and sponsor • Investigator/institution and CRO • Sponsor and CRO (where required) • Investigator/institution and authority(ies) (where required) 		O	C
		O	C
		O	C
		O	N/A

Title of Document	Purpose	Located in Files of	
		Investigator-Sponsor (IND Holder)	Ancillary Study Site
Dated, document approval/favorable opinion of IRB/IEC of the following: <ul style="list-style-type: none"> • Protocol and any amendments • CRF (if applicable) • Informed consent form(s) • Any other written information to be provided to the subject(s) • Advertisement for subject recruitment (if used) • Subject compensation (if any) • Any other documents given approval/favorable opinion 	To document that the trial has been subject to IRB/IEC review and given approval/favorable opinion. To identify the version number and date of the document(s).	O	C
Institutional review board/independent ethics committee composition (where required)	To document that the IRB/IEC is constituted in agreement with GCP	O	C
Regulatory authority(ies) authorization/approval/notification of protocol (where required)	To document appropriate authorization/approval/notification by the regulatory authority(ies) has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s)	O	C
Curriculum vitae and/or other relevant documents evidencing qualifications of investigator(s) and subinvestigators	To document qualifications and eligibility to conduct trial and/or provide medical supervision of subjects.	O ¹ O ²	N/A O ²
Normal value(s)/range(s) for medical/laboratory/technical procedure(s) and/or test(s) included in the protocol	To document normal values and/or ranges of the tests	O ¹ C ²	N/A O ²
Medical/laboratory/technical procedures/tests (where required) <ul style="list-style-type: none"> • Certification, or • Accreditation, or • Established quality control and/or external quality assessment, or • Other validation (where required) 	To document competence of facility to perform required test(s), and support reliability of results	O ¹ C ²	N/A O ²
Sample of label(s) attached to investigational product container(s)	To document compliance with applicable labeling regulations and appropriateness of instructions provided to the subjects	O	C
Instructions for handling of investigational product(s) and trial-related materials (if not included in protocol or Investigator's Brochure)	To document instructions needed to ensure proper storage, packaging, dispensing, and disposition of investigational products and trial-related materials.	O	C

Located in Files of

Title of Document	Purpose	Investigator-Sponsor (IND Holder)	Ancillary Site	Study
Shipping records for investigational product(s) and trial-related materials	To document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. Allows tracking of product batch, review of shipping conditions and accountability	O ¹ C ²	N/A ¹ O ²	
Certificate(s) of analysis of investigational product(s) shipped	To document identity, purity and strength of investigational products to be used in the trial	O	C	
Decoding procedures for blinded trials (third party, if applicable)	To document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining subjects' treatment.	O	C	
Master randomization list (third party, if applicable)	To document method for randomization of trial population	O	C	
Investigator's Brochure updates	To document that investigator is informed in a timely manner of relevant information as it becomes available	O	C	
Any revisions to: <ul style="list-style-type: none"> • Protocol/amendment(s) and CRF • Informed consent form • Any other written information provided to subjects • Advertisement for subject recruitment (if used) 	To document revisions of these trial-related documents that take effect during trial	O	C	
Dated, documented approval/favorable opinion of institutional review board (IRB)/independent ethics committee (IEC) of the following: <ul style="list-style-type: none"> • Protocol amendment(s) • Revisions of: <ul style="list-style-type: none"> ✓ Informed consent form ✓ Any other written information to be provided to the subject ✓ Advertisement for subject recruitment (if used) • Any other documents given approval/favorable opinion • Continuing review of trial 	To document that the amendment(s) and/or revision(s) have been subject to IRB/IEC review and were given approval/favorable opinion. To identify the version number and date of the document(s)	O	C	
Regulatory authority(ies) authorization/approvals/notifications where required for: <ul style="list-style-type: none"> • Protocol amendment(s) and other documents (where required) 	To document compliance with applicable regulatory requirements.	O	C	
Curriculum vitae for new investigator(s) and/or subinvestigators	To document qualifications and eligibility to conduct trial and/or provide medical supervision of subjects	O ¹ C ²	N/A ¹ O ²	

Title of Document	Purpose	Located in Files of	
		Investigator-Sponsor (IND) Holder)	Ancillary Study Site
Updates to normal value(s)/range(s) for medical laboratory/technical procedure(s)/test(s) included in the protocol	To document normal values and ranges that are revised during the trial	O ¹ C ²	N/A ¹ O ²
Updates of medical/laboratory/technical procedures/tests: <ul style="list-style-type: none"> • Certification, or • Accreditation, or • Established quality control and/or • Other validation (where required) 		O ¹ C ²	N/A ¹ O ²
Documentation of investigational product(s) and trial-related materials shipment	To document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. Allows tracking of product batch, review of shipping conditions and accountability	O ¹ C ²	N/A ¹ O ²
Certificate(s) of analysis for new batches of investigational products	To document identity, purity and strength of investigational products to be used in the trial	O	N/A
Monitoring visit reports	To document site visits by, and findings of, the monitor	O	N/A
Relevant communications other than site visit <ul style="list-style-type: none"> • Letters • Meeting notes • Notes of telephone calls 	To document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting	O	C
Signed informed consent forms	To document that consent is obtained in accordance with GCP and protocol and dated prior to participation of each subject in trial. Also to document direct access permission	O ¹ C ²	N/A ¹ O ²
Source of documents	To document the existence of the subject and substantiate integrity of trial data collected. To include original documents related to the trial, to medical treatment and history of subject	O ¹ —	N/A ¹ O ²
Signed, dated and completed case report forms (CRFs)	To document that the investigator or authorized member of the investigator's staff confirms the observations recorded	O ¹ —	N/A ¹ O ²
Documentation of CRF corrections	To document all changes/additions or corrections made to CRF after initial data were recorded	O ¹ —	N/A ¹ O ²

O, Original; **C**, Copy, **N/A**, Not Applicable; **1**, UAB; **2**, Ancillary Study Site

References

www.fda.gov/cder/regulatory/applications/ind_page_1

www.fda.gov/cder/guidance

Federal Register, 5/9/97 (62 FR 25692)

APPENDIX B

CLINICAL TRIALS REVIEW COMMITTEE MEMBERS

BOARD 1

Chairman: Mansoor Saleh, M.D. (Professor, Hematology Oncology)

Al LoBuglio, M.D.	Professor	Hematology Oncology
Alma DelGrosso, RN	RN, BSN, OCN	Hematology Oncology
Francisco Robert, M.D.	Professor	Hematology Oncology - Lung Cancer
Andres Forero, M.D.	Associate Professor	Hematology Oncology
James Posey, M.D.	Assistant Professor	Hematology Oncology - G.I. Malignancies
Jeannette Lee, Ph.D.	Research Professor	Biostatistics
Lisle Nabell, M.D.	Assistant Professor	Hematology Oncology -Head and Neck Cancer
Ruby Meredith , M.D., Ph.D.	Associate Professor	Radiation Oncology
James Foran, M.D.	Assistant Professor	Hematology Oncology – Hem. Malignancies
Robert Oster, Ph.D.	Research Assistant Professor	Biostatistics
Sharmila Makhija, M.D.	Assistant Professor	Gynecology Oncology
John Carpenter, M.D.	Professor	Hematology Oncology
Ronda Carlisle, RN	RN, BSN, OCN	Hematology Oncology
William Vaughan, M.D.	Professor	BMT Program
Michael Straughn, M.D.	Assistant Professor	Gynecology Oncology
Graeme Bolger, M.D.	Associate Professor	Hematology Oncology – G.U. Malignancies

CTRC Ad hoc members include:

Marshall Urist, M.D.	Professor	Surgery – Breast and Melanoma
Roger Berkow, M.D.	Professor	Pediatric Oncology

CLINICAL TRIALS REVIEW COMMITTEE MEMBERSHIP

BOARD 2

Chairman: Mansoor Saleh, M.D. (Professor, Hematology Oncology)

Al LoBuglio, M.D.	Professor	Hematology Oncology
Andres Forero, M.D.	Associate Professor	Hematology Oncology
Alma DelGrosso, RN	RN, BSN, OCN	Hematology Oncology
Carla Falkson, M.D.	Professor	Hematology Oncology - Breast Cancer
Donna Salzman, M.D.	Assistant Professor	BMT Program
Jeannette Lee, Ph.D.	Research Associate Professor	Biostatistics
John Fiveash, M.D.	Associate Professor	Radiation Oncology
Kevin Harris, M.D.	Assistant Professor	Hematology Oncology
Richard Lopez, M.D.	Assistant Professor	BMT Program
Burt Nabors, M.D.	Associate Professor	Neuro-Oncology
Jennifer De Los Santos, M.D.	Assistant Professor	Radiation Oncology
Robert Oster, Ph.D.	Research Assistant Professor	Biostatistics
Vishnu Reddy, M.D.	Professor	Clinical Pathology
Katri Selander, M.D., Ph.D.	Research Assistant Professor	Hematology Oncology
Ruiwen Zhang, M.D., Ph.D.	Associate Professor	Pharmacology
Ronda Carlisle, RN	RN, BSN, OCN	Hematology Oncology
Larry Lamb, Ph.D.	Research Associate Professor	Hematology Oncology
Joseph Pressey, M.D.	Assistant Professor	Pediatric Oncology
Eben Rosenthal, M.D.	Associate Professor	Surgery – Otolaryngology

CTRC Ad hoc members include:

Marshall Urist, M.D.	Professor	Surgery – Breast & Melanoma
Roger Berkow, M.D.	Professor	Pediatric Oncology

APPENDIX C
Disease Oriented Working Groups (DOWGs)

Brain Tumor Working Group
Chairperson – Burt Nabors, M.D.

Yancey Gillespie, Ph.D.	Neurosurgery
James Markert, M.D.	Neurosurgery
John Fiveash, M.D.	Radiation Oncology
Sreelatha Meleth, Ph.D.	Biostatistics

Breast Cancer Working Group
Co-Chairs– Lisle Nabell, M.D.
Andres Forero, M.D.

Kirby Bland, M.D.	Surgery
Carla Falkson, M.D.	Hematology Oncology
John Carpenter, M.D.	Hematology Oncology
Helen Krontiras, M.D.	Surgical Oncology
Valerie Kracke, RN	Hematology Oncology
Karen Watters, RN	Hematology Oncology
Yufeng Li, Ph.D.	Biostatistics

Chemoprevention Working Group
Chairman - Clinton Grubbs, Ph.D.

Stephen Barnes, M.D.	Pharmacology
Craig Elmets, M.D.	Dermatology
William Grizzle, M.D., Ph.D.	Pathology
Carol Lamartiniere, Ph.D.	Pharmacology
Donald Muccio, Ph.D.	Chemistry
Wen Wan, Ph.D.	Biostatistics

G.I. Working Group
Chairman – James Posey, M.D.

Mohamad Eloubeidi, M.D.	Gastroenterology
Marty Heslin, M.D.	Surgery
Tina Wood, M.D.	Hematology Oncology
Dayle Craig, RN	Hematology Oncology
Sreelatha Meleth, Ph.D.	Biostatistics

G.U. Working Group
Chairman – John Fiveash, M.D., M.D.

William Grizzle, M.D., Ph.D.	Clinical Pathology
Hui-Yi Lin, Ph.D.	Biostatistics

Gynecology Oncology Working Group
Chairman – Mack Barnes, M.D.

Main Members:

Sharmila Makhija, M.D.	Gyn. Oncology
Warner Huh, M.D.	Gyn. Oncology
Ronald Alvarez, M.D.	Gyn. Oncology
Hui-Yi Lin, Ph.D.	Biostatistics

Head and Neck Working Group
Co-Chairs –Lisle Nabell, M.D.
William Carroll, M.D.

Sharon Spencer, M.D.	Radiation Oncology
Glenn Peters, M.D.	Surgery – Otolaryngology
Ronda Carlisle, R.N.	Hematology Oncology
Deli Wang, Ph.D.	Biostatistics

Hematologic Malignancies Working Group
Chairman – James Foran, M.D

Andres Forero, M.D.	Hematology Oncology
Ruby Meredith, M.D., Ph.D.	Radiation Oncology
Jeanne Connor, R.N.	Hematology Oncology
Jeff Worrell, R.N.	Hematology Oncology
Renee Desmond, Ph.D.	Biostatistics

Melanoma Working Group
Chairman – Marty Conry, M.D.

Marshall Urist, M.D.	Surgery
Ronda Carlisle, RN	Hematology Oncology
Seng-jaw Soong, Ph.D.	Biostatistics

Lung Cancer Working Group
Chairman – Francisco Robert, M.D.

Robert Cerfolio, M.D.	Cardiovascular Surgery
James Bonner, M.D.	Radiation Oncology
Betty Prescott, RN	Hematology Oncology
Deli Wang, Ph.D.	Biostatistics

APPENDIX D

UAB Gene Therapy Project Review Panel Chairman: Jeffrey Kudlow, M.D.

Charles Alford, M.D.

David Curiel, M.D.

Charles Elson, M.D.

Albert LoBuglio, M.D.

Eric Sorscher, M.D.

Mansoor Saleh, M.D.

John Anthony Thompson, Ph.D.

William Carroll, M.D.

Graeme Bolger, M.D.

Michael Ruppert, M.D., Ph.D.

Burt Nabors, M.D.

Richard Whitley, M.D.

Ronald Alvarez, M.D.

Roger Berkow, M.D.

Yancey Gillespie, Ph.D.

Raymond Lyrene, Ph.D.

John Mountz, M.D.

Judith Thomas, Ph.D.

Mack Barnes, M.D.

James Markert, M.D.

Kevin Harris, M.D., Ph.D.

Tim Townes, Ph.D.

John Kappes, Ph.D.

APPENDIX E

CLINICAL TRIALS MONITORING COMMITTEE

Chairman: Albert F. LoBuglio, M.D.
Andres Forero, M.D.; Mansoor Saleh, M.D.

Albert LoBuglio, M.D.	Acting Associate Director for Clinical Research
Andres Forero, M.D.	Medical Director, CCC-CSU
Mansoor Saleh, M.D.	Hematology Oncology
Ruby Meredith, M.D., Ph.D. (or representative)	Radiation Therapy
Seng-jaw Soong, Ph.D. (or representative)	Biostatistics Unit Shared Facility
William Grizzle, M.D., Ph.D. (or representative)	Tissue Procurement Shared Facility
Mona Fouad, M.D., MPH (or representative)	Recruitment Shared Facility
Donald Buchsbaum, Ph.D.	Translational Research
Alma DelGrosso, R.N.	Nurse Manager, CCC-CSU Operative office
Research Nurses (11)	CCC-CSU
Tracey Bailey	Coordinator Data Managers, CCC-CSU
Data Managers (9)	CCC-CSU
Tina Ayer, B.S.	Manager, CCC-CSU Regulatory Office
Principal Investigators	With active protocols in the CCC-CSU
Lisa Clemons, R.N.	Radiation Oncology
JoLane Gable, R.N.	Gynecology Oncology

II. CTMC of the Pediatric Oncology-CSU:

The majority of the Phase I, II, and III clinical trials conducted by the pediatric oncology section of the CCC are generated through and monitored by the Children's Oncology Group (C.O.G.). Occasional studies will be conducted outside the auspices of the C.O.G. and will be audited using the phase II monitoring (if applicable) and auditing systems established within the Department of Pediatrics and at the Children's Hospital, the site of the conduct of these trials. The rare study (usually within the pediatric bone marrow transplant program) being conducted by pediatric investigators that may involve adult patients will be registered and monitored within the CCC Data Safety and Monitoring Plan.

Roger Berkow, M.D.	Chairman
Norma Maxvold, M.D.	Associate Professor
J.P. Clancy, M.D.	Assistant Professor

APPENDIX F
QUALITY ASSURANCE COMMITTEE

John Fiveash, M.D.	Chairperson
Yufeng Li, Ph.D.	Biostatistics
Michael Ann Markiewicz, Pharm.D.	Pharmacology
Pablo Arnoletti, M.D.	Surgical Oncology
Ronald Alvarez, M.D.	Gyn. Oncology
Molly DeShazo, M.D.	Medical Oncology

APPENDIX G

Members, UAB Institutional Review Board

UAB has two IRBs for human use. These boards have been appointed by the President, the Provost, and/or the Acting Vice President for Research of UAB in accordance with the requirements of 45 CFR 46.107 and 21 CFR 56.107. A prisoner representative's attendance will be required when an IRB reviews a protocol involving prisoners.

Members and alternates are appointed to the IRB with varying backgrounds to promote complete review of Covered Research. The IRBs will have the professional competence to review Covered Research.

To access the current membership of the UAB Institutional Review Board, use the following web address:

<http://main.uab.edu/show.asp?durki=30253>

APPENDIX H

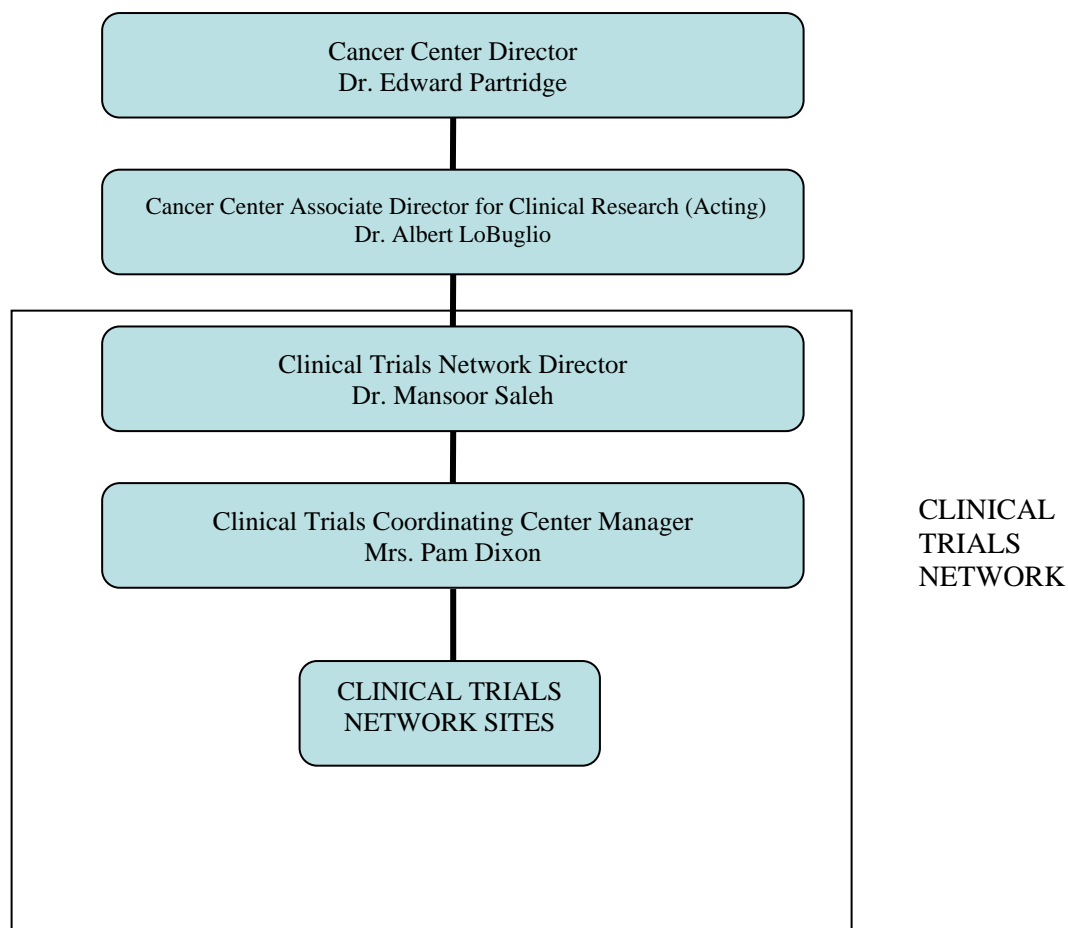
IMPLEMENTATION PLAN FOR OFF-SITE CONDUCT OF UAB COMPREHENSIVE CANCER CENTER INVESTIGATOR-INITIATED PHASE I AND II STUDIES

CLINICAL TRIALS NETWORK (CTN)

1.0 INTRODUCTION

The Clinical Trials Network (CTN) of the UAB Comprehensive Cancer Center (CCC) conducts investigator-initiated clinical trials under Good Clinical Practice conditions at CTN sites to achieve timely study subject enrollment and to provide subjects at CTN sites with access to CCC investigator-initiated phase I and II studies. The CCC CTN Coordinating Center oversees this effort. The CTN sites are required to have 1) an experienced staff of investigators, research nurses, and data managers; 2) a designated IRB and significant experience in undertaking clinical trials; and 3) accrual of at least five study subjects annually into CCC investigator-initiated CTN site studies, as well as successful completion of annual audits. CTN sites must adhere to guidelines in the CCC Data Safety and Monitoring Plan (DSMP).

2.0 ADMINISTRATION OF THE CLINICAL TRIALS NETWORK



Overall responsibility for the CTN lies with the Director of the CCC with primary oversight by the CCC Associate Director for Clinical Research. The Director of the CTN coordinates the overall efforts of the CTN, while day-to-day activities are supervised by the CTN Coordinating Center Manager.

2.1 Current CTN Personnel

- CTN Director: Mansoor Saleh, MD
- CTN Coordinating Center Manager: Pam Dixon, RN, BSN, OCN, CCRP
- CTN Coordinating Center Data Manager: Gladys Johnson, LPN

3.0 IMPLEMENTATION PLAN FOR CTN SITE STUDIES

The Implementation Plan for off-site conduct of CCC investigator-initiated Phase I and II studies receives UAB IRB approval via an expedited review mechanism. Each study identified for activation at CTN sites is added to the IRB-approved Implementation Plan by way of an addendum, which identifies the CTN sites where the study is to be conducted. The addendum is submitted to the IRB for expedited review and approval. A proposed CTN site study must also be processed through the CTN site IRB.

Serious Adverse Events (SAEs) are reported by the CTN site Lead Investigator within 24 hours to the CTN Coordinating Center Manager by email (pam.dixon@ccc.uab.edu) or by fax (205) 975-9875. The 24 hour paging number for the CTN Coordinating Center Manager is (205) 934-3411, beeper #5904. The CTN Coordinating Center Manager is then responsible for reporting SAEs to the UAB IRB in accordance with study-specific requirements. SAEs occurring at CTN sites are reported to the UAB IRB as “non-UAB” events.

The CTN Coordinating Center Manager also ensures that the following are accomplished:

- Develop and implement plans for monitoring and auditing CTN site studies
- Provide initial protocol and consent documents to CTN sites
- Coordinate CTN site initiation visits / teleconferences
- Receive and evaluate documents from CTN sites and determine the need for further evaluation
- Submit required regulatory documentation to the UAB IRB
- Generate study-specific queries and develop resolutions
- Perform monitoring visits at CTN sites
- Provide for needed fiscal management including development of CTN site budgets and sub-contracts
- Provide for distribution of study-specific funds to CTN sites.

4.0 CTN SITE REQUIREMENTS

All CTN sites are formally accredited and must adhere to the CCC DSMP. During the accreditation process, an Accreditation Checklist is completed (Appendix III).

4.1 Personnel

A Lead Site Investigator is identified for each CTN site study. Adequate CTN site staff is provided for administration, data management, and research nurse activities. The administrative staff provides clerical assistance to support CTN site studies. The data management staff collects and manages necessary research data on study subjects enrolled onto CTN site studies. The research nurses coordinate the study subjects' care in conjunction with study-specific requirements to ensure patient safety, continuity of care and to provide ongoing assessment of the impact of the study on the CTN site and on patient resources. The CTN site staff has expertise in study management and data collection. Training in necessary computer applications, Human Subject Research, and HIPAA regulations is provided and documentation of this training is provided to the CTN Coordinating Center Manager. CTN site staff cooperates in all data management activities with the CTN Coordinating Center Manager, including participation in monitoring and audit activities.

4.2 Equipment and Facilities

CTN sites have equipment and facilities to conduct CTN site studies. These include:

- Patient care facilities, equipment, and supplies
- Required information systems
- Equipment and facilities for processing and storage of study-related tissues, tissue extracts, and blood products
- The capability to transport study-related tissues, tissue extracts, and blood products per study specifications
- Dedicated fax machine for transmitting and receiving study-specific correspondence.

The CTN site provides adequate facilities for secure storage of study documents and for study monitoring activities. A designated monitoring area is provided that includes a workstation, copier, and fax machine. The workstation is located in proximity to the workstations of the CTN site study-specific research nurse and data manager. A secure facility, with restricted access, is provided for storing study drugs, specimens, and other study-specific materials. Systems to assure maintenance of drug receipts and drug dispensing documents and to assure secure disposal of sensitive documents are in place.

CLINICAL TRIALS NETWORK (CTN) STANDARD OPERATION PROCEDURES

1.0 PROCEDURES FOR INITIATING AND ACTIVATING CLINICAL TRIALS

1.1 Letter of Understanding

An Initial Study Offering Document addressed to the Lead Investigator at a CTN site is developed by the CTN Director. This document enables the CTN site to provide assurances that all responsibilities have been defined and that all necessary resources are available to conduct the proposed CTN site study. The document includes a synopsis of the study, enrollment targets, and estimated funding. The document is signed by the Lead Investigator at the CTN site and is on file at the CTN Coordinating Center before the study can be initiated at the CTN site.

1.2 Budget Development

Designated personnel at the CTN site coordinate budget development and budget negotiations for the study with the CTN Coordinating Center Manager. Acceptable payment terms are also addressed by both parties in conjunction with any sub-contracting requirements.

1.3 Regulatory Procedures

Prior to activation of a study at a CTN site, the following documents must be on file at the CTN Coordinating Center:

- A signed Master Affiliate Agreement (APPENDIX I)
- A signed study-specific Addendum to the Master Affiliate Agreement (APPENDIX II)
- A signed FDA Form 1572, with a current signed and dated CV for each CTN site investigator listed on the form and a copy of the investigators' current medical license
- Current resume and contact information for the study-specific CTN site research nurse and study-specific data manager
- Human Subjects Research Training certification for key CTN site study personnel
- Documentation of HIPPA Compliance Training for key CTN site study personnel
- A copy of all current CTN site laboratory certifications (CAP and / or CLIA) and current laboratory reference ranges for all tests specified in the study. Current CV and license of the CTN site laboratory director, if listed on the FDA Form 1572
- Name of and contact information for the CTN site's IRB Chairperson, contact information and current CTN site IRB membership roster
- Assurance Identification / CTN site IRB Certification
- CTN site IRB approval of the study protocol and consent form
- CTN site IRB acknowledgement of receipt of the study-specific Investigational Brochure
- Any special study-specific approvals such as radiation licensing
- Signed copy of Initial Study Offering Document

- Signed final CTN site budget / contracting documents
- Signed CTN site Financial Disclosure Forms / Conflict of Interest Forms
- CTN site signature logs
- Yearly updates of the above information are required during the course of the CTN site study

All documents are mailed to the CTN Coordinating Center:

UAB Comprehensive Cancer Center
 Clinical Trials Network Coordinating Center
 c/o Pam Dixon, RN
 1802 6th Avenue South
 North Pavilion Room 2523
 Birmingham, Alabama 35294

CTN sites are responsible for the timely submission of safety reports, protocol amendments, protocol exceptions and deviations, ancillary study documentation (such as advertisement materials), and annual renewals to their CTN site IRB. Copies of CTN site IRB approvals for all documents are forwarded to the CTN Coordinating Center.

1.4 Initiation Visit

An initiation visit is conducted the first time a CTN site participates in a CCC investigator-initiated study. The initiation visit provides instruction and orientation and reviews the facilities and study staff to ensure that all study-specific requirements are satisfied. CTN site personnel who must attend the initiation visit include the research nurse, data manager, study investigators, research pharmacist, and other study-specific personnel.

The CTN Coordinating Center Manager presents: 1) receipt, review and filing of the Investigator's Brochure; 2) maintaining up-to-date study-specific protocols; 3) study objectives and design; 4) participant screening log and participant identification log; 5) clinical and laboratory evaluations and schedule of evaluations; 6) specimen collection, processing, storage, and shipping; 7) informed consent process and randomization procedures; 8) missed evaluations and protocol deviations and violations; 9) adverse event reporting guidelines, procedures and forms for adverse event reporting, and toxicity management; and 10) receipt, review, and filing of addendums to the Investigator's Brochure. Study specific data collection procedures are presented including: CRF guidelines; common errors and corrections; CRF update procedures; missed visits; data inquiries; source documentation; record keeping; and disposition of CRFs. Investigational agent procedures are reviewed including: dissemination of information to the CTN site research pharmacist; agent storage and accountability; pharmacy guidelines; and quality assurance. A review of the CTN site Lead Investigator's responsibility is carried out with the CTN site Lead Investigator. The CTN site Regulatory Document Binder is reviewed including: CTN site IRB documentation, study-specific approval letter, study-specific informed consent, advertisements and participant information sheets when applicable, annual renewal, and roster. Assurance number, laboratory certification, laboratory norms, documentation of submission of the Investigator's Brochure, and signature logs are also reviewed.

A CTN site may not enroll a patient on a study until all of the regulatory documents have been received and CTN site IRB documentation is reviewed and approved by the CTN Coordinating Center manager.

2.0 PROCEDURES FOR CONDUCTING CLINICAL TRIALS

All studies conducted at CTN sites must adhere to the study-specific protocol.

2.1 Patient Registration

The CTN site maintains an accurate screening log for each study and forwards this to the CTN Coordinating Center Manager on a monthly basis.

Once a study subject has been screened and deemed eligible for study entry by the CTN site, a study-specific study subject eligibility checklist, a copy of the dated and signed consent form, and corresponding source documentation are faxed to the CTN Coordinating Center Manager for eligibility verification. Subsequently, a study-specific number is assigned to the study subject and sent to the CTN site. Finally, a Patient Registration Form is completed and faxed by the CTN site to the CTN Coordinating Center Manager.

Queries regarding data accuracy are forwarded from the CTN Coordinating Center Manager to the CTN site for clarification or correction. Once queries are addressed by the CTN site, any corrected data forms or copies of corrected source documentation are faxed to the CTN Coordinating Center Manager.

2.2 Study Monitoring

Each study subject is discussed at the CTN site's weekly Clinical Trials Monitoring Committee meeting by the CTN site research nurses and Lead Investigator and is, in turn, presented at the next weekly CCC Clinical Trials Monitoring Committee meeting by the CTN Coordinating Center Manager.

All questions and concerns regarding the conduct of a study at a CTN site are directed to the site Lead Investigator who consults with the CTN Director and / or the CTN Coordinating Center Manager when necessary. The CTN Director and the CTN Coordinating Center Manager are the primary contacts for study-specific questions such as dose modifications, toxicities, and supportive care. The CTN Coordinating Center Manager is the primary contact for issues regarding patient registration, regulatory documents, completion of CRFs, data collection, and data submission.

Comprehensive monitoring of all CTN site studies (100% of patients) is conducted "off-site" at the CTN Coordinating Center using the CRFs and supporting source documents that are transmitted from the CTN site on a monthly basis.

Following each monitoring exercise, a report is generated by the CTN Coordinating Center Manager, which includes queries and / or requests for additional documentation. The report is generated within 2 weeks of receipt of the CTN site documents. Subsequently, the CTN site reviews the monitoring report, responds to queries, and implements the necessary corrective

action(s). Within two weeks, the CTN site submits a written summary of corrective actions to the CTN Coordinating Center Manager. When necessary, the CTN Coordinating Center Manager conducts “on-site” monitoring visits to provide staff education and to assist in implementing corrective action at the CTN site.

2.3 Auditing of CTN Site Studies by the CCC Quality Assurance Committee

Audits of all CCC investigator-initiated studies are audited on a yearly basis, two to three months prior to the selected study’s UAB IRB renewal date. Ten percent of the patient charts are audited. As part of this process, 10% of the CTN site “shadow charts” maintained at the CTN Coordinating Center are also audited. Following the audit of the CTN site “shadow charts”, a summary of the audit findings are forwarded to the CTN site IRB, the UAB IRB, the CTN site Lead Investigator, the CTN Director and the CCC Associate Director for Clinical Trials. The CTN site Lead Investigator, in consultation with the CTN director, has 2 weeks to respond to any deficiencies prior to formal UAB IRB action concerning the audit findings.

2.4 Data Collection and Submission

Data collection and submission is the responsibility of the CTN site Lead Investigator. Data collection forms are provided by the CTN Coordinating Center Manager. Each CTN site maintains a study-specific research data file (research chart) for study subjects enrolled into a study. The research chart includes completed CRFs and copies of all source documentation. Completed CRFs are reviewed, signed and dated by CTN site Lead Investigator. Any deviations from the study protocol are documented in the study subject’s medical record and research chart. Missing data is documented in the research chart. Copies of the completed CRFs, other study-related documents, and source documents are faxed to the CTN Coordinating Center Manager on a monthly basis.

Failure to submit the required documents in a timely fashion (within one week of the due date) results in a Letter of Notification. Subsequent failure to comply can result in the following:

- Suspension of CTN site study subject accrual until all delinquent data is submitted to the CTN Coordinating Center
- Permanent suspension of study subject accrual to a CTN site
- Other action determined by unique circumstances.

2.5 Adverse Event Reporting

IN CANCER CLINICAL TRIALS, AN ADVERSE EVENT (AE) IS ANY UNFAVORABLE PHYSICAL SIGN, SYMPTOM, SIGNIFICANT LABORATORY TEST ABNORMALITY OR DISEASE THAT IS TEMPORALLY ASSOCIATED WITH THE USE OF A MEDICAL TREATMENT, PROCEDURE OR DEVICE. ALL AEs MUST BE RECORDED ON STUDY-SPECIFIC CRFs. AE INFORMATION IS COLLECTED FROM THE INITIATION OF THE TREATMENT, PROCEDURE OR USE OF A STUDY DEVICE AND CONTINUES UNTIL THE TREATMENT, PROCEDURE OR USE OF A STUDY DEVICE IS STOPPED AND FOLLOW-UP IS COMPLETED. SEVERITY IS GRADED ACCORDING TO COMMON TOXICITY CRITERIA. THE CTN SITE LEAD INVESTIGATOR MUST EVALUATE THE SEVERITY OF EACH AE, ASSESS CAUSAL RELATIONSHIPS, DETERMINE THE ACTION TO BE TAKEN AND DOCUMENT THE OUTCOME. THE CTN SITE STUDY-SPECIFIC RESEARCH NURSE IS

RESPONSIBLE FOR DOCUMENTING, FILING, AND REPORTING AEs ON A WEEKLY BASIS TO THE CTN COORDINATING CENTER MANAGER, WHO IN TURNS REPORTS THE AE AT THE NEXT WEEKLY CCC CLINICAL TRIALS MONITORING COMMITTEE MEETING.

A Serious Adverse Event (SAE) is an AE that 1) results in patient hospitalization or prolongation of hospitalization; 2) results in persistent or significant disability or incapacity; 3) results in death; 4) is a cancer or congenital abnormality or 5) results in the development of drug dependence or abuse. An AE must be considered an SAE when the nature or severity of the event is not consistent with the current Investigator's Brochure. CTN site SAEs must be reported by the CTN site Lead Investigator to the CTN Coordinating Center Manager by email or by fax. It is also the responsibility of the CTN site Lead Investigator to report SAEs to the CTN site IRB and to submit copies of that report to the CTN Coordinating Center Manager. It is the CTN Coordinating Center Manager's responsibility to report the SAE to the appropriate regulatory agency and / or industry sponsor.

3.0 PROCEDURES FOR STUDY CLOSURE

3.1 Closeout Visit

A closeout visit at the CTN site is conducted by the CTN Coordinating Center Manager when a CTN site study reaches its accrual goal or is closed prematurely. The visit includes close out and storage of study subject records and resolution of all outstanding regulatory, data management, and pharmacy issues. The CTN site retains study documents pertaining to an investigational agent for two years when a marketing application is approved or, if a marketing application is not approved, for two years after shipment and delivery of the investigational drug is discontinued.

3.2 Manuscripts, Publications, Press Releases

Any reports or manuscripts describing study results are reviewed by the CTN Director and circulated to contributing CTN sites for their review prior to any presentation, submission for publication or press release. The CTN Director, in consultation with the CCC Principal Investigator, determines the time and place of any presentation, submission for publication or press release and is the final arbiter of authorship.

APPENDIX I

MASTER AFFILIATE AGREEMENT

This Agreement is between The Board of Trustees of The University of Alabama for the University of Alabama at Birmingham, located at 701 20th Street South, Birmingham, Alabama 35294-0111 (herein called "UAB") and _____ (herein called "Affiliate").

RECITALS

- A. UAB, through its School of Medicine, engages in medical research and clinical trials for experimental drugs and medical devices, either initiated by UAB investigators or through contracts with outside companies, institutions, and agencies (herein called "Sponsors").
- B. UAB occasionally has a need for additional participants in these clinical trials.
- C. Affiliate is interested in participating in selected clinical trials under subcontract with UAB.
- D. Affiliate agrees to fulfill annual accreditation and compliance requirement, and to recruit a minimum of five patients for UAB studies annually.
- E. This Agreement provides Affiliate with the following options for participating in clinical trials with the UAB Cancer Center. Affiliate will perform these clinical trials in conjunction with the UAB Cancer Center.

Option 1

Clinical trials originating from UAB faculty for Affiliate participation which are funded by UAB and/or Sponsors. These trials will be performed under the direction of UAB including data collection and auditing functions.

Option 2

Clinical trials for which Affiliate is recruited for participation by UAB but which the Affiliate negotiates directly with the Sponsor. The Affiliate will have financial and regulatory responsibilities independent of UAB.

Option 3

Clinical trials for which Affiliate is recruited for participation by UAB and trials are contracted through and supervised by UAB with data collection and auditing directly with Sponsor.

- F. Therefore, UAB and Affiliate are executing this umbrella Agreement to facilitate participation by the Affiliate in one or more of these clinical trial arrangements.

AGREEMENT

1. By execution of this Agreement and by execution of addendums to this Agreement (the form of which is attached) for performance of specific clinical trials, the Affiliate agrees to participate in clinical studies of investigational drugs and medical devices.
2. Prior to the participation of the Affiliate in any specific clinical trial the Affiliate and UAB shall execute an addendum to this Agreement which shall indicate the type of trial arrangement (Options 1, 2 or 3) and incorporate the protocol of the specific clinical trial, detail the compensation of the Affiliate for participation in the trial, and any other terms and conditions which are specific to that clinical trial. Each clinical trial funded by UAB (or its Sponsor) as part of the CTN Agreement will be subject to an indirect cost for the first \$25,000. All subsequent funds will not be subject to UAB indirect cost.
3. The performance of each clinical trial by Affiliate shall be subject to all terms and conditions of this Agreement, the applicable addendum to this Agreement, and of the contract (if one occurs) between UAB and the Sponsor for performance of that clinical trial.
4. Affiliate agrees to fulfill all responsibilities of a Affiliate under the protocol for each clinical trial. Specifically, the Affiliate agrees to conduct those clinical trials in accordance with the applicable protocol and all applicable Institutional Review Board (“IRB”) regulations according to the requirements described in 62 FR 900-10 dated February 3, 1997 and 67 FR 11792 dated March 6, 2000, Food and Drug Administration (“FDA”), and all Financial Disclosure requirements. Among other duties for each clinical trial the Affiliate agrees go:
 - a. comply with all applicable rules, policies, and procedures of UAB and the affiliate’s IRB.
 - b. assure that all uses of any drug or device involving human subjects will be conducted by the Affiliate or co-Affiliates under the Affiliate’s supervision in compliance with all applicable IRB and FDA requirements.
 - c. obtain informed consent from all study participants, documented by written informed consent materials approved by the affiliate’s IRB.
 - d. maintain in confidence proprietary technical and other information disclosed to the Affiliate concerning the drugs or devices, unless written approval to release that information is received from UAB or the Sponsor.
 - e. assume reasonable responsibility for devices or drugs used in the studies by keeping them in secure storage and not releasing them to any unauthorized person.
 - f. for trial options #1 or 2, to report to the UAB Principal Investigator responsible for the conduct of the trial at UAB, all study patient adverse events, patient deaths, IRB actions, or deviations from the study protocol.
 - g. permit site monitoring by the Sponsor or its employees or representatives, representatives of the FDA, or representatives of UAB as appropriate. Such monitoring may include examination of any records relating to the clinical trial under review.
 - h. maintain complete and accurate written records, accounts, notes, reports, and data relating to each study. Such records shall include completed Case Report Forms and signed Consent Form. The records will be retained in accordance with FDA regulations (21 CFR 312.62) or longer, if required by Sponsor. If the record retention requirement for a particular clinical trial varies from FDA regulation, the specifics will be detailed in the individual addendum.
 - i. comply with all rules, policies, and procedures concerning investigator financial disclosure and conflict of interest management, including compliance with FDA requirements described in 21 CFR Part 54 and 59 FR 33242.
 - j. Affiliate will comply with all requirements related to the use and disclosure of protected health information in compliance with all UAB, IRB and HIPPA requirements.
5. The Affiliate agrees that it will supervise all testing of patients under any clinical trial and certifies that the Affiliate has adequate facilities and personnel to conduct each study for which an addendum is executed. Affiliate certifies that it will maintain professional liability coverage for all full-time and part-time employees, agents, or consultants participating in the clinical trials that are subject to this Agreement.

6. The Affiliate shall receive compensation for each clinical trial in accordance with the provisions of addendums to this Agreement. The Affiliate shall invoice UAB following each successfully completed study milestone (as defined in the Addendum). Successfully completed study milestone will be documented by completion of CRFs and receipt of monitoring report attesting to such completion as well as resolution of queries. Payment shall be made by UAB (or Sponsor) to the Affiliate within 60 days of invoice of after receipt of study funding at UAB.
7. Either Party may terminate this Agreement or any addendum to this Agreement at any time upon written notice to the other Party. In the event of termination, both Parties agree to fulfill treatment and financial obligations related to all patients enrolled in clinical trials covered by this Agreement at the time of termination.
8. Affiliate and its employees and agents shall be considered independent contractors for all purposes under this Agreement.
9. This Agreement shall be interpreted in accordance with Alabama law without regard to conflicts of law rules.
10. This Agreement, any addendum to this Agreement, and any rights under this Agreement may not be assigned or transferred by the Affiliate without the prior written approval of UAB and Sponsor.
11. While this Agreement is in effect, the Affiliate may characterize its relationship with UAB in print or electronic media in the following manner: "a clinical study affiliate of the UAB Comprehensive Cancer Center"; or "Affiliated for clinical trials with the UAB Comprehensive Cancer Center"; or "working with the UAB Comprehensive Cancer Center to bring leading-edge cancer care to _____". Characterization of Affiliate's relationship with UAB is limited to patient recruitment into specific clinical trials and dissemination of information related to those clinical trials. For any other use of UAB's name, specific permission in writing from UAB is required.
12. This agreement and any addendums to this agreement which are executed by the parties constitute the entire agreement between the parties and any prior written or oral agreements or understandings concerning the subject matter of this agreement and those addendums are void. This agreement and the addendums to this agreement may only be amended by mutual written agreement of the Affiliate and UAB.
13. This agreement shall extend for a term of one year and shall be automatically renewed for additional terms of one year each unless either party shall give written notice of a desire to terminate prior to the end of the then current term.

IN WITNESS WHEREOF, UAB and the Affiliate have executed this Agreement on the ____ day of _____ 20__.

THE BOARD OF TRUSTEES
 OF THE UNIVERSITY OF ALABAMA
 FOR THE UNIVERSITY OF
 ALABAMA AT BIRMINGHAM

BY _____
 Name:
 Title:
 Date _____

BY _____
 Name:
 Title:
 Date _____

APPENDIX II ADDENDUM

Sponsor _____ Protocol _____ Site _____

This is an Addendum to the Affiliate Agreement between _____ (“Affiliate”) and The Board of Trustees of The University of Alabama for the University of Alabama at Birmingham (“UAB”) dated _____.

1. This Addendum shall be subject to all of the terms and conditions of the Agreement referred to above. The clinical trial will operate under option _____.
2. Affiliate agrees to participate in the clinical trial entitled “_____” which is described in the protocol which is attached to and made a part of this Addendum.
3. The Affiliate shall be compensated for performance of the clinical trial under this Addendum as follows:
4. The following special terms and conditions are applicable to this clinical trial and Clinical Trial Agreement amend the Agreement between the Affiliate and UAB:

TERMS AND CONDITIONS

LIABILITY – Each party will be responsible for their own acts and omissions during the performance of the Protocol. Each party will carry liability insurance or self-insurance to support this certification.

PROPRIETARY INFORMATION – The drug, protocol, case report forms, or data designated as confidential or proprietary are the property of UAB or Sponsor. The Affiliate shall have no claim to proprietary information.

GENERIC DRUG ENFORCEMENT ACT OF 1992 – The Affiliate certifies that it or its employees, affiliates and agents have never been i) debarred or ii) convicted of a crime of which a person can be debarred, under Section 306(a) or (b) of the Generic Drug Enforcement Act of 1992 (“Section 306(a) or (b)”). The Affiliate certifies that it has been and, to the best of its knowledge after due inquiry, none of its employees, affiliates or agents has ever been i) threatened to be debarred or ii) indicated for a crime of otherwise engaged in conduct for which a person can be debarred, under Section 306(a) and (b). the Affiliate agrees that it will promptly notify Sponsor in the event of any such debarment, conviction, threat, or indictment. The terms of the preceding sentence shall survive the termination of expiration of the Agreement.

SUBJECT INJURY – This language will be study-specific.

ADVERSE EVENT REPORTING – The Affiliate agrees to notify the Sponsor and/or UAB Principal Investigator within twenty-four (24) hours after learning of any serious and/or unexpected adverse drug reactions affecting any patient in the Study. The Affiliate further agrees to follow-up such notification of adverse drug reaction with appropriate reports in compliance with the Protocol and all applicable legal and regulatory requirements.

CONFIDENTIAL INFORMATION – During and for a period of _____ (____) years after the term or early termination of this Agreement, the Affiliate shall retain in confidence all test articles and proprietary data and/or information obtained from the Sponsor or generated pursuant to the Study including, but not limited to, the Protocol, the investigator’s brochure, interim results, and any other information or material disclosed under secrecy agreements previously entered into between the parties.

Dated the ____ day of _____ 20____.

THE BOARD OF TRUSTEES OF THE
UNIVERSITY OF ALABAMA FOR THE
UNIVERSITY OF ALABAMA AT BIRMINGHAM

Affiliate

APPENDIX III

CTN SITE ACCREDITATION CHECK LIST

CTN Site Name:

CTN Site PI:

CTN Site Research Manager:

CTN Site Review Date:

Accreditation	Yes	No	Comments
Existing and functional administrative staff for the conduct of clinical research?	<input type="checkbox"/>	<input type="checkbox"/>	
Existing regulatory staff for the conduct of clinical research?	<input type="checkbox"/>	<input type="checkbox"/>	
Existing clinical staff for the conduct of clinical research?	<input type="checkbox"/>	<input type="checkbox"/>	
Successful completion of appropriate training and certification of personnel involved in the conduct of clinical trials involving human subjects to include: copy of investigators licenses copy of current investigators CV's signed and dated copy of human subjects training for all investigators and research personnel copy of HIPAA training for all investigators and research personnel?	<input type="checkbox"/>	<input type="checkbox"/>	
Ability to conduct independent clinical trials under GCP?	<input type="checkbox"/>	<input type="checkbox"/>	
WIRB Member Listing?	<input type="checkbox"/>	<input type="checkbox"/>	
Copy of CTN site laboratory certifications-CLIA /CAP?	<input type="checkbox"/>	<input type="checkbox"/>	
Copy of Laboratory Norms for each site?	<input type="checkbox"/>	<input type="checkbox"/>	
Copy of key site research personnel with complete names, phone numbers, fax numbers, and e-mail for each to include: research manager regulatory research nurses	<input type="checkbox"/>	<input type="checkbox"/>	

data managers			
research pharmacist (s)			
Adequate equipment and facilities to conduct clinical research: equipment for processing and storage of research related materials; dedicated fax machine for receiving and transmitting protocol specific correspondence adequate facilities and space for storage of test related articles, specimens, and record retention designated monitoring space with adequate space for research chart review, easily accessible to copy of transmittal equipment locked area with access restricted to designated study personnel.	<input type="checkbox"/>	<input type="checkbox"/>	
Standard Operating Procedures for Research at affiliate site?	<input type="checkbox"/>	<input type="checkbox"/>	
Listing of scheduled research meetings at affiliate site?	<input type="checkbox"/>	<input type="checkbox"/>	
CTN site pharmacy review in compliance for the conduct of clinical trials?	<input type="checkbox"/>	<input type="checkbox"/>	
Signed Master Agreement?	<input type="checkbox"/>	<input type="checkbox"/>	

General Observations:

Actions:

ID	Action Item	Assigned To	Due By
			[mm/dd/yyyy]
			[mm/dd/yyyy]
			[mm/dd/yyyy]
			[mm/dd/yyyy]
			[mm/dd/yyyy]

Comments:

Approvals:

CTN Manager : _____

Date: ___/___/___

CTN Director: _____

Date: ___/___/___

