DISCLOSURES

• I have no conflicts of interest to disclose
• I am funded by NIH and FDA to study new and existing therapeutic agents to improve outcome of newborn infants
• I Chair the Neonatal Advisory Committee in the Office of the Commissioner at the FDA. My presentation reflects my own opinions and does not necessarily represent the opinions of the FDA
Newborn Intensive Care

- 6% of the 4,000,000 births each year in the US require NICU admission
- Term (congenital defects, infection, respiratory distress) and preterm infants
- Prematurity rates (12%) place us 131st in the world; worst of any developed country
- Total cost of prematurity >$29 billion each year
- Only marginal improvements in outcome in the last 20 years – minimal drug development
Pediatric Initiatives

55% of Medicines Still Do Not Have Data in Labels to Guide Appropriate Use in Children

Proportion of medicines in Physician’s Desk Reference with information relating to children

- AAP Guidelines Issued
- PPRU launch
- US BPCA Renews “carrot”
- EU Pediatric Regulation “carrot & stick”
- US FDAAA Renews “carrot & stick”
- US FDASIA Makes “carrot & stick” permanent!

Key initiatives


Proportion: 78% Yes, 22% No

Proportion: 54% Yes, 46% No
Registered Trials in ClinicalTrials.gov*

*Children represent 20% of the population; only 300 registered studies involve neonates
Pediatric Studies are Not Enough, How About Neonates?

Studies must be clinically relevant

- Of 406 medicines studied in the pediatric population to achieve 6 months of exclusivity, only 28 (or 7%) had been studied in neonates
- These 28 drugs are rarely used
- Priorities of academic community, regulators, and industry not well aligned

1 Stiers, J., et al. Newborns, One of the Last Therapeutic Orphans to Be Adopted. JAMA Pediatrics,
Pediatric Mission

- Provide a national forum to identify collaborative opportunities to facilitate child health clinical and translational research
- Set priorities and increase visibility for child health research
- Build partnerships (industry), sustainable infrastructure
- Identify barriers, develop solutions
- Improve outcomes through high quality science
Point Person Project: Multisite Clinical Trials

- Modeled after the Finnish project to increase opportunities, lower costs, improve efficiency
- A Point Person designated at 55 sites to review and respond to child health collaborative opportunities
- Point Person functioned as a navigator – directed trial opportunities to local investigators with appropriate expertise and potential interest
- This contact also used by industry or individual investigators for protocol development / implementation
Point Person Project: Protocols

- 23 protocol synopses distributed in the 1\textsuperscript{st} year with 40/55 sites actively participating
  - Source:
    - 15 CRO
    - 6 Industry
    - 2 Individual Investigators
  - Disease Focus
    - Wide range of disorders affecting children
  - Age Range
    - Newborn to Adolescent
- After a review of the full protocol, 50\% of interested investigators decided not to participate
Reasons for Not Participating

- Lack of appropriate subjects
- Complex study design
- Problems with inclusion, exclusion criteria
- Concern over safety of proposed study drug
- Lack of study support staff
- Source of study (Industry)
- Competing trial
- 20% of protocols withdrawn by Sponsor after protocol review
Developing Drugs for Infants & Children: National and Global Efforts

- Designing neonatal studies is “Team Science” - pediatricians, pharmacologists, statisticians, bioethicists, regulators, support staff, Industry sponsors, foundations, families
- Early in the protocol development phase
- Better communication/collaboration among FDA, NIH, Industry, CROs, and Academia
- Global network initiatives most promising, especially for rare diseases
Global Initiatives to Facilitate Neonatal Drug Development

- Multisite clinical trials with sites from US, EU, and Canada conducting the same protocol
- Enabled by better communication among regulatory agencies – FDA, Critical Path Inst
- All key stakeholders agree on study design and outcome measures
- Approval in multiple countries - save years off the development process (most attractive to industry)
Partners and Stakeholders

- Patients/Families
- Patient Advocacy Groups
- Clinicians & Nurses
- Professional Societies
- Hospitals, Health Centers & Systems
- Research Investigators & Staff
- Industry

- Government
- Regulators
- Payers
- Public
- Research Agency Funders
- Research Ethics Boards
Stakeholders
- Pharmaceutical Companies
- Professional Organizations
- Patient Advocacy Groups
  - Academia
  - Others

Neutral Third Party Convener (501C3)

Neonatal Consortium

Coordinating Committee

Clinical Trial Designs

Data Standards

Biomarkers

PBPK Modeling

Standard of Care

Outcome measures

Review/Feedback From Partners/FDA/Others
Common Conditions in the NICU

- **Neonatal Brain Injury**: Prevention and treatment of seizures, asphyxia, stroke, intraventricular hemorrhage (IVH) and white matter injury (WMI), leading factors in the development of neurodevelopmental impairment (NDI)
- **Neonatal Lung Injury**: Prevention and treatment of Bronchopulmonary Dysplasia (BPD) and Persistent Pulmonary Hypertension of the Newborn (PPHN)
- **Neonatal Gastrointestinal Injury**: Prevention and treatment of Necrotizing Enterocolitis (NEC)
- **Perinatal Infection**: Prevention and treatment of bacterial and viral infections
- **Retinopathy of Prematurity (ROP)**: Prevention and treatment
- **Neonatal Abstinence Syndrome (NAS)**: Treatment of the withdrawal that results from *in utero* exposure to opiates
- **Prevention of preterm labor and delivery**
Advancing Maternal - Child Health

Sustainable Infrastructure

Global Networks

Knowledgeable Workforce

Efficient Regulatory Processes