CLINICAL RESEARCH REQUIRED TRAINING

a. RASCAL - CITI TRAININGS

Research Compliance and Administration System (RASCAL) - CUIMC’s online proprietary information system for research regulatory management and compliance [www.rascal.columbia.edu](http://www.rascal.columbia.edu)

Collaborative Institutional Training Initiative (CITI Program) - training resource [https://about.citiprogram.org/](https://about.citiprogram.org/)

**REQUIRED TRAININGS:**

RASCAL:

- TC0019 - HIPAA: Health Insurance Portability and Accountability Act
- TC6500 - HICCC Clinical Protocol and Data Management Investigator Standard Operating Procedure Training

REDIRECTED TO CITI:

- TC0087 - Human Subjects Protection (HSP) Training
- TC0094 - Responsible Conduct of Research Training
- TC3450 - Good Clinical Practice (GCP) Training
  - FDA-Regulated Research
  - GCP for Clinical Trials with Investigational Drugs and Medical Devices (U.S. FDA Focus)
  - Human Subjects Protection Biomed
  - RCR Biomedical
  - Research with Minors - BIOMED

b. OTHER TRAININGS

*Pis should log in with their UNI and complete the required trainings in Training Finder*

[Training Finder | Columbia | Research](https://research.columbia.edu/research-policies-and-handbooks) *(REQUIRED TRAININGS DEPEND ON PI)*

c. OTHER CUIMC RESEARCH RESOURCES

[Resources for Researchers](https://www.vagelos.columbia.edu/about-us/explore-vps/leadership-and-administration/academic-affairs/faculty-professional-development-diversity-inclusion/faculty-resources/resources-researchers)

[Clinical Research Handbook](https://research.columbia.edu/research-policies-and-handbooks)

[Human Research Policy Guide](https://research.columbia.edu/human-research-policy-guide)
CLINICAL TRIALS PROCESS STEPS

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   d. MONITORING, AUDITING, AND INSPECTIONS
1. INTERNAL APPROVAL PROCESS

In addition to informational questions, the survey requires submission of a protocol & budget allocation outline to determine feasibility for investigator-initiated and industry-sponsored studies.

1. Protocol outline components including:
   a. Study summary paragraph
   b. Objectives/aims
   c. Study Calendar
   d. Protocol Schema
   e. Eligibility criteria

2. Budget allocation outline

b. RADONC FEASIBILITY APPROVAL - RADONC CLINICAL TRIALS COMMITTEE MEETING

c. CUIMC FEASIBILITY APPROVAL - MULTIDISCIPLINARY DISEASE BASE TEAM MEETING
2. COST ESTIMATE FORMS

a. OTHER CUIMC DEPARTMENT COST ESTIMATE FORMS

Cost estimate forms must be obtained from other involved departments.
Cost Estimate Forms | Columbia | Research

Commonly required cost estimate forms for Radiation Oncology clinical trials:
- Research Pharmacy
- Radiology
- Pathology
  - A request cost estimate form for biostatistician services is also obtained.

b. RADIATION ONCOLOGY COST ESTIMATE FORM

If the study is NOT Standard of Care, a Radiation Oncology Cost Estimate Form should be completed.
3. STUDY DESIGN PLANNING

**a. PROTOCOL**

**PROTOCOL** – document that describes the objectives, design, methodology, and organization of the study

**i. BIOSTATISTICS, EPIDEMIOLOGY & RESEARCH DESIGN (BERD)** – service that provides study design consultations at the initial stage of study planning (before IRB submission) [https://www.irvinginstitute.columbia.edu/about-us/resources-and-cores/biostatistics-epidemiology-and-research-design-berd](https://www.irvinginstitute.columbia.edu/about-us/resources-and-cores/biostatistics-epidemiology-and-research-design-berd)

*If the protocol changes throughout the process:

- PI must communicate to the Clinical Research Team:
  - Mariamne Reyna, Clinical Trials Manager (mro2213@cumc.columbia.edu)
  - Michelle Tuz, Clinical Research Coordinator (mt3457@cumc.columbia.edu)
  - Cindy Walters, Grants Manager (cw102@cumc.columbia.edu)
- Modification Process through CTO:
  - Protocol, Informed Consent Form, Budget, Contract
- IRB approval of the protocol change is required before implementation

**KEY**

| PI Responsibility |
b. INFORMED CONSENT FORM

INFORMED CONSENT FORM (ICF) – fully discloses to the Study Subject the purposes, procedures, risks, costs, payment, and use of biospecimens, data, and results of a Clinical Research Study. CTO advises the clinical teams on select provisions of the Informed Consent, to ensure the language is clear and in agreement with the contract.

c. BUDGET

CTO Required Components of a Study Budget

1. Start-Up Costs
   a. Standard site costs – non-refundable – study start-up costs, etc
   b. Per patient costs
   c. Direct costs
   d. Tests/procedures
   e. Supplies, pharmacy dispensing, stipends, transportation
   f. Time and effort of study personnel (e.g., PI, Research Nurse, Data Manager, Study Coordinator)

2. Variable (Invoiceable) Costs
   a. Bill (invoice) only if the costs occur
   b. Not included in list of per-patient costs

➔ CTO reviews and negotiates the budget

d. CONTRACT

The sponsor provides the contract.

➔ CTO reviews and negotiates the contract
➔ CTO executes the contract after IRB approval

Commented [NER7]: If the study is investigator-initiated, the PI must provide budget details.

Commented [NER8]: If the study is investigator-initiated, the PI should consult with CPDM to formulate the budget.

Commented [NER9]: Contracts should be signed only after IRB Approval and CTO execution.
4. CUIMC SUBMISSIONS FOR APPROVAL

KEY
PI Responsibility
a. CTO SUBMISSION

CLINICAL TRIALS OFFICE (CTO) – the main administrative arm of clinical research for CUIMC
https://research.columbia.edu/clinical-trials-office

Study submissions to CTO Clinical Trials for Investigators | Columbia | Research
The CTO requires the following documents to review and properly negotiate the legal and budget items for a study:
1. Protocol
2. Informed Consent Form
3. Cost Estimate Forms
4. Budget
5. Contract

Email template for CTO Submission

In From: Submitting PI
To: CTO BUDGET NEGOTIATION PROCESS

CTO BUDGET NEGOTIATION PROCESS

1. Review protocol, budget, and informed consent.
2. Review Budget Checklist with Principal Investigator (PI) and Study Coordinator.
3. Determine Standard of Care (SOC) vs. Research Specific Billing.
4. Create Internal CTO Draft Budget to ensure financial feasibility and compare with Sponsor’s budget.
5. Negotiate budget and payment terms with Sponsor and finalize budget.

CTO CONTRACT NEGOTIATION PROCESS

2. Determine whether Master Agreement applies or duplication of previous Agreement terms is possible.
3. Review in accordance with Institutional and legal policies; coordinate payment terms with Budgets.

KEY
PI Responsibility
b. PRMC SUBMISSION

HICCC PROTOCOL REVIEW AND MONITORING COMMITTEE (PRMC) – is responsible for conducting clinical protocol reviews (the scientific merit, scientific priorities, and progress of all clinical protocols involving cancer patients). PRMC reviews all new protocols involving cancer treatment or risk intervention. The specific elements of the protocol that are addressed by reviewers include, but are not limited to:

- the merit of the research question
- the innovation of the study design
- feasibility
- proper allocation of institutional resource
- if the appropriate number of patients are available locally
- whether the statistical plan is adequate to test the study hypothesis
- ensuring that trials do not overlap in eligibility criteria (which may lead to competition for the same pool of patients)

PRMC INITIAL REVIEW
PRMC reviews all new protocols involving cancer treatment or risk intervention. The specific elements of the protocol that are addressed by reviewers include, but are not limited to:

- the merit of the research question
- the innovation of the study design
- feasibility
- proper allocation of institutional resource
- if the appropriate number of patients are available locally
- whether the statistical plan is adequate to test the study hypothesis
- ensuring that trials do not overlap in eligibility criteria (which may lead to competition for the same pool of patients)

PRMC CONTINUING REVIEW
The PI is required to submit a continuing review application to the IRB and PRMC 60 to 90 days before the annual expiration date of the protocol. This progress report needs to include: (1) the number of subjects enrolled in the trial, (2) the number of subjects treated, (3) a summary of all Unanticipated Problems (UPs) in accordance with the CUIMC IRB UP policy, (4) and significant literature developments that may affect the safety of participants or the ethics of the study.

c. DSMC SUBMISSION

HICCC DATA AND SAFETY MONITORING COMMITTEE (DSMC) – in accordance with NIH policy and CUIMC IRB policy, is responsible for the data and safety monitoring of ongoing oncology clinical trials; review of Data Safety Monitoring Plan (DSMP)

DSMC RESPONSIBILITIES

- Review the protocol data and safety monitoring plan and proposed study specific monitoring plan. Based on the level of risk, the DSMC will determine the frequency of reporting, which may be monthly, quarterly, biannually, or annually.
- Conduct a thorough review of the unanticipated problems, SAEs, adverse events, and toxicity profile associated with each study subject. When it is deemed necessary, the DSMC may suspend or terminate a study based on toxicity, adverse events reported, or unanticipated problems. The DSMC may mandate revision to the protocol and informed consent to increase on study monitoring and proper participant notification.
- Track safety and efficacy issues throughout the duration of the study and request additional relevant data from the PI. If needed, the DSMC will suspend or terminate the study when there is a significant concern for participant safety.
- Review requests for waivers and other significant protocol deviations.

KEY

| PI Responsibility |
Review compliance and adherence to the approved protocol and mandate appropriate action when deviations are identified. If significant deviations are observed, which alters the overall integrity of the study, the DSMC may recommend suspension or termination of the study.

Consider the rationale for continuation of the study based on the overall safety and compliance.

Prepare correspondence communicating DSMC recommendations to the PI and Study Team. Any findings of unacceptable performance will be forwarded promptly to the PI and the IRB. The PRMC/DSMC Program Manager will also inform the PRMC.

If CUIMC is the coordinating/lead site of a multicenter study, the CUIMC PI is responsible for sending the DSMC reports to sub-site PIs. The sub-site PI is required to submit the HICCC DSMC report to the sub-site IRB pursuant to the NIH “Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials” (NIH Guide for Grants and Contracts, June 11, 1999).

**DSMC REVIEW**

- Unanticipated Problems (UP)
- Serious Adverse Events (SAE)
- Safety reports
- DSMC Recommendations
- Integration with HICCC Clinical Protocol and Data Management (CPDM) Office Compliance Core
- Study specific Data and Safety Monitoring Plans
- Monitoring Summary Reports
- Criteria for Study Suspension or Termination

**d. IRB SUBMISSION**

**INSTITUTIONAL REVIEW BOARD (IRB)** – a review committee established to help protect the rights and welfare of human research subjects


**Forms included in IRB submission:**

- Protocol
- Informed Consent Form
- PRMC approval
- Signed Data Safety Monitoring Plan (DSMP)
- Forms to be reviewed and completed by patients (e.g., quality of life questionnaire)
- HIPAA forms
- Recruitment forms
- HICCC website posting form
- IND approval, CUIMC acknowledgment and supporting forms
- IND exemption/IDE CUIMC acknowledgment
- Package Insert and Investigational brochure
- JRSC approval (if study is not standard of care)
- Pathology approval (if study involves tissue collection)
- Executed Data Use/Transfer Agreement (if study involves analyzing data outside of CUIMC)
- Executed Materials Transfer Agreement (if study involves analyzing materials (tissue/cells) from outside of CUIMC)
5. STUDY INITIATION

a. CLINICALTRIALS.GOV REGISTRATION

CLINICALTRIALS.GOV – national registry of federally and privately supported research studies
https://clinicaltrials.gov/

After receiving IRB approval, registration is required for all clinical trials:

i. PI – PRS ACCOUNT
https://clinicaltrials.gov/ct2/manage-recs/register

ii. CLINICAL TRIAL REGISTRATION

b. SITE INITIATION VISIT

A site initiation visit is held via Zoom.

ATTENDEES:
Principal Investigator
Other CUIMC department representatives
Mariamne Reyna, Clinical Trials Manager (mo2213@cumc.columbia.edu)
Michelle Tuz, Clinical Research Coordinator (mt3457@cumc.columbia.edu)
Cindy Walters, Grants Manager (cw102@cumc.columbia.edu)

*Signatures of attendees are required

c. SYSTEMS SET UP

- Informed Consent Form - Spanish translation
- Project Chart String
- Data Collection systems
- Payment invoicing systems
- Core Services systems

KEY
PI Responsibility
6. RECRUITMENT

6. Recruitment

Department Recruitment
CUIMC Recruitment Website
HICCC Clinical Trials Website

PI orders diagnostics if required

Enrollment
Informed Consent Form Signature

Accrual
Eligibility Approved

a. DEPARTMENT RECRUITMENT
   - Review of patient information
     → Informed consent form review for eligible patients (email or in-person review)

b. CUIMC’S RECRUITMTE WEBSITE https://recruit.cumc.columbia.edu/

c. HICCC CLINICAL TRIALS WEBSITE
   Find a Cancer Clinical Trial | Herbert Irving Comprehensive Cancer Center (HICCC) - New York (columbia.edu)

   i. ENROLLMENT = Informed Consent Form signature
      ➢ Informed consent form is uploaded to Epic

   ii. ACCRUAL = eligibility approved
7. STUDY MANAGEMENT

a. DATA COLLECTION
   ELECTRONIC DATA CAPTURE (EDC) SYSTEMS
   i. VELOS – accrual information (feeds Clinical Trial Reporting Program (CTRP))
   ii. REDCAP – patient information
   iii. QUALTRICS – survey-based research (e.g., quality of life questionnaire)

b. PAYMENT INVOICING
   i. IBM CLINICAL TRIALS MANAGEMENT SYSTEM (CTMS) – used by CUIMC to track, invoice, and reconcile financial activities for clinical trials (flags patients as participants in clinical trials in CUIMC Electronic Medical Records (EMR) systems)
   ii. EPIC RESEARCH BILLING INQUIRY RECONCILIATION – daily process (4 day policy)

c. CORE SERVICES
   i. iLAB ORGANIZER – online scheduling, ordering, and billing system
   ii. SAARP – Small Animal Radiation Research Platform
   iii. Institute of Comparative Medicine (ICM)

d. MONITORING, AUDITING, AND INSPECTIONS

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<th>WHO</th>
<th>WHAT</th>
<th>WHY</th>
<th>WHEN</th>
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<td>MONITORING</td>
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<td>AUDITING</td>
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KEY
PI Responsibility