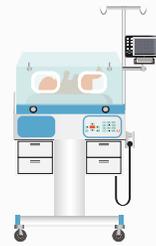


## Critical Path Institute's International Neonatal Consortium (INC)

- Public-private partnership of diverse stakeholders consisting of Industry members, academic researchers, nurses, families, and regulators
- Mission to accelerate drug development in neonates
- Operating as a pre-competitive collaboration to:
  1. Address the measurement and assessment of clinical outcomes in neonates, through teams that share data and expertise to advance regulatory science
  2. Improve the predictability of neonatal drug development

## INC AND THE NICU

The INC concentrates its efforts on those conditions most commonly encountered in neonatal intensive care units (NICUs), and on the prevention of preterm birth.



- NEONATAL LUNG INJURY AND CIRCULATORY FAILURE
- RETINOPATHY OF PREMATURITY (ROP)
- NEONATAL GASTROINTESTINAL INJURY
- NEONATAL BRAIN INJURY
- PERINATAL/NEONATAL INFECTIONS
- DRUGS TO PREVENT PRETERM LABOR
- HEMODYNAMIC ADAPTATION (HA)
- NEONATAL ABSTINENCE SYNDROME (NAS)/  
NEONATAL OPIOID WITHDRAWAL SYNDROME (NOWS)



## UNMET DRUG DEVELOPMENT NEEDS IN NEONATES

- Neonates are therapeutic orphans
- Last drug that significantly impacted survival in preterm neonates was approved over 30 years ago
- Clinical trial activity in neonatal population remains limited (<1% of currently registered trials are in neonates)
- Vast majority of drugs (>60-90%) in this population are used off-label<sup>1</sup>, which greatly impacts an objective evaluation of safety and efficacy of these drugs



## CHALLENGES IN DRUG DEVELOPMENT IN NEONATES

- There are significant temporal changes in neonatal physiology by gestational and postnatal age, concurrent illness, and underlying disease. These changes have not been described in sufficient detail to allow predictable drug development
- Most commonly used laboratory values have not been defined in neonates, which greatly limits their utility as markers of adverse events
- The currently used adverse event reporting system is heterogeneous and not tailored to neonates
- There are differences in how various neonatal research processes are perceived by key stakeholders integral to the care of neonates in the NICU
- Insufficient multidisciplinary working and engagement with families and nurses to promote research in NICUs
- These issues increase the cost of doing trials and aggravate safety concerns, which greatly impacts the feasibility of conducting clinical trials in this small population of neonates



## MOVING NEONATOLOGY RESEARCH TOWARDS DRUG DEVELOPMENT SOLUTIONS

**Neonatal Adverse Event Severity Scale:** An effort to standardize safety assessment and reporting in neonatal clinical trials

- Recognition and classification of adverse events in the neonatal population is challenging because of complex physiology, multi-organ system involvement, and symptoms not similar to classification systems in adults and older children
- INC developed and published a standardized 5-grade, 35-point Neonatal Adverse Event Severity Scale that will make safety reporting more reliable and comparable across neonatal clinical trials<sup>2</sup>
- This scale has been published on the NCI/NIH website<sup>3</sup>, translated into Japanese, and is being adopted by regulatory agencies for safety reporting in neonatal clinical trials

### Standardizing measurements of Blood Pressure (BP) in neonates

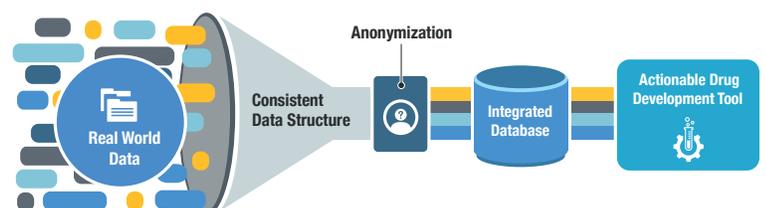
- Current gold standard methods of accurately measuring BP in neonates involve invasive methodologies
- INC's Hemodynamic Adaptation workgroup provided recommendations based on a systematic review and analysis of published literature on methods of measuring BP in neonates<sup>4</sup>
- These recommendations will form the basis of a standardized BP measurement protocol in neonates, reduce variability as well as improve routine clinical care



## REAL WORLD DATA ANALYTIC PLATFORM (RW-DAP) PROJECT

INC has been awarded FDA funding to create a RW-DAP. This project will involve aggregation, standardization and integration of patient-level EMR real-world data to:

- Establish reference laboratory value ranges by gestational and postnatal age
- Construct a quantitative disease progression model for Bronchopulmonary Dysplasia





## INC MEMBERSHIP

INC Membership consists of a diverse array of organizations spanning the globe.



### Neonatal Nurses

- National Association of Neonatal Nurses (USA)
- The Council of International Neonatal Nurses (USA)

### Pharmaceutical Companies

- Bayer (Germany)
- By Heart
- Chiesi (Italy)
- Eli Lilly (USA)
- Infant Bacterial Therapeutics (Sweden)
- Johnson & Johnson (USA)
- Novartis (Switzerland)
- Pfizer (USA)
- Sanofi (France)
- Takeda (Japan)
- Trove Therapeutics (USA)

### Families/Advocacy Organizations

- Bliss (UK)
- EFCNI (Germany)
- I-ACT (USA)
- March of Dimes (USA)
- NEC Society (USA)
- NICU Parent Network (USA)
- Once Upon a Premie
- Premieworld (USA)
- Speaking for Moms and Babies, Inc. (USA)

### Academic Researchers from Institutions Located in:

- Australia (1)
- Canada (5)
- Europe (11)
- Japan (5)
- UK (9)
- USA (24)

**Thank you for everything you do. We look forward to your support in making a meaningful and positive impact in the lives of neonates worldwide!**

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## FOSTERING INNOVATION

The INC enables **pre-competitive collaboration** with industry, academic researchers, nurses, family and parent organizations, and regulatory agencies to enable **evidence-based science** for all stakeholders.



## OTHER 2019-2020 SUCCESSES

- 2019 Held public webinar sharing the results of a multi-stakeholder survey on "The Culture of Communication Regarding Research in Neonatal Intensive Care Units"
- 2019 Developed a scale to define a common source of blindness in preterm infants<sup>5</sup>
- 2019 Developed framework to identify and treat neonatal gastrointestinal injury<sup>6</sup>
- 2019 Published recommendations about neurodevelopmental follow-up<sup>7</sup>
- 2020 PAIN workgroup established to address validated endpoints for evaluating treatment of pain in infants with the potential expansion of existing drug labels
- 2020 Added parent/family and nurse representation to the INC Leadership team



## 2020-ONWARDS OBJECTIVES

- **Data Sharing Initiative:** Neonatology is a data-rich community. In the upcoming years, INC will work towards implementing a data sharing and aggregation model which will accelerate drug development in this population. We will build on C-Path's expertise in data aggregation, collation, curation, analysis, and regulatory submissions.
- **Multidisciplinary contributions to research, and emphasis on family involvement in research**
- **Evaluating how conditions during pregnancy impact neonatal development**