Opportunities for Public-Private Partnerships in Pediatric Research Networks

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*On behalf of the pediatric working group for the development of the Global Pediatric Clinical Trial Network

Disclaimer

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Developing a Clinical Trials Infrastructure in the United States: Discussion Paper, Institute of Medicine, 2012

- Paul Eisenberg, Amgen, Inc.; Petra Kaufmann, National Institute of Neurological Disorders and Stroke; Ellen Sigal, Friends of Cancer Research; and Janet Woodcock, U.S. Food and Drug Administration
- Over time, clinical trials in the U.S. have become too expensive, difficult to enroll, inefficient to implement, and ineffective to support the development of new medical products using modern evidentiary standards."
- "There are few clinical research structures in the U.S. that combine mature clinical trials infrastructure, experienced staff, and established procedures that also have access to large numbers of patients with a specific disease or disorder."
- "How could such networks be supported? Funding such an enterprise in the face of current budgetary constraints is the primary issue......Despite these problems, the question remains: How can the U.S. afford not to have a clinical trials infrastructure?"

Public-Private Collaboration in Clinical Research During Pregnancy, Lactation and Early Childhood

- Joint position statement of the Early Nutrition Academy and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition
- JPGN, April 2014; Academic pediatricians, obstetricians in the EU, UK, Ireland, and Australia

"Collaborative clinical research between academia and commercial enterprises is in the mutual and the public interest, and it can provide major contributions to improving maternal and child health."

What are the Current Challenges? (Why do we need a Global Pediatric Network?)

- Across pediatric populations there is difficulty in:
 - Accessing the necessary patient populations for studies
 - Assessing feasibility of studying indications in the designated population
 - Finding qualified sites and Identifying experienced pediatric investigators
- Time, expense, and effort to operationalize sites, only to disperse that infrastructure and start all over again for the next study
- Trials in children take longer, recruit fewer patients, but cost much more on a per subject basis
- It currently takes approximately 7 years between NDA approval for adults and pediatric labeling in the US.
- There is a legal mandate in EU and US to provide children with same access to our drug products



Why Build a Network?

- 1. Do the right thing for children globally
- 2. Speed up and facilitate the development of medications for children
- 3. Leverage broad spectrum of expertise inherent in the faculty/physicians and scientists at member sites to inform planning of drug development programs
- 4. Maximize quality and usefulness of data with uniform quality standards and platforms for data collection that allow cross-study data sharing and collaboration
- 5. Encourage cooperative multi-arm protocols between pharma companies with drugs for the same pediatric indication
- 6. Improve ability to identify relevant clinical trials for patients and their families to participate in
- 7. Avoid costs for sponsors and investigative sites by leveraging an established network rather than continually creating and dismantling networks
- 8. Shorten the time of trial execution
- 9. Make it more feasible to meet regulatory timelines
- 10. Accelerate feasibility studies necessary to propose PSPs (FDA) and PIPs (EU)
- 11. Increase likelihood that industry complies with regulatory requests by being better prepared with feasible proposals

Type of Pediatric Networks

- Country, state, regional, networks
- Sub-specialty networks
- Academic networks
- Disease specific networks
- NIH networks
- Foundation networks
- Trial recruitment networks
- Office-based networks
- Children's hospital networks
- Patient advocacy networks
- Networks of networks



CTSA CC-CHOC

CC-CHOC

A Facilitator of Child, Maternal, and Llfecourse Clinical and Translational Research



Examples of Public-Private Partnerships



What Is SOATT?

Advances in Therapeutics and Technology

Mission: To advance pediatric health and well-being through collaboration, communication and education on innovation and the discovery, development and translation of therapeutics and technology

- A professional home within the American Academy of Pediatrics for providers and researchers with a passion for medical innovation for children
- Established July 2010 and now includes ~350 members from industry, academia, clinical practice, the Food and Drug Administration, government agencies and non-profit groups
- Opened to Affiliate Members in May 2011

- Objectives
 - Communication
 - ListServ, Newsletters
 - Education
 - AAP National Conference and Exhibition Educational Programs, webinars, patient education brochure on clinical trials
 - Networking
 - COPR Policy Statement on importance of pediatric research, guest articles
 - Integration
 - Global Alliance for Pediatric Therapeutics, NCE research abstract program, KIDS, global pediatric clinical trials network

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Data: Trials Across Stakeholders



• There are over 360,000 pediatric patients enrolled or enrolling in trials currently.

• Nearly 20,000 pediatric patients were planned for trials that were terminated.

*in pediatric-only trials; interventional only Source: clinicaltrials.gov as of November 9, 2013

Who should be engaged to build the Network?



The Partnership Landscape

What pediatric sites are looking for

- Access to new medicines
- Consistent, ongoing access to research & participation in meaningful clinical trials
- Investigator-led research
- Thought leadership opportunities
 - Pediatric development planning
 - Expert committees
- Development opportunities for junior staff / fellows
- Education opportunities & training of residents, fellows, and staff in clinical research
- Funding for internal programs

What industry is working to provide

- Access to new medicines
- Early access to pipeline
- Feedback and consultation on study startup processes
- Pediatric studies across multiple therapeutic areas
- Staff education
- Funding through sponsored studies and/or investigator-initiated research

Areas for Improvement

- Ongoing and steady flow of studies within therapeutic areas
- Structured approach and more consistent involvement in thought leadership activities (including development plan and protocol design, feasibility, etc)
- Funding beyond study participation

Landscape Questionnaire: What have We learned?

- Networks are partnerships; not sponsor-vendor relationships
- Networks need a constant stream of studies to pay for dedicated research staff and optimize profitability.
- Early and strategic view of the network pipeline allows for appropriate resource planning and feasibility review.
- Supplemental resources are typically necessary to overcome enrollment challenges and to focus on identifying appropriate trial patients.
- Reducing or removing administrative site burden supports routine, consistent enrollment.
- Successful site networks require ongoing nurturing, training.
- Investigator 'ownership' key to success
- Resources for supplemental studies needed from public sector
- Opportunities for academic career development critical

Concept of a Children's Therapeutic Clinical Trials Network

- Initial funding from a public-private partnership (industry, public/ private research institutions)
- □ Multi-specialty capable; phase I-IV; neonatal-adolescence
- Global: US, EU, Canada, and beyond
- □ 50-60 of the best children's medical centers in the world
- Heterogeneous study sponsors including industry, NIH (government research), private foundations, patient advocacy groups, investigator/academic medical center-initiated
- Global resource for advancing science of pediatric drug development and advocating for sound regulatory policy
- Cooperate and partner with existing networks

What is Different?

- Real (not virtual) network
- Primary focus is development and approval of new therapies
- All disease indications, therapeutic areas
- All age groups (including neonates)
- All phases (I-IV, IIS, registries)
- Sustainable infrastructure
 - Governing board (industry;academia; NIH)
 - Independent corporate non-profit entity with full time FTEs to operationalize and manage the network (Site Management Organization)
 - Financial support and central management of on-site employees in clinical trials units; and of site PI champions to foster long-term community of investigators

• Sustainable Funding

- Founding partner initial capitalization
- Subsequent additional partner's buy-in
- Partner yearly dues (including non-industry partners and partnering sites)
- Ad-hoc fees to non-partner companies utilizing services for specific studies
- Ad-hoc fees to patient advocacy groups/foundations utilizing network for studies
- Grants from NIH, other government, foundation sponsors

Conceptual Design: Global Pediatric Clinical Trials Network



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*geographic (MCRN) or therapeutic focus (COG)

Upcoming Initiatives, Timelines in the US for Consideration of a Pediatric Clinical Trials Networks*

- Transcelerate
- American Academy of Pediatrics; SOATT
- Critical Path Institute/ FDA
- NICHD
- EFPIA/IMI collaboration

- Year-long exploration in 2014
- 3rd quarter 2014
- Sept 23,24, 2014
- March, 2014 and ongoing
- Initial discussions May-June, 2014

*Other interested parties in the conversations include the **DIA and NCATS/CTSA**

Role of Transcelerate

- Objectives:
 - Lead the development and implementation of solutions which improve the operative feasibility and conduct of pediatric clinical trials
- Develop a model for efficiently accessing and using multiple types and sources of data (EHR) for evidence based feasibility assessments
- Explore models for collaborative patient sharing (master trials) across sponsors and protocols

We Are in Phase I of a Complex Process

- Diagnostics: Meet with member companies, government partners, academia, as well as existing investigator networks to identify what is needed to build, support and maintain a global pediatric clinical trials network.
- Partnership Selection: Investigate pediatric landscape and determine with whom to partner (and how).
- Requirements Building: Determine scope, establish standards needed to identify or qualify a site. Determine governance, operating model, including technical infrastructure needed
 Construct a business case: Focus on sustainability

Our Goals

- To catalyze a paradigm shift in pediatric therapeutic research by:
 - Understanding that this is a subspecialty and must be conceived, designed and executed by partnering subspecialists (in academia, industry, government and private research foundations)
 - Creating a unique, global network of sites that reliably enroll pediatric patients in industry/non-industry therapeutic trials.
 - Employing innovative regulatory strategies.
 - Using novel methods to design feasible pediatric drug development programs and protocols.
 - Building a sustainable community of pediatric researchers dedicated to bringing new therapies to children

Background Slides

Networks for Pediatric Drug Development

- European network for pediatric research (enpr-EMA):
 - PRINTO, PENTA, ITCC, BFM, MCRN, European Research Network in Diabetes and Endocrinology. Qualified networks
- US:
 - NIH related networks Phase 1: Pediatric Trials Network (off-patent)
 - Phase 3: CTSA, COG, PHN, neonatal
 - Association/Foundation networks CFF, NAPRTCS, AAP PROS, Rare disease (NIH)
 - PCORI or state funded consortia of children's hospitals: PCORI consortia not designed for clinical trials; other's in early stages.
 - Preferred site program: multiple academic sites and children's hospitals in US and EU
- Global:
 - PAIDION (newly forming pediatric research organization)
 - CRO Pediatric Centers of Excellence

Pediatric Therapeutics Development: CCHOC Goals

Provide Leadership in Product Development

- Set the agenda and act as the primary Pediatric conduit through which interactions flow between all stakeholders
- Work with FDA and International Regulatory Authorities
- Establish and Implement Federated IRB Model
- Move child health multisite trials to completion
- Improve the regulatory environment for pediatric therapeutics development
- Partner with existing networks US and International
- Promote best Practices standards in neonatal and pediatric trials
- Product development training curriculum for pediatric investigators
- Data Quality Workshop CTSA, NIH, FDA, CRO, Industry
- Pediatric Academic Societies Symposia

Examples of Public-Private Partnerships in Drug-Development Research

- <u>Biomarker Consortia</u> (biomarkers for drug development)
- <u>CTTI</u>-Clinical Trials Transformation Initiative (increase quality and efficiency of clinical trials)
- <u>Smart Tots</u> (funding pediatric anesthesia research)
- <u>**iSAEC**</u> (international Serious Adverse Event Consortia)

- FDA, NIH, PhRMA, BIO, multiple pharma companies, Centers for Medicare/Medicaid Services
- FDA, Duke University grant; members OHRP, NIH, VA, multiple pharma companies, PhRMA, DIA, BRANY, academia
- FDA, IARS (International Anesthesia Research Society), corporate partners
- Welcome Trust, multiple pharma companies, FDA, academia, medical societies

The Role of the Critical Path Institute

- Facilitator of public-private collaborations centered around critical disease indications, neglected patient populations, and issues in clinical research
- Originally partnership between Univ of Arizona, Tucson business community, and FDA
- Successful collaborations between industry, academic, and regulatory scientists
- Examples:
 - **PRO**: Patient Reported Outcome Consortia
 - MSOAC: Multiple Sclerosis Outcome Assessment Consortia
 - **PKD**: Polycystic Kidney Disease Consortia
 - CFAST: Coalition for Accelerating Standards and Therapies (data standards, tools, methods)

Transcelerate: Engagement with the Clinical Ecosystem Launched Sept, 2012 by 10 global Pharma companies

The intent is not to recreate, but partner whenever feasible. Clinical trial execution identified as a key priority



PhARMA Support



- Pharmaceutical Research and Manufacturers of America (Industry lobbying, Washington DC)
- □ 46 member companies with global reach
- Children's Therapeutic Clinical Trials Network endorsed by Scientific Review Committee 4rth quarter of 2013
- Unrestricted educational grant given to non-profit (AAP)
- To convene stakeholder meeting(s) including regulatory agencies during 2014

Eroom's Law: Number Of New Drug Approvals Per Billion US Dollars Halved Every Nine Years

a Overall trend in R&D efficiency (inflation-adjusted)



Source: Nature Reviews – Drug Discovery: Diagnosing the decline in pharmaceutical R&D efficiency Vol 11, March 2012, page 191 - 200