

Introduction and Workshop Objectives

FDA-UMD CERSI on Pediatric Extrapolation

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Disclaimer: The opinions expressed are those of the speaker and should not be interpreted as the position of the U.S. Food and Drug Administration.

Acknowledgment

- Workshop planning committee:
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 - Dr. Joga Gobburu
 - Dr. Vikram Sinha
 - Dr. Ann Anonsen
 - Dr. Jim Polli
 - Dr. Gilbert Burckart
 - Dr. Lynne Yao
 - Dr. Skip Nelson
 - Dr. Andrew Mulberg
 - Dr. Sarah Yim
 - Dr. Phil Sheridan
 - Dr. Kevin Krudys
 - Dr. Greg Reaman
 - Dr. Lisa Yanoff
 - Dr. Vasum Peiris
 - Dr. Barbara Buch
- Office leadership (Dr. Issam Zineh)
- Office of Commissioner (OCS/ORSI)

Challenges in Pediatric Drug Development

Data limited situations

- › Small populations
- › Ethical and practical constraints

Significant developmental/maturational changes

- › Trial design considerations
- › Dose selection



Lag in Labeling

Difference between Adult NDA and Pediatric Label (years)

1998-2007

7.55

N=69

2008-2015

8.21

N=99

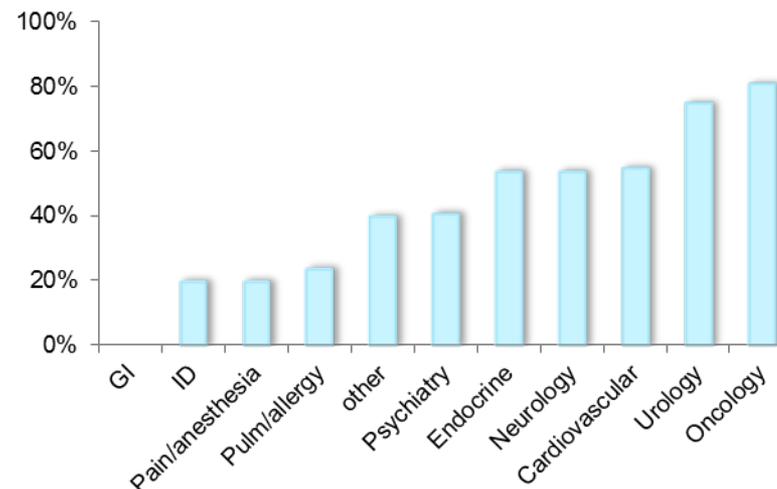
Accessed November 2015 (OPT pediatric labeling database).
Sample size N = 168 pediatric labels randomly selected

On average, pediatric labeling lags behind adult approval by > 8 years



High Failure Rate

Pediatric exclusivity studies that did not demonstrate efficacy (1998-2012)



Wharton et al. Pediatrics 2014

- › Large number of failed trials
- › Reasons for failure are multifactorial

Pediatric Extrapolation: Regulatory and Statutory Milestones

2011 FDA Review



Review of application of extrapolation in pediatric studies submitted to the Agency btwn 1998-2008

EMA Reflection Paper



Introduces the use of a quantitative approach

Additional Guidances



CDRH draft guidance on pediatric extrapolation
Pediatric Clinical pharmacology draft guidance

CDER Guidances



Exposure response guidance outlines general approach to pediatric extrapolation

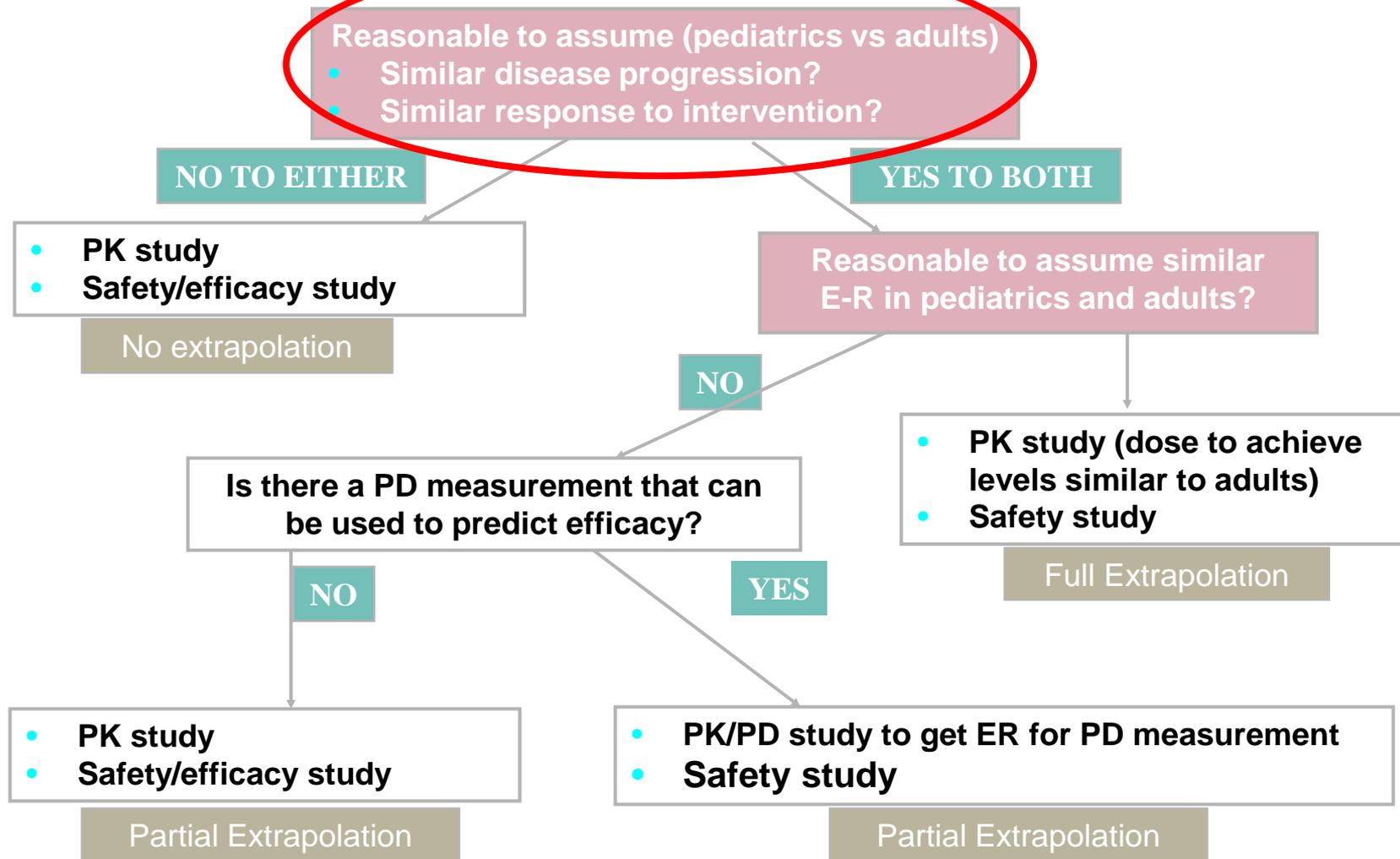
1994 Pediatric Rule



Introduced the concept of pediatric extrapolation
Further reflected in Regulations (21 CFR 314.55)



The FDA Pediatric Extrapolation Framework



Opportunities to Optimize Pediatric Drug Development

Systematic Application of extrapolation*

- ~60% of pediatric programs require at least 1 confirmatory pivotal phase 3 study
- Need for consistent approach to defining and establishing disease and response similarity

Dunne et al. *Pediatrics* 2011

Leverage Rich Prior Data

- Adult clinical trial data
- Access to data from pediatric trials from >600 development programs submitted to the Agency over the last 2 decades

Early Planning for Pediatric studies

~300 initial Pediatric Study Plans submitted annually at end of Phase 2 in adults

- Systematic assessment of prior data to support extrapolation
- Ensure collection of informative data in adult phase 3 trials and pediatric trials

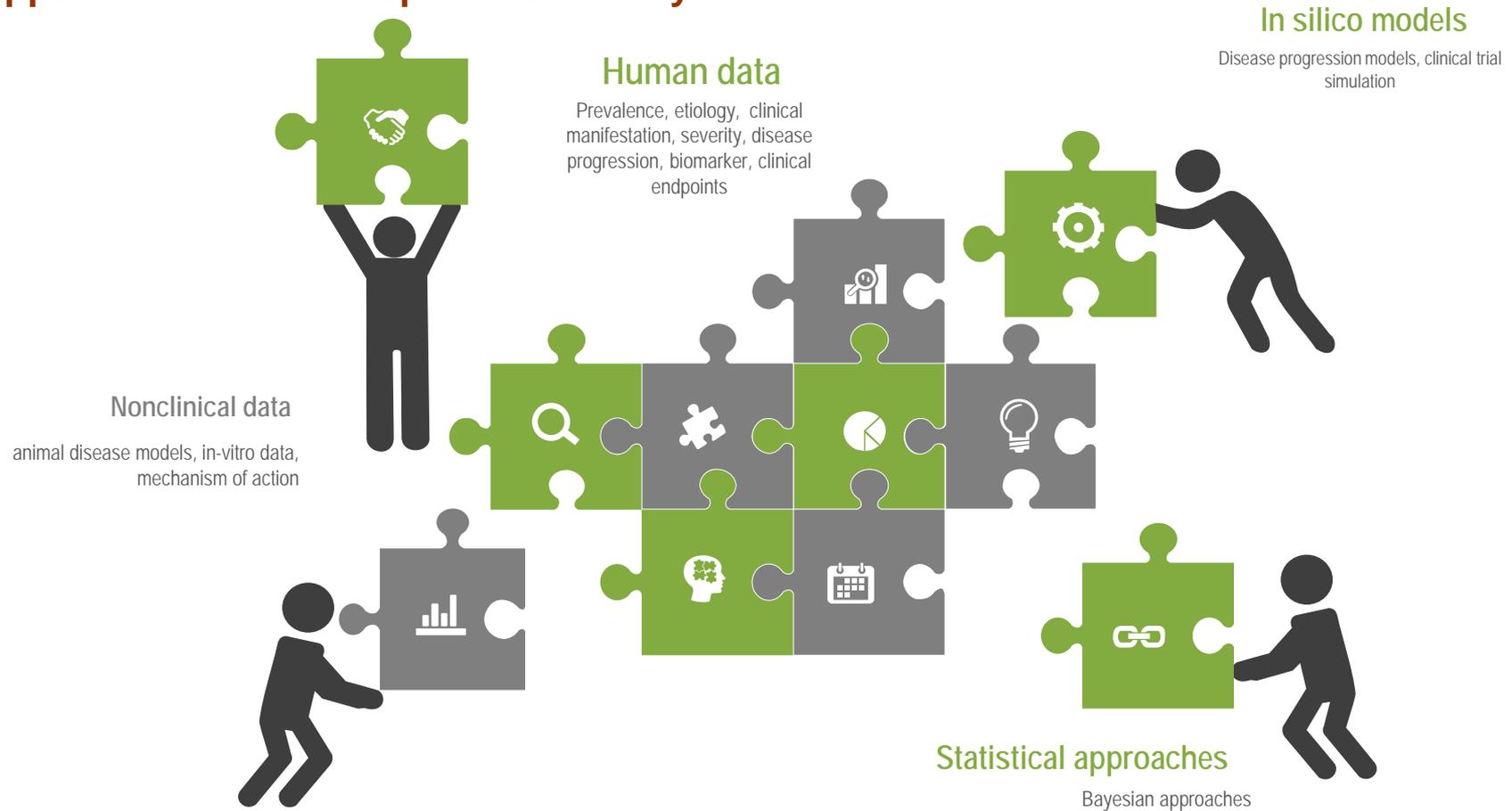
Use of innovative approaches/tools

- › Modeling and simulation
- › Bayesian approaches



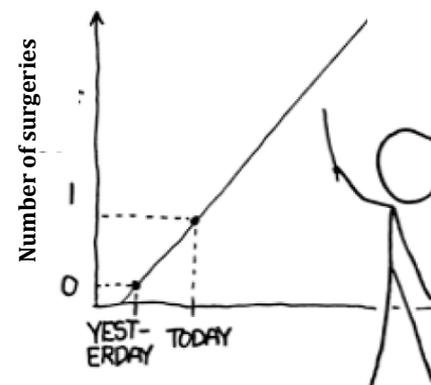
Building Evidence to Support Pediatric Extrapolation

Strength and limitations of different level evidence/approaches to support disease and response similarity?



Minimizing Uncertainties in Pediatric Extrapolation Assumptions

Stating extrapolation assumptions explicitly and designing pediatric trials to validate assumptions

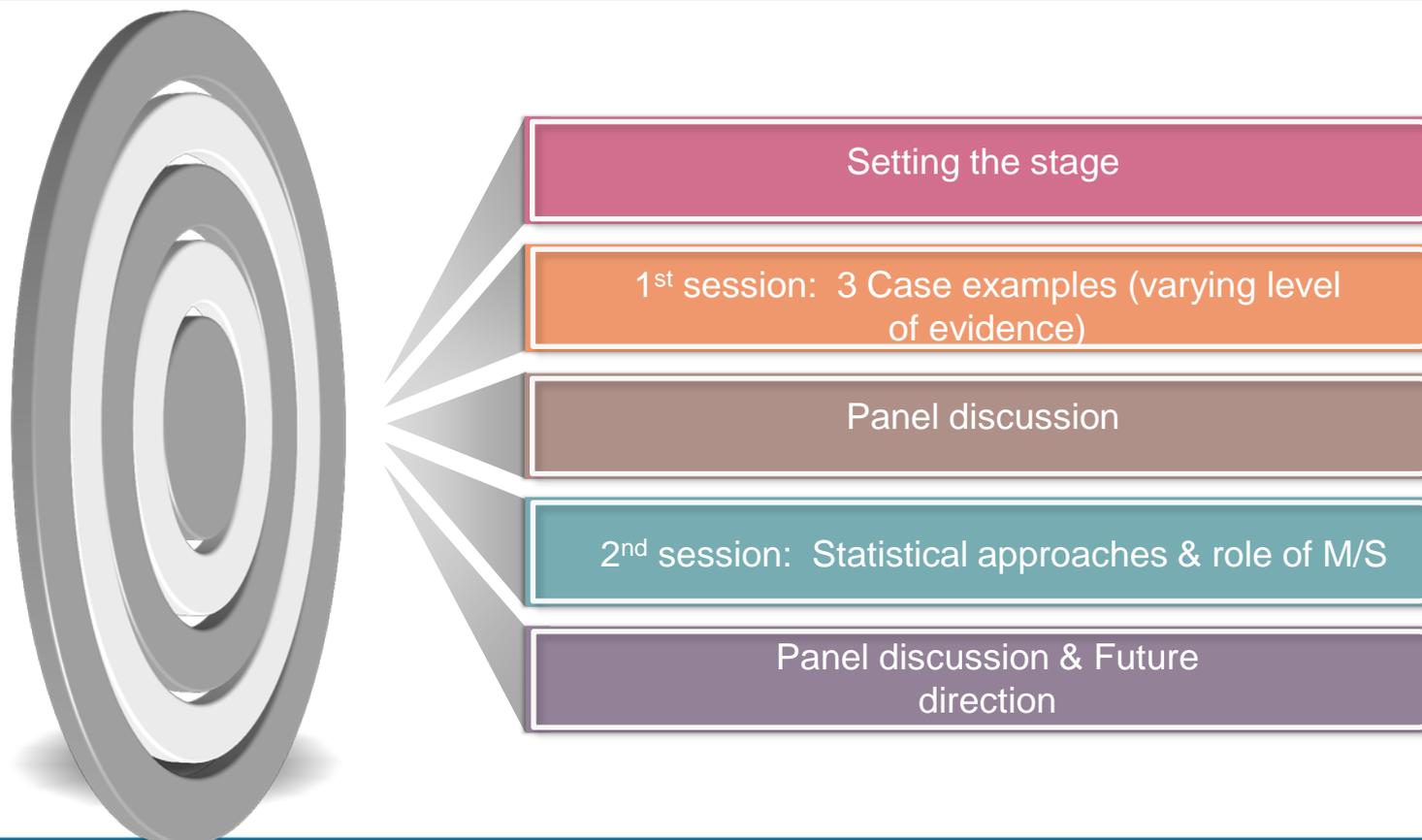


By late next month, you will have had over a dozen surgeries. Better get a bulk rate on deductibles.

Workshop Outline

Goals

1. Define critical data to provide evidence of disease/response similarity
2. Discuss the added value of quantitative assessment (vs. qualitative)
3. Identify conditions to serve as useful model to demonstrate proof of principle in the use of quantitative data in support of pediatric extrapolation
4. Discuss challenges with conducting a systematic assessment and potential path forward



In Memoriam



Dr. Jack Pellock, Neurologist (VCU) and co-chair of the Pediatric Epilepsy Academic Consortium on Extrapolation (PEACE)