Transportation and Logistics for Cell Therapy Projects

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ISCT Regional Meeting
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Objectives

• Offer perspective of laboratory tasked with coordinating cellular therapy clinical trials (CT) with external sponsors

• Focus on internal logistics and coordination with clinical service and sponsor

• Provide lessons learned from participating externally-sponsored CT INDs
What are External Sponsor Clinical Trials?

- Biotech/Industry sponsor
- Usually multi-center
- ± Central manufacturing laboratory
  - Company owned
  - Contract Manufacturing Organization (CMO)
- ± Logistics Contractor
- ± Contract Research Organization (CRO)
- Sometimes collaboration/partnership
  ± contract manufacturing
Background

• Increasing number of inquiries about participating in external sponsor CT trials.

• No coordination of communication
  • Direct recruitment of local PI
    • Contacted lab
  • Request to Research Pharmacy
    • Forwarded to lab
  • Direct request to laboratory

• Cell Therapy Lab was common denominator
Cell Therapy Lab as Logistics Coordinator

- Required mindset change
  - Less direct benefit than for IND held by Mayo PI
  - Not our typical CT product development

- Broadened our internal customer base
  - Future internal collaboration

- Raised our profile within the institution

- Matched institutional priorities of regenerative and individualized medicine
Company/Biotech Sponsored CT Trials: Variations on a Theme

1. Starting product (apheresis, bone marrow, tumor) collected and shipped to a laboratory
2. Manufactured into final product
3. Final product returned to hospital
   - Fresh (non-frozen)
   - Frozen ± in multiple doses
4. Final prep in lab or direct delivery to patient care area.

*Off the shelf (allo) product trials usually begin with #3*
Cross-Functional Process Flow - HCTL

Project Development – HCTL Review

Personnel
- Mayo personnel (CRAs/Investigators)

Process
- Complete HCTL Request Form

Tools
- HCTL Request Form

Output

External Sponsor
Cross-Functional Process Flow - HCTL

**Project Development – HCTL Review**

**Personnel**
- Mayo personnel (CRA/Investigator)
- HCTL Coordinator
- HCTL Coordinator

**Process**
1. Complete HCTL Request Form
2. Does Study Pass Initial Review?
   - Yes: Does Study Require Non-HCTL Service Partner?
     - Yes: Stop
     - No: Stop
   - No: Protocol & Investigator’s Brochure

**Tools**
- HCTL Request Form
- HCTL Request Form

**Output**
Cross-Functional Process Flow - HCTL

**Project Development – HCTL Review**

**Personnel**
- Mayo personnel (CRA/Investigator)
- HCTL Coordinator
- HCTL Coordinator
- HCTL Coordinator

**Process**
- Complete HCTL Request Form
- Does Study Pass Initial Review?
  - If yes, Does Study Require Non-HCTL Service Partner?
    - If yes, Non-HCTL Service Partner Review
    - If no, Stop
  - If no, Protocol & Investigator's Brochure

**Tools**
- HCTL Request Form
- Protocol & Investigator’s Brochure
- HCTL Request Form
- Protocol & Investigator’s Brochure

**Output**
Cross-Functional Process Flow - HCTL

Project Development – HCTL Review

Personnel

- Mayo personnel (CRA Investigator)
- HCTL Coordinator
- HCTL Coordinator
- HCTL Coordinator
- HCTL Coordinator
- HCTL Development Technologist

Process

- Complete HCTL Request Form
- HCTL Request Form
- Non-HCTL Service Partner Review
- Protocol Review & Budget Creation

Tools

- Protocol & Investigator’s Brochure
- HCTL Request Form
- Budget Form
- Protocol Review Form

Output

- Non-HCTL Service Partner Approval
Cross-Functional Process Flow - HCTL

**Project Development – HCTL Review**

**Personnel**
- HCTL Review Board

**Process**
- HCTL Scope of Service Defined and Approved?
  - If yes
    - Site C (as i)
  - If no
    - Stop

**Tools**
- Budget Form
- Protocol Review Form
- HCTL Request Form

**Output**
- HCTL Approval (to include budget & PAU request for charges)
Cross-Functional Process Flow - HCTL

Project Development – HCTL Review

Process

Personnel

HCTL Review Board

Sponsor, Investigator, HCTL

Sponsor, Investigator, HCTL

Mayo personnel (GRA/Investigator)

Investigator

If yes

If yes

If yes

If no

If no

If no

Stop

Stop

Stop

HCTL Scope of Service Defined and Approved?

Site Qualification Visit (as applicable)

Approval Received – IRB Sponsor, OSPI? Contract Signed?

Logistics Meeting

Site Initiation Visit (as applicable)

HCTL to receive documentation that the protocol has been approved by the appropriate regulatory authorities at Mayo

Trial Open

Tools

Budget Form

Protocol Review Form

HCTL Request Form

Logistics Agenda

Output

HCTL Approval (to include budget & PAU request for charges)
Initial Protocol Review

• Coordinator submits online request to HCTL
• HCTL review – using Project Review Criteria
• Budget completed
• Final approval by Laboratory Review Board
  • Template memo to local PI with agreement and budget details
• Coordinator submits online request to HCTL
  • HCTL web page links to the request form

• Minimal information required
  • Company name
  • Protocol
  • Investigator’s Brochure
  • # of patients
## Initial Protocol Review

### HCTL Project Review Criteria

<table>
<thead>
<tr>
<th>General</th>
<th>Receipt</th>
<th>Final prep</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Company</td>
<td>• Time constraints</td>
<td>• New techniques?</td>
<td>• Documentation requirement</td>
</tr>
<tr>
<td>• FDA Warning Letters</td>
<td>• Inventory system compatibility for frozen products</td>
<td>• Equipment?</td>
<td>• Appropriate lab skill set?</td>
</tr>
<tr>
<td>• Enrollment – overall and Mayo</td>
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<td>• Time constraints</td>
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<tr>
<td><strong>Procurement</strong></td>
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<tr>
<td>• Product type</td>
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<tr>
<td>• Mayo expertise</td>
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<tr>
<td><strong>Shipping</strong></td>
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<td></td>
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<tr>
<td>• Time constraints</td>
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<td></td>
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<tr>
<td>• Unique requirements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
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Initial Protocol Review

• Budget - based on review
  • Set up fee - fixed, independent of enrollment
  • Per patient/product fee
    • One of three fixed amounts based on complexity
      • No need to create new fees for each study (variations on a theme)
The Budget Process

- There isn’t enough information
- Information doesn’t arrive before the budget is due
- The requirements change after the budget is finalized
- Repeat process for the next study
Laboratory Checklist

- Ensures key items are completed
- Lab process flow is key

External Sponsor Cellular Therapy Clinical Trial Initiation Checklist

| Trial Name: |  
| Project Sponsor: Mayo PI: |  
| Clinical Coordinator: Lead Development Tech: |  
| Back up/Additional HCTL Staff: |  
| Expected Number of Mayo Patients: |  
| Estimated Trial Open Date at Mayo: |  

<table>
<thead>
<tr>
<th>Project Milestones</th>
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<tbody>
<tr>
<td>Preliminary laboratory visit from sponsor</td>
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<tr>
<td>Review of protocol by HCTL Development Coordinator or designee</td>
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<tr>
<td>Budget developed and submitted to protocol development coordinator</td>
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<tr>
<td>Training provided by sponsor</td>
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<tr>
<td>HCTL staff attendance at investigator meeting</td>
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<tr>
<td>HCTL Process flow created</td>
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<tr>
<td>Training required for Mayo developed processes</td>
</tr>
<tr>
<td>Trial Logistics meeting with Mayo personnel</td>
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<tr>
<td>Final qualification visit by sponsor</td>
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<tr>
<td>Final budget approval and PAU received</td>
</tr>
<tr>
<td>Record IRB # and approval date</td>
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<tr>
<td>Record IND #</td>
</tr>
</tbody>
</table>

Reviewed by: ______________________________ Date: __________________

Laboratory Director
Trial Planning

• Investigator meeting
• Preliminary review of lab by sponsor/CRO
• Training
• Preparation of lab processes/documents
• IRB submission/approval
• Site initiation visit
• Internal logistics meeting
• Trial open
Sample Process Flow

Clinical coordinator will contact HCTL staff when a subject has been identified.

Subject undergoes nephrectomy

Specimen is sent to Frozen Section (FS) lab. Tumor for study collected and placed in RNALater vials by FS lab. Tumor is retrieved from FS lab by HCTL and shipped.

Clinical Coordinator will request slide from Anatomic Pathology and ship.

Subjects will be screened for eligibility between 2 and 5 weeks post-nephrectomy.

If eligible, subjects will be randomized in a 2:1 fashion, combined therapy to standard alone. Standard alone will not undergo apheresis.

Subjects randomized to combination therapy undergo apheresis 0-3 days before Visit 1 (Day 0).

Therapeutic Apheresis unit will contact HCTL at completion of apheresis. HCTL staff will transport product to HCTL, package, and ship.

Product for administration will ship directly to unit, no HCTL involvement anticipated

- Subject’s DOB and scheduled date of surgery will be provided by coordinator.
- Coordinator will notify TRAG of collection.
- Give kit to Frozen Section lab day prior to surgery or no later than 8:00 a.m. on day of surgery.
- Subject ID is determined by the tumor collection kit chosen.

- Ship tumor on day of collection. If unable to ship on same day, place in refrigerator and ship next available day. Do not ship day before weekend or holiday.
- Package and ship per Collection guide.
- Enter shipment in IVRS.

- Slide does not need to be shipped on same day as tumor.

- Approximately 180 mL of leukocytes and approximately 150 mL of autologous plasma will be collected in separate bags.
- System boxes should be stored at room temp. for 72 hours prior to use.
- Place plasma and leukocytes into individual bags and package for shipping per Leukapheresis Manual.
- Enter shipment in IVRS.
Process Flow - Internal Documentation

Patient Specific Summary

Patient Name: Lastname, Firstname
Clinic Number:
Subject identifier: Identifier Assigned to HPC-A: Qxxxxx

Tumor Collection Date: DD/MM/YY
Tumor shipped by:_____________

Leukapheresis Date: DD/MM/YY
Leukapheresis shipped by: _____________

All product handling and processing were according to the clinical trial agreement.

Reviewed by ____________________________________________________ Date___________________

Laboratory Director

• Regardless of (in addition to) company required documentation this is the laboratory standard for internal recordkeeping

• This text block, or variation, is part of every process flow

• Deviations are described here and per study procedures
Internal Logistics Meeting

• Required for every clinical trial (lab requirement)
• Operational details are worked out
  • Internal contact list
  • Who calls who
  • Weekend coverage
  • Adverse event notification
• Internal, or company provided forms?
• Agreement to reconvene after first few patients, depending on enrollment speed
  • Discuss what worked and what didn’t
Trial Open Phase

• Follow procedures and process outlined in trial documentation
• Maintain inventory of supplies, if not resupplied automatically
• Communicate with CRO and sponsor as necessary
• Strict attention to communication restrictions for blinded studies
  • Lab is typically the only unblinded group at the clinical site
Trial Open Phase - Documentation

- Chain of custody
  - Shipping and receipt of products
- Technical
  - Product preparation documentation
- Many studies utilize online randomization and supply re-ordering
- Training additional staff
- Changes to study procedures
External Sponsor Clinical Trials: Our Philosophy

• Follow the instructions provided even if you know there are better ways
  • The Golden Rule: “Just shut up and do it”

• Unless there are concerns about:
  • Patient safety
  • Patient identification procedures
  • Regulatory issues

• Don’t expend much effort until the contract is final
  • Studies sometimes disappear after initial inquiries

• Budget for contingencies (repeats, failures, unplanned visits)
External Sponsor Clinical Trials: Lessons Learned

• Create a process for external trials so nothing gets forgotten
• Advertise internally so your hospital knows you can provide this service
  • Coordinators, PI groups
  • Possibility of institutional support
• Structure budget so you recover your costs even with no enrollment
• Wide range of expertise and savvy among sponsors
  • We’re not being asked to be (or paid as) consultants
• Communication between sponsor, CRO, logistics, and clinical team is critical