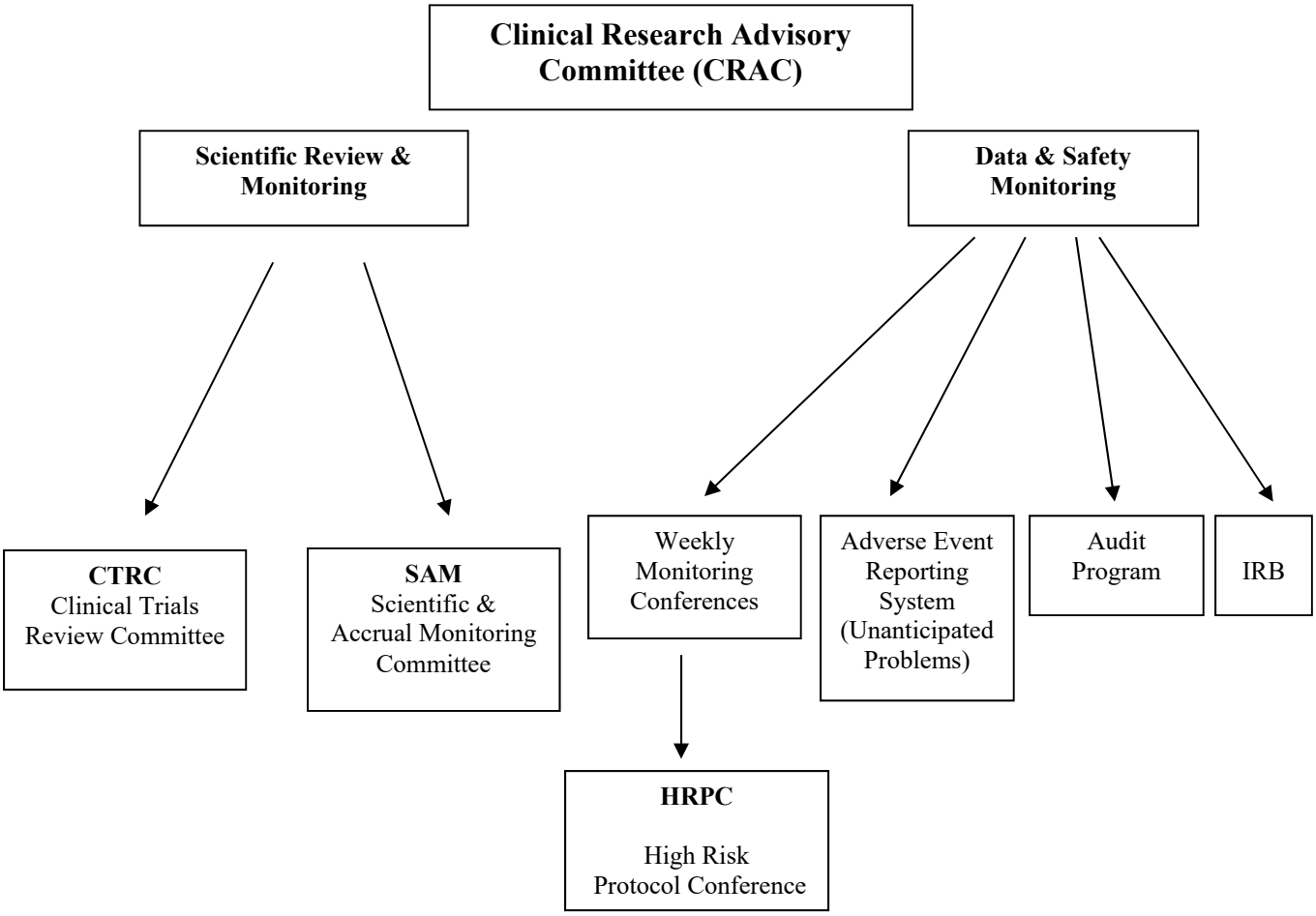
The Protocol Review and Monitoring System
Guidelines and Procedures

Clinical Trials Review Committee
Scientific and Accrual Monitoring Committee

The University of Chicago Comprehensive Cancer Center
5841 South Maryland Avenue, MC 1140
Chicago, Illinois 60637-1470

Table of Contents

1.0 – Organizational Structure



2.0 - Clinical Trials Review Committee

2.1 - Introduction

The Protocol Review Monitoring System (PRMS) at the University of Chicago Comprehensive Cancer Center (UCCCC) is comprised of two committees, one of which is the Clinical Trials Review Committee (CTRC). The Committee is appointed by, and is under the overall direction of the Associate Director for Clinical Sciences, who is also the Chair of the Clinical Research Advisory Committee (CRAC). The CTRC is responsible for the initial scientific review of new cancer-related clinical trials.

2.2 - Purpose

The CTRC is responsible for the evaluation of scientific merit and data and safety monitoring plans for all cancer-related clinical research performed at the UCCCC. The Committee meets once a month to:

a) Review all new clinical trials for scientific merit. The review takes into account the scientific rationale, study design, type of support required to implement the research, adequacy of

biostatistical input, anticipated accrual, study feasibility, and the estimated period for completion.

b) Assess adequacy of data and safety monitoring plans (including audit procedures and frequency) for each protocol.

c) Determine the level of study risk (criteria described in the UCCCC DSM plan) and recommend frequency with which the study is to be audited.

d) Verify that the protocol is assigned to a weekly safety monitoring conference.

e) Assess the prioritization of proposed trials in the context of patient and staff resources.

f) Affirm relevance of the proposed clinical trial to the mission of the UCCCC.

g) Score protocols for subsidy awards.

h) Terminate/close a research project.

2.3 – Scope

Studies cannot be activated without CTRC approval, a pre-requisite for IRB approval. As a general policy, protocols undergo full review as outlined below. Protocols that have undergone prior peer review (e.g. NIH, NCI, FDA, ACS, Cooperative Group) will be eligible for expedited CTRC review, which involves review by the Committee Chair or Vice-Chair who has the option of bringing them to the full committee if there are specific concerns (e.g. regarding merit, design, and prioritization). The CTRC has the authority to develop policies and procedures regarding initial review and approval of cancer clinical trials.

a) Standard Protocols (not previously peer-reviewed)
The UCCCC Clinical Trials Review Committee will conduct a full Committee review of all cancer-related clinical protocols that have not otherwise undergone external peer review. Multi-institutional protocols supported by the pharmaceutical industry and single institution (investigator IND) industry-supported protocols are also subject to review.

b) Clinical Protocols
Protocols whose primary objective is to develop a novel technology, procedure, or clinical tool, and that enroll a broad spectrum of patients, only some of whom carry a cancer diagnosis, will not require CTRC review. On the other hand, protocols whose primary objective is to test the validity or limitations of a cancer diagnostic procedure or that enroll a cohort of patients with a defined cancer or cancer-prone syndrome will be subject to CTRC review.

c) Consortium Protocols
Protocols submitted through a consortium can be expedited providing that the following two criteria are met: 1) The consortium review process must be approved by the Clinical Research Advisory Committee (CRAC) as meeting the standards for robust peer review and 2) the review by the consortium must be protocol specific. All protocols submitted by a research consortium that do not meet the above criteria will receive full Committee review.

d) Exempt Protocols

Studies given an exempt status by the IRB will also be exempt by the CTRC and will not be reviewed.

e) Externally Peer-Reviewed Protocols
Protocols that have been externally peer reviewed, such as Cooperative Group protocols or studies conducted in the context of an NIH grant or contract (i.e. Phase II contract), will undergo expedited review only.

f) Compassionate Use and Expanded Access Protocols
Compassionate use protocols will not require a full Committee review. They will receive expedited review.

Expanded access studies in which the study drug has shown good activity but has not yet been approved by the FDA will be reviewed by the Committee using slightly different criteria. These studies permit use of an effective drug that may be beneficial to subjects and may provide additional information on long term use. At the discretion of the CTRC, such studies could receive special approval on the basis of "compassionate use".

g) Clinical Databases and Banks
HIPAA and Human Investigation Regulations require that collection of any human specimens or clinical data must be conducted under an IRB approved protocol. In order to maintain a consistent policy, any such protocols that are specific for cancer patients will require CTRC approval. However, because the only objective of these protocols is to collect data, they will not require full Committee review but will receive expedited review. Any hypothesis-directed research that utilizes the resources in such a database or bank will then require a follow-up formal clinical protocol, a full CTRC review, and presumably IRB approval. An investigator can request expedited CTRC review of a protocol, but final determination as to whether a protocol represents a "data and specimen collection device" or a clinical trial requiring full scientific review rests with the CTRC.

Protocols in which the only objectives are to evaluate/study previously collected tissue in standard clinical archives or established tissue banks do not require CTRC review if they undergo review by the Pathology Biospecimen Utilization Committee. Cancer- focused tissue protocols not reviewed by this committee or protocols requiring prospective tissue collection and/or prospective clinical data collection will require full CTRC review.

h) Annual Reviews
Annual reviews will be conducted by the Scientific Accrual Monitoring (SAM) Committee to ensure compliance with the initially approved data and safety monitoring plan (for more detail please see SAM Guidelines) and accrual goals.

2.4 - Structure

Profile of members:
Membership includes the Chair, Vice-Chair, the PRMS Coordinator and committee members from various departments within the Division of Biological Sciences including faculty and nurses engaged in cancer research. Currently, the Committee has representation from Medical Oncology, Surgery, Pediatrics, Pathology, Radiation and Cellular Oncology, Radiology, and Nursing, as well as

representation from the Biostatistics Core Facility, the Human Imaging Research Office (HIRO), and the Cancer Clinical Trials Office (CCTO).

Appointment:
Members are appointed by the Associate Director for Clinical Sciences with approval of the UCCCC Director. Although appointments are for a three-year term, there is some degree of flexibility to ensure broad representation from all cancer-related specialties and departments. Members are selected based on an interest in and experience with cancer clinical research.

3.0 - Protocol Submission Process

3.1 - Overview

With the exception of the Department of Pediatrics, and a small minority of protocols managed by the Clinical Research Support Office (CRSO), the CCTO currently manages the CTRC submission of cancer-related protocols for all departments, including Medicine, Surgery, Obstetrics and Gynecology, Radiation and Cellular Oncology, and Radiology. In general, Principal Investigators (PIs) submit their protocols to the Cancer Clinical Trials Office (CCTO) and they are given to the appropriate Regulatory Manager. The required documentation is compiled (see below) and the protocols are then submitted to the CTRC. Once the protocol receives full CTRC approval, the protocol is eligible for review and approval by the Institutional Review Board (IRB).

3.2 – Prospective Study Submission

To conduct a prospective study, the Principal Investigator **must** submit the following ***(see Appendix 1 for details of submission process***):

a) A written protocol that includes background information and references to support the study, clear objectives, specific research questions, research methods, a definition of study endpoints and statistical considerations, a data and safety monitoring plan, and projected patient accrual. If this is a multi-institutional study, the DSM plan must include procedures for managing SAEs/UPs from affiliate/participating institutions.

b) A completed Clinical Trial Submission Form.

c) Protocol priority tree (a list of all protocols, including the study being submitted, which are competing for the patient population under study).

d) Investigational Brochure (if applicable).

e) Other submission documents (questionnaires, package inserts, assessment forms, etc as applicable).

3.3 - Retrospective Study Submission

To conduct a retrospective study the Principal Investigator **must** be submit the following:

a) A written protocol with background information and references to support the study, study objectives, specific research questions to be addressed, and a definition of study

endpoints and statistical considerations. **The protocol should list all the data items to be analyzed**, the status of the data (i.e. paper records, on computer), and the total number of patients.

b) The completed CTRC Submission Form..

3.4 - Pre-Meeting Preparation

The PRMS Coordinator maintains a log of all protocol submissions. This includes the name of the Principal Investigator, title of the protocol and dates of the committee review. The CTRC Chair assigns at least two reviewers, as well as a biostatistician to review and present the protocol at the meeting. Review from additional committee members with special areas of expertise such as pathology or pharmacology may also be requested. The PRMS Coordinator posts the protocols to the password protected web-based electronic protocol review application and notifies members that they have protocols to review. .

4.0 - Clinical Trials Review Committee Meetings

4.1 - Meeting Policies

Meetings are conducted by the Committee Chair, or in his/her absence, the Vice-Chair. In the absence of the Chair or Vice-Chair, the Chair appoints a member of the committee to conduct the meeting. At least eight committee members must to be present to achieve a quorum. Meetings are held monthly and minutes are recorded by the PRMS Coordinator and saved in electronic files.

The CTRC review process is consider an "open" review and reviewers are encouraged to directly contact Principal Investigators for clarification at any time during the review process. A Principal Investigator is welcome to attend the CTRC meetings to hear his/her protocol discussed, and to address comments that are raised by the Committee. If a reviewer is unable to attend the meeting, he/she may provide a written review to the Chair or Vice-Chair for presentation at the meeting.

The Chair, with the assistance of the Vice-Chair and the PRMS Coordinator, are responsible for correspondence to the Principal Investigator regarding necessary revisions, approval or deferral of the study. Copies of the outcomes letters are sent to the Principal Investigator and the Regulatory Affairs Manager. When the study is approved by the CTRC, the PRMS Coordinator uploads the approval or approval with revisions letter into AURA IRB, the electronic administrative system used by the University of Chicago IRB.

For protocols that receive an "approval with revision", the Principal Investigator must respond to the CTRC review within 60 days. The PRMS Coordinator mails one reminder prior to the deadline date. If the Principal Investigator fails to respond, the protocol is deferred and will need to be resubmitted and reviewed at a full Committee meeting.

Upon receipt of revisions, the CTRC Chair or Vice-Chair can grant full approval to protocols initially receiving an "approved with revisions". The full committee must discuss revised protocols that were deferred.

A new protocol that appears to be a resubmission of a previous disapproved protocol must be accompanied by the previous protocol and a detailed letter indicating how the new protocol differs. If the PI wishes to appeal the decision, the PI must present a detailed justification letter to the CRAC committee for consideration.

4.2 - Meeting Outcomes

After a full presentation and discussion of a protocol by the reviewers, the Committee arrives at a consensus and protocols receive either:

a) Approval: Protocol requires no changes (no action required).

b) Approval with Revisions: Protocol has minor issues needing clarification. Studies that receive an "Approval with Revisions" for which no response is received from the Principal Investigator within 60 days are deferred.

c) Deferral: Protocol has major issues. This could include major concerns with study design, scientific rationale, or adequacy of biostatistical input. Protocol must be re-reviewed at a full CTRC meeting before approval will be granted.

d) Disapproval: Protocol disapproved due to poor scientific merit and/or as the study design is unlikely to meet the study objectives. If a PI wishes to appeal the CTRC decision, the PI can appeal the decision to the Clinical Research Advisory Committee (CRAC).

4.3 - Subsidy Scoring

Based on the implementation by the Cancer Center of a Chargeback System for CCTO services, a new scoring system has been added to the CTRC review for institutional trials. Scoring is based on the study's scientific merit and scientific priority. The descriptor score (1. outstanding; 2. good solid study design; 3. adequate; 4. deferred; 5. disapproved) determines the study's eligibility for a UCCCC subsidy to cover regulatory management fees. Studies receiving a score of one or two are eligible to receive a subsidy, with specific fund allocations made by the Clinical Research Advisory Committee (CRAC).

4.4 – Amended Protocol Review

In the event a protocol previously reviewed and approved by the CTRC has been modified significantly to change the scope of the trial (e.g. doubled sample size, addition of treatment arm, etc), the protocol can be resubmitted to the CTRC for full committee re-review. This re-review option will be based on the Principle Investigator's or IRB's discretion.

5.0 – Scientific and Accrual Monitoring Committee

5.1 - Introduction

The second PRMS Committee, the Scientific and Accrual Monitoring Committee (SAM), is responsible for the ongoing annual review of study progress. The Committee is appointed by the Chair and approved by the UCCCC Director.

5.2 - Purpose

The purpose of the Scientific and Accrual Monitoring Committee is to monitor the progress of CTRC-approved studies in terms of both accrual and scientific priority. Specifically SAM reviews trials to:

a) Ensure that the conduct of the study is in compliance with the approved Data Safety Monitoring plan.

b) Evaluate compliance with any stipulations placed on the research at the time of CTRC initial review.

c) Review study progress, specifically accrual to date compared to projected accrual, to determine if the trial should be continued based upon the likelihood of timely completion in meeting its scientific goals.

d) Review the rate of accrual to ensure the study has not exceeded the targeted accrual as stated in the protocol. Review accrual of women and minorities relative to the proportion of these sub-groups in the disease specific population. If a multi-center study is reviewed, only institutional accrual rate will be taken into account.

e) The SAM is authorized to change the risk level initially assigned by the CTRC on the basis of accumulating data and number of Unanticipated Problems.

5.3 - Scope

The SAM committee has the authority to develop policies and procedures regarding annual review of cancer clinical trials. Studies recommended for study closure by SAM are brought to the CRAC for further discussion. After CRAC review, the study is brought to the CTRC for final determination on closure. On studies for which the Associate Director for Clinical Sciences is participating, or otherwise has a conflict of interest, SAM recommendations are submitted to the UCCCC Director, who works with the CRAC to review the study and then forwards the recommendation to the CTRC to determine study closure.

5.4 - Structure

Profile of members:
The SAM Committee includes diverse representation from various departments in the Division of Biological Sciences comprised of individuals with representation from Pediatrics, Surgery, Medicine, Section of Hematology Oncology, Health Studies, Neurology, Obstetrics/Gynecology, and Nursing who engage in cancer clinical research.

Appointment:
. Members will serve for a term of 3 years, although membership duration will be flexible to maintain the required depth and breadth of expertise related to the spectrum of clinical research conducted at the UCCCC.
.

6.0 – Scientific and Accrual Monitoring Committee Procedures and Meetings

6.1 - Pre-Review Process

a) All open protocols are reviewed annually, generally near the time of IRB continuing review.

b) The PRMS Coordinator generates a protocol and accrual summary (including study status and DSM plan) from the centralized database (Velos) for each protocol being reviewed.

c) PRMS Coordinator assigns studies to specific Committee members for review.

d) The PRMS Coordinator uploads electronic copies of the annual renewal material (protocol, consent, IRB continuing renewal form, Velos summary of accrual, and any study progress reports).

e) PRMS Coordinator emails members informing them of their assignments.

6.2- Review Process

a) SAM members are given materials at least one week prior to the meeting and they are responsible for completing an online Reviewer Worksheet for each assigned study.

b) Reviews and recommendations are then presented to the committee and discussed at the monthly meetings.

6.3 - Review Outcome, Notification and Study Closure

a) Each study reviewed receives one of the following designations:
   - Approval: the study can continue without change.
   - Conditional approval/decision pending: the committee requests clarification or more information in order to formulate a recommendation.
   - Recommendation of Closure.

b) The PRMS Coordinator distributes an automatic email generated during the meeting to the study PIs, outlining the committee's recommendations, including requests for additional information.

c) If the study PI receives a conditional approval/decision pending, the PI is required to complete the SAM PI Response Form/Corrective Action Plan (Appendix 2).

d) If the PI has not responded within two weeks, a reminder email is issued by the PRMS Coordinator.

e) All responses are reviewed by the SAM Chair and members of the Committee at the next SAM Committee meeting to determine the final outcome.

f) In instances where closure has been recommended by the Committee and the investigator declines to follow the recommendation, the matter is referred to the CRAC committee for discussion. After CRAC review, the study is brought to the CTRC for final determination on closure.

6.4 - Review of Amendments

The committee approves all protocol amendments which are reviewed at the time of the annual review.

6.5 – Studies Exempt from Review

Non-therapeutic trials, such as retrospective chart reviews, tissue-banking trials, and umbrella grants, are exempt from SAM review.

6.6 - Meeting Policies

Meetings are conducted by the Committee Chair, or in his/her absence, the Vice-Chair. A quorum must include the Chair or Vice Chair and at least 2 committee members. The PRMS Coordinator assists the Chair and/or the Vice-Chair in the development of meeting agendas, policies and procedures, assures that minutes are written and maintained, and coordinates distribution of protocols to committee members and distribution of committee recommendations to the Principal Investigators of the studies. Meetings are held monthly and minutes are recorded by the PRMS Coordinator and placed in the electronic SAM folder in the T-Drive.

6.7 - Subsidy Scoring

Based on the implementation by the Cancer Center of a Chargeback System for CCTO services, a new scoring system has been added to the SAM review for institutional trials. Scoring is based on the study's scientific merit and scientific priority. The descriptor score (1. excellent; 2. adequate; 3. poor) determines the study's eligibility for a UCCCC subsidy to cover regulatory management fees. Studies receiving a score of one or two are eligible to receive a subsidy, with specific fund allocations made by the Clinical Research Advisory Committee (CRAC).

Appendix 1

New Submission to the CTRC

1) Must meet the deadline date of 12 noon the Monday a week and a half before the meeting. For example, for a CTRC Meeting held on Thursday, March 1, 2012, the protocol submission deadline would be Monday, February 20, 2012. If a holiday falls on the Monday, the submission would be due the Tuesday after the holiday.
2) Must provide one electronic copy of:
   A) The protocol (see appendix 2 for a template for Non-Therapeutic Trials)
   B) The Clinical Trials Submission Form **(Can be obtained from Velos or below in Sub-Section A)**
   C) Priority Tree [This is a list of all studies (including the study being submitted) which are competing for the same patient population; if applicable].
   D) Investigational Brochure (If applicable)
   E) Other Submission Documents (Questionnaires, Package Insert, Assessment forms, etc)

PLEASE NOTE: ALL submitted items MUST be emailed to the PRMS Coordinator. The email MUST be titled NEW CTRC SUBMISSION

Meeting

1) CTRC Meetings are generally held the first Thursday of each month, unless rescheduled by the CTRC Chair.

2) Acknowledgment letters will be emailed **one week after the meeting** at the end of the business day. If distribution of the letters is expected to be greater than one week, an email will be sent by the PRMS Coordinator of the expected delivery date.

Response based on Outcomes of the CTRC Meeting

1) Approved – No response is needed

2) Approved with Revisions – A response is required from the PI. The letter must address all the committee's queries. The letter should be addressed to the attention of the Chair and Vice-Chair. The letter must address each query point by point. All changes to any submitted document must be highlighted. ONE electronic (emailed) copy of all updated materials must be submitted with the response. The changed sections should be highlighted. **Do not provide copies of documents which have not been altered**.

3) Deferred - A response is required from the PI. The letter addressing all the committee's queries must be submitted. The letter should be addressed to the attention of the Chair and Vice-Chair. The letter must address each query point by point. All changes to any submitted document must be highlighted. One electronic (emailed) copy of the protocol,

priority tree and clinical trial submission form must be submitted. If any of the above documents have been updated, submit those copies with the changed section highlighted. **The study MUST go back for a full committee review and must be submitted in time to meet the CTRC meeting submission deadline**. The PRMS Coordinator will notify the IRB, Program Leaders and Contract Specialists of the protocol deferral by the CTRC.

4) Disapproval – The trial cannot be activated at the U of C. If the PI of the study chooses to seek further approval, an appeal can be submitted to the Clinical Research Advisory Committee (CRAC)**.**

Expedited Studies

1) A study can be expedited if it is one of the following:

   A) Compassionate Use Study
   B) Co-Operative Group Study (i.e. CALGB, SWOG, GOG, COG, etc)
   C) NCI Funded Study – Grant Information should be provided
   D) Tissue Banking Study
   E) Database Collection Study
   F) Retrospective Chart Review
   G) Grant
   H) Otherwise peer-reviewed (e.g. NIH grant or consortium trials)

If the submitted study meets one of the above definitions, one copy of the following documents is needed:

   A) The protocol
   B) The Clinical Trials Submission Form can be obtained from Velos or see Sub-Section A.
   C) Priority Tree: This is a list of all studies competing for the same patient population which should include the study being submitted for review.
   D) Investigational Brochure (if applicable).

PLEASE NOTE: ALL submitted items MUST be emailed to the PRMS Coordinator. The email MUST be titled NEW CTRC SUBMISSION

Expedited studies DO NOT need to meet the CTRC meeting deadline. The study can be submitted at any time. Although there is NO set turnaround time for distribution of approval letters, delivery usually takes 7 days to allow time for review by the Chair or Vice-Chair.

Sub-Section A
Clinical Trial Submission Form

A. STUDY SUMMARY

Principal Investigator:

IRB#:

Study Title:

1.) Is this an investigator-initiated study? Investigator-initiated studies are those for which you generated the idea and had majority input into design and writing of the protocol.

☐ Yes ☐ No

2.) Division (check one):

☐ CRC_Anesthesia
☐ CRC_Gyn
☐ CRC_Peds
☐ CRC_Health Studies
☐ CRC_Psychiatry
☐ CRC_Hem/Onc
☐ CRC_Rad/Onc
☐ CRC_Medicine
☐ CRC_Radiology
☐ CRC_Pathology

3.) Disease Site(s): _____

4.) National Accrual Goal (If applicable): _____

5.) Local (U of C) Sample Size: _____

6.) How long (months/years) will it take to complete accrual?: _____

7.) Phase:

☐ N/A
☐ Pilot/Feasibility
☐ Phase I
☐ Phase I/II
☐ Phase II
☐ Phase II/III
☐ Phase III
☐ Phase III/IV
☐ Phase IV
☐ Phase IV/V
☐ Phase V

8.) Sponsor(s): _____

9.) Is this an Investigator IND/IDE study? _____
If so, what is the IND/IDE number? _____

10.) Research Type (Sponsor Type):

☐ **National Cooperative Group Trials**

☐ **Other Externally Peer-Reviewed Trials:** *R01s and P01s or other trial mechanisms funded by NIH or supported by other peer-reviewed funding organizations, including the following:*

a. *Agency for Healthcare Research and Quality (AHRQ)*
b. *American Cancer Society (ACS): national office only*
c. *American Foundation for AIDS Research (AFAR)*
d. *American Institute for Cancer Research (AICR)*
e. *Cancer Research Foundation of America*
f. *Center for Disease Control (CDC)*
g. *Central Office of the Veterans Administration (VA) – excluding local/regional awards and "block" grants*
h. *Environmental Protection Agency (EPA)*
i. *Food and Drug Administration (FDA)*
j. *Howard Hughes Foundation*
k. *Leukemia and Lymphoma Society 2*
l. *Multiple Myeloma Research Foundation*
m. *National Institute for Occupational Safety and Health (NIOSH)*
n. *National Science Foundation (NSF)*
o. *Susan G. Komen Breast Cancer Foundation*
p. *University of California-Wide Breast Cancer Research Program*
q. *U.S. Army (DOD) special research programs in ovarian, breast and prostate cancer*

☐ **Institutional Trials:** *In-house, internally reviewed trials, including those collaborative studies conducted with industry sponsorship in which the center is a primary contributor to the design, implementation, and monitoring of the trial, or participation in a multi-site trial initiated by an investigator at another center.*

☐ **Industrial Trials:** *Design and implementation of the study is controlled by the pharmaceutical company*

11.) Study Scope: ☐ Single-Center ☐ Multi-Center

a. If Multi-center study, total # of sites participating? _____

b. Is U of C the lead institution? (If so, please list participating sites below): ☐ Yes ☐ No

Study Type (please select one):

☐ a. **Therapeutic Trial:** *Clinical trials with **therapeutic** intent using drugs, radiation, surgery, other biological agents, or behavioral or other interventions.*

☐ b. **Prevention Trial:** *clinical trials for the modulation of cancer risk and inhibition of cancer progression using chemoprevention drugs, nutritional, dietary, behavioral, or other interventions.*

☐ c. **Supportive Care:** *Clinical trials intended to improve the comfort and quality of life for the*

patient using drugs, nutritional, dietary, behavioral or other interventions.

☐ d. **Screening, Early Detection, or Diagnostic Trials:** *Clinical trials directly testing the efficacy of devices, techniques, procedures; or tests for earlier or more accurate detection or diagnosis of disease.*

☐ e. **Epidemiologic, Observational, or Outcome:** *Studies among cancer patients and healthy populations that involve no intervention or alteration in the status of the participants, e.g., surveillance, risk assessment, outcome, environmental, andbehavioral studies.*

☐ f. **Ancillary:** *Auxiliary studies that are stimulated by, but are not a required part of, a main clinical trial/study, and that utilize patient or other resources of the main trial/study to generate information relevant to it. Ancillary studies included must be linked to an active trial or epidemiologic or other study and should include only patients accrued to that trial or study. Only studies that can be linked to individual patient or participant data should be reported*

.

☐ g. **Correlative:** *Laboratory based studies using specimens to assess cancer risk, clinical outcomes, response to therapies, etc. Only studies that can be linked to individual patient or participant data should be reported.*

☐ h. **Healthy Volunteer:** *A healthy volunteer is a person with no known significant health problems who participates in clinical research to test a new drug, device, or intervention. Research procedures with healthy volunteers are designed to develop new knowledge, not to provide direct benefit to study participants.*

☐ **i. Registry**

☐ **j. Retrospective Chart Review**

☐ **k. Tissue/Specimen Bank**

☐ **l. Umbrella Grant**

☐ **m. Other**

B. MORE STUDY DETAILS:

1.) CDUS study? (applicable to NCI sponsored studies only):

☐ Yes ☐ No

2.) Consent required?:

☐ Yes ☐ No

3.) Summary 4 Clinical Research Category (**MUST** select one):

☐ ***Clinical trials involving an Agent or Device***

☐ ***Clinical trials involving other types of interventions*** (i.e. behavioral modification, nutritional protocols, etc.)

☐ ***Epidemiologic, outcome, or other observational studies***

☐ ***Companion, ancillary or correlative studies*** associated with a clinical trial and other biological studies using clinical specimens that can be linked to individual patient or participant data

☐ ***N/A*** **–** check only for the following types of studies:

i. Tissue banking or Patient Registry protocols with no hypothesis/research question

ii. Retrospective chart review

iii. Companion, ancillary or correlative studies using clinical specimens that can UNOTU belinked to individual patient or participant data

4.) UCCCC Program Code (Please select program to which study PI is a member)

☐ Molecular Mechanisms of Cancer
☐ Immunology and Cancer
☐ Pharmacogenomics and Experimental Therapeutics
☐ Advanced Imaging
☐ Cancer Risk and Prevention
☐ N/A

5.) What is your minimal ANNUAL accrual? _____

6.) Will patients be registered in Velos?

☐ Yes ☐ No

*Note: Therapeutic trials U**MUST**U register patients into Velos. For additional information and to request a user account, please download the Velos Access Request Form from: http://clinicalresearch.bsd.uchicago.edu/faculty_staff/velos/velos-access.shtmlU

a.) If "yes", please list the name of the individual(s) registering: _____

b.) If "No", please select from the following options:

☐ Paper registrations forms will be completed for every patient enrolled and submitted to the CRC for entry into Velos

☐ A summary of study enrollment will be reported monthly on Monthly Accrual Form and submitted to the CRC for entry into Velos

☐ Special arrangements will be made with the CRC (e.g. data migration, annual reports, etc) for migration Contact Jia Cheng – jcheng1@bsd.uchicago.edu. Please specify.

_____

_____

_____

☐ N/A – check if "N/A" is selected for Summary 4 Category (#3) above

7.) Study Team Members (please list all relevant individuals – names can be entered for multiple roles, all roles must be completed):

a.)

Role	Name(s)
Regulatory Manager	
Data Manager	
Research Nurse	

b.) With whom will the regulatory files for this study be located?: _____

C. DISEASE SITE FOR UCCRC WEB POSTING:

Should the protocol title listed above be posted on the public UCCRC web site?

☐ Yes ☐ No

If yes, please check the disease areas below under which you want the titled posted.one area).

○ Non-Hodgkin's Lymphoma	○ Bladder	○ Bone
○ Brain and Nervous System	○ Breast	○ Cancer Control
○ Cancer Risk	○ Cervix	○ Colorectal
○ Esophagus	○ Gastrointestinal (GI) Other	○ Gastrointestinal Stromal (GIST Sarcoma)
○ Head and Neck	○ Hodgkin's Lymphoma	○ Leukemia
○ Liver/Hepatobiliary	○ Kidney/Renal	○ Lung/Chest
○ Melanoma (skin)	○ Mesothelioma	○ Myelodysplastic Syndrome (MDS)
○ Myelofibrosis	○ Multiple Myeloma	○ Developmental Therapeutics (Phase I)
○ Ovary	○ Pancreas	○ Pediatric Brain
○ Pediatric Leukemia	○ Pediatric Lymphoma	○ Pediatric Other
○ Pediatric Solid Tumors	○ Pediatric Transplant	○ Prostate
○ Soft Tissue Sarcoma	○ Stomach/Gastric	○ Thyroid
○ Transplant (Hematologic)	○ Uterus/Endometrium	◉ Vulva

D. SUPPLEMENTAL QUESTIONS

1) Do you anticipate being an author on the final manuscript? ***This must be completed.**

☐ Yes ☐ No

If yes, briefly explain why:

If no, briefly justify the scientific or programmatic reasons for opening this trial (What are the benefits to the institution?):

2) Is there a potential institutional conflict of interest involved with this trial (i.e., is there institutional intellectual property associated with this trial)? ***This must be completed.**

☐ Yes ☐ No

If yes, please explain:

3) Is this trial a single arm phase II with a **primary efficacy endpoint** (e.g., response rate, progression free survival, or overall survival) or a phase I study with a disease specific expansion cohort with a primary efficacy endpoint? ***This must be completed.**

☐ Yes ☐ No

If yes:

Review the following references regarding optimal designs for Phase II clinical trials testing cancer therapeutics:

-- Seymour: American Association for Cancer Research
http://clincancerres.aacrjournals.org/content/16/6/1764

-- Tang: American Society of Clinical Oncology
http://jco.ascopubs.org/content/28/11/1936.full.pdf+html

Select the design of your single-arm study:

☐ A) This study is evaluating monotherapy with response rate as the primary objective.

☐ B) This study is evaluating
a) combination therapy with response rate, progression-free survival and/or overall survival endpoints or
b) monotherapy with progression-free and/or overall survival endpoints. Robust, published reproducible historical control data are available (as exemplified by Korn et al for 1 year overall survival in melanoma in the pre-B-raf inhibitor era - Journal of Clinical Oncology http://www.ncbi.nlm.nih.gov/pubmed/18235113).

In the box below please list the relevant citation(s) documenting a robust, reproducible historical control data.

☐ C) This study meets neither of the study designs described in A or B: Please contact CTRC Chair; Vice-Chair; or the Associate Director for Clinical Sciences before completing the CTRC application.

4) Will research specific biopsies be required and are you participating? ***This must be completed.**

☐ Yes ☐ No

If yes, are serial biopsies mandatory? ☐ Yes ☐ No How many biopsies? _____ (enter a number) ***This must be completed.**

5) Are you participating in all aspects of this protocol (including all research related biopsies)? ***This must be completed.**

☐ Yes ☐ No

If no, please explain:

6) Clinical trials, except for those designated 'minimal' or 'low' risk, require a weekly data and safety monitoring conference.

a.) Is there an existing weekly conference in which this trial can be monitored?

☐ Yes ☐ No ☐ N/A

b.) If yes, please provide the name of the conference _____

c.) If no, please indicate how this protocol will be monitored _____

_____

E. Federal Regulations

The Principal Investigator agrees to comply with all federal regulations for investigator initiated trials including but not limited to clinicaltrials.gov, NCI, and NIH requirements. PI Initials _____

F. CCTO Chargeback Information (ONLY FOR THE SECTION OF HEMATOLOGY/ONCOLOGY)

All subsidy-eligible studies (both therapeutic and non-therapeutic) will automatically be assessed to determine if the Cancer Center subsidy will be awarded. A Cancer Center subsidy may be awarded if the CTRC determines the study to be highly meritorious. Please note that subsidies awarded at study initiation of therapeutic protocols are for the initial year only. Subsidies for annual maintenance costs of therapeutic protocols may be awarded based on study progress as determined by the SAM Committee. Therapeutic trials that did not receive a subsidy at start-up will, in general, not be eligible for an annual subsidy and will be charged the annual maintenance fee. Non-therapeutic studies will not be charged annual maintenance fees. It will be assumed (unless the Regulatory Manager is specifically told otherwise at the time of submission) that investigators plan to move the study forward whether or not a subsidy is awarded, and that they will cover the CCTO fees as applicable if a subsidy is not awarded.

PRINCIPAL INVESTIGATOR APPROVAL

_____ _____

Signature **Date**

Appendix 2

Protocol Template For Non-Interventional Studies

TITLE PAGE (should include the following):

- Title:
- Principal Investigators:
- Co-Investigators (if any):
- Sponsor:
- Study Type (Please Select from the following):
  a) Tissue Banking Study
  b) Database Collection Study
  c) Retrospective Chart Review
  d) Correlative
  e) Ancillary
- Protocol Number: (IRB #, other agency number)
- Single center or multi-center (if multi-center - indicate number of other centers)

PROTOCOL (should include the following):

- Background:
  - Describe the problem being addressed by the study, including
    a) Background research that provides scientific justification (animal and/or human) for goals and methods
    b) Outline of study's overall goals

- Objectives:
  a) List primary and secondary specific aims of the study and corresponding hypotheses.

- Study Design and Methods – should include the following:
  - Describe data to be collected
    a) How will the data be collected?
    b) How will the data be protected (based on HIPAA compliance)?
    c) Where will the data be stored?
    d)
  - Study duration – how long will it take to complete
  -
- Statistical Methods – should include:
  a) Justification for sample size
  b) Data elements to be analyzed; how will data quality be ensured
  c) Statistical methods for data analysis to address the hypotheses and objective

- References

Appendix 3

Scientific and Accrual Monitoring Committee
PI Response Form/Corrective Action Plan

Date: _____

PI: _____

IRB #: _____

Protocol Title: _____

_____

Please check one of the boxes below:

- ❑ I believe that SAM does NOT have accurate accrual data for this study. I am providing you with updated accrual data. Actual accrual on this study is acceptable, and the study should remain open to patient enrollment. ***(If selected: please provide patient registration forms for missing patients or confirm that your data manager will enter those patients).***

  _____
  _____
  _____

- ❑ I plan to close the study to patient enrollment**.** ***(Please provide date)***

  Date: _____

- ❑ I plan to terminate the study. ***(Please provide date)***

  Date: _____

- ❑ The study has been closed to patient entry ***(Please provide actual date of study closure).***

  Date: _____

- ❑ The study has been terminated ***(Please provide actual date of study closure).***

  Date: _____

- ❑ I believe that the study should remain open. **IF THIS BOX IS CHECKED YOU MUST COMPLETE THE CORRECTIVE ACTION PLAN FORM WHICH FOLLOWS.**

In order to have SAM's recommendation for study closure reconsidered, you MUST complete a corrective action plan which includes specific actions for increasing accrual, and your expected result in terms of accrual.

Examples of possible action steps are provided in the table below. Please check any that you will use and provide specific detail (e.g., what eligibility criteria will be changed? What, specifically, will you do differently in the recruitment process? Etc) as to how the strategy will be applied to your protocol. Feel free to add any additional actions you plan to take.

Plan to use: (check if yes)	Strategy	Specific application to your protocol
	Change in eligibility criteria	
	Change in procedures for recruitment	
	Increase in project staff	
	Increase in participating sites	
	Compensating subjects	
	Study promotion/advertising	
	Changing Study Priority	
	Other ***(please specify):***	
	Other ***(please specify):***	

New yearly minimal target accrual: _____