Pediatric Drug Development

- 1998: essentially no trials
- Mandate (Pediatric Research Equity Act)
- Incentive (Exclusivity)
- Virtually no studies in young infants
- Off Patent (Best Pharmaceuticals Children Act)
  - Authorization by Congress
  - NICHD sponsored trials
  - 2002-2010
  - 6 molecules, one trial enrolled on-time
What Is The Pediatric Trials Network PTN?

- Sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

- The primary objective of the Pediatric Trials Network:
  Create an infrastructure for investigators to conduct trials that improve pediatric labeling and child health.

- PTN is studying product formulation, drug dose, efficacy, safety, and device validation

- Evidence of success will be completed trials that improve dosing, safety information, labeling, and ultimately child health
<table>
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<tr>
<th>Project</th>
<th>Date Signed</th>
<th>Protocol Status</th>
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<tr>
<td>TO1 Administration</td>
<td>Oct 2010</td>
<td>NA</td>
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<td>TO2 - Hypertension protocol</td>
<td>Oct 2010</td>
<td>Protocol Complete</td>
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<td>TO3- Metronidazole</td>
<td>Dec 2010</td>
<td>Protocol Complete</td>
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<td>TO4 - Hydroxyurea</td>
<td>May 2011</td>
<td>Protocol Complete</td>
<td>Interim analysis on time</td>
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<td>TO5 Acyclovir</td>
<td>Jun 2011</td>
<td>Protocol Complete</td>
<td>Interim analysis, on time</td>
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<td>TO6 Opportunistic (POPS)</td>
<td>Aug 2011</td>
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<td>TO7 -Lisinopril PK</td>
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<td>TO8 -Tape</td>
<td>Sep 2011</td>
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<td>TO9 -Midazolam</td>
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<td>TO10 Ampicillin</td>
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<td>TO11 -Obesity</td>
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Lessons Learned Main Contract Timelines

- Meropenem RFP release to signature 24 months
- IND 31 months
- First patient 34 months
- Last infant 48 months
- Clinical Study Report 60 months from RFP release
- Pediatric Trials Network RFP 3/2010, signature 6 months
- IND 7 months
- First patient 9 months
- Last patient 18 months
- Clinical study report 22 months from RFP release
Innovations and Track Record That Made it Go

- DCRI operations team—job vs. mission
  - Contracting—risk to NIH and to investigators
  - POPS
  - IRB
- Meropenem—give it away to keep it
- Trial leadership and PI selection
- Per patient cost—between and within trial
- Success in first trial—support of NICHD
- Success in 2011—support of the members
- Only decisions that impact timelines and budget
Protocol Title: Pharmacokinetics of Understudied Drugs Administered to Children per Standard of Care

Objectives:
- Evaluate the PK of understudied drugs currently being administered to children.

Study Population: 500 children (birth-20 years) who are receiving understudied drugs of interest per standard of care as prescribed by their treating caregiver.

Study Duration: each child will participate in the study for up to 90 days per drug; study conduct for 3 years.

Number of Sites: 45

First Patient Enrolled: November, 2011
PTN and POPS Continued

- 15 therapeutics bundled into one protocol
- Samples stored locally and sent in batch
- Flexibility to add molecules
- Provide preliminary and supportive data for subsequent trials
  - Compare to epi-data
  - Metronidazole example
- Provide a testing ground for sites—enrollment
- Facilitate contracts and infrastructure—enrollment in between more traditional trials
Comparison Legacy Trials Pediatric Trials Network

- Legacy 10 years
  - website
  - 6 molecules
  - 1 trial completed on time

- Pediatric Trials Network
  - 30 molecules
  - All trials on time and on budget to date
  - 16 trials over 7 years requested, will have started 14 trials in 2 years
  - 2 CSR
  - Website [www.pediatrictrials.org](http://www.pediatrictrials.org)
Applications infectious disease trials

- Success in ID trials already
- POPS
  - Site selection and reduce start up time
  - Post-marketing safety
  - Feasibility
- Interacting with industry
- Pharmaco-epi
- Piggyback of diagnostics