The Business of Clinical Trials: Who Pays? Who Profits?

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Acknowledgements

- Cystic Fibrosis Therapeutics Development Network
- Cystic Fibrosis Foundation
- Kate A. Hilliard, BA. CCRC
  - Director of Clinical Research Operations, Rainbow Babies & Children’s Hospital
- Patrick Flume, MD
  - Director or Cystic Fibrosis Center, Medical University of South Carolina
Objectives and Goals for Forum and Panel Discussion

• Understand and review the business of clinical trials
• Develop fair and appropriate budgets
• Understand both straightforward and under-recognized cost
• Developing a system for effective cost recovery
• Present tips and tools for successfully negotiating your budget
What do we mean by “The Business of Clinical Trials”

- **Managing the Program**
  - Hiring/Firing
  - Training and Certification, equipment maintenance, supplies
  - Developing a performance portfolio

- **Managing the Clinical Trials**
  - Performing feasibility assessments
  - Matching participation to interest
  - Recruitment
  - Recognizing and managing lack of success *(no activity does not equal no cost)*

- **Managing the Money**
First things First...Know Your Cost

• **Indirect Cost**
  • Money paid to the institution for basic infrastructure cost

• **Patient Care Cost**
  • Budgeted Items paid for services rendered (x-ray, labs, etc)

• **Personnel time**
  • PI, RC, Pharmacist, Administrative support to conduct the study visits
  • Poorly defined but often extensive, between patient demands on the team

• **Study Start-Up Cost**

• **Invoice Items**

• **Study Close out**
  • FDA audits, document storage
# UAB Cystic Fibrosis Program Start-up Fees

<table>
<thead>
<tr>
<th>Activity</th>
<th>PI Hours</th>
<th>RC Hours</th>
<th>Admin hours</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feasibility Questionnaire</td>
<td>2</td>
<td>2</td>
<td></td>
<td>$770</td>
</tr>
<tr>
<td>IRB Preparation</td>
<td>8</td>
<td>40</td>
<td></td>
<td>$5600</td>
</tr>
<tr>
<td>Budget/Contract Preparation</td>
<td>8</td>
<td>40</td>
<td>20</td>
<td>$7200</td>
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<tr>
<td>eCRF Training</td>
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<td>2</td>
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<td>$1220</td>
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<tr>
<td>Source Document Development</td>
<td>2</td>
<td>16</td>
<td></td>
<td>$1940</td>
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<td>CHRU FEE</td>
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<td>$1500</td>
</tr>
<tr>
<td>Pharmacy Start Up Fee</td>
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<td></td>
<td></td>
<td>$950</td>
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<td>Subtotal start Up Cost</td>
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<td></td>
<td></td>
<td>$19,790</td>
</tr>
<tr>
<td>Institutional Indirects (30%)</td>
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<td></td>
<td></td>
<td>$5,937</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td>$25,727</td>
</tr>
</tbody>
</table>

Personnel Rates:
- PI: $250/hr
- RC: $90/hr
- Admin: $80/hr
- RA: $50/hr
Invoiceable Items
Know what your Invoiceables items are and plan ahead!!!

Procedures that **MIGHT** happen
- Screen Fails
- Pregnancy Test
- Unscheduled Visits
- Travel, Overnight Stays
- Adverse Events
- Creating Source Documentation
- Dry Ice
- Amendments, Renewal Fees
- IND safety Reports
- Document Retrieval (after close out)
- FDA Audit

Procedures that **Will** Happen
- Monitoring Visits
- Archiving, Data Storage
- Pharmacy Dispensing Fees
- Close out Fees
- Conference Calls

Develop your PI and RC time for these Invoiceables and be prepared!!!
Go into the Negotiation Prepared!

Use the Tools you have:

- Synopsis, study schedule, study design
- Subject Selection
  - Population, Inclusion/Exclusion
  - Study Drug
- Study procedures and guidelines
- Evaluations by visits
- Adverse event reporting
- Data Collection

Remember!!
A CRO/Sponsor will never offer the amount of compensation your deserve, only the amount you negotiate!!!
Negotiation Considerations

Study Visits

• Before the Visit
  • Prescreening, Recruitment, prep time,

• During the Visit
  • Study Activities, lab processing, shipping, dry Ice, complicated medical history review

• After the Visit
  • Data entry, queries
  • Processing Specimens/Shipping
  • Invoicing and reconciliation
For Example....

- Identify the length of each visit
- Identify the test that are billable
- Are there both Tech/Professional costs associated with the test
- Central Lab vs Local Lab
- Review all footnotes, may find hidden cost
- Determine personnel time

<table>
<thead>
<tr>
<th>APPENDIX 1. SCHEDULE OF EVENTS</th>
<th>VISIT 1 SCREENING/ BASELINE (Day 1)</th>
<th>VISIT 2 (Week 13)*</th>
<th>VISIT 3 (Week 26)*</th>
<th>VISIT 4 (Week 39)*</th>
<th>VISIT 5/ FINAL STUDY VISIT (Week 52)*</th>
<th>EARLY WITHDRAWAL VISIT</th>
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</thead>
<tbody>
<tr>
<td>Review study/ obtain Informed Consent/ HIPAA/ Specimen Banking Consent/ Consent to collect CFF Registry ID</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Assess child screening number</td>
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<tr>
<td>Record Demographics Data</td>
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<td>X</td>
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<tr>
<td>Record Medical History</td>
<td>X</td>
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<td></td>
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<tr>
<td>Record most recent respiratory microbiology culture</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Concomitant Medications</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Confirm Eligibility</td>
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<td>X</td>
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<tr>
<td>Administer study instruments b</td>
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<td>X</td>
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<td>X</td>
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<td>- 1. CFVRIID</td>
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<td>X</td>
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<tr>
<td>- 2. CFQ-R</td>
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<td>X</td>
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<tr>
<td>- 3. TAC-CF</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>- 4. FAADS</td>
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<td>X</td>
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<td>X</td>
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<td>- 5. MOLI-SSS</td>
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<td>X</td>
<td>X</td>
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<td>Complete Physical Exam</td>
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<td>Vital signs, height, weight</td>
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<td>Blood for Repository a</td>
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<td>Randomization</td>
<td></td>
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<tr>
<td>Early Intervention group training</td>
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<td>X</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Review standard approach to exacerbation management</td>
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<tr>
<td>Pulmonary Signs and Symptoms Evaluation</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

a Subject questionnaires should be administered at the start of each study visit. 

b For subjects randomized to the Early Intervention arm, training includes use of AM2 monitor for both spirometry and CFASD, demonstration of data transmission, and providing subjects with AM2 monitor and data transmission equipment. Baseline for AM2 monitor for both spirometry and CFASD will be performed at this study visit.

* Protocol Amendment 1, a baseline specimen for the clinical biorepository can be collected at a subsequent visit provided the subject is not exacerbating (is in a clinically stable state).
For Example...

**TIPS:**
- Use this as a worksheet!!!!
- Allows you to identify SOC
- You may find things in the protocol not listed on the schedule of events
- Every visit should include PI time
- Include RC prep time
- Include data entry and query resolution
- Don’t shortchange yourself

**Study Procedures with Time Costs**

Please use the Schedule of Events below to estimate staff time to complete the visit.

Procedures that are typically charged with a set procedure cost (and not based on time) are not included in this list and the procedure cost should be entered on the Site Standard Costs tab.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Visit 4</th>
<th>Visit 5</th>
<th>Acute Visit w/ Blood Draw</th>
<th>Acute Visit w/o Blood Draw</th>
<th>Acute FU Visit</th>
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<td>Informed Consent and consent</td>
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<tr>
<td>Demographics/ICD Diagnosis</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Medication History</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signs and Symptoms (Baseline and Attn)</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
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<td>SOC</td>
</tr>
<tr>
<td>Concomitant Medications Review</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
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<td>Administration of CPRS</td>
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<td>X</td>
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<td>Administration of CRL/MOC/HCAL/MOS</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Administration of Treatment Burden</td>
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<tr>
<td>Physical Exam (P)</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
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<tr>
<td>Physical Exam (P) Abbreviated</td>
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<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
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<tr>
<td>Vital Signs</td>
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<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
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<td>Weight and Height</td>
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<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
<td>SOC</td>
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<td>Oximetry</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Randomization</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early Intervention training</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Review, medication management</td>
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<td></td>
</tr>
<tr>
<td>Visit Prep and Follow-up</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

**Key:** Only procedures done for research purposes will be reimbursed.
- X Procedure should be included in the estimate for staff time as this procedure is being performed for research only.
- SOC Procedure is performed as part of standard of care. Do not include as part of estimate for staff time.
- [X] Only need to perform for half of subjects.
Now you're ready to Negotiate!!

How do we come to an agreement?

**Negotiation process steps**

1. Follow the same process for every study
2. You must know how far you can lower your charges without losing money
3. You should understand the concept of fair market value
4. Establish a site specific checklist for all aspects of the process
5. Know when to walk away, even if temporarily

“Let us Never negotiate our of fear, but let us never fear to negotiate”

- John F. Kennedy
Fair Market Value

What is Fair Market Value?

• Average cost/charge of a procedure across all markets
• May be based on previously negotiated amounts from other trials at your site or an aggregate of other sites
• A sponsor may determine the lowest negotiated amount for an item and apply it across all sites.
• Fair market value must be addressed per site (i.e. past performance) and per market
  • As well as per disease
  • And in response to protocol specifications (in patient vs outpatient)
Billing and Reconciliation

You Negotiated the Contract
and
You Did the Work
so
COLLECT THE MONEY
Business of Clinical Trials Trivia

What is the average percentage of the Budget that research sites do not collect due to lack of invoicing???

26%

Source: Quintiles, SCRS (2016), Tufts CSDD
Billing and Reconciliation

While we wait for Oncore….

- Develop a system for tracking all charges and events
- Submit invoices for all of these items according to the time schedule outlined in the contract
- Reconcile the payments with invoices on a periodic basis
- Do not close the grant until you are assured you have received all payments
Filemaker, billing program designed by Isabel Virella-Lowell, MD
Filemaker, billing program designed by Isabel Virella-Lowell, MD
Filemaker, billing program designed by Isabel Virella-Lowell, MD
Wednesday, June 28, 2017 at 12:20:06 PM Eastern Daylight Time

Subject: Invoice #014 - COA/UAB PULMONARY CLINICAL RESEARCH CENTER
From: Isabel Lowell
To: Smith, John
CC: hhathorne@peds.uab.edu, tiryby@peds.uab.edu, thyrzajohnson@uabmc.edu, miriammiles@uabmc.edu
Attachments: Invoice 014.pdf

Please review attached invoice and remit payment by due date.

Thank you,

UAB/COA Pulmonary Clinical Research Center

---

**INVOICE**

COA/UAB PULMONARY CLINICAL RESEARCH CENTER

---

**DATE:** 6/28/2017

**TS**

**Sponsor ID:** 1010

---

**To:**

**TS**

123 research drive

Birmingham, AL 35233

USA

---

**Payment in full is due by:** 7/28/2017

---

**ITEM** | **QTY** | **UNIT PRICE** | **AMOUNT**
---|---|---|---
Budget Preparation | 1 | 8,240 | $8,240.00
IRB Preparation and Submission | 1 | 4,640 | $4,640.00
Lab Set Up Fee | 1 | 1,300 | $1,300.00
Site Initiation Visit | 1 | 1,140 | $1,140.00

**Subtotal** | $15320.00

**Indirect Costs** | $4596.00

**TOTAL** | $19916.00

---

Filemaker, billing program designed by Isabel Virella-Lowell, MD
**Example Budget Tool**

**Site Standard Cost**

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item 1</td>
<td>Example item 1</td>
</tr>
<tr>
<td>Item 2</td>
<td>Example item 2</td>
</tr>
<tr>
<td>Item 3</td>
<td>Example item 3</td>
</tr>
</tbody>
</table>

**Institutional Support**

- Institutional Support: 100

**Financial Data**

- Financial Status: Operating
- Financial Year: 2023

**Project Specifics**

- Project Name: Example Project
- Project Code: X123

**Budget Breakdown**

- Breakdown for...
  - Category A: $10,000
  - Category B: $5,000
  - Category C: $15,000
Example Budget Tool

Study Phase Cost
Example Budget Tool

Subject Cost
### Example Budget Tool

#### Schedule of Events

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
<th>Location</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/01/2023</td>
<td>Opening Ceremony</td>
<td>Auditorium</td>
<td>$500</td>
</tr>
<tr>
<td>01/02/2023</td>
<td>Welcome Dinner</td>
<td>Restaurant</td>
<td>$300</td>
</tr>
<tr>
<td>01/03/2023</td>
<td>Keynote Session</td>
<td>Convention Center</td>
<td>$1000</td>
</tr>
<tr>
<td>01/04/2023</td>
<td>Panel Discussion</td>
<td>Hotel Ballroom</td>
<td>$200</td>
</tr>
</tbody>
</table>

*Note: Costs are estimated and subject to change.*
Example Budget Tool

Summary Budget
The table below includes tasks associated with study start up, typical turn-around time and target dates for completion. The table also identifies the personnel responsible for completing the task. This tool can be customized for your site specific requirements.

<table>
<thead>
<tr>
<th>Task</th>
<th>Personnel</th>
<th>Time Required</th>
<th>Target Start Date</th>
<th>Target Complete Date</th>
<th>Actual Completed Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review budget</td>
<td>PI/RC/Business Manager</td>
<td>3 – 5 hours</td>
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</tr>
<tr>
<td>IRB prep/review by sponsor</td>
<td>PI or RC</td>
<td>Prep (10 hours) Sponsor (2-5 days)</td>
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<tr>
<td>IRB submission</td>
<td>RC</td>
<td>2-3 hours</td>
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<tr>
<td>IRB review</td>
<td>By Committee</td>
<td>Depends on schedule</td>
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<tr>
<td>Peds IRB review</td>
<td>By Committee</td>
<td>Ad hoc 2 weeks</td>
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<tr>
<td>PRC-GCRC review</td>
<td>By Committee</td>
<td>3 weeks to get on schedule</td>
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<tr>
<td>PRC-GCRC preparation</td>
<td>RC</td>
<td>2-3 hours</td>
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<tr>
<td>Contract review/ negotiations</td>
<td>By Legal</td>
<td>4-6 weeks</td>
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<tr>
<td>Obtain IRB approval</td>
<td>PI/RC</td>
<td>Concurrent w/contract</td>
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<tr>
<td>Finalize contract</td>
<td>PI/RC</td>
<td>Concurrent w/IRB approval</td>
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<tr>
<td>Investigator Meeting</td>
<td>PI/RC</td>
<td>1-2 days</td>
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<td></td>
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<tr>
<td>Site Initiation Visit</td>
<td>PI/RC</td>
<td>1 day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enroll 1st Subject</td>
<td>PI/RC</td>
<td>1 day</td>
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Panel Discussion

• Steven Rowe, MD, MSPH
  Director, Gregory Fleming James Cystic Fibrosis Research Center
  Co-Director, CCTS Children's Health Research Unit

• Mansoor Saleh, MD
  Medical Director, UAB Clinical Trials Administration Office
  Director, CCTS/CCC Phase I Clinical Trial Unit

• Mark Dransfield, MD
  Department of Medicine Professor, Division of Pulmonary, Allergy, and Critical Care, Director UAB Lung Health Center