INC
CRITICAL PATH INSTITUTE

International Neonatal Consortium

May
18–19, 2015

Applying Regulatory Science to Neonates:

Launch of the International Neonatal Consortium

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10 YEARS

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Introduction

Welcome to the launch of the International Neonatal Consortium (INC). INC is a coalition of industry, academia, patient representatives, the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), other governmental agencies, professional organizations, foundations and the Critical Path Institute (C-Path) that will focus on accelerating the development of safe and effective treatments for neonates.

The initial workshop that led to the formation of the consortium was held at the FDA on October 28–29, 2014 and co-sponsored by the FDA, Critical Path Institute (C-Path), and the Burroughs Wellcome Fund. With the recognition that individual organizations lack the requisite data, resources, or expertise to tackle the gaps in regulatory science for neonates, participants discussed collaborative approaches for addressing the most pressing needs of this underserved population.

Today and tomorrow we will collectively prioritize an array of high-impact initiatives for conditions that are commonly observed in neonatal intensive care units. By applying a consensus science model and working directly with regulators, INC will develop practical tools that can be incorporated into clinical trials for neonates.

We look forward to your active engagement, both in these discussions and the follow-up collaborative activities that will lead to more successful, efficient trials and provide neonates with better treatments.

Ralph Bax and Lynn Hudson, Workshop Co-Organizers
Workshop Planning Committee:

- Ralph Bax, MD (European Medicines Agency)
- Jon Davis, MD (Tufts University)
- Lynn Hudson, PhD (Critical Path Institute)
- Sam Maldonado, MD, MPH, FAAP (Johnson &Johnson)
- Susan McCune, MD, MA Ed (U.S. Food and Drug Administration)
- Ron Portman, MD (Novartis)
- Stephen Spielberg, MD, PhD (Drug Information Association)
- Mark Turner, PhD (University of Liverpool)

Meeting Objectives

- Reach consensus on priority project(s) to accelerate the development of therapeutics for the neonatal population
- Initiate collaborations on priority projects to develop safe and effective treatments for neonates

Session Objectives

- Provide the rationale for forming a new neonatal consortium
- Define “regulatory science” and how it relates to treating neonates
- Describe the projects the new consortium could take on
- Explain the role of C-Path in an International Neonatal Consortium
- Explore what sources of data may be available for consortium projects
- Prioritize consortium projects

Agenda

May 18, 2015

11:00 a.m. ***Welcome and Overview***
LYNN HUDSON, Critical Path Institute (C-Path)
JORDI LLINARES GARCIA, European Medicines Agency (EMA)

11:10 a.m. ***The Value of a Neonatal Consortium: A Regulator's Perspective***
RALPH BAX, European Medicines Agency (EMA)

11:30 a.m. ***The ABCs of Regulatory Science***
SUSAN McCUNE, U.S. Food and Drug Administration (FDA)

11:50 a.m. ***Moving Neonatology into the Modern Era of Drug Development: Overview of potential consortium projects and deliverables***
STEPHEN SPIELBERG, Drug Information Association
RON PORTMAN, Novartis
MARK TURNER, University of Liverpool
WOLFGANG GÖPEL, German Neonatal Network

1:00 p.m. **Lunch available at EMA**

2:00 p.m. ***The C-Path Vision: Sharing Data and Expertise to Accelerate the Development of Safe and Effective Therapies for Neonates***
MARTHA BRUMFIELD, Critical Path Institute (C-Path)

2:20 p.m. ***Data for Executing the Consortium's Research Plan***
Participants will identify sources of data, types of available data (clinical trial, registry, longitudinal studies), and data standards.
Moderator: TOM DIACOVO, Columbia University
NEENA MODI, Imperial College
BRIAN SMITH, Duke University
DOMINIQUE HAUMONT, St. Pierre University Hospital

3:20 p.m. ***Results of the Pre-Workshop Survey***
PAMELA SIMPKINS, Johnson & Johnson

3:30 p.m. **Transfer to Hilton for Breakout Sessions**

4:00 – 6:00 p.m. **Breakout Sessions at Hilton**

Each breakout session will be facilitated by 1-2 moderators and one C-Path staffer and will include subject matter experts and representatives from academia, industry, regulatory agencies, and foundations. The breakout groups will consider both therapeutic areas and projects that could be conducted in those therapeutic areas.

Breakout #1: Neonatal Brain Injury

HEIKE RABE, MODERATOR
NEIL MARLOW, MODERATOR

GERALDINE BOYLAN
SERENA COUNSELL
MARIANA CATAPANO
DAVID EDWARDS
NICK HALL
GIOVANNI LESA
BARRY MANGUM
VANIA OLIVEIRA
MEHALI PATEL
RON PORTMAN
RONIT PRESSLER
AGNES SAINT-RAYMOND
PRAKASH SATODIA
LINDA STORARI
GERT VAN STEENBRUGGE
LYNN HUDSON, C-Path

By Telecon

ALBERT ALLEN
ROBIN HUFF
KAREN LUYT
STANLEY ZENGEYA
QING ZHAO

Breakout #2: Neonatal Lung Injury

ROBIN STEINHORN, MODERATOR
MARY SHORT, MODERATOR

WOLFGANG GÖPEL
ANNE GREENOUGH
MAREK MIGDAL
VADIVELAM MURTHY
CECILE OLLIVIER
THORSTEN OLSKI
DOBROMIR PENKOV
P. BRIAN SMITH
STEPHEN SPIELBERG
MARTHA BRUMFIELD, C-Path

By Telecon

CHRISTINA BUCCI-RECHTWEG
VALENTINO COMITO
DOLORES ELORZA
LISA BETH FERSTENBERG
DARREL HEISELMAN
ROSEMARY HIGGINS
SHINYA HIRANO
SATOSHI KUSUDA
MARY PURUCKER
ANNE ZAJICEK

Breakout #3: Neonatal Gastrointestinal Injury

KATE COSTELOE, MODERATOR

TOM DIACOVO
NEENA MODI
CHRISSI PALLIDIS
LUANA PESCO KOPLOWITZ
YOSHIHIKO SANO
ALAN BEDRICK, C-Path

By Telecon

AGNES V KLEIN

Breakout #4: Neonatal Sepsis

DANNY BENJAMIN, MODERATOR
CATHERINE SHERWIN, MODERATOR

RAAFAT BISHAL
PAUL HEATH
ANDREA ECKER
SAM MALDONADO
MIN-SOO PARK
CHARLIE THOMPSON
MARK TURNER
SABITA UTHAYA
SIRI WANG
LIZ WALKER, C-Path

By Telecon

ARIEL ARIAS
CYNTHIA JACKSON

Breakout #5: Retinopathy of Prematurity (ROP)

BOUBOU HALLBERG, MODERATOR

GILL ADAMS
IRMGARD EICHLER
ALISTAIR FIELDS
DINA APELE FREIMANE
AGNES GYURASICS
MELISSA S. H. LIEW
JANE MOSELEY
HIDE NAKAMURA
STEVE BROADBENT, C-Path

By Telecon

ROBERT MARTIN
EVA-MARIA SIMANK
DAVE TRUEBLOOD

Breakout #6: Neonatal Abstinence Syndrome

JOHN VAN DEN ANKER, MODERATOR

KAREL ALLEGAERT
ROBERTO DE LISA
CHRISTINE GLEASON
PAMELA SIMPKINS
MERRAN THOMSON
PAOLO TOMASI
ALICIA WEST, C-Path

By Telecon

WAKAKO EKLUND
CECILIA FALKENBERG

6:30 p.m. ***Working Dinner at the Hilton: Incorporating the Voice of Families***

Panel representing families, neonatal and children's advocacy groups, foundations, and neonatal nurses

Moderator: NICK HALL, Graham's Foundation
SILKE MADER, European Foundation for the Care of Newborn Infants (EFCNI)
MEHALI PATEL, Bliss
G.J. VAN STEENBRUGGE, Vereniging van Ouders van Couveusekinderen (VOC)
WAKAKO EKLUND, National Association of Neonatal Nurses (NANN)
CHARLIE THOMPSON, iCAN

8:30 p.m. **Close of Day One**

May 19, 2015

9:00 a.m. **Reconvene at EMA**

The two subject matter leaders of each breakout session will include the initial prioritization of Consortium projects and identify three potential projects.

Moderator: SAM MALDONADO, Johnson & Johnson

10:30 a.m. **Coffee Break**

11:00 a.m. **Expert panel sessions begin**

JON DAVIS, Tufts University, Co-chair
ROSEMARY HIGGINS, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), Co-chair

12:00 p.m. **Lunch**

1:00 p.m **Expert panel sessions continue**

MARK TURNER, University of Liverpool, Co-chair
CHRIS GLEASON, University of Washington/March of Dimes, Co-chair

2:00 p.m. **Expert panel sessions continue**

CHARLIE THOMPSON, Pfizer, Co-chair
ANNE ZAJICEK, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), Co-chair

3:00 p.m. **Closing session**

RALPH BAX, European Medicines Agency (EMA)
MARK TURNER, University of Liverpool
CHARLIE THOMPSON, Pfizer
NICK HALL, Graham's Foundation
ALAN BEDRICK, Critical Path Institute (C-Path)

Participants will evaluate projects using preset criteria. Each participant will also identify how they or their organization could contribute to specific projects.

3:30 p.m. **Close of Workshop**

Priority Therapeutic Areas and Project Areas

Priority Therapeutic Areas based on conditions commonly observed in Neonatal Intensive Care Units (NICUs):

- **Neonatal Brain Injury:** For Term infants – Prevention and treatment of seizures, asphyxia, stroke. For Preterm infants – Prevention and treatment of severe intraventricular hemorrhage (IVH) and white matter injury (WMI), both leading factors in the development of Cerebral Palsy (CP)

- **Neonatal Lung Injury:** Prevention and treatment of Bronchopulmonary Dysplasia (BPD) and associated pulmonary hypertension. Prevention and treatment of Persistent Pulmonary Hypertension of the Newborn (PPHN)

- **Neonatal Gastrointestinal Injury:** Prevention and treatment of Necrotizing Enterocolitis (NEC)

- **Neonatal Sepsis:** 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

Priority Project Areas

- **Standardized methods and consensus-derived standards-of-care**, which could include draft master protocols, general guidance on standardizing assessment and collection methods for the conduct of clinical trials in neonates, and consensus-derived optimal clinical endpoints. Innovative trial designs tailored to this population as well as trial designs for a particular class of drugs could also be developed.

- **Draft position papers to assist the regulatory agencies in preparing guidance** on the appropriateness of extrapolation of research results from other populations to the neonatal population.

- **Revised definition of neonates** to take into account - physiology, etc.

- **Draft decision criteria for conducting clinical trials of new therapies**, including recommendations on which pharmacologic agents are best suited for intervention trials in the neonate.

- **Drug Development Tools** endorsed or qualified by the regulatory agencies for a specific context of use. Such tools can also be used to evaluate interventions designed to prevent pre-term birth.

    - Safety and Efficacy Biomarkers

    - Clinical Outcome Assessments (COA)

    - Modeling approaches such as physiologically based pharmacokinetic and disease progression models, as well as clinical trial simulation tools.

- **Guidance on safer formulations** encompassing ease of administration, including drugs that are used to prevent or treat pre-term labor.

- **Applying personalized medicine to the treatment of neonates.**

Questions to be Addressed by each Breakout Group

1. What indications in this therapeutic area (e.g. neonatal lung injury) are in most need of effective therapies? Include an estimate of the incidence and the severity of the indication.

2. What non-clinical studies need to be carried out prior to designing clinical trials of new and/or existing drugs?
    a. What juvenile animal toxicity studies are needed?
    b. Are animal models available for the indication (e.g. gestational age equivalent)?
    c. Can the non-clinical data be extrapolated to inform clinical development, including initial dosing?

3. For each indication, what information would be needed before starting a clinical trial?
    a. Can existing pediatric or adult studies be extrapolated to neonates?
    b. Could a master protocol be developed for use when evaluating treatments for this indication?
    c. Would the use of different drug classes alter the inclusion/exclusion criteria?
    d. Do the inclusion criteria drive formulation, mode of administration and/or dose?
    e. What parameters are needed for constructing a meaningful modelling and simulation tool?

4. Are there impediments to establishing a master protocol (do multiple approaches exist – comparative effectiveness studies)? Is there equipoise?

5. What potential biomarkers and clinical trial endpoints could be used?
    a. Are adequate clinical outcome measures available? If not can they be developed?
    b. Are any prognostic, predictive, pharmacodynamic, and safety biomarkers available? Are any regulatory ready?

6. What long-term outcome measures are available to assess the safety and efficacy of the therapy?

7. In light of your responses to Questions 1-6, where are the gaps in knowledge and how would you prioritize the studies needed to approach this indication?

Sponsors and Supporters

Applying Regulatory Science to Neonates: Launch of the International Neonatal Consortium (INC) is co-sponsored by the European Medicines Agency.

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This workshop is supported in part by contributions from the Burroughs Wellcome Fund, the March of Dimes and Graham's Foundation.

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