IT STARTS WITH ONE

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Why Pediatric Clinical Trial Networks?

Current Challenges to Run Global Paediatric Interventional Clinical Trials

CHILD
Child Health Innovation Leadership Department

Sam Maldonado
June 5, 2019
As a Society We Have Work To Do...

Over 50% of medicines used to treat children have not been studied in children

Over 90% of them have not been studied in infants
Different Doses, Different Formulations
Small Populations and Sub-Populations

At least Five Pediatric Sub-Populations

<table>
<thead>
<tr>
<th>Preterm Newborn Infants</th>
<th>Term Newborn Infants</th>
<th>Infants and Toddlers</th>
<th>Children</th>
<th>Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-term</td>
<td>0–28 days</td>
<td>29 days to 23 months</td>
<td>2 Years to 11 Years</td>
<td>12 Years to 18 Years</td>
</tr>
</tbody>
</table>

- Heterogenous population
- Low incidence of diseases
- For each sub-population, separate clinical studies are often required
- Eligibility criteria further narrow the pool eligible to be enrolled in a study
## Adult vs. Pediatric Trial with the Same Anti-hypertensive

<table>
<thead>
<tr>
<th>Adult</th>
<th>Pediatrics (6-16 y/o)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• N = 220 subjects</td>
<td>• N = 253 subjects</td>
</tr>
<tr>
<td>• Countries: One (USA)</td>
<td>• Countries: Three</td>
</tr>
<tr>
<td>• No. Sites: 9</td>
<td>• No. Sites: 70</td>
</tr>
<tr>
<td>• Study time: 5 months</td>
<td>• Study time: 1 year</td>
</tr>
<tr>
<td>• 24 subjects per site</td>
<td>• 3 – 5 subjects per site</td>
</tr>
</tbody>
</table>

*Thank you to Dr. Ron Portman for providing this example*
Opportunities for Efficiency

Efficiency lowers R&D investment and increases likelihood of success

1. Site Selection & Throughput
   - Approached: 500
   - Selected: 93
   - Enrolled Patients: 65
   - 2-5 Patients Per Site over 1-2 Years

2. Aligning CDA, Contracts and have a single ICF

3. Minimize Protocol Amendments
   - amendments slowed enrollment

4. Staffing Consistency
Paediatric Trials – Still Struggling

Status of PIP Completion
Snapshot as of June 2017
N = 261 PIPs

Source: Adapted from EMA Annual Report to the European Commission dated April 2018, J&J CHILD Analysis, May 2019

- 57% PIPs Completed On Time
- 31% PIPs Not Completed On Time (Valid Justification)
- 12% PIPs Not Completed On Time (No Justification)
Pediatric Trials – Still Struggling

Annual Snap Shot at Year End
Last 5 Years ~60% Have Not Yet Enrolled Patients or Have Been Released from Obligations

Total # Pediatric Studies: FDA Annual Status Summary
CDER and CBER, by Year
Adapted from FDA Website, FDAAA Pediatric Tracking Requirements
J&J CHILD Analysis, May 2019

United States
Potential Solutions?

Pediatric Clinical Trials Networks

c4c *
IACT *
Others
PAVING THE FUTURE FOR THE TREATMENT OF PAEDIATRIC DISEASES THROUGH A PAN-EUROPEAN CLINICAL TRIALS NETWORK

c4c
Vision

Better medicines for babies, children and young people through a pan-European clinical trial network
c4c will use a coordinated approach to deliver high quality “regulatory grade” clinical trials in:

- Multiple countries
- Multiple sites
- All paediatric age groups

by supporting:

- Trial implementation using resources shared between studies
- Trial design through a combination of information about natural history, feasibility, appropriate innovation, and expert opinion
- Education and awareness within and beyond the network
Key Objectives

• More efficient trial implementation through the set-up of **national hubs** and qualified sites
• Input in clinical trial design and implementation from **pilot expert advisory groups** and other fora
• **Educational programme** for health professionals and **awareness raising campaigns** for the general public
• Identification of **Data standards** and performance metrics
• Business cases for **sustainability** beyond IMI funding
The c4c consortium members

- 10 EFPIA companies
- 18 paediatric national networks
- 2 large patient advocacy groups
- 8 EU multinational specialty networks
- 3 global research networks
- 2 large children’s hospitals
Core Elements of I-ACT’s Approach

I-ACT for Children is an independent 501(c)3 public-private collaboration designed to advance innovative medicines and device development and labeling to improve child health.

Pediatric Product Development
Skills and experience for regulated pediatric product development, labeling and post-marketing for innovative medicines and devices

Innovation
Clinical development strategy and trial design

Efficiency
Operational efficiency with high quality
The Current U.S. Site Network

- Innovative medicines and devices
- Regulatory-quality clinical trials
- Therapeutic-area agnostic
- Partnered with specialty & international networks
- Participate in I-ACT for Children metrics & QI program
- Utilize central IRB
- Contract agreements in place
- Dedicated medical & operational points of contact
- Peer-to-peer engagement
- Mentoring program
- Communications & troubleshooting

44 US sites as of March 2019; 2019 goal of 60 sites

- Pre-competitive projects
- Advice & guidance on proprietary projects
- Facilitation of clinical trials, feasibility
- Trial conduct, enrollment etc.
Key Global Collaborators - GPCTN

Example Research Alliance Organizations

Example Advocacy Relationships
I-ACT for Children: Key Staff

- **Chief Executive Officer**: Laura Gordon
- **Interim Chief Medical Officer**: Ed Connor, MD, MBE, FAAP
- **Chief Operating Officer**: Karen King, MS
- **Director, Strategy & Operations**: Stephen McConoughey, PhD, PMP
- **Director, Research, Quality & Education**: Janelle Allen, MS
- **Clinical Project Manager**: Christina Stanley, MS, CCRA
- **Quality Improvement Project Manager**: Carol Rosenberg, ND, DNP, RN
- **SVP, Clinical/Scientific Development**: Collin Hovinga, PharmD, MS, FCCP
- **SVP, Research, Quality & Education**: Lisa Benson, BS, CCRP, CRCP
Thank you