Duke | MARGOLIS CENTER *for* Health Policy

Advancing Endpoint Development for Preterm Neonates with Pulmonary Morbidities

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Preterm neonates are often at risk of ongoing pulmonary morbidity, particularly due to developmental immaturity of the lungs at birth as well as damage caused by mechanical ventilation and long-term use of supplemental oxygen. One measure of pulmonary morbidity is captured by a diagnosis of bronchopulmonary dysplasia (BPD), which has been typically defined as the need for oxygen, with or without positive pressure respiratory support, at 36 weeks post-menstrual age (PMA) or "corrected" age. In clinical trials designed to improve pulmonary and respiratory outcomes, the most commonly used endpoint has been BPD. However, there is no consensus on whether BPD is a clinically meaningful endpoint to predict pulmonary and respiratory outcomes at infancy, childhood, and beyond. Therefore, it can be challenging to encourage the development of products in this space because there is uncertainty over whether BPD is an optimal efficacy endpoint for regulatory submissions.

Efforts are underway to support the development of validated efficacy endpoints, including Clinical Outcome Assessments (COAs), that incorporate longer-term improvement or changes in pulmonary outcomes and are more data-driven. However, there are outstanding questions about how best to support the development of such endpoints. This expert workshop will provide stakeholders the opportunity to explore and discuss the work that has been done to date, highlight gaps and limitations in existing data and research, and identify a path forward to develop validated endpoints and COAs that better represent short- and long-term outcomes associated with pulmonary morbidities of prematurity.

9:00 a.m. **Welcome and Introductions**
Gregory Daniel, Duke-Margolis Center for Health Policy

9:10 a.m. **Opening Remarks from FDA**
Susan McCune, U.S. Food and Drug Administration

9:20 a.m. **Session I: Current State of Research and Challenges in Developing Endpoints for Preterm Neonates with Pulmonary Morbidities**

Objective: Provide an overview of how today's workshop fits into broader efforts to advance the science on endpoints for preterm neonates with pulmonary morbidities, as well as the key issues and current limitations in this space

Presentation: Overview of preterm respiratory disease in the NICU

- *Judy Aschner, Albert Einstein College of Medicine*

Presentation: Overview of long-term pulmonary insufficiency outcome data

- *Prakesh Shah, Mount Sinai Hospital*

Q&A *(10 min)*

10:00 a.m. **Session II: Identifying What is Clinically Meaningful to Stakeholders in Endpoint Development for Preterm Neonates with Pulmonary Morbidities**
Moderator: Mark Turner, University of Liverpool

Objective: Explore what is clinically meaningful to stakeholders in endpoint development

Lead Discussants:

- *Parent Advocates*
  - *Deb Discenza, PreemieWorld*
  - *Keira Sorrells, Preemie Parent Alliance*
  - *Jennifer Degl, Speaking for Moms and Babies, Inc.*
- *Sharon McGrath-Morrow, Johns Hopkins University*

Moderated Discussion *(30 min)*

Questions to address:

- What does the disease process look like and what are you trying to prevent/improve?
- What is important to you, your child, and your family?

10:45 a.m. **Break**

11:00 a.m. **Session III: Defining the Potential for Endpoint Development for Preterm Neonates with Pulmonary Morbidities**
Moderator: Greg Daniel

Objective: Outline the components that should be measured as well as the domains that may be included in potential clinically meaningful alternatives such as endpoints and COAs, and strategies to advance the development of these tools

Lead Discussants:

- *Wakako Eklund, National Association of Neonatal Nurses*
- *Laura Fabbri, Chiesi*
- *Nancy Leidy, Evidera*

Moderated Discussion *(30 min)*

Questions to address:

- What should the timing of endpoints be? 1 year, 2 years, or some other time frame?
- What type of endpoint(s) would best serve the needs of all the stakeholders? (These include COA, clinical endpoint, biomarker, among others)

11:45 p.m. **Lunch**

12:45 p.m. **Session IV: Exploring Endpoint and COA Development**
Moderator: Greg Daniel

Objective: Review how these instruments are developed, including a discussion of key concepts that should be considered such as validity and reliability, as well as other important attributes

Presentation:

- *Carole Tucker, Temple University*

Panelists:

- *Anna Maria Hibbs, UH Rainbow Babies & Children's Hospital*
- *Erik Jensen, Children's Hospital of Philadelphia*
- *Elektra Papadopoulos, U.S. Food and Drug Administration*

Moderated Discussion *(25-30 min)*

Questions to address:

- What are the most important components in endpoint development and how are these incorporated when developing new endpoints?
- Do you foresee particular measurement areas that could hinder endpoint development in this space?
- Are there exemplar COAs that could be helpful as we begin to develop COAs for neonates with pulmonary insufficiency?
- What is the feasibility of follow-up programs and how do we address family, researcher, and sponsor concerns?

1:45 p.m. **Session V: Characterizing Data Sources for Endpoint and COA Development Opportunities**
Moderator: Jonathan Davis, Tufts University

Objective: Examine the current availability in data and how to translate that data to support endpoint and COA development for preterm neonates with pulmonary morbidities

Lead Discussants:

- *Rosemary Higgins, National Institutes of Health*
- *Roberta Ballard, University of California, San Francisco*
- *Alexandra Mangili, Shire*
- *Allen Fischer, Permanente Medical Group*

Moderated Discussion *(25-30 min)*

Questions to address:

- What is possible with existing sources?
- What data are needed and how might they be obtainable?

- Is there an instrument/endpoint ready for testing? If not, what would be needed to make it ready for testing?

2:45 p.m. **Break**

3:00 p.m. **Session VI: Synthesis Discussion and Potential Paths Forward**
Moderators: Greg Daniel and Gerri Baer, U.S. Food and Drug Administration

Objective: Reflect on the day's discussion, identify the areas of consensus and potential paths forward, and highlight major gaps in knowledge and prioritize them for future research and discussion

Moderated Discussion

Questions to address:

- What are actionable steps we can take or recommend to make real progress in the development of these endpoints?

4:15 p.m. **Closing Remarks**
Greg Daniel

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