Logistics of a Clinical Research Trial: Overview

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Contributors:
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Deborah Quint
Connie Trexler

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Learning Objectives

1. Describe the process for study start-up at Children’s National Medical Center (CNMC) and other pertinent study logistics

2. Identify timing for study start-up and real-time examples of opening a research study
Where do you begin?

Oh what to do, what to dooo?
Departments & offices to consider before you begin

• Clinical Research Center (CRC)
• Clinical Research Management Office (CRMO)
• CNMC Human Research Protection Program (OPHS-IRB)
  – Western Institutional Review Board (WIRB)
• Grants and Contract Administration Office
• Investigational Drug Service (IDS) Pharmacy
• Office of Innovation Development
• Public Relations and Marketing
Grants and Contract Administration Office

**Function:** Oversee financial planning, management, budgets, and compliance for every grant - whether the grant is federal, local, or a philanthropic donation

**Office includes:**

- **Pre-award** services to help investigators and grant applicants prepare accurate and effective budget tools for their submissions

- **Post-award** services to assist investigators and grant recipients to manage the grant’s budget and requirements, remain compliant with the financial terms of the grant, assist with purchasing, and other related tasks
Before you begin the clinical trial

Send Confidentiality Agreement (CDA), Clinical Trial Agreement (CTA), Clinical Study Agreement (CSA), Business Associate Agreement (BAA), Data Use Agreement (DUA) and/or study contract to the Grants and Contract Administration Office* for review by the Legal Department

* Note - Consortium studies (COG, PBCT, etc.) may not need to seek internal approvals by the Grants and Contract Administration Office prior to submitting study to IRB for approval
Clinical Research Management Office (CRMO)

- **Function:** Provides consultation and guidance prior to initiating and during study implementation.

- Examples include (but are not limited to):
  - Budget negotiation for industry sponsored clinical trials
  - Patient-care budgets for all clinical trials
  - Assistance with audit preparation
  - **ClinicalTrials.gov** registration assistance
  - General clinical trial troubleshooting
Before you begin the clinical trial

If **industry-sponsored** study, contact the **CRMO**:  

1. Forward study protocol, Investigator Brochure, draft trial agreement (CSA/CTA) and sponsor’s proposed budget to **Amy Gross, MS, MPH, CCRP**

2. Complete:
   i. Logistic Review Questionnaire
   ii. Separation of Allowable Charges
   iii. Investigational Drug Service (IDS) Pre-IRB Review and Cost Estimate Request (if using IDS pharmacy)

3. Schedule meeting to determine study costs and prepare internal budget to begin budget negotiations with sponsor
CRMO Forms

Logistics Review Questionnaire

IDS Pre-IRB Review and Cost Estimate Request Form
CRMO Forms

Separation of Allowable Charges Form

<table>
<thead>
<tr>
<th>Children's National Medical Center - Separation of Allowable Charges</th>
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<tbody>
<tr>
<td>Principal Investigator</td>
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<tr>
<td>Department</td>
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<tr>
<td>Study Name</td>
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<td>Study Begin Date:</td>
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<tr>
<th>Visit #</th>
<th>Service</th>
<th>CPT</th>
<th>Department Providing Service</th>
<th>Bill to Insurance</th>
<th>Bill to Grant/Sponsor</th>
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PI SIGNATURE/DATE
Human Research Protection Program (OPHS-IRB)

- **Function**: The Institutional Review Board (IRB) and the Office for the Protection of Human Subjects (OPHS), under the Human Research Protection Program (HRPP), protect the rights and welfare of all participants in research studies.

  - **IRB**: Review and evaluate research protocols, and identify potential ethical and safety issues.

  - **OPHS**: Act as the liaison between the IRB committees and the research investigators, documents compliance with federal research regulations, and educates CNMC research community about the ethical and safe conduct of research.
Before you begin the clinical trial

Initiate CNMC IRB submission in IRBear

1. **Industry-sponsored:**
   i. Facilitated review by CNMC IRB must be approved prior to submitting regulatory documents to Western Institutional Review Board (WIRB)
      • Required Division Approvals
      • Ancillary Reviews (ex: Investigational Drug Service, Radiation Safety Committee, Institutional Biosafety Committee, Radiation Oncology, Nursing Research Council, Laboratory Medicine, Medical Records, PR & Marketing)
   ii. Submit study to WIRB once approved by CNMC IRB

2. **Non-industry sponsored (consortium, sub-contract):**
   i. CNMC IRB review (full-board, exempt, expedited)

IRBear website: www.irbear.org
Clinical Research Center (CRC)

- **Function**: Outpatient/inpatient facility for pediatric patients and healthy volunteers participating in clinical trials
  - Staff are trained in the management and execution of research protocols, IRB requirements, subject monitoring, sample collection and processing, and data collection according to Good Clinical Practice Guidelines

- **Services available**: phlebotomy, infusion of experimental medications, blood transfusions, spirometry, patient monitoring, anthropometric measurements, laboratory sample collection and processing including DNA sequencing, nutrition, overnight availability, nursing services (including beyond the CRC walls)

**Location**: 3rd Floor Main Hospital
Before you begin the clinical trial

Seek approval by the CRC* Advisory Committee

- Contact the CRC Nurse Manager, Marlene Lee, RN to set up a study activation meeting

* Note – not all studies will utilize the CRC or its services. This is determined by available resources, study team needs and subject enrollment
Investigational Drug Service (IDS) Pharmacy

- **Function**: Ensures the proper ordering, dispensing, and administration of all experimental medications. The research pharmacy:
  - Approves drug-related protocols
  - Performs procedures, stores, dispenses and keeps records of study medications and test articles
  - Maintains inventory control
  - Provides participants with study drug information and ensures study compliance
  - Provides drug information to investigators, nurses, and their associates
Before you begin the clinical trial

If you will be storing investigational drug in the IDS Pharmacy, you will need to complete a protocol activation meeting prior to enrolling any patients and dispensing any drug

- Contact the IDS Pharmacy Supervisor, Henry Choi, PharmD to set up pre-IRB and protocol activation meetings

* Note – members of the study team that must be present for the activation meeting include: PI, study coordinator, study nurse (if applicable)
# IDS Protocol Activation Checklist

<table>
<thead>
<tr>
<th>ITEM</th>
<th>Check if reviewed</th>
<th>Document to be provided by P(team)</th>
<th>COMMENTS</th>
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<tbody>
<tr>
<td>Final Study Protocol (Is there a Pharmacy Manual?)</td>
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<td>Investigator’s Brochure</td>
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<td>IRB Approval Letter</td>
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<td>IRB #</td>
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<td>Approved Consent Form (Checkbox on order form)</td>
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<td>Who is on this study team (PI, Coordinator, etc.)/Who can sign for drug</td>
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<td>Enrollment expectations</td>
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<td>Storage conditions of drug</td>
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<td>Study complexity (sponsorship, randomization, multiple drug arms, IVRS, etc.)</td>
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<td>Notification timing for patients to come in for dosing 24-48 hrs</td>
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<td>Notification timing for monitoring visits also 24-48 hrs</td>
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<tr>
<td>IDS Operational Procedures for notification and drug order</td>
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<td>Investigational Pharmacist (IP) Responsibilities (IP Point Of Contact @ 2089)</td>
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<td>Tracking of investigational supplies (Inventory, expiry date, recovery/recall)</td>
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<tr>
<td>Approved Budget with IDS feedback</td>
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<tr>
<td>What services are required of IDS - Return on Expectations of the IDS/Will any Drug need to be shipped to patients?</td>
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<tr>
<td>Date Discussion Took Place (Day/Month/Year)</td>
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Principal Investigator Name __________________________ Initiated ________  A scanned copy will be provided

IDS Representative Name _____________________________ Initiated ________

OCRMA Representative Name __________________________ Initiated ________  A scanned copy will be provided

IDS Protocol Activation Meeting, Page 2 of 3
Version 2.0 (03/16)
Public Relations and Marketing

**Function:** Provide effective, strategic communications that strengthen CNMC’s brand. Specifically, develop integrated marketing strategies and resources to promote awareness and preference to CNMC to external consumer and physician audiences.
Recruitment Materials

- Recruitment flyers/posters and telephone scripts must be approved by Public Relations and Marketing prior to IRB submission
  - Contact Senior PR & Marketing Specialist, Emily Hartman with any questions about recruitment materials
  - Recruitment sources should reflect target population and research goals
    - Inpatient units
    - Emergency Department
    - Specialty Clinics
    - Primary Care Clinics (Goldberg Center)
    - Community (schools, child care centers, radio or newspaper ads)
  - Approved documents must be included in IRB submission
Registering Research Participants

**Why is this important?:** Incorrect billing of research costs is a compliance issue placing CNMC at risk of fraud

- All clinical studies will have an assigned study specific research requisition form with a unique plan code

- Investigators/staff must register research participants using the plan code and research registration process

- Outpatient clinics may not register participants without the study specific registration form
Registering Research Participants

• If a study participant is scheduled for standard of care and research procedures at the same visit, two registrations, including labels are required
  – Laboratory or other services that are not part of the study must be submitted on a separate requisition with a valid non-research registration

• If you need help registering a research subject, contact Ianka Laidlow in the CRC
Research Registration Request and Billing Form & Study Subject Reimbursement Form

* If applicable - not all studies provide subject reimbursement
Inpatient Study Logistics

Oftentimes tests are ordered differently when subjects are inpatient versus outpatient.

- Different billing implications

You may need to work with the inpatient nursing staff to coordinate research-related activities.
Internal Processes

PRE-STUDY

1 Notification
- Study Notification
- Confidentiality Agreement
- Feasibility Questionnaire

2 Pre-Site Selection
- Pre-Site Selection Visit
- Budget*
- Clinical Trials Agreement*
- Recruitment Materials
- IRB/WIRB*

3 Pre-Study Initiation
- Plan Code Issuance
- Pre-Study Initiation Meeting (Internal & External)
- Study Registration (clinicaltrials.gov)

STUDY

4 Study Implementation
- Enrollment
- Randomization
- Follow-up
- Monitoring & Audits
- Study Completion

POST-STUDY

5 Study Close-out
- Study Close-out
- Record Keeping
- Complete Billing/Payment review

* Steps can occur in parallel
**Submission & Approval Timeline**

- **Study concept/site identified** immediately

- **Grants and Contract Administration Office**

- **CRC**

- **CRMO***

- **IDS**

- **CNMC IRB**

- **PR & Marketing***

- **WIRB**

- **PR & Marketing***

- **CNMC IRB**

  - 2 weeks after PI submission
  - 4-6 weeks after PI submission (may take longer)

  - 10 days

  - 2-3 weeks

* Can submit to IRB while negotiating budget
** Can be done concurrently if study is utilizing CRC
*** Only if submitting material for approval
**** Only if utilizing IDS Pharmacy

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Industry-sponsored study

Non-industry sponsored study

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Begin Study

**Children’s National Medical Center**

**CTSI CN**

**Clinical and Translational Science Institute of Children’s National**

**Washington DC**
Challenges & Things to Keep in Mind

• Challenges vary by setting and protocol requirements

• Importance of maintaining privacy and confidentiality

• Provide potential participants time to consider study participation and ask questions to assess level of understanding and willingness to participate
Things to Keep in Mind: Intellectual Property

- The **Office of Innovation Development** manages all aspects of intellectual property development, creates strategic business partnerships with external stakeholders, and conducts education programs to foster academic entrepreneurship.

  - Contact the Director, Innovation and Business Development, **Lawrence Mahan, PhD** if your research involves intellectual property.
Things to Keep in Mind: Emergency INDs (EIND)

• FDA regulations allow for the emergency use of an unapproved investigational drug/biological product or an unapproved medical device if:
  – the physician considers the product may be urgently needed for the patient’s serious or life-threatening condition;
  – no satisfactory alternative therapy is available; and
  – the patient cannot receive the product through any existing clinical trials or expanded access protocols

• CNMC IRB has a document, “Emergency Use of a Test Article, posted on the intranet for reference/guidance
  – outlines steps to take when initiating an EIND
  – Amy Gross will speak more about EINDs in the Introduction to the Investigational Pharmacy presentation (next)
EIND, con’t

FDA instructions available at:


IRB Emergency Use Exemptions from Prospective IRB Approval Policy and Procedure:

Case Studies

Real-time experiences with start-up processes for a(n):

1. Industry-sponsored clinical trial

2. Grant-funded study
DAY 0
• PI is interested in opening clinical trial and wants the RC to initiate dialogue with the study sponsor
• RC contacts sponsor expressing CNMC's interest in clinical trial
• Sponsor responds to RC’s e-mail and states a member of CRO will send CDA

Grants & Contract Administration Office
• RC forwards CDA

DAY 7
• RC still hasn't heard from CRO with CDA so a f/u e-mail is sent to sponsor contact
• CDA is forwarded to RC

DAY 19
• CDA is executed and signatures obtained from PI and sponsor

DAY 67
• Sponsor conducts phone site selection visit

Day 67
• Site receives start-up regulatory documents including budget and contract

Grants & Contract Administration Office
• RC forwards contract

Day 102
• RC completes study application in IRBear

OPHS-IRB
• RC enters study information into IRBear to initiate a facilitated review of study (WIRB protocol)

CRMO
• RC forwards budget, protocol and IB

Cont.
Industry-Sponsored Clinical Trial:
Highlights, continued

DAY116
• IDS initiation meeting with PI and RC

IDS
• Study initiation meeting

DAY130
• CNMC IRB approved facilitated review

OPHS-IRB
• Authorization for Protocol Review by WIRB letter

DAY140
• RC submits study to WIRB

WIRB
• Initial protocol review application is submitted to WIRB for review

DAY159
• WIRB approves study and accompanying regulatory documents

DAY165
• Site Initiation Visit (SIV) is conducted by sponsor: PI, RC, secondary RC and IDS staff are present

DAY174
• Study contract is executed by the Grants and Contract Administration Office

STUDY IMPLEMENTATION

KEY:
External Communications/Actions (   )
Internal Actions (   )
What went wrong?

• Did you notice anything (processes, etc.) that could have been done differently?
Grant-Funded Study: Highlights

**DAY 0**
- PI has communicated with sponsor about participating in the study (CNMC has already been selected as a site)
- CDA from sponsor is sent to the Office of Grants and Contracts

**Grants & Contract Administration Office**
- RC forwards CDA from sponsor

**DAY 32**
- CDA is approved by the Grants & Contract Administration Office

**DAY 38**
- Sponsor sends substitute agreement and non-negotiable budget to the Grants & Contract Administration Office

**DAY 40**
- Sponsor sends protocol and other regulatory documents to RC

**DAY 48**
- RC submits new study application to IRB via IRBear

**DAY 124**
- Substitute agreement executed by Office of Grants & Contracts

**DAY 139**
- IRB approves study

**STUDY IMPLEMENTATION**

**KEY:**
- External Communications/Actions ( )
- Internal Actions ( )
What went wrong?

• Did you notice anything (processes, etc.) that could have been done differently?
Key Research Contacts

Clinical Research Center (CRC)

Marlene Lee, Nurse Manager
Phone #: (202) 476-2298
mlee@childrensnational.org

Clinical Research Management Office (CRMO)

Amy Gross, Clinical Research Management Office
Phone #: (202) 476-4881
agross@childrensnational.org

Grants and Contract Administration Office

Monique Foxx, Manager, Office of Grants and Contracts
Phone #: (301) 565-8483
mfoxx@childrensnational.org

Human Research Protection Program (OPHS-IRB)

Phone #: (301) 565-8452

Investigational Drug Service Pharmacy (IDS)

Henry Choi, Supervisor, IDS Pharmacy
Phone #: (202) 476-2088
hchoi@childrensnational.org

Office of Innovation Development

innovation@childrensnational.org

Public Relations and Marketing

Emily Hartman, Senior PR & Marketing Specialist
Phone #: (301) 244-6728
ehartman@childrensnational.org

Research Finance

Carmen Mendez, Executive Director, Office of Grants and Contracts
Phone #: (301) 565-8484
cmendez@childrensnational.org

Western Institutional Review Board (WIRB)

Phone #: (800) 562-4789
www.wirb.com
QUESTIONS?!