

Challenges in Newborn Drug Development – US Perspective

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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

Key initiatives

AAP Guidelines Issued

PPRU launch

US FDAMA "carrot"

ICH E11 Guidelines

US BPCA Renews "carrot"

EU Pediatric Regulation "carrot & stick"

US FDAAA Renews "carrot & stick"

PPRU sunset

US FDASIA Makes "carrot & stick" permanent!

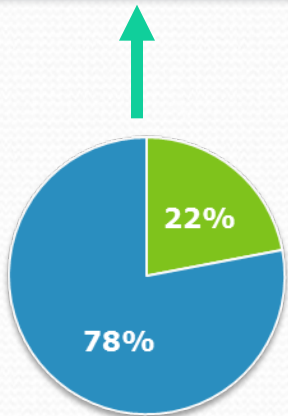
1970

1980

1990

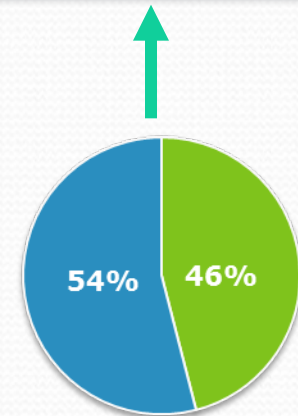
2000

2010



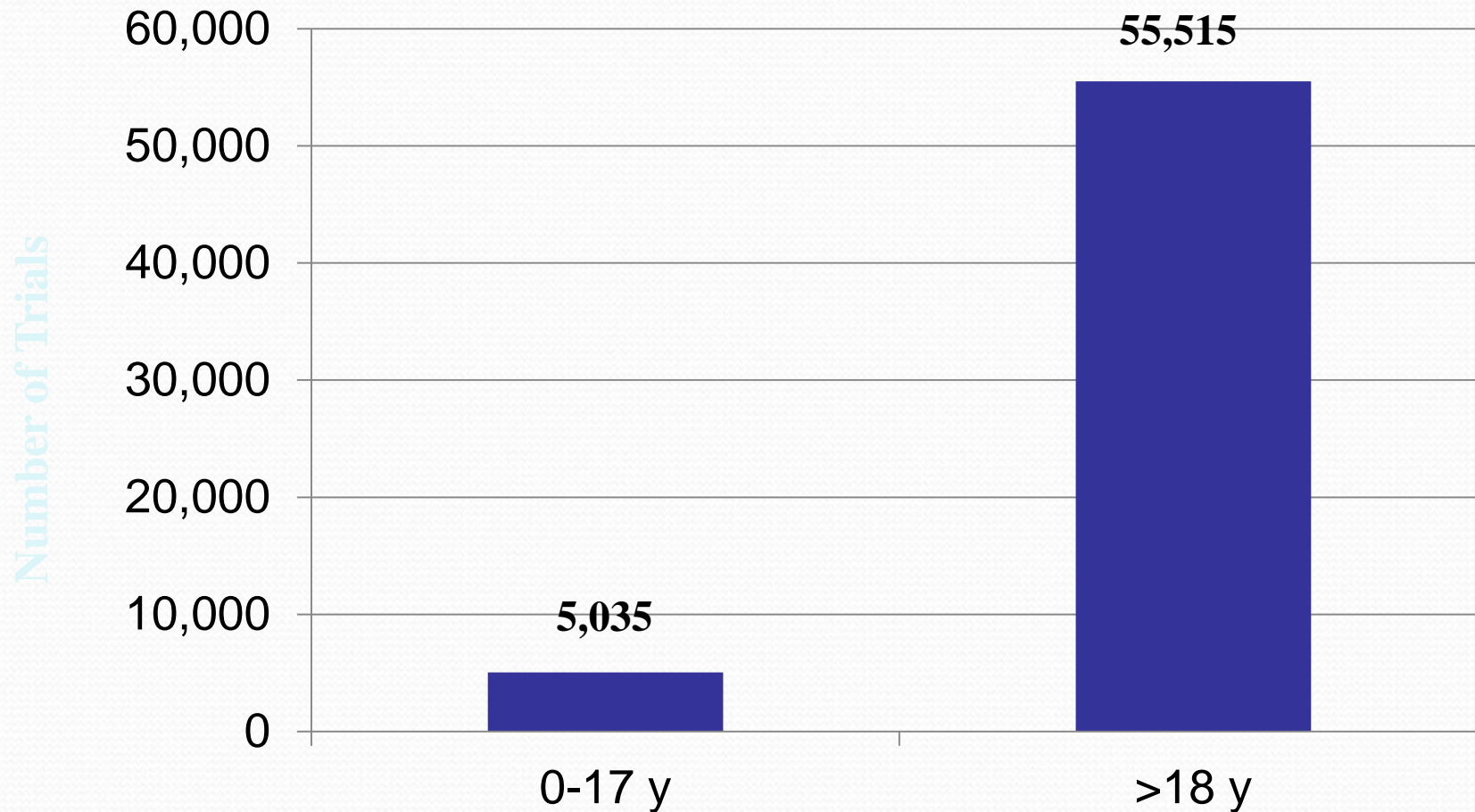
■ Yes
■ No

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



■ Yes
■ No

Registered Trials in ClinicalTrials.gov*



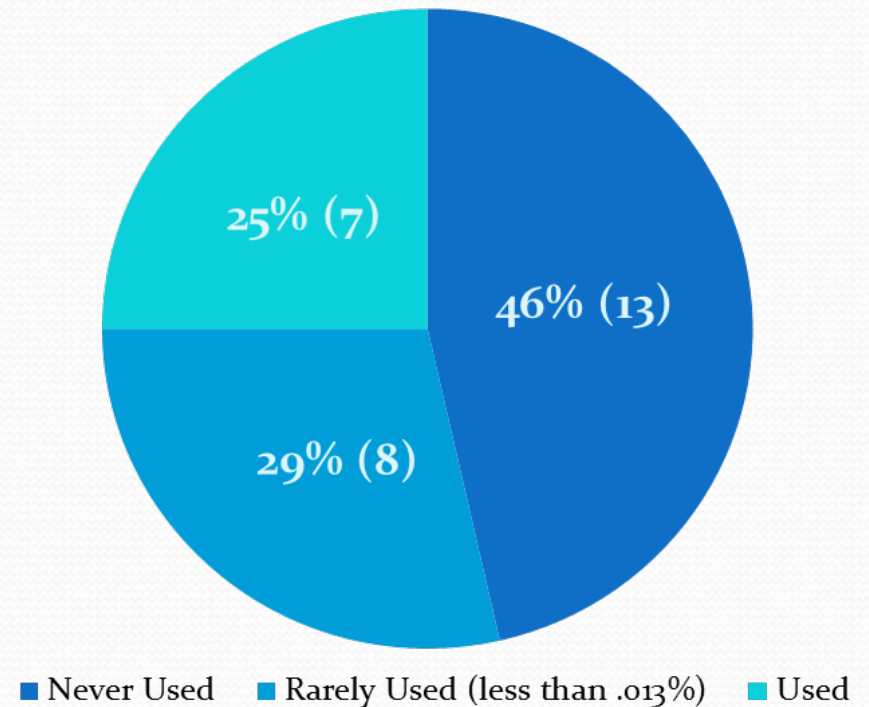
***Children represent 20% of the population; only 300 registered studies involve neonates**

Pediatric Studies are Not Enough, How About Neonates?

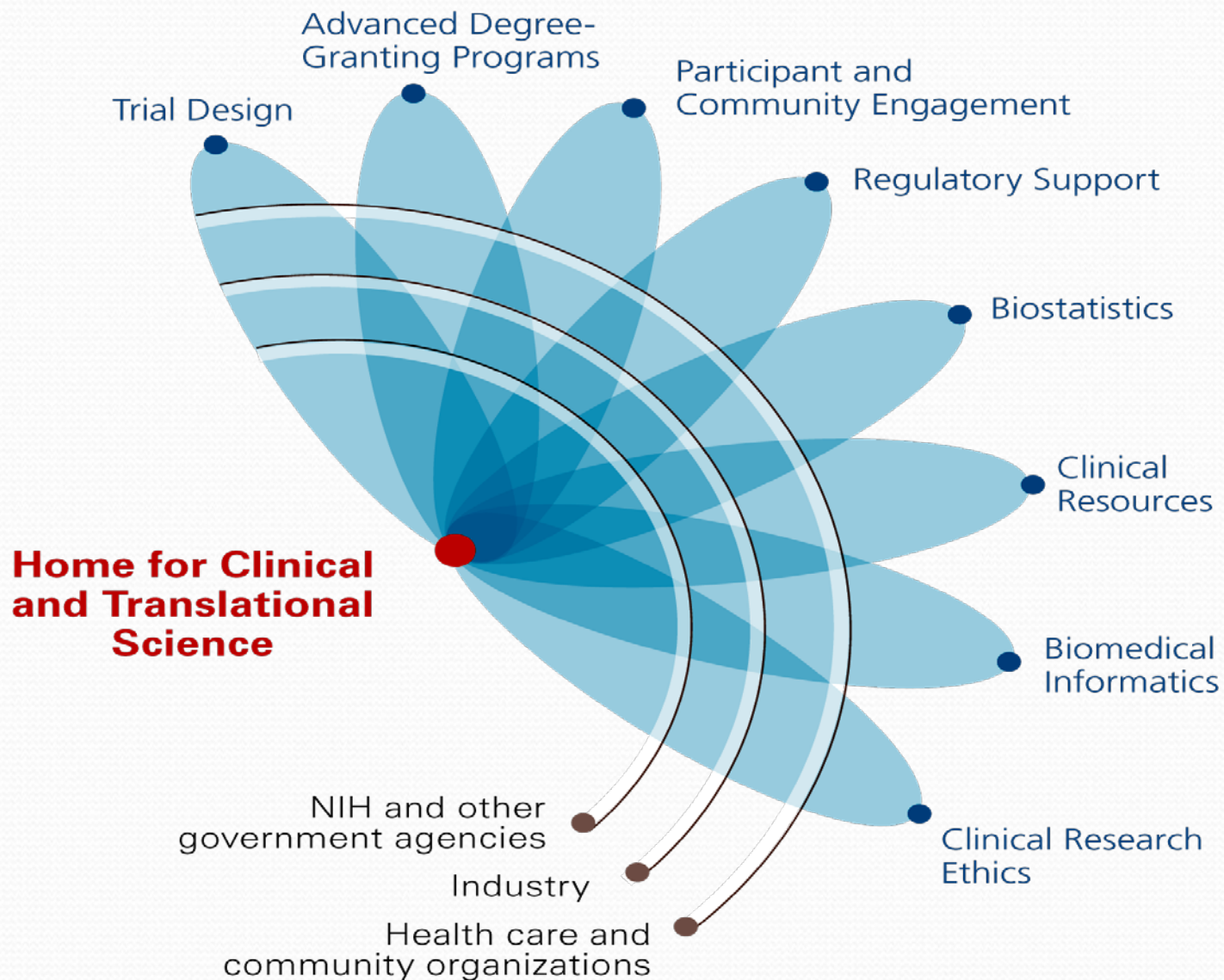
Studies must be clinically relevant

- 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

% of Medicines Studied in Neonates
N = 28



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



Visit CTSAcentral.org to learn more.

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**

Visit CTSAcentral.org to learn more.

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**

Visit CTSAcentral.org to learn more.

Point Person Project: Protocols

- **23 protocol synopses distributed in the 1st 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**

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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

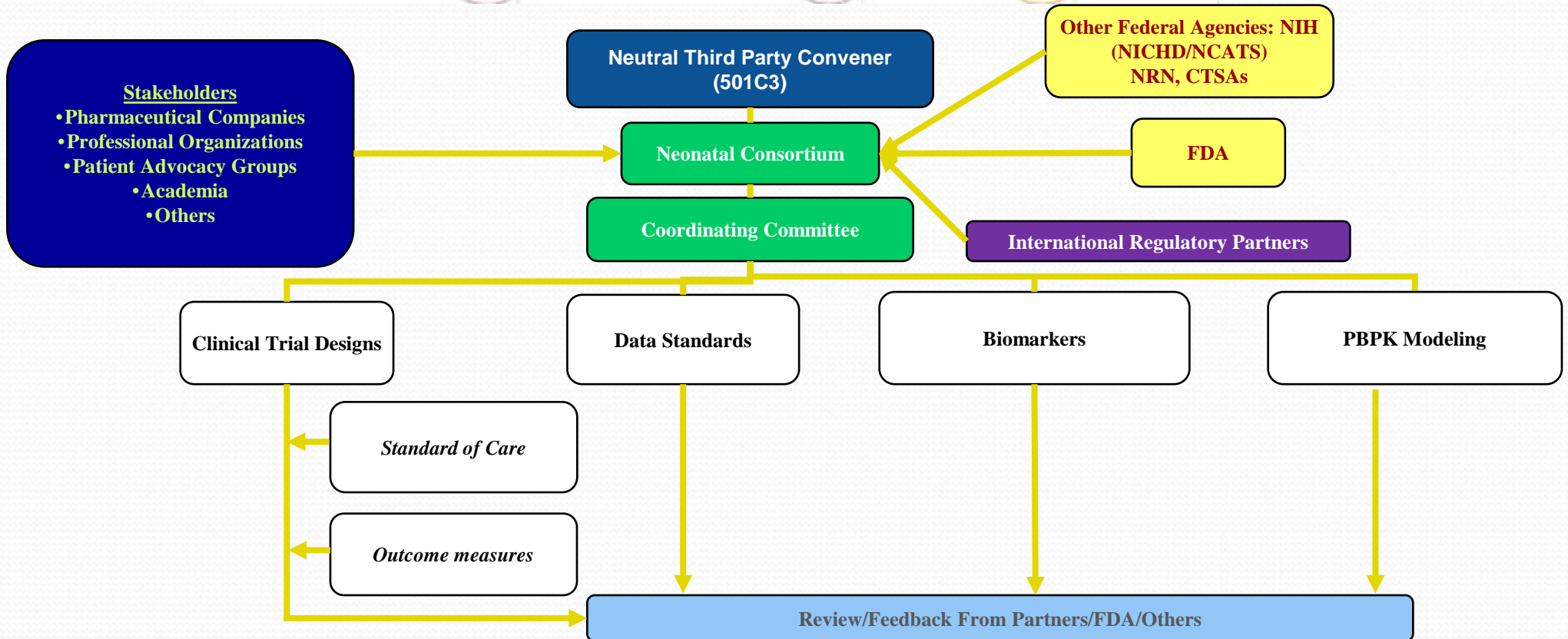
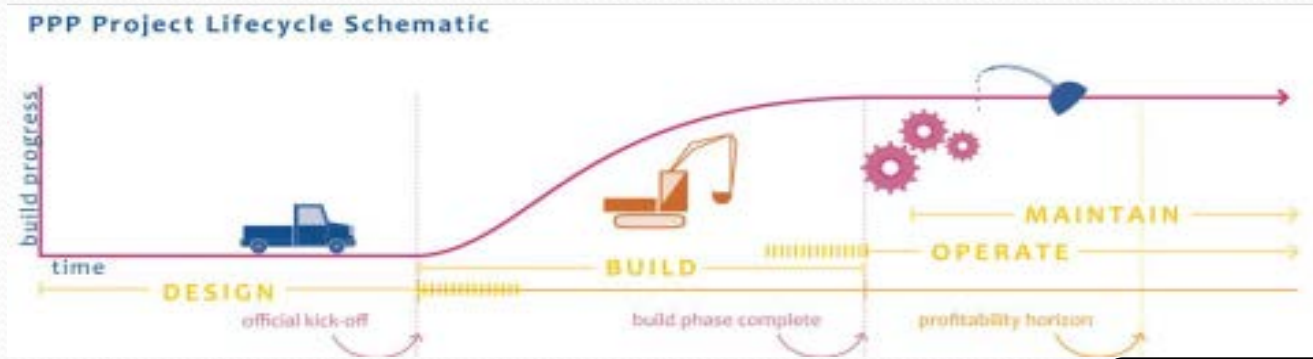
Public

Research
Agency
Funders

Research
Ethics
Boards



Neonatal Consortium Concepts



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**
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Advancing Maternal - Child Health

Sustainable
Infrastructure

Global
Networks

Knowledgeable
Workforce

Efficient
Regulatory Processes

