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

Collaborative Institutional Training Initiative (CITI Program) - training resource 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

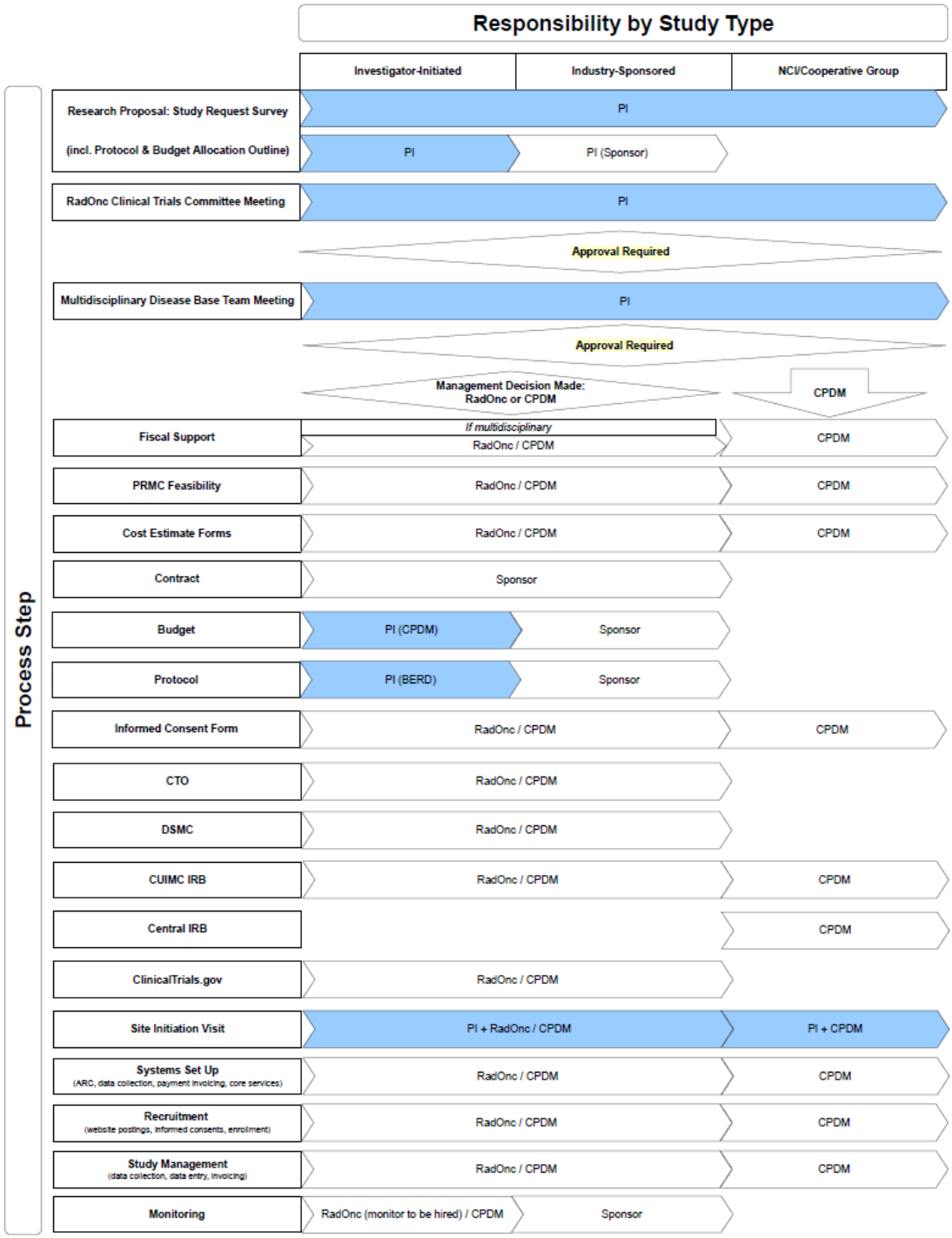
b. OTHER TRAININGS

PIs should log in with their UNI and complete the required trainings in Training Finder
Training Finder | Columbia | Research *(REQUIRED TRAININGS DEPEND ON PI)*

c. OTHER CUIMC RESEARCH RESOURCES

Resources for Researchers https://www.vagelos.columbia.edu/about-us/explore-vp-s/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

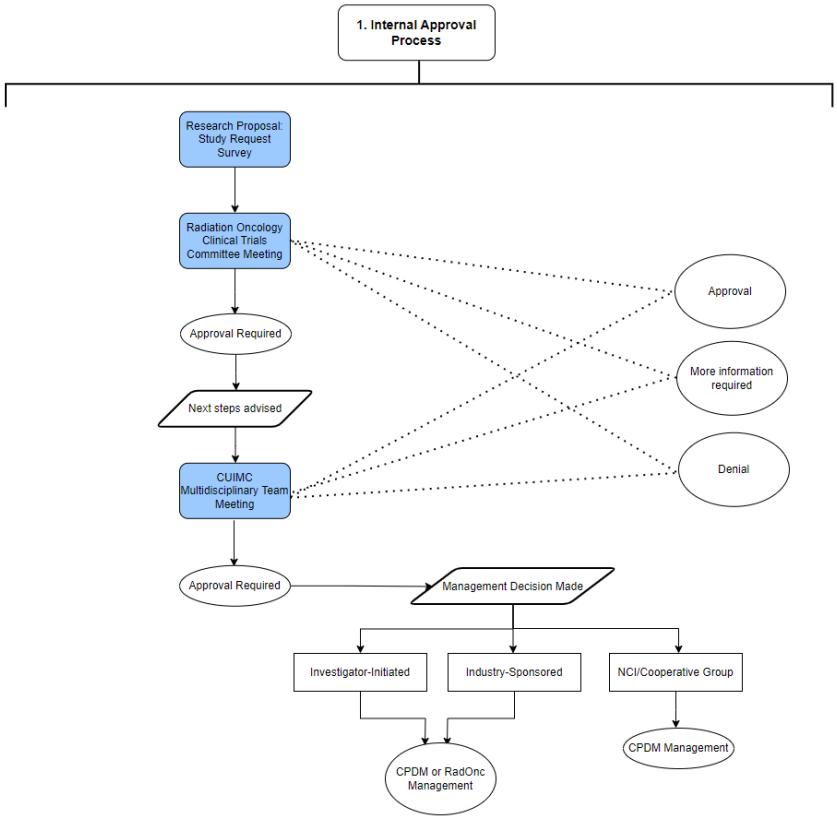
KEY
PI Responsibility


Responsibility by Study Type
Process Step
Investigator-Initiated
Industry-Sponsored
NCI/Cooperative Group
Research Proposal: Study Request Survey
(incl. Protocol & Budget Allocation Outline)
PI
PI
PI (Sponsor)
RadOnc Clinical Trials Committee Meeting
PI
Approval Required
Multidisciplinary Disease Base Team Meeting
PI
Approval Required
Management Decision Made: RadOnc or CPDM
CPDM
Fiscal Support
If multidisciplinary
RadOnc / CPDM
CPDM
PRMC Feasibility
RadOnc / CPDM
CPDM
Cost Estimate Forms
RadOnc / CPDM
CPDM
Contract
Sponsor
Budget
PI (CPDM)
Sponsor
Protocol
PI (BERD)
Sponsor
Informed Consent Form
RadOnc / CPDM
CPDM
CTO
RadOnc / CPDM
DSMC
RadOnc / CPDM
CUIMC IRB
RadOnc / CPDM
CPDM
Central IRB
CPDM
ClinicalTrials.gov
RadOnc / CPDM
Site Initiation Visit
PI + RadOnc / CPDM
PI + CPDM
Systems Set Up
(ARC, data collection, payment invoicing, core services)
RadOnc / CPDM
CPDM
Recruitment
(website postings, informed consents, enrollment)
RadOnc / CPDM
CPDM
Study Management
(data collection, data entry, invoicing)
RadOnc / CPDM
CPDM
Monitoring
RadOnc (monitor to be hired) / CPDM
Sponsor

CLINICAL TRIALS PROCESS STEPS

KEY
PI Responsibility

1. INTERNAL APPROVAL PROCESS



a. RESEARCH PROPOSAL: STUDY REQUEST SURVEY

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

Commented [NER1]: The PI must submit a Research Proposal: Study Request Survey.

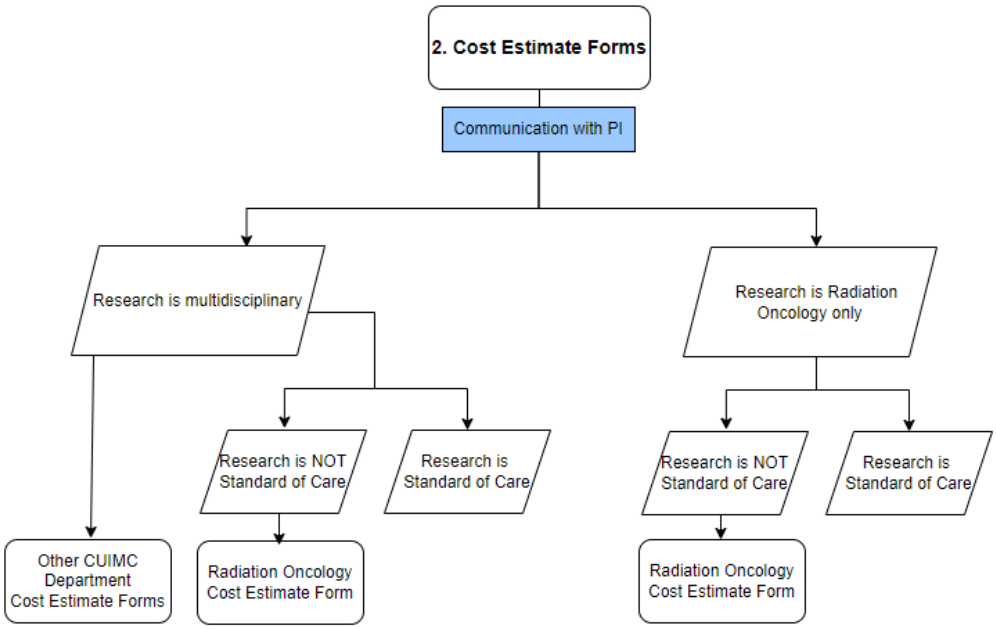
Commented [NER2]: If the study is investigator-initiated or industry-sponsored, the PI must submit a protocol & budget allocation outline in the study request survey.

Commented [NER3]: The PI must attend a Radiation Oncology Clinical Trials Committee Meeting for feasibility approval.

Commented [NER4]: If approved and advised in the Radiation Oncology Clinical Trials Committee Meeting, the PI must attend a CUIMC Multidisciplinary Disease Base Team Meeting for feasibility approval.

KEY
PI Responsibility

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

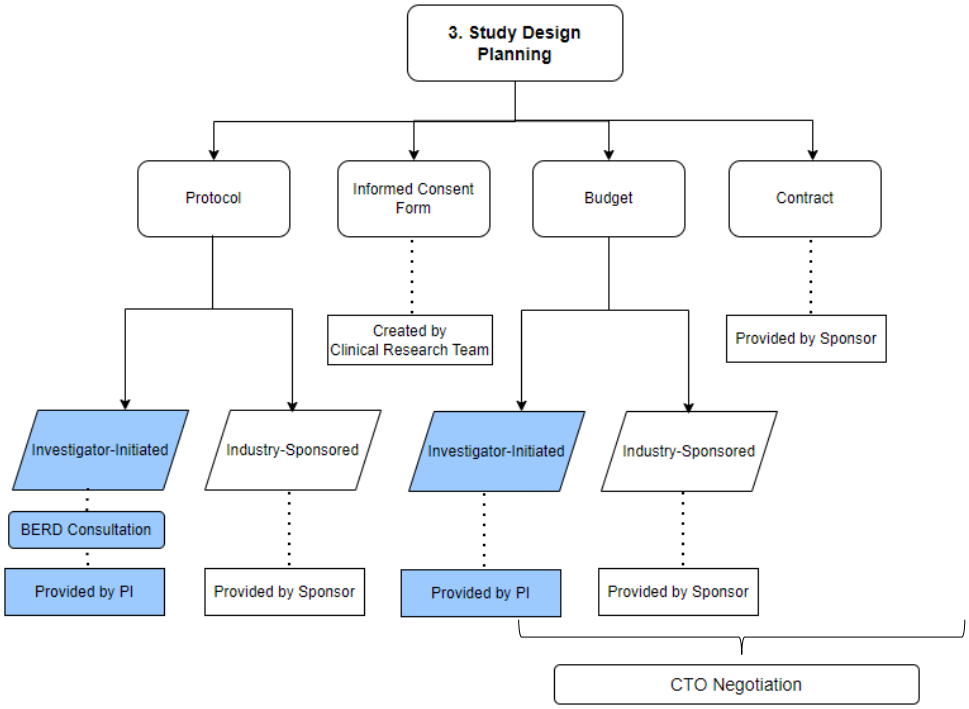
- A request cost estimate form for biostatistician services is also obtained.

b. RADIATION ONCOLOGY COST ESTIMATE FORM

If the study is **NOT Standard of Care**, a Radiation Oncology Cost Estimate Form should be completed.

KEY
PI Responsibility

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

Commented [NER5]: If the study is Investigator-Initiated, the PI must create the protocol.

Commented [NER6]: If the study is Investigator-Initiated, the PI should schedule a study design consultation with BERD during the protocol creation step.

***If the protocol changes throughout the process:**

- PI must communicate to the Clinical Research Team:
  - 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)
- 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

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

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

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

➔ CTO reviews and negotiates the budget

d. CONTRACT

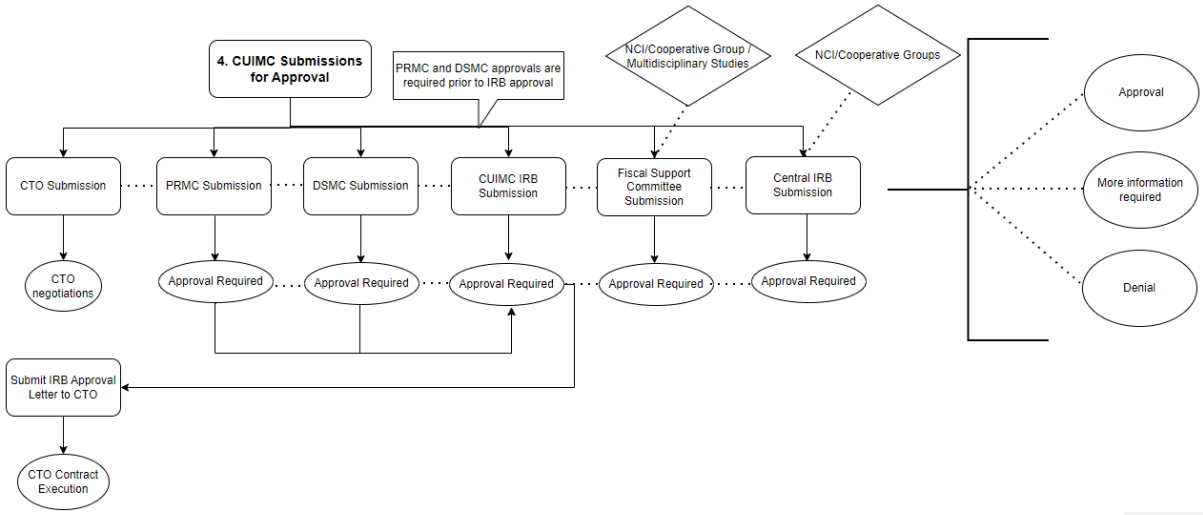
The sponsor provides the contract.

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

Commented [NER9]: Contracts should be signed only after IRB Approval and CTO execution.

KEY
PI Responsibility

4. CUIMC SUBMISSIONS FOR APPROVAL



KEY

PI Responsibility

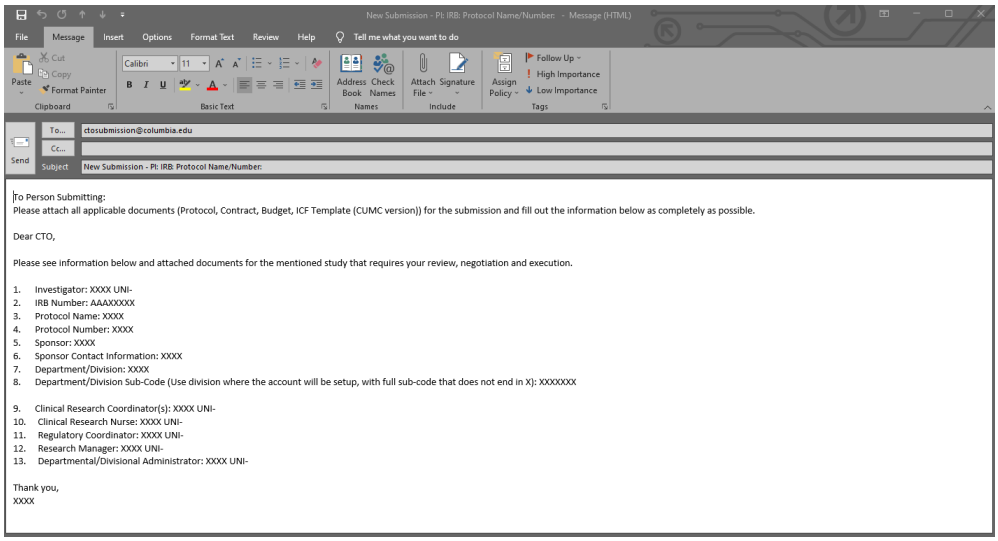
a. CTO SUBMISSION

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



CTO BUDGET NEGOTIATION PROCESS	CTO CONTRACT 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.	1. After execution of Confidentiality Agreement: Receive Protocol, Informed Consent Form, budget, and contract. 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. 4. After negotiation complete, confirm Informed Consent language matches Contract language; route for signatures.

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) chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://research.columbia.edu/sites/default/files/content/HRPO/Herbert%20Irving%20Comprehensive%20Cancer%20Center%20Data%20Safety%20and%20Monitoring%20Plan.pdf

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) chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://research.columbia.edu/sites/default/files/content/HRPO/Herbert%20Irving%20Comprehensive%20Cancer%20Center%20Data%20Safety%20and%20Monitoring%20Plan.pdf

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

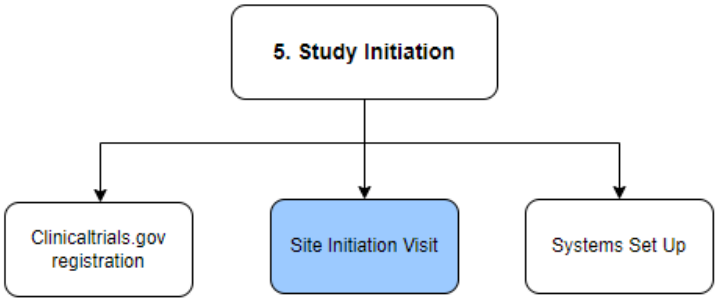
INSTITUTIONAL REVIEW BOARD (IRB) – a review committee established to help protect the rights and welfare of human research subjects
CUIMC HUMAN RESEARCH PROTECTION OFFICE https://research.columbia.edu/human-research-protection-office-and-irbs

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)

KEY
PI Responsibility

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

Commented [NER10]: The PI must create a PRS Account on clinicaltrials.gov.

ii. CLINICAL TRIAL REGISTERATION

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)

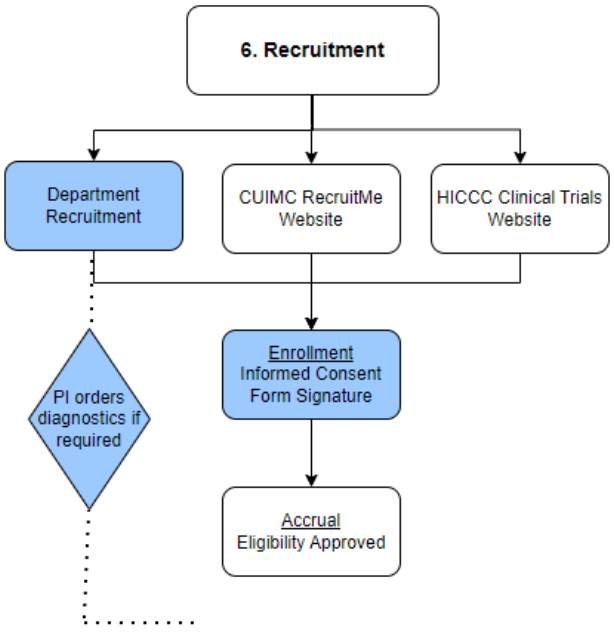
***Signatures of attendees are required**

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



a. DEPARTMENT RECRUITMENT

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

b. CUIMC'S RECRUITME 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

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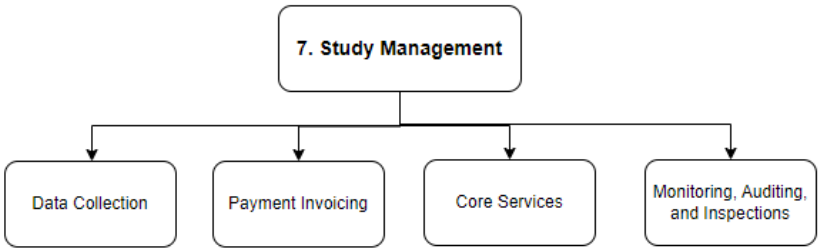
PI Responsibility

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

WHO	WHAT	WHY	WHEN
MONITORING			
Involved in the trial	Protection, safety and data accuracy	To bring a trial to compliance	Continuously
AUDITING			
Independent of the trial (e.g., IRB)	Protection, safety and data accuracy	To ensure compliance	During, After
INSPECTION			
Regulatory Agency (e.g., FDA)	Safety, integrity of the data	To assess compliance	During, After

KEY

PI Responsibility