



Protocol Development

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Concept Submission

- Concepts must include:
 - Title
 - Study Chair/Co-chairs
 - Rationale (include description of how protocol fits into committee's portfolio)
 - Objectives
 - Eligibility Criteria
 - Statistical Considerations
 - Treatment Plan (or study design/methods/intervention for non-treatment studies)
 - References
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Submission to Executive Committee (EC)

- Concept is submitted with concept submission Form A-007 to Central Office by committee chair and placed on agenda for next EC conference call/meeting (approximately every 6 to 8 weeks).
- Deadline for submission of new concepts to faculty statistician is 2 weeks prior to EC submission deadline.
- Concept submission form MUST be signed off by the statistician, as well as chairs of other disease/modality committees as appropriate.

Submission to Executive Committee (EC)

- All Phase III studies must be submitted using the CTEP concept template (available on CTEP web page: <http://ctep.info.nih.gov>).
 - If correlative science is embedded within Phase III trial, detailed description of correlative science studies, including objectives, methods, statistics, must be incorporated within Phase III concept template prior to EC submission of treatment trial.
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Executive Committee Outcomes

- EC members will vote a priority score using NIH scale of 1-5; Group Chair sets payline.
 - Protocol Coordinator will inform study team of outcome of EC meeting and provide summary of the discussion.
 - Concepts tabled must be resubmitted with a detailed response to the EC review along with revised concept.
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Concept Submission to CTEP/DCP

- Phase I/II: If NCI is providing an agent to be used in the protocol, a Letter of Intent (LOI) must be routed through the Central Office.
 - Phase III: All Phase III clinical studies are submitted to NCI for concept review using NCI Phase III concept template.
 - Cancer Control concepts must be submitted to DCP, regardless of study phase or sample size.
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Protocol Development

- If the concept is approved by the EC, the Study Chair will be notified by the Protocol Coordinator and referred to the CALGB website (<http://www.calgb.org>) for protocol development materials, including:
 - Study development guidelines
 - Model Protocol
 - Common Toxicity Criteria
 - Password is required to access this information; obtain your participant ID (User Name) from your Lead CRA or the CALGB Central Office.
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Regulatory Documentation

- Submit to Central Office:
 - Conflict of interest disclosure form must be submitted or study will not be activated.
 - Additional requirements for correlative studies:
 - Documentation of IRB approval at performance site(s)
 - Letter of investigator agreement
 - Letter of germline agreement (if applicable)
 - Registration of laboratory for LabTrak (lab address, phone, fax, contact information)
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Creating the First Draft of Your Protocol

- First protocol draft due at Central Office within 6 weeks of the notification of EC approval, or sooner for studies subject to CTEP expedited development procedures (phase III, LOI).
 - Modify the CALGB model protocol according to the needs of your study by inserting new sections or deleting non-relevant sections.
 - Keep required tests (# and frequency) to a minimum needed to meet study objectives.
 - Draft model consent using simplified consent form template.
 - Send electronic version of your protocol to the Protocol Coordinator.
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Initial Review

- After formatting and editing the protocol, the Protocol Coordinator will distribute a first draft (Initial Review) to:
 - Study Chair and Co-Chairs
 - Statistician
 - Committee Chair and Vice Chair
 - Data Coordinator
 - Executive Officer
- * Comments due within one week.
- Study chair informs protocol coordinator of changes needed as a result of initial review.

Author Review

- After revisions from initial review are incorporated, the protocol is then distributed for Author Review to:
 - Initial reviewers
 - Nursing, CRA, Pathology, Imaging, Patient Advocate, and Pharmacy reviewers
 - Group Chair
 - Audit Coordinator
 - Quality Assurance Coordinator
 - Director of Regulatory Affairs
 - QARC (if RT used), Surgical Quality Assurance Subcommittee (if applicable)
 - * Comments are due within one week.
- Study Chair informs Protocol Coordinator of changes needed as a result of author review.

NCI Submission

- After revisions from author review are incorporated, a protocol draft sent to NCI, and posted at CALGB website.
- NCI provides a written review within approximately 30 days. Protocol coordinator distributes review to study team. The review can contain either items requiring a response or recommendations. All items must be addressed in response in a point-by-point fashion.
- A response to NCI review is drafted by Study Chair, and sent to NCI with a revised protocol by Central Office within two weeks.
- Any changes to protocol not requested by CTEP must be identified.
- All correspondence must be routed through Central Office.

NCI Expedited Development Process

- Phase III
 - complete protocol, including all substudies, required within 45 days
 - drafts distributed via e-mail for review by CALGB/NCI joint study team
 - respond to comments from reviewers as they arise
 - Phase I/II (if drug supplied by CTEP via LOI mechanism)
 - complete protocol required within 60 days
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Cancer Trials Support Unit (CTSU)

- Replaces traditional intergroup process for participation in Phase III trials
 - Groups may “endorse” trials
 - All registrations, other than those from coordinating group go, through CTSU
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Central IRB

- Reviews all Phase III studies on CTSU menu
 - Review is performed sequentially, i.e. CIRB review occurs after CTEP review is completed
 - Study chair needs to be available by phone during CIRB meeting
 - CIRB approval is required prior to activation for these studies
 - Amendments require review and approval prior to implementation
 - Annual review coordinated by Central Office
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Study Activation

- Once written approval is received from the NCI, the protocol will be activated via the website (15th of the month).
 - Approval from the Central IRB (CIRB) must be obtained for Phase III studies prior to activation.
 - All forms **MUST** be finalized and any contract/drug distribution mechanism finalized
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Correlative Science Studies

“Stand Alone”	Prospective
“Embedded” within treatment study	Retrospective

Studies Using Samples from Intergroup Studies

- Concepts proposing to use specimens banked under intergroup studies must be submitted to appropriate Intergroup Correlative Science Committee after EC approval.
- If no Intergroup Correlative Science Committee exists for the disease site, proposal needs to be circulated to groups participating in the trial.
- Exception: If correlative study is embedded in clinical trial at time clinical trial is submitted to CTEP for review, further review by Intergroup is not required.

NCI Review of Correlative Science Studies

- NCI review is required of all studies using more than 100 samples (retrospective or prospective). If the project has been peer reviewed and funded (i.e. R01 grant), CTEP comments will be limited to recommendations.
 - If correlative science study is embedded in a clinical trial, review of the correlative science will be included in the review of the clinical study. Any points raised regarding the correlative science component must be addressed by the Correlative Science Chair.
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NCI Review of Correlative Science Studies Continued

- NCI review is not required for studies using less than 100 samples not obtained from intergroup banks. These studies may be activated once all internal review stages are completed. A study summary must be included in the CALGB grant renewal application.
 - If study uses specimens from intergroup banks, NCI will accept the scientific review of the appropriate Intergroup Correlative Science Committee. NCI review will be administrative only. If no Intergroup Correlative Science Committee exists for the disease site, NCI will perform scientific review.
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Specimen Submission

- Institutions
 - Mandatory?
 - Optional?
 - Limited to subset of institutions participating in study or open to all?
 - Patients
 - Required of all patients?
 - Opt in/opt out consent form options
 - Prepare lay language explanation for the consent form explaining why the research is important and what we hope to learn
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Specimen Submission

- Be explicit about the intended use of the specimen. For example, will remainder of specimen be banked for future studies after planned studies are completed, or will it be returned/destroyed?
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Protocol Amendments

- Keep to a minimum
 - Amendments affecting scientific intent, study design, patient safety, or human subject protection must be approved by CTEP prior to implementation.
 - If Phase III study, significant amendments must receive prior review from the DSMB, CTEP, and the CIRB
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Protocol Amendments

- Issued on the 15th of each month
 - ALL changes made to a protocol after CTEP approval but prior to activation must be reviewed and approved by CTEP. If Phase III, it must also be reviewed and approved by the CIRB.
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Trouble Shooting Tips

- E-mail is the most effective means of communication.
 - Do NOT concentrate on the format of your protocol, especially tables and schemas.
 - Cite references by #, not author. If you use Endnote, send the library.
 - Communicate frequently with the Protocol Coordinator, Statistician, and Data Coordinator to ensure that protocol and forms development proceeds in tandem.
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Trouble Shooting Tips

- After initial submission of the electronic version of your protocol, further revisions must be made on hard copy. If substantive new material is added, it can be sent via e-mail to the Protocol Coordinator.
 - Review all drafts of your study; be responsive to requests from the study team and NCI.
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Troubleshooting Tips

- If converting grant to protocol : “we” = CALGB, not your lab.
 - If your correlative science component is embedded in another trial, communicate frequently with the study team to ensure that development of your section keeps pace with development of the overall trial.
 - Grant approval \neq protocol approval
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Committee Assignments

Committee	Protocol # Assigned by Database	Protocol Coordinator
Breast	4YYXX	Heather Becker
Cancer Control & Health Outcomes	7YYXX	John, Colleen, Kathy
Cancer in the Elderly Committee	36YYXX	Heather Becker
Corr. Sciences for Leukemia	2YYXX	Mike Kelly
Gastrointestinal (GI)	8YYXX	TBN
Genitourinary (GU)	9YYXX	John Taylor
Leukemia	1YYXX	Mike Kelly

Committee Assignments

Committee	Protocol # Assigned by Database	Protocol Coordinator
Lymphoma	5YYXX	Mike Kelly
Melanoma	50YYXX	Heather Becker
Pharmaceutical and Therapeutics (P.E.T.)	6YYXX	Colleen Watt
Respiratory	3YYXX	Colleen Watt
Transplant	10YYXX	Mike Kelly

The first one or two digits represent the committee, the second two digits indicate the year the concept was introduced, and the final two digits are assigned consecutively as concepts are submitted to the EC.

For example: The first concept submitted to the EC by the Breast Committee in 2005 is protocol #40501.

Protocol Coordinator Contact Information

Coordinator	E-Mail Address	Phone #
Heather Becker	hpbecker@uchicago.edu	773-834-2546
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