Trends in Pediatric Modeling and Simulation
(What Formulators Should Know)

Jon Collins, PharmD
Senior Director, Clinical Pharmacology
ViiV Healthcare

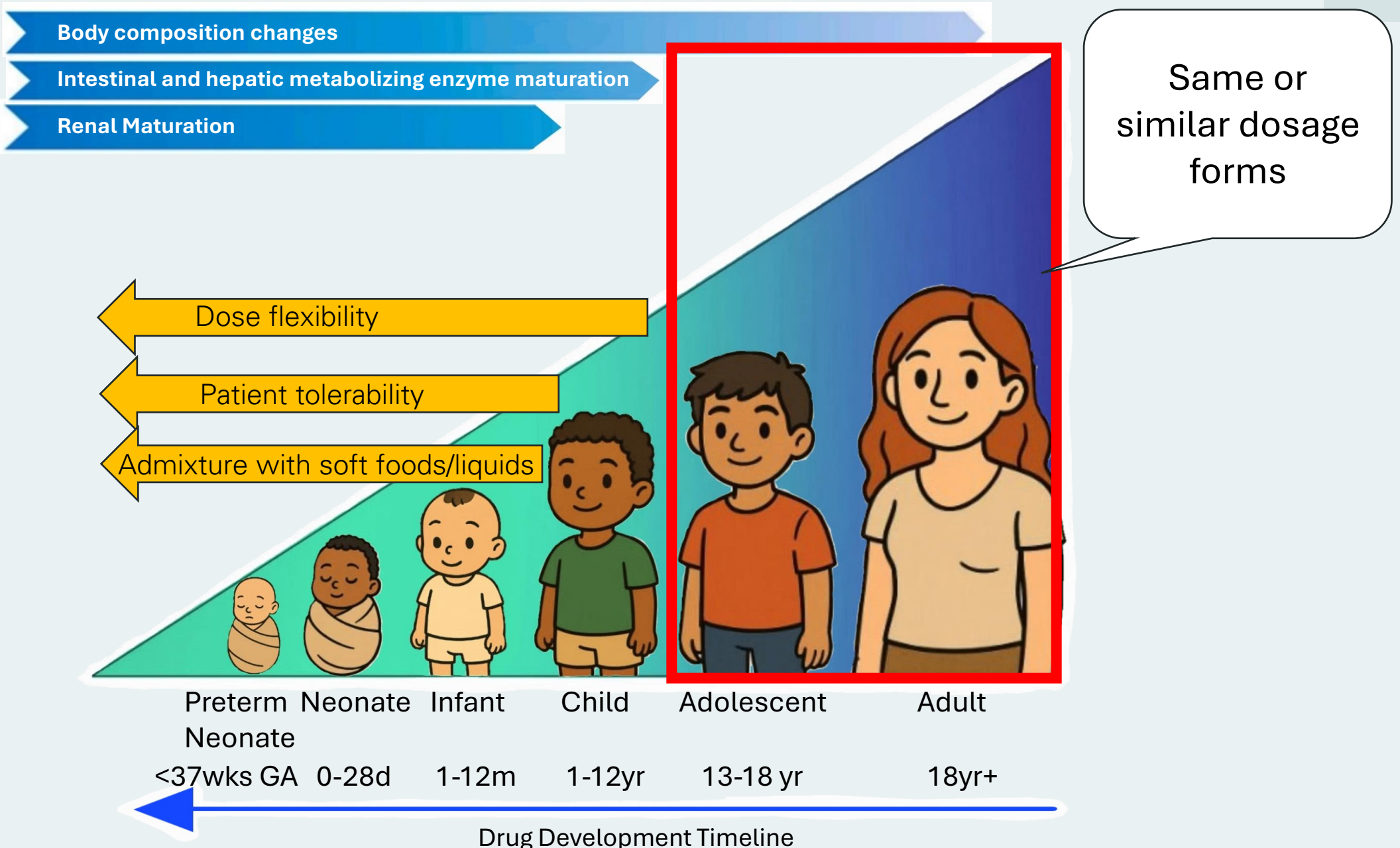
Disclaimer/Disclosure

- Presenter is an employee of ViiV Healthcare
- Views and opinions expressed are solely those of the presenter, and not those of GSK / ViiV Healthcare
- Materials, products and services mentioned are for illustration purposes only and do not represent any endorsement for use

Challenges in Pediatric Formulation Development

- Pediatric patients have distinct physiological and developmental needs
- Clinical opportunities to optimize formulations through extensive trials are limited
- Formulation development timelines can constrain program execution
    - Multiple formulations may be required

Why is Pediatric Drug Development Unique?



Why Model-Informed Drug Development?

- Turns emerging evidence into better decisions

The MIDD operating loop

1 Integrate evidence

Preclinical, clinical, biomarker and real-world inputs.

2 Model & simulate

Quantify uncertainty, test scenarios and predict trade-offs.

3 Decide & document

Select dose, refine trial design and prepare rationale.

Executive value: faster, better-supported decisions across the development path

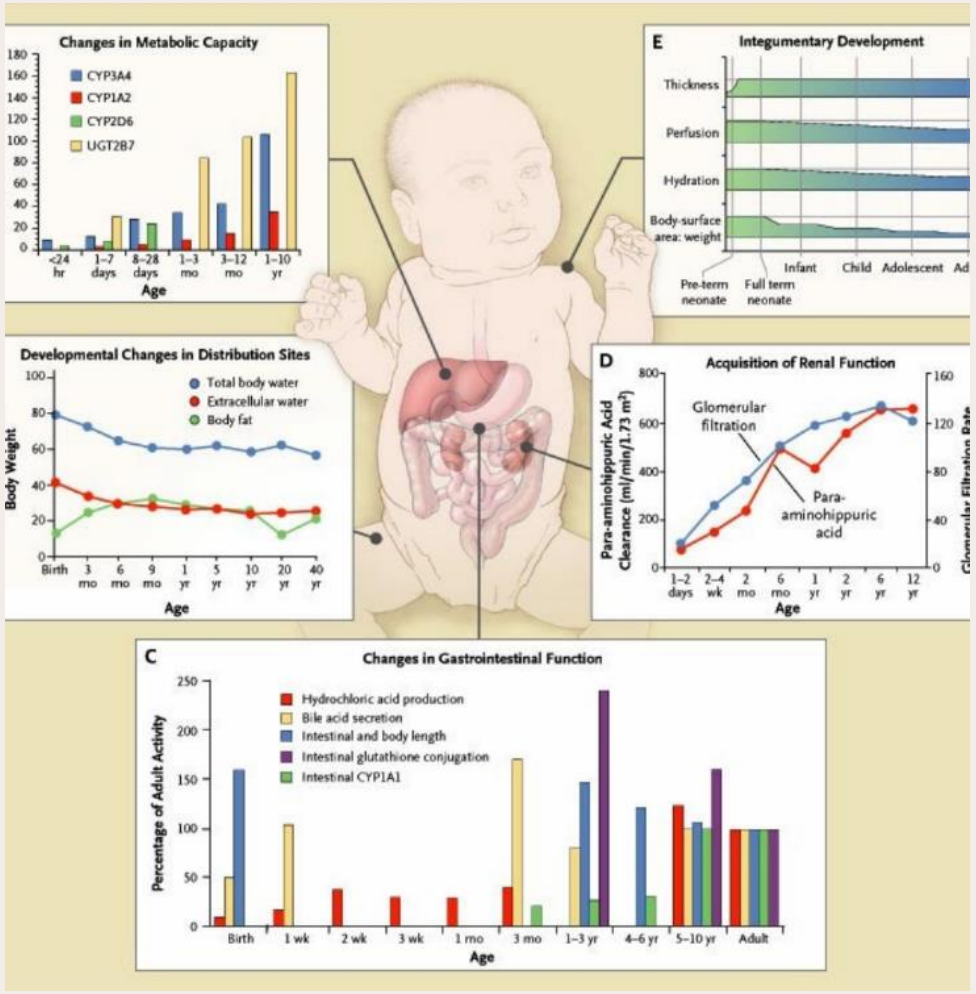
Sources: FDA, M15 General Principles for Model-Informed Drug Development, 2026; FDA MIDD Paired Meeting Program.

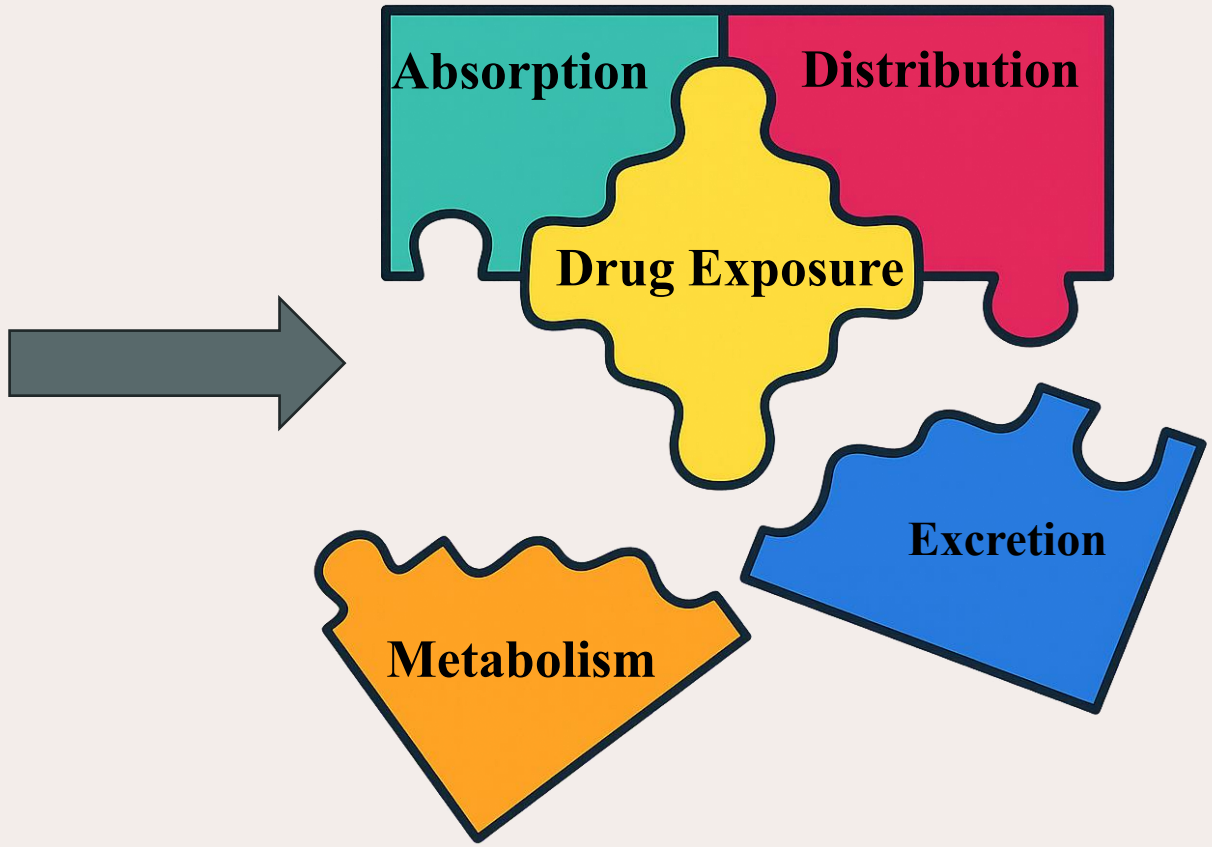
Central Role of Modeling in Pediatric Development

- Supports critical decisions across pediatric development
- Informs dose selection in collaboration with formulation teams
- Strengthens study design for pediatric programs
- Enables scientifically grounded extrapolation from adults to pediatric populations

What Are The Modeling Inputs Needed ?

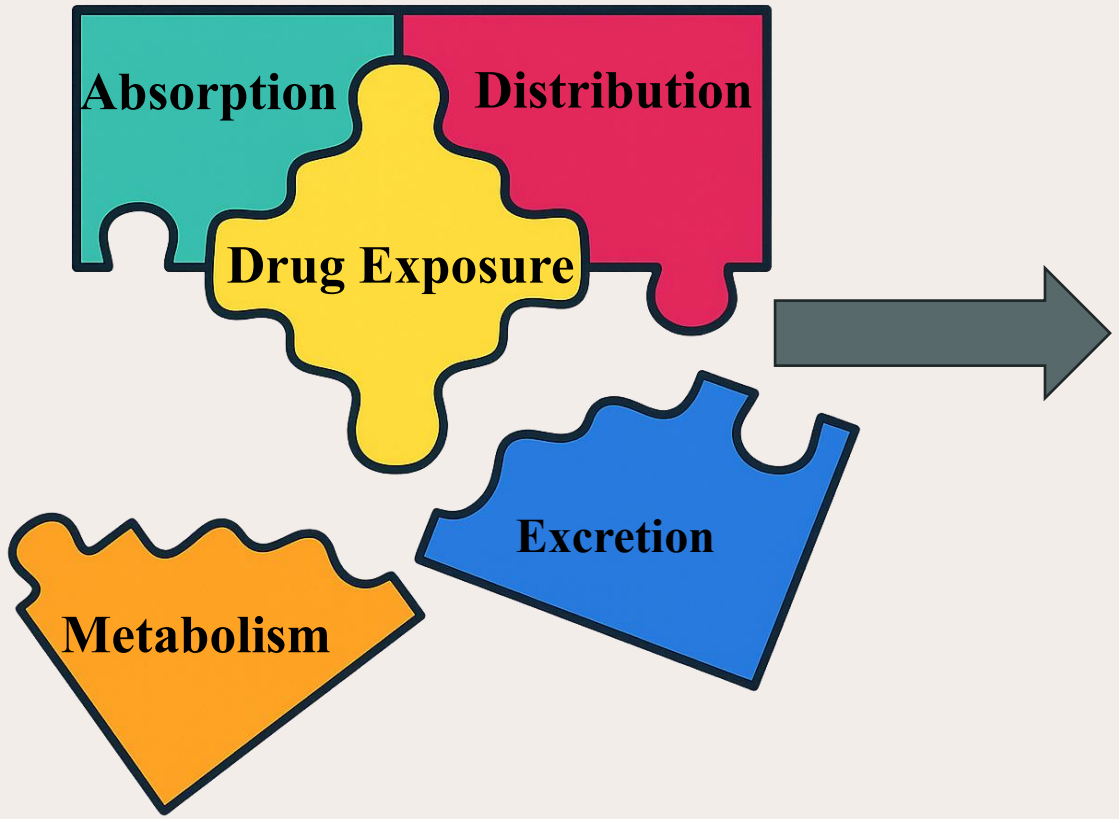
What Makes Pediatrics Different?



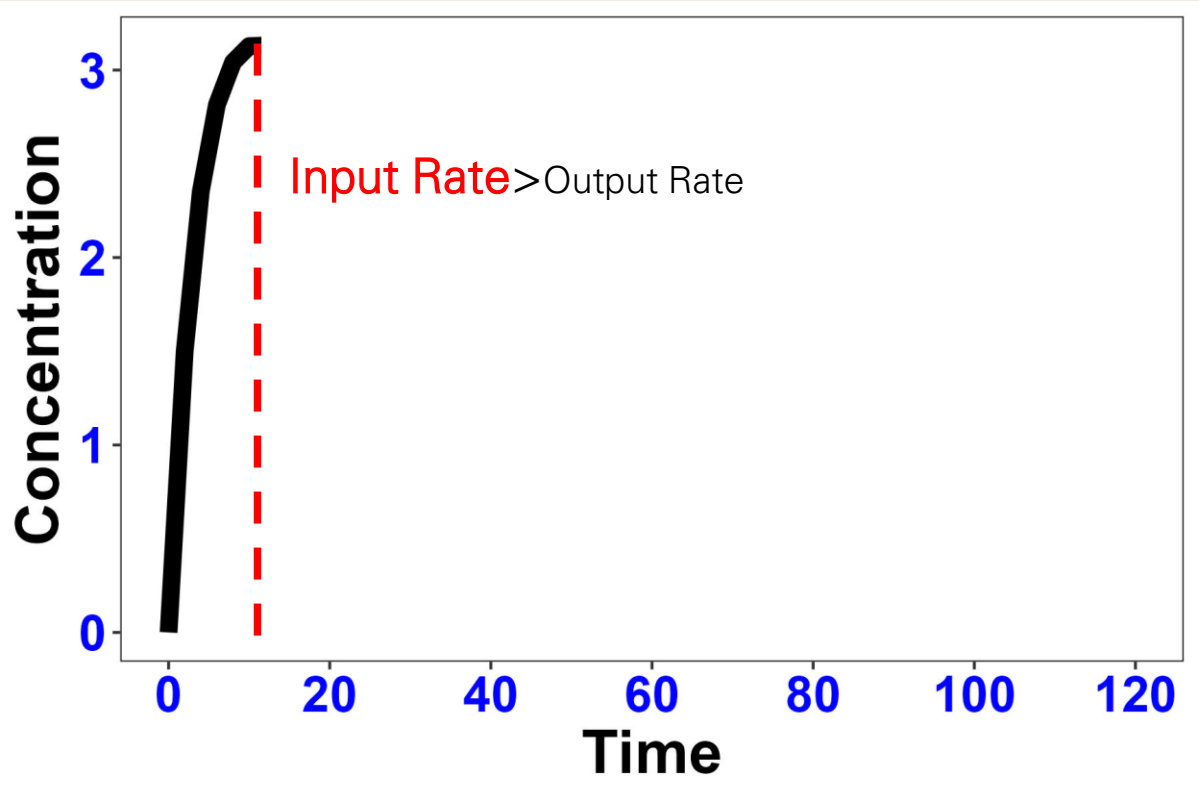


Used with permission.
Kearns G, et al N Engl J Med. 349:1157-1167(2003)

How Does ADME Determine Kinetic Profile?

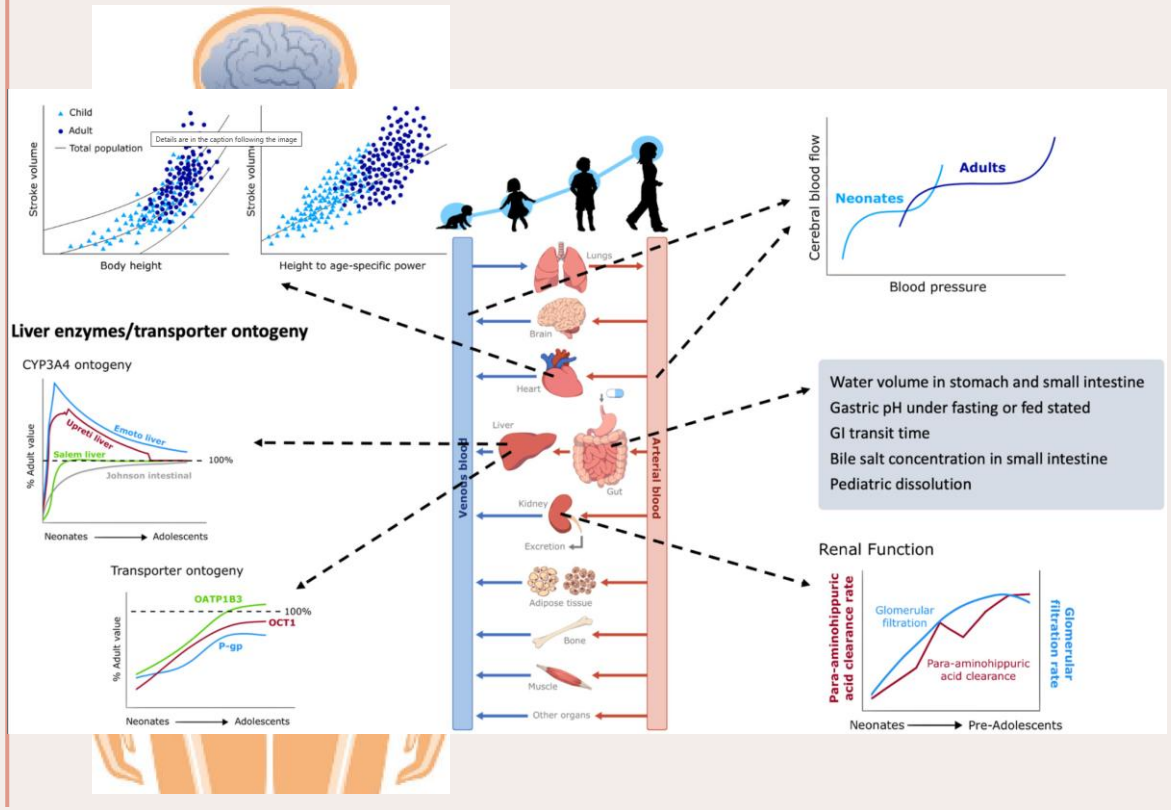


Typical plasma concentration-time profile after oral absorption

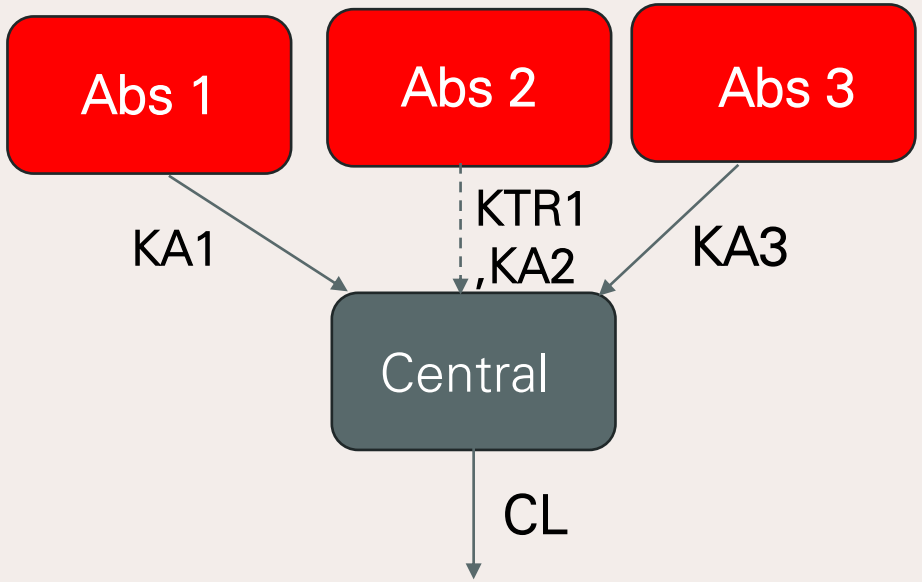


What are Modeling Approaches to Pediatric Development?

Physiological Based Modeling (PBPK)



Population Pharmacokinetic Modeling (POPPK)



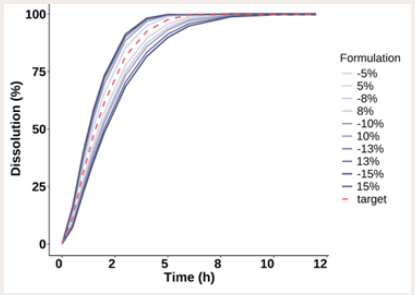
10

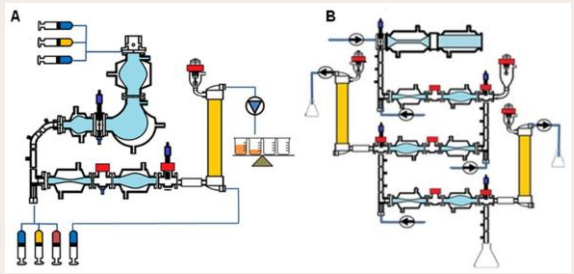
Yates, et al., CPT Pharmacometrics Syst. Pharmacol.; 15:e70141(2026)

Physiological Based Biopharmaceutics Modeling (PBBM)

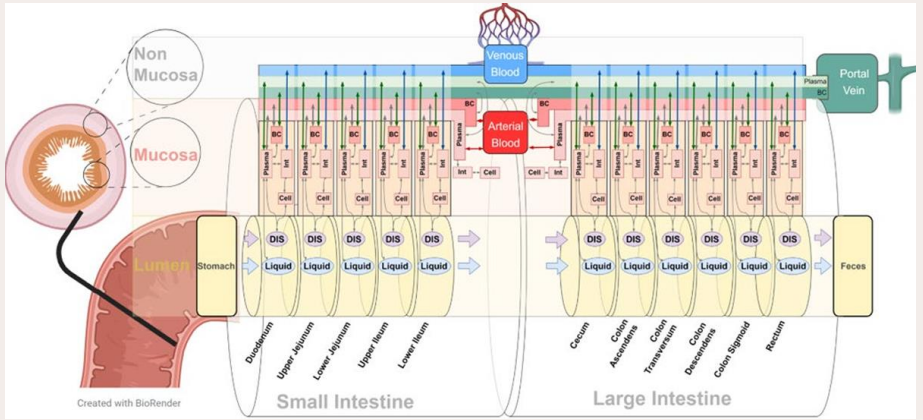
Links Formulation Attributes to *in vivo* Performance

Mechanistic Absorption





O'Farrell C, et al. Pharmaceutics. Mar 24;18(4)(2026)

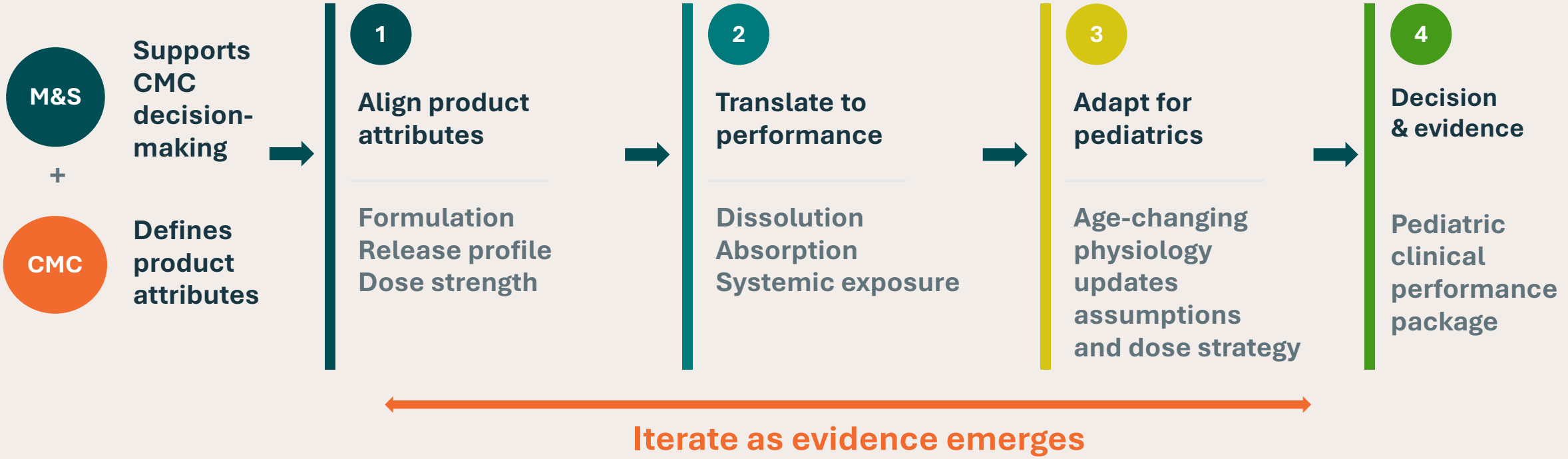


Guimares, M et al. , ACoP 2024, Abstract#T-050

Collaboration Key to Accelerate Pediatric Development

A shared decision process links formulation attributes, pediatric physiology, and clinical performance.

Collaboration engine



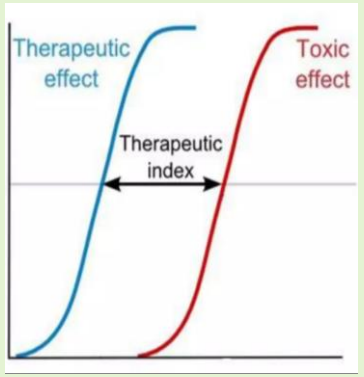
Outcome: modeling links formulation attributes to clinical performance in pediatric populations

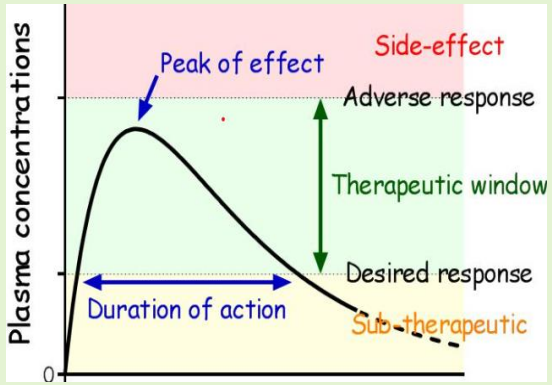
Use of Modeling and Simulation to Address Formulation Questions

Modeling and Simulation Has Been Used Across the Spectrum of Pediatrics

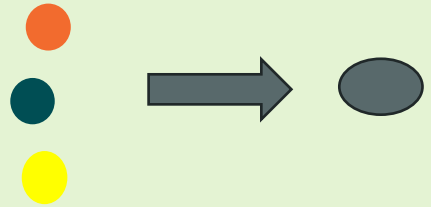
Early dosing volume predictions

Dose predictions for narrow therapeutic drugs





FDC from single entities (DTG/3TC/ABC)



Bioequivalence of pediatric formulations

Food-effect prediction for pediatric formulations

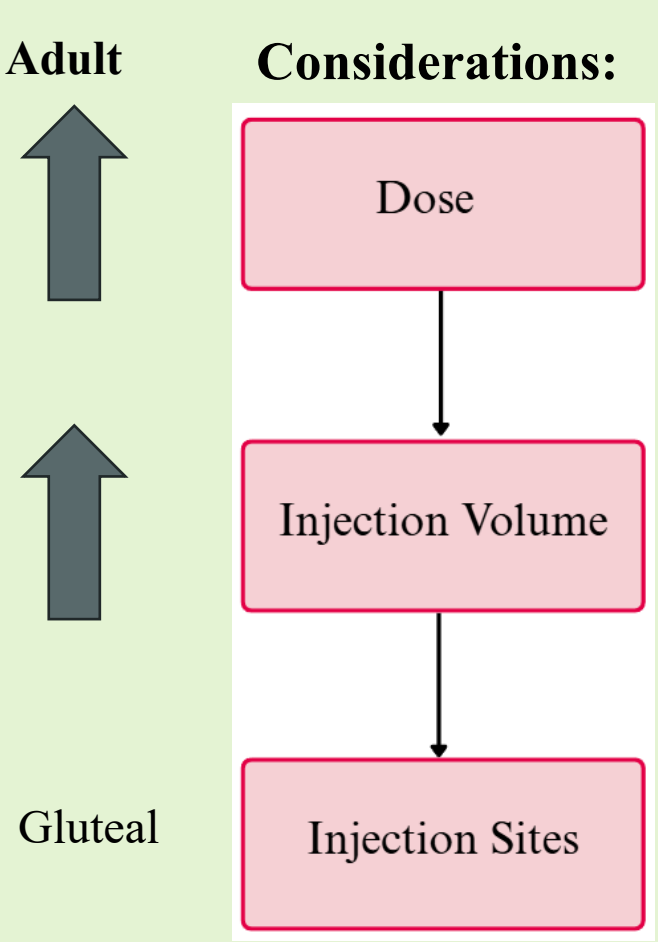
Neonate Drug Exposure with Formula/Breast Milk

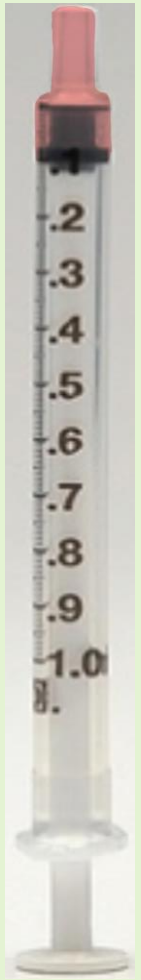
Optimized Dosing for Novel Thin Film (DTG)

Modeling and Simulation to Aid Early Investigations into Neonate Formulation Development: Long Acting Injectable

- Cabotegravir Intramuscular Suspension for Injection used in HIV Prevention and Treatment

CAB Dosing:
600mg=3mL





PBPK ~20 mg* Dose yields equivalent exposure in neonates
20 mg = 0.1 mL

*Bunglawala, et al CROI 2021 Abstract 606

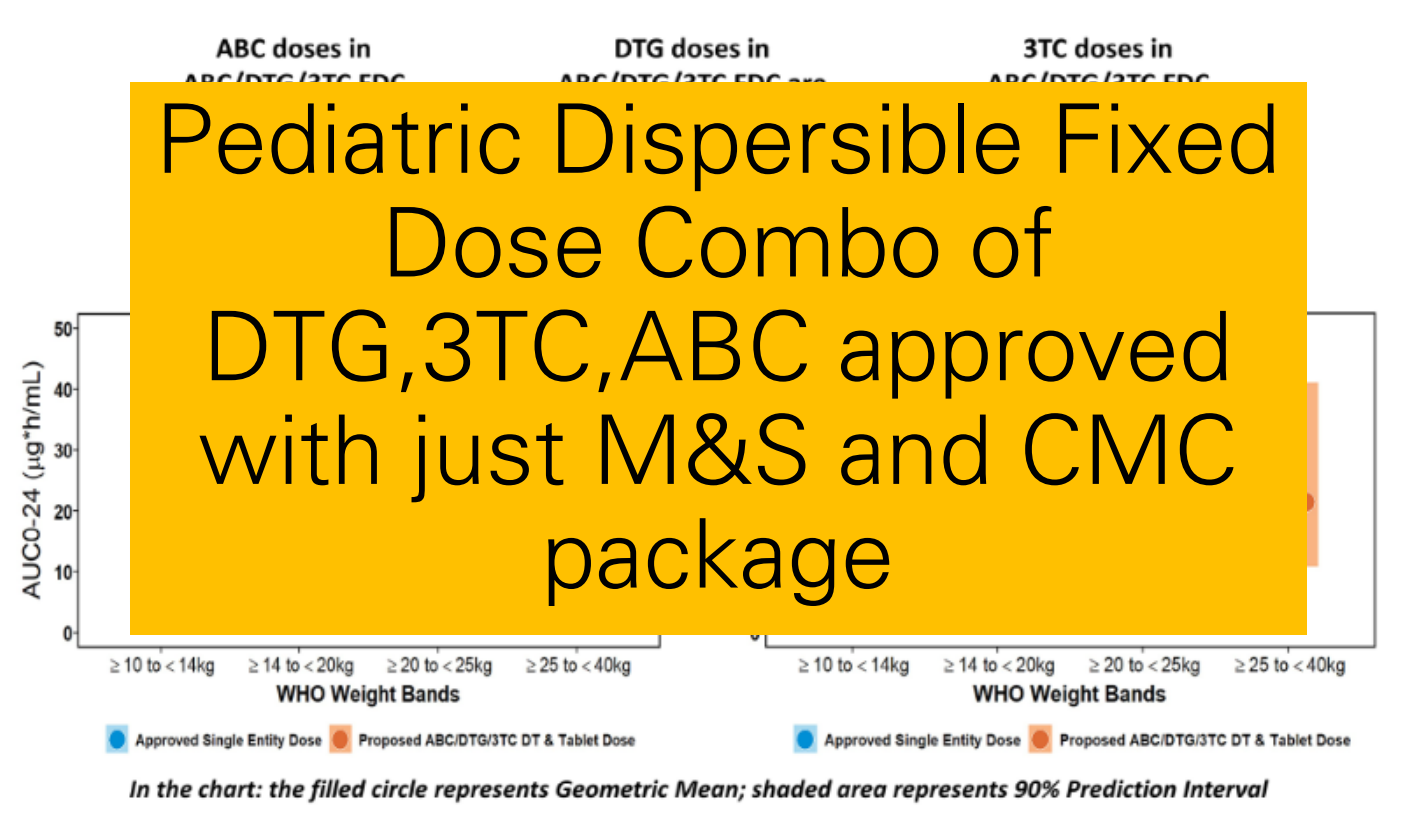
Accelerating Dolutegravir Formulation Development

Single Entity DTG Pediatric Data

Single Entity 3TC Pediatric Data

Single Entity ABC Pediatric Data

RBA/Food Effect Study



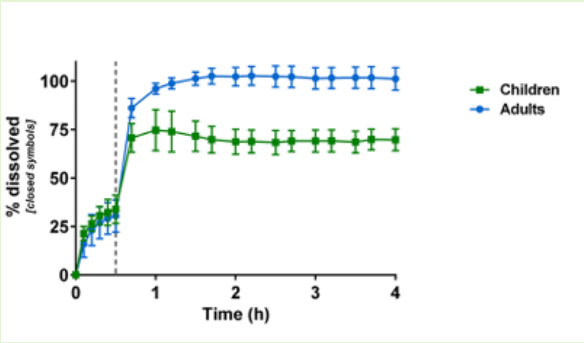
Pediatric Dispersible Fixed Dose Combo of DTG,3TC,ABC approved with just M&S and CMC package

Chandasana H, et al., J Clin Pharm, 65:18-27. (2025)

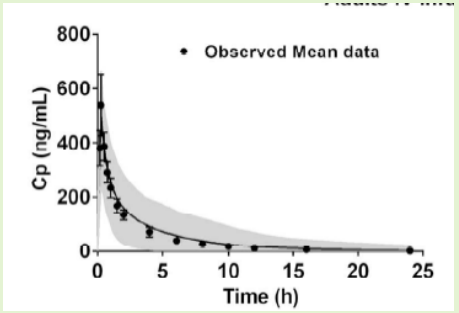
Montelukast Case Study as Framework to Drive Decision Making during Pediatric Development

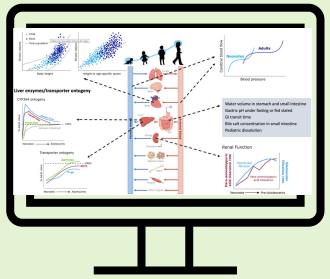
Goal: Combine age-appropriate *in vitro* dissolution with PBPK to explain and predict **oral exposure across pediatrics**, supporting formulation selection and administration recommendations.

Age appropriate in-vitro dissolution

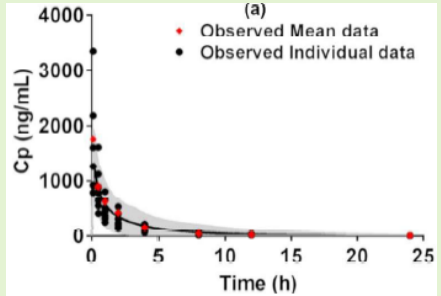


Adults IV

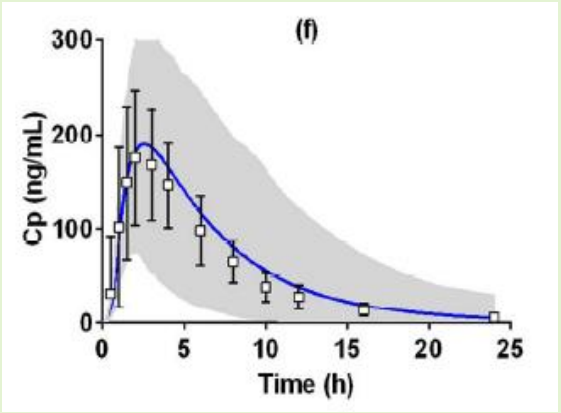




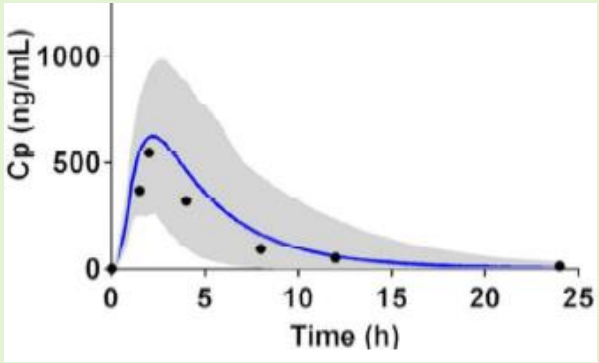
Pediatrics IV



Adults Tablet



Pediatric Tablet

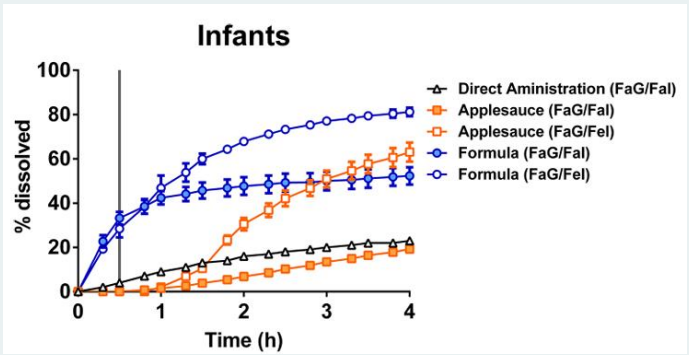


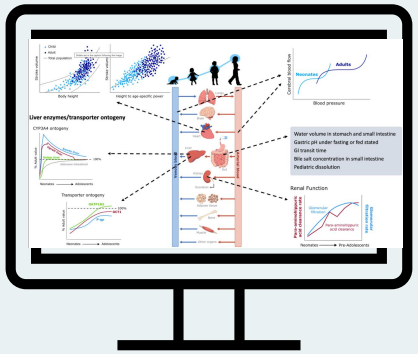
Guimarães, M., et al. *AAPS J* **24**, 27 (2022).

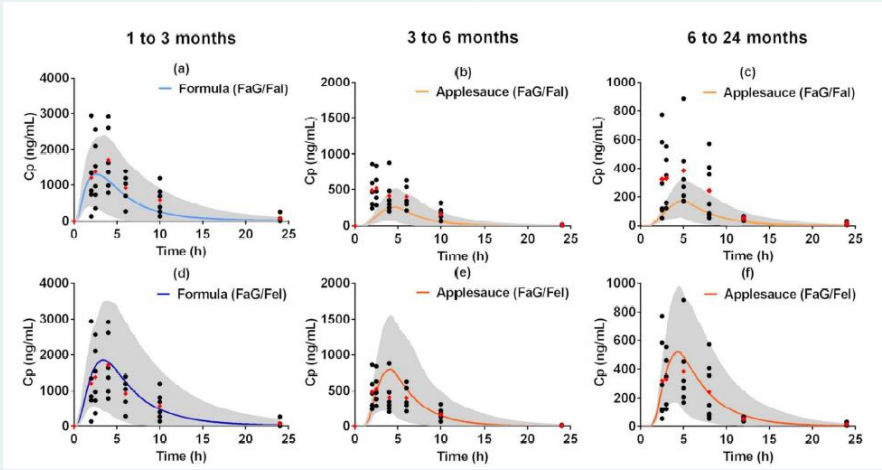
Montelukast Case Study as Framework to Drive Decision Making during Pediatric Development

Goal: Combine age-appropriate *in vitro* dissolution with PBPK to explain and predict **oral exposure across pediatrics**, supporting formulation selection and administration recommendations.

Applesauce or Formula

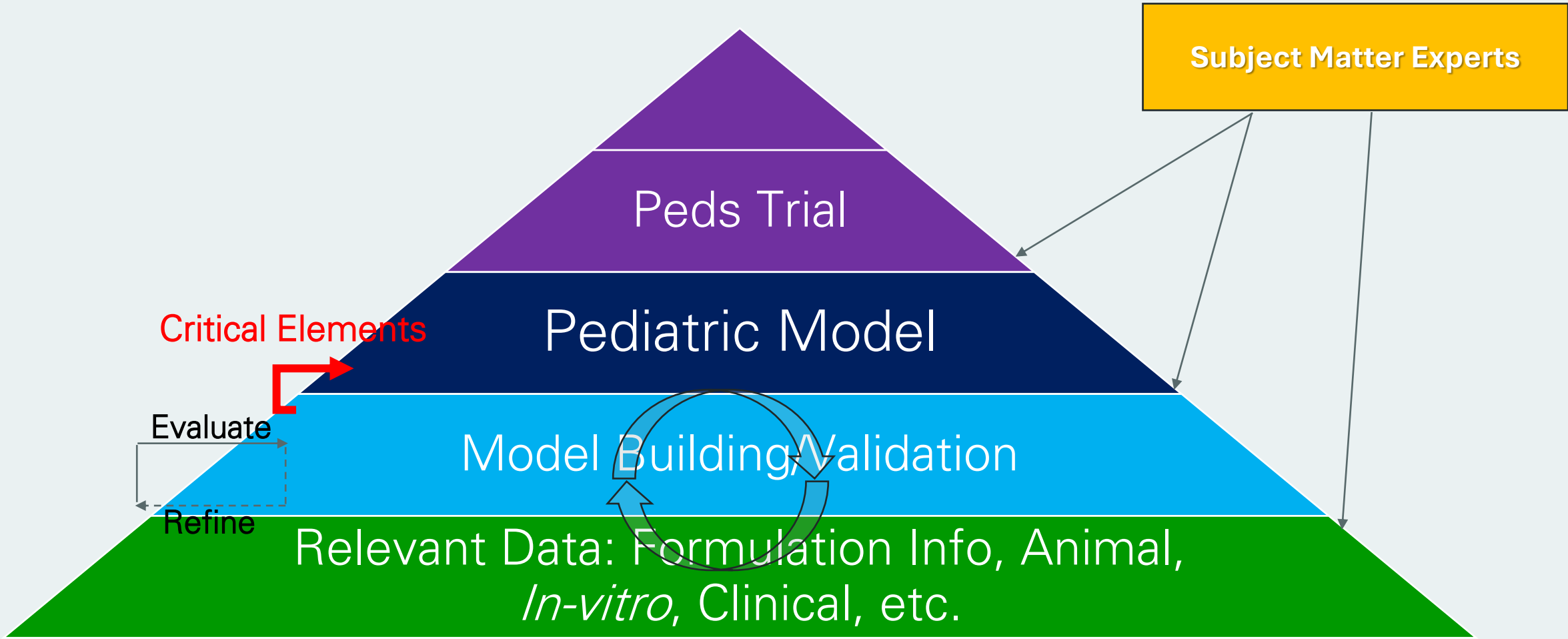






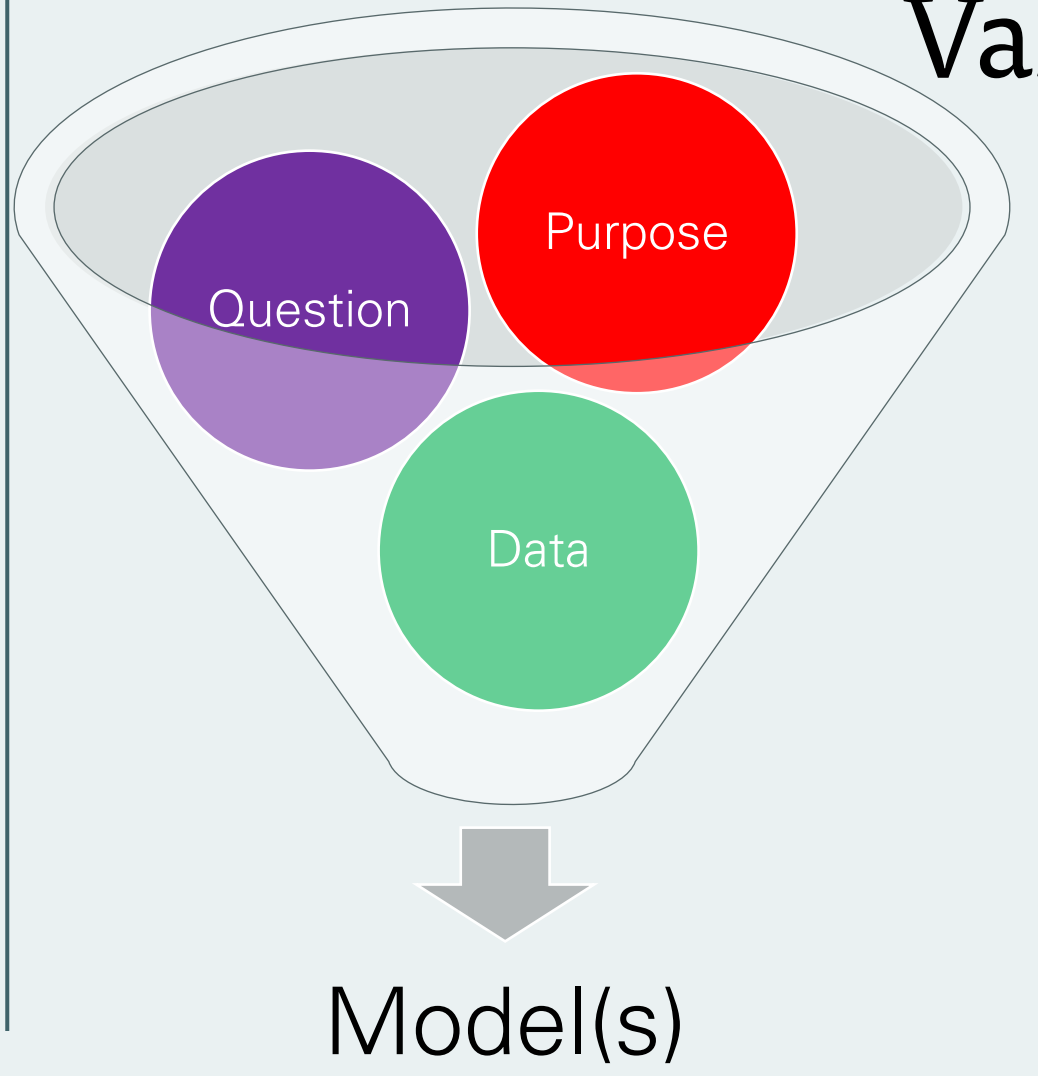
Guimarães, M., et al. *AAPS J* **24**, 27 (2022).

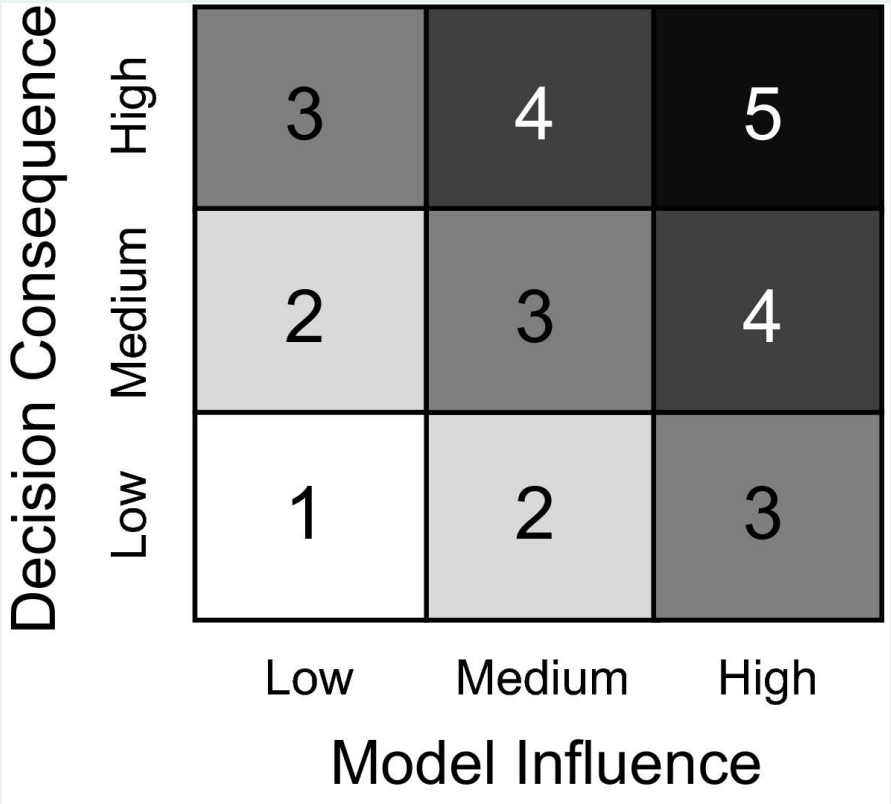
Modeling Paradigm to Translate to Pediatrics



Modified from Guimarães, M., et al., Journal of Pharmacy and Pharmacology. 71(4):603-642 (2019)

Which Modelling Approach and How Much Validation





Kuemmel, C., et al. CPT Pharmacometrics Syst. Pharmacol., 9: 21-28.(2019)

Take Aways

- Innovation Does Not Happen in Isolation
- Communication, Communication, Communication

Thank You
Questions?