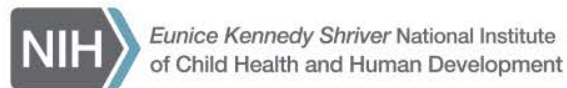


PRGLAC meeting: Lessons Learned from Pediatric Research

Implementation of NICHD'S Pediatric Drug Development Program
Best Pharmaceuticals for Children Act (BPCA)
February 26, 2018





Best Pharmaceuticals for Children Act

- The Need: 60-70% of drugs used in children NOT labeled for dosing, safety, effectiveness, or indication (*percentages ^^^ in neonates*)
- One (*of many needed*) Answer: Legislation
- Purpose: to implement a pediatric drug development program improve pediatric labeling of on-patent and off-patent drugs; to improve treatment in various therapeutic areas

BPCA Overview

BPCA Legislation

FDA (*On-patent)

NIH (*off-patent)

Pharmaceutical
Companies' Drug
Studies

Pediatrics Division
Oversight

Prioritization
Clinical Trials
Training



Contemporary Drug Development Paradigm

- Opportunity for profit – population to be treated
- Frequency, severity, chronicity of disease
- Pathophysiology of disease
- Pre-clinical testing for efficacy, safety, pk/pd
- *Clinical testing for efficacy and pk/pd
- FDA Approval
- Aggressive marketing and distribution

Where does
NIH fit?



“*Pediatric*” Drug Development...twists and turns*

Many issues hamper the testing of drugs in children. These include:

- The lack of incentives
- Ethical issues involving parental permission and the child's assent;
- Need for new technology to provide means to monitor patients and test very small amounts of blood;
- The unforeseeable nature of some clinical responses in immature individuals; leading to the possibility of unanticipated adverse reactions;
- The threat of effects on growth, development or health long after the drug's administration;
- Difficulty in predicting dose-response or concentration-response relationships by extrapolation from data obtained in adults;
- Need for a suitable infrastructure for the conduct of pediatric pharmacology research



NIH BPCA RECAP

PRIORITIZATION

- Identify drugs needing further study

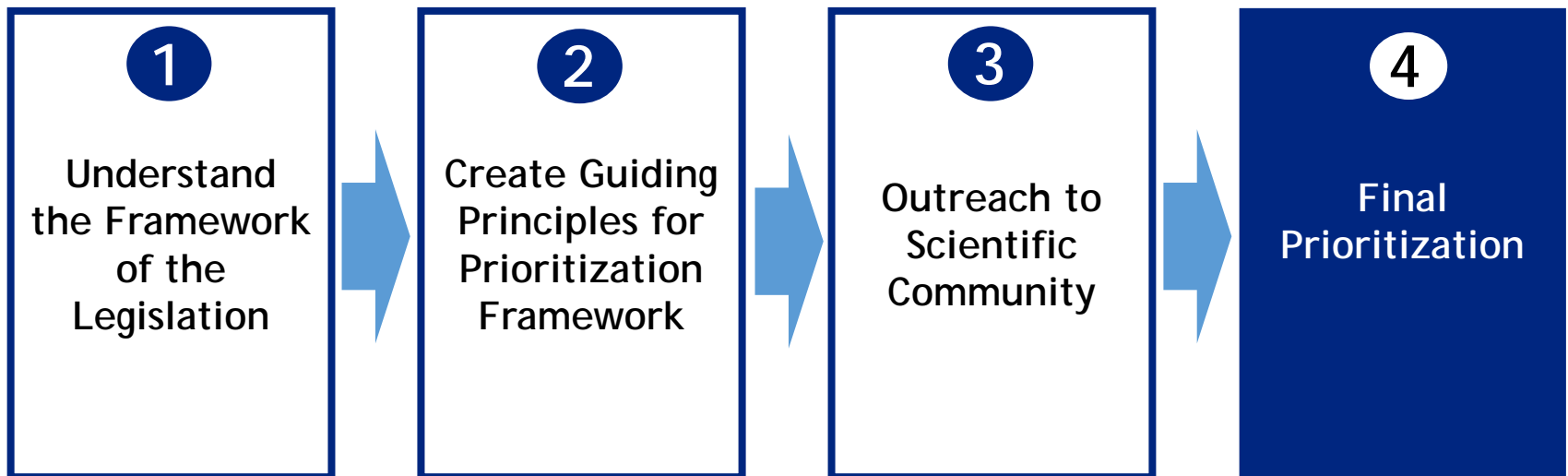
CLINICAL STUDY/LABELCHANGE

- Performing those prioritized studies
- Submitting to FDA



How to prioritize...

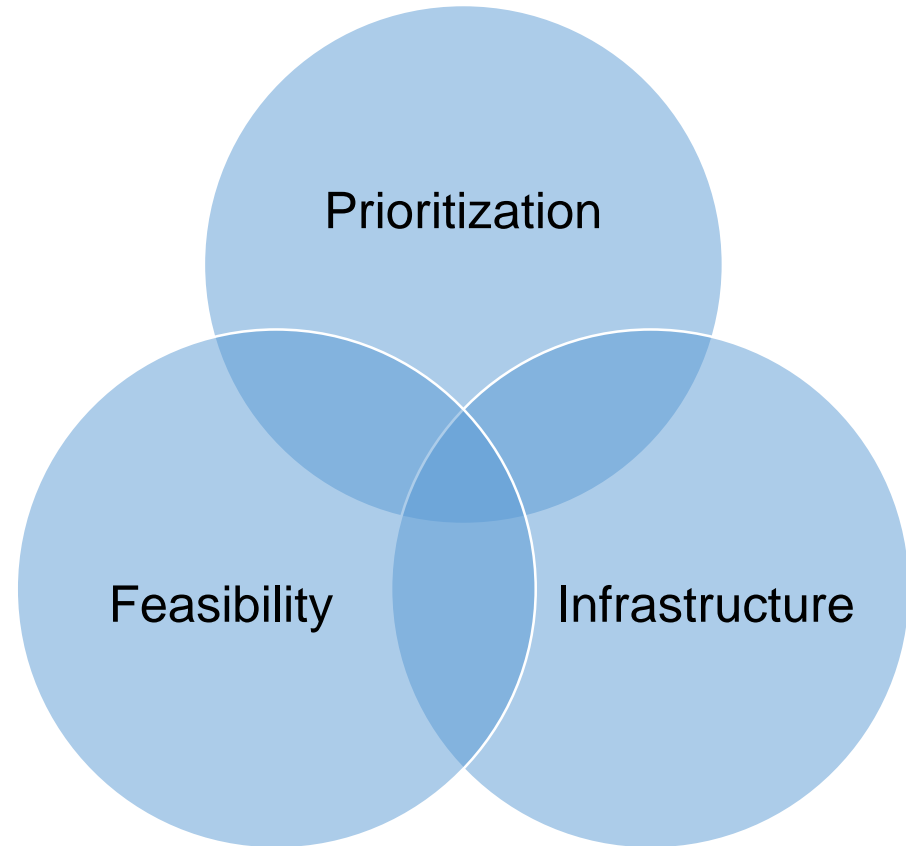
Over the years, OPPB has collaborated with pediatric experts to determine the greatest needs in pediatric pharmacology research. As it is not possible to pursue all such needs, NICHD has taken the following steps to define a priority setting process:





Prioritization Complexities

- Frequency of medication use in children
- Drug availability/cost
- Therapeutic index (including side effect profile)
- Use in life-threatening conditions
- Physicians preferences
- Patient factors
- Indications for use





Clinical Studies

Lessons learned 24 years later...

In Implementing Pediatric Drug Trials:

- Need for epidemiology data for the drug and the condition
 - Are people using this drug? What is the SOC (Indication/Approach)

- Need for data on the natural history of the disease and/or on the treatment effect
 - How to determine outcome measures of disease and endpoints for treatment effects

- Need for Pharmacokinetic and Statistical expertise up front (in protocol design)

- Practicalities of Conducting Pediatric trials, especially RCTs
 - Sample size/Recruitment
 - Expertise (PI and sites)/Training
 - Ethical concerns / Informed consent



Continuing Lessons

- Extrapolation
Key to feasibility in pediatric trials
- Collaboration



Current BPCA Clinical Program* Infrastructure

T32 Training

- NICHD
- NIGMS

U54 Centers Program

- CNMC
- University of Indiana
- SUNY Downstate
- UCSD
- Indiana University

Pediatric Trials Network

- Management
- Clinical Pharmacology
- Pharmacometrics
- Safety and Ethics
- Devices

Data Coordinating Center

- Regulatory Submissions
- Statistical Support
- Site monitoring/auditing

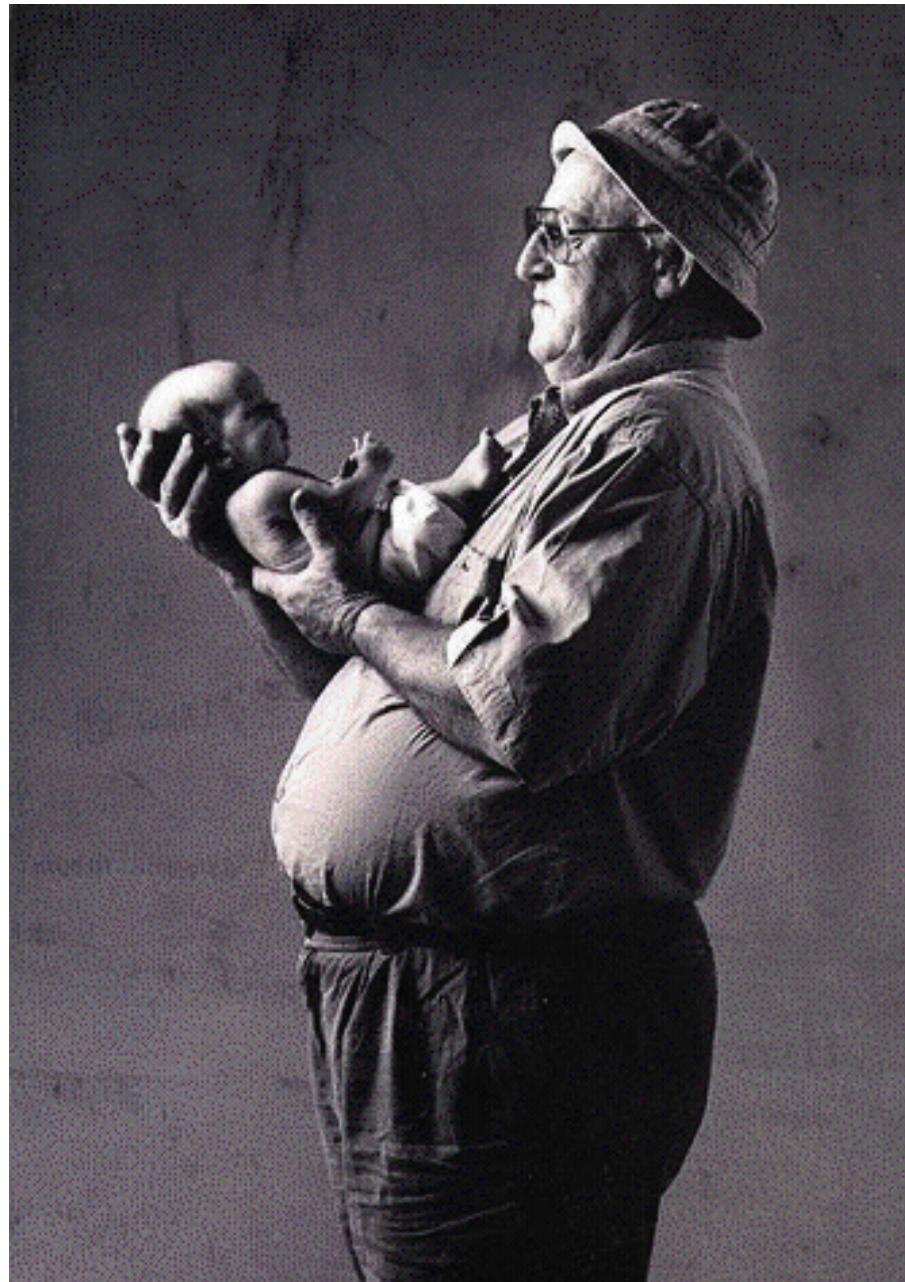


Progress

- Extensive range of therapeutics categories
Prioritized thus far:
 - ✓ >150 Drugs Listed to date
 - ✓ ~60 Drug Moieties studied to date
 - ✓ >20 Studies submitted for Label Change to date

" Pediatrics does not deal with miniature men and women, with reduced doses and the same class of diseases in smaller bodies, but....it has its own independent range and horizon..."

**Dr. Abraham
Jacobi, 1889**



Thank you

- NICHD Leadership
- Obstetric and Pediatric Pharmacology and Therapeutics Branch
 - Dr. Rohan Hazra
 - Dr. Zhaoxia Ren
 - Dr. Katerina Tsilou
 - Dr. George Giacoia
 - [Dr. Anne Zajicek]