Institute for Advanced Clinical Trials for Children

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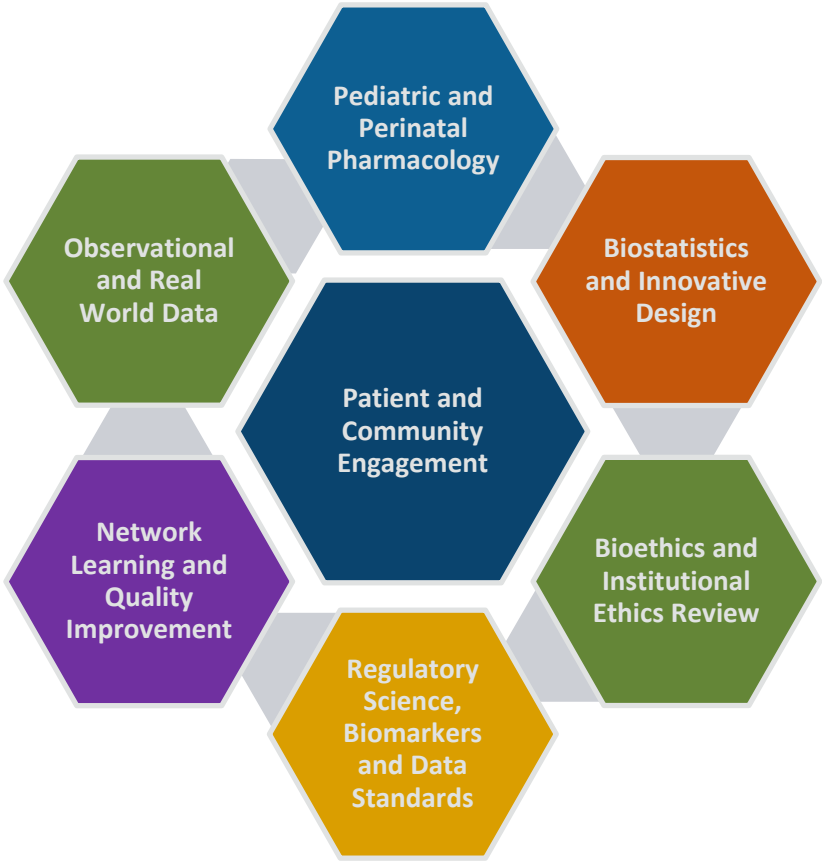
Chairman and Interim Chief Medical Officer
I-ACT for Children

Mission: To serve as a neutral and independent organization on behalf of children everywhere, bringing a dedicated voice to the advancement of new medicines and devices needed now and in the future. Our work is to engage public and private stakeholders through research and education to ensure that healthcare for children is continually improved by enhancing the awareness, quality and support for pediatric clinical trials.

- An independent 501(c)3 public-private collaboration launched in 2017 to advance innovative medicines/device development and labeling to improve child health
- Addressing the challenges and opportunities in pediatric clinical trials of new medicines/devices
- Focus on product development science, innovation, efficiency, quality, child-health impact
- Early and continuous cross-stakeholder engagement, including patients/parents
- Funded by membership, FDA U18 grant, donations/philanthropy
- Scope:
  - **Strategy/Planning** including innovative trial design, feasibility, pediatric program development
  - **Infrastructure/Trials Execution** – 60 centers, international reach, multidisciplinary experts
  - **Best Practices** – trial readiness, harmonized processes, points of contact
  - **Thought Leadership** – moving the field forward

Medicine and Devices Expertise

I-ACT for Children alliance partners and collaborators provide deep expertise in critical elements of pediatric medicines and devices development



I-ACT for Children's Collaborative Network

Example Research Organizations

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

MICYRN
better health for mothers and children

Duke Clinical Research Institute

INC
INTERNATIONAL NEONATAL CONSORTIUM

Japan Clinical Trials Network

Multiple Specialty Networks

CHILDREN'S HOSPITAL ASSOCIATION

Example Alliance Organizations

PEDSnet
A Pediatric Learning Health System

Children's Hospital of Philadelphia

Nationwide Children's Hospital

CRITICAL PATH INSTITUTE

National Capital Consortium for Pediatric Device Innovation

Cincinnati Children's

James M. Anderson Center for Health Systems Excellence

Tufts CTSI Tufts Clinical and Translational Science Institute

MyOwnMed

Example Advocacy/Care Relationships

iCAN
International Children's Advisory Network

Parent Project Muscular Dystrophy

National Eczema Association

PPA
Preemie Parent Alliance

IMPROVECARENOW™

Other healthcare improvement networks

Example Biopharmaceutical Collaborators

Johnson & Johnson

NOVARTIS

Lilly

BAYER

Chiesi

PhRMA
AMERICA'S BIOPHARMACEUTICAL COMPANIES

Bio Biotechnology Innovation Organization

I-ACT INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

I-ACT for Children's Collaborative Network

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

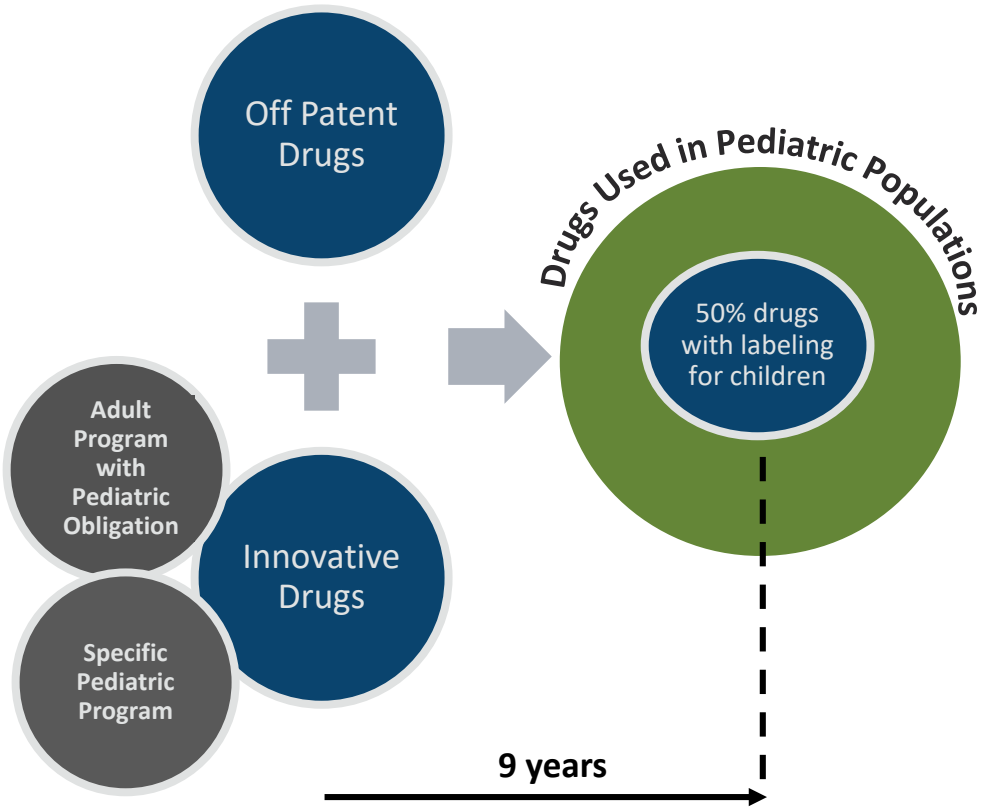
- 60 sites in the network by EOY; 80+ in 2020
- Site champion and operational lead
- Pre-qualification process
- Process efficiency
- Rapid site engagement
- Pediatric relevant training
- Peer-to-peer engagement
- Central IRB
- Communications and troubleshooting
- Mentoring program
- Quality improvement program

Project Scope 2019

I-ACT for Children engagement in high priority projects in the pre-competitive and proprietary space

- **Innovative trial designs:** extrapolation, simulation, master protocols, inclusion of adolescents in adult trials
- **Innovative methodology**: Bayesian methods, adaptive designs
- Model-informed drug development and MOA-based drug development
- **Landscape** and **feasibility** assessments
- Pediatric plans, PIPs, PSPs etc.
- **Independent expert position papers**
- **Implementation science**, including site identification and engagement
- Novel methods for **patient recruitment**
- **Developmentally appropriate endpoints/biomarkers**
- **Digital tools and technology** in pediatric trials
- **Pediatric-specific education** and training
- Human subject protection, bioethics, consent/assent
- **Data and safety monitoring**
- Pediatric formulations/delivery

Pediatric Product Development History



Increasing Trial Demand

Regulations in US and EU require pediatric trials for innovative medicines and devices

High Infrastructure Demand

Typically multicenter/multinational trials
Average of **1-3** patients per site per year

Trials Take Too Long

12-16 months to start up
Up to **15 years** to complete

Many Trials Stall or Fail

60% of trials stall
40% of trials fail
30% of sites never enroll a patient

- Progress in reducing gap in labelling for BPCA drugs and stimulating pediatric studies and labelling in PREA
- Some progress in reducing failed trials
- Still significant work to do and nearly a decade of pediatric off-label use in not acceptable
- Advances in innovation, product development infrastructure and public-private collaboration are key

Pediatric Drug Development Progress

- Pediatric regulations continue to be essential for catalyzing drug and device development
- Permanent pediatric legislation (FDASIA) has resulted in pediatric development moving more to a forethought than an afterthought
- Scientific advancement has yielded opportunity in pediatric therapeutics, with estimates that 30% of the current biopharmaceutical pipeline includes pediatric applications
- FDA's leadership in advancing innovative trial methodologies is foundational
  - Extrapolation, modeling and simulation, Bayesian methodologies, master protocols/platform trials
- FDA's engagement of the scientific and patient community continues to be critical

Pediatric Drug Development Progress

- Public-private collaboration has emerged as a mainstay in pediatric development
  - Critical Path Institute, I-ACT for Children, C4C (EU)
- Regulatory and development science are essential to reduce development risk and applications are advancing to practice
  - Natural history, biomarkers, endpoints, innovative designs and analytical methods, real world data
- Trial networks skilled in pediatric product development and implementation science are creating needed global sustainable infrastructure
  - PTN (NIH BPCA Program), Global Pediatric Trials Network (I-ACT for Children, DCRI), C4C (EU)

Still needed… as we go forward

- Culture change: protecting children *through* research and integration of research and care
- Consideration of pediatric development even earlier in the process and the responsibility of adult programs to inform pediatric product development and routine consideration of trial innovation as a methodology for pediatrics
- Science vs age as the driver of pediatric product development
- Closing the 9-year gap in labelling to not later than 2-3 years, ideally 0 years
- Evolution of models, regulations/policy to address underserved pediatric populations (e.g. neonates)
- Programs to maintain and grow the pediatric product development workforce
- Interoperable/sustainable global infrastructure designed to use innovative development and implementation science to close the gap and support novel approaches, including adaptive platform trials, diversity of trial subjects, and long-term safety assessment.

This is a time of significant progress and substantial optimism for closing the gap in pediatric product development…