The Evolution of Pediatric Product Development: Progress, Remaining Gaps, and Future Directions

Joanna Koziara, PhD

Executive Director, Gilead Sciences

Where We Started (2016-2019)

M-CERSI Pediatric Workshops: From Insight to Impact

Challenges and Strategies to Facilitate Formulation Development of Pediatric Drug Products (2016)	Pediatric Formulation Development: Challenges of Today and Strategies for Tomorrow (2019)	Shaping the Future of Pediatric Formulation Development (2026)
▪ Age-appropriate design ▪ Acceptability (swallowability & palatability) ▪ Food effects ▪ Excipient safety ▪ Biopharmaceutics	▪ Acceptability (standardization focus) ▪ Excipients (data + safety frameworks) ▪ Drug–device integration ▪ Multiparticulates & analytical strategies ▪ Pediatric PK & study design ▪ Global regulatory alignment	▪ Patient centricity (including compounding, human factors and neonatal dev challenges) ▪ Mini-tablets ▪ Excipients ▪ Innovation in drug delivery, modeling and use of AI/ML

10 years of progress: from problem identification to solution alignment

Despite Alignment on Principles, Critical Gaps Remained

Aligned on core principles

Early cross-functional & regulatory alignment

Patient-centric design → acceptability drives outcomes

Focus on younger pediatric populations

Shared data & frameworks as enabler

Opportunities

Knowledge & Data Gaps

- Limited pediatric PK understanding (neonates)
- Gaps in excipient safety data

Lack of Standardization

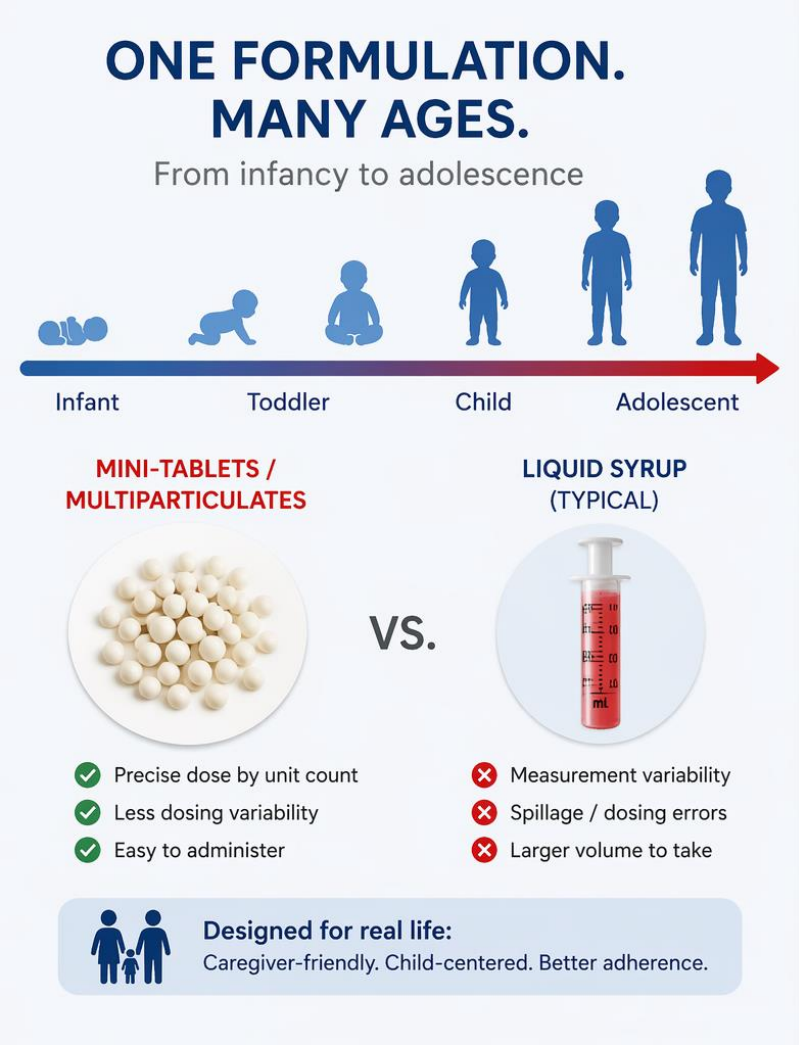
- Acceptability & food effect approaches inconsistent
- Variability in analytical/testing frameworks

Real-World Implementation Challenges

- Dosing accuracy, devices, feeding tubes
- Caregiver practices inconsistent

What Has Progressed

Mini-tablets: Emerging Default Pediatric Platform



Key advantages

- One platform: infancy → adolescence
- Flexible dosing (unit count)
- High acceptability & adherence

Operational advantages

- Better stability vs liquids
- Scalable manufacturing
- Supply-chain efficient

Regulatory traction

- 14 US approvals
- Majority in last decade
- Expanding pipeline (8 in clinical trials)[1]

[1] ClinicalTrials.gov and EU Clinical Trials Register

Acceptability Science Has Advanced, But Lacks Standardization

RPS Pharmacy and Pharmacology Reports, 2025, 4, rqaf006

Approximately 300 unique peer-reviewed publications[1] addressed pediatric medicine acceptability

- Palatability and swallowability ~ 225 studies
- Swallowability studies ~ 90 studies
- Mini-tablet specific acceptability ~ 60 studies
- Patient/caregiver dosage-form preferences ~ 50 studies

Methodologies

Defined endpoints and developed assessment tools

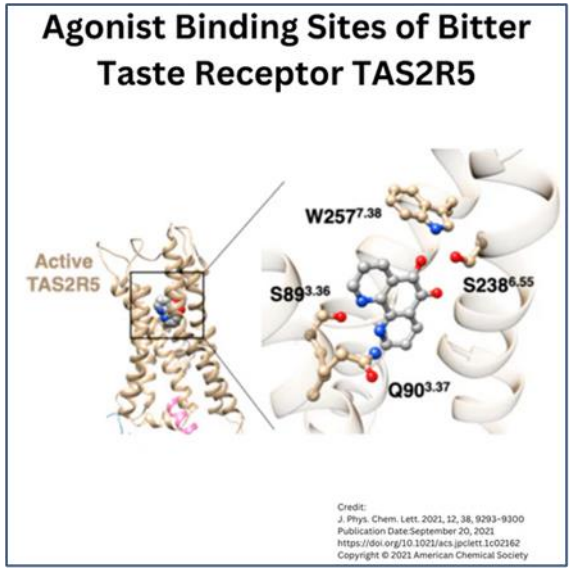
Standardization

- No centralized acceptability database
- No standard metadata model
- No global, agreed assessment standard
- Limited pre-competitive data sharing infrastructure

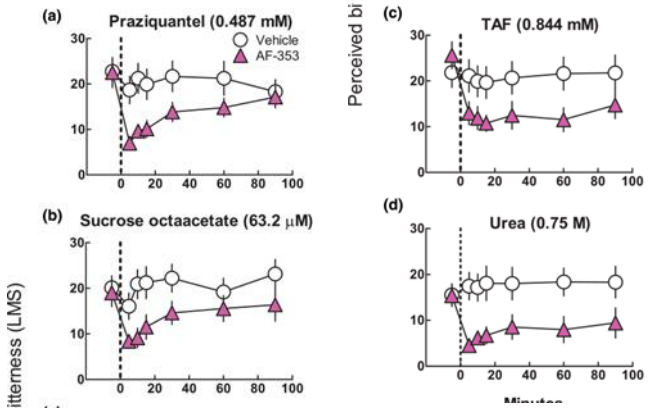
[1] Literature search results (2019 thru June 2026) for pediatric product acceptability in PubMed and Embase

Emerging Strategies for Bitter Taste Suppression

Intensified research to identify bitter blockers that interrupt the taste pathway



Monell researchers identified novel target for bitter blocking[1]



Topical application of a P2X2/P2X3 purine receptor inhibitor suppresses the bitter taste of medicines

Flavor houses/food industry are extending their knowledge to pharmaceuticals

ModulaSENSE® Bitter[2] (DSM-Firmenich)

“Taste Solutions” (Givaudan)

TruBlock™ (TastesNatural™)

[1] British Journal of Pharmacology 181 (17) 2024, 3282-3299

[2] https://www.dsm-firmenich.com/en/businesses/health-nutrition-care/news/press-releases/2026-03-19-dsm-firmenich-launches-modulasense-bitter.html

Advancing Pediatric Excipient Safety: Data, Tools, and Regulatory Momentum

STEP database

Safety & Toxicity of Excipients For Paediatrics

PERA

Paediatric Excipient Risk Assessment

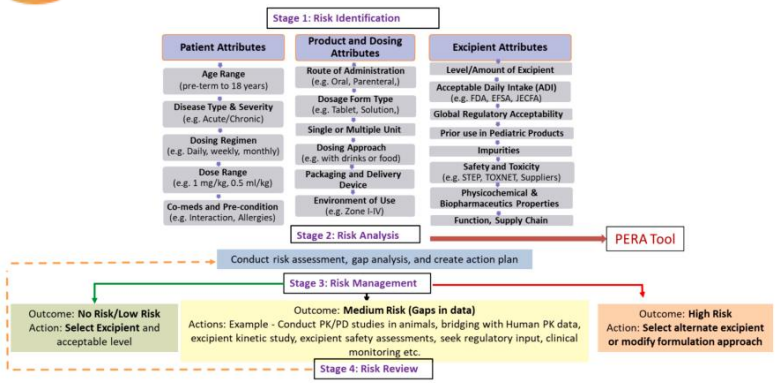


Fig. 1. Paediatric Excipient Risk Assessment (PERA) Framework.

STEP[1] database grew from initial 10 excipients to 75 by 2022, providing centralized safety information. STEP 2.0 to leverage AI/ML tools

IQ Consortium and EuPFI developed PERA tool[2,3], a systematic risk-benefit assessment framework for pediatric excipient selection

European Commission revised excipient labeling guideline in 2019 (updated in 2022, 2024 and 2025), specifying warnings for 50+ excipients

FDA piloting AI-enabled ELSA tool to evaluate maximum daily exposure for excipients

2021 FDA launched Novel Excipient Review Pilot Program

[1] https://step-db.ucl.ac.uk/eupfi
[2] European Journal of Pharmaceutics and Biopharmaceutics 203 (2024) 114458
[3] European Journal of Pharmaceutics and Biopharmaceutics 203 (2024) 114447

Dosing Accuracy and Administration Are Becoming Standardized, But Still Fragmented

Drug/food compatibility

Risk-based approaches with considerations of physicochemical and biopharmaceutical factors

Development of a standard toolbox for compatibility testing of pediatric drug products with common dosing vehicles (fruit juice, apple sauce, yogurt, and pudding)[2]

Device innovation

Low volume oral syringe (0.01 ml accuracy!)

Pacifier Medicine Dispenser (MediFrida)

Smartphone integrated autoinjectors e.g. SemPresto

Omnipod 5 waterproof insulin “patch-pump” children 2+

Dosing devices

ISO 20695 Standard Published
Global standard for enteral feeding systems

FDA Draft Guidance on Enteral Tube Administration (2021)

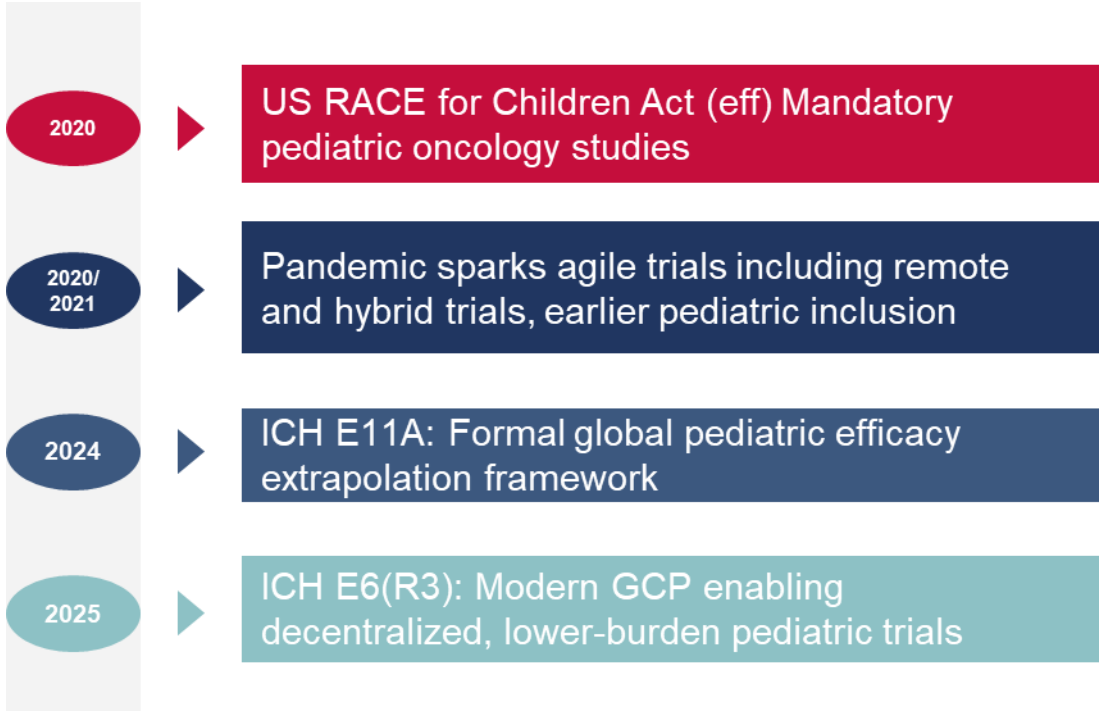
EMA integrates feeding-tube compatibility requirements into quality guidelines (effective 2026)

Industry experts publish a risk-based testing paradigm aligning with regulatory guidance [1]

[1] The AAPS Journal (2024) 26:43
[2] European Journal of Pharmaceutics and Biopharmaceutics 217 (2025) 114868

Faster And More Flexible Clinical Trials

Regulatory Shifts and Global Alignment



Innovative Study Designs

- Adaptive
- Seamless

Master Protocols & Platform Trials

Earlier Inclusion of Pediatric Cohorts

- Adolescents are frequently included in adult Phase III trials
- Parallel enrollments for various age/weight cohorts

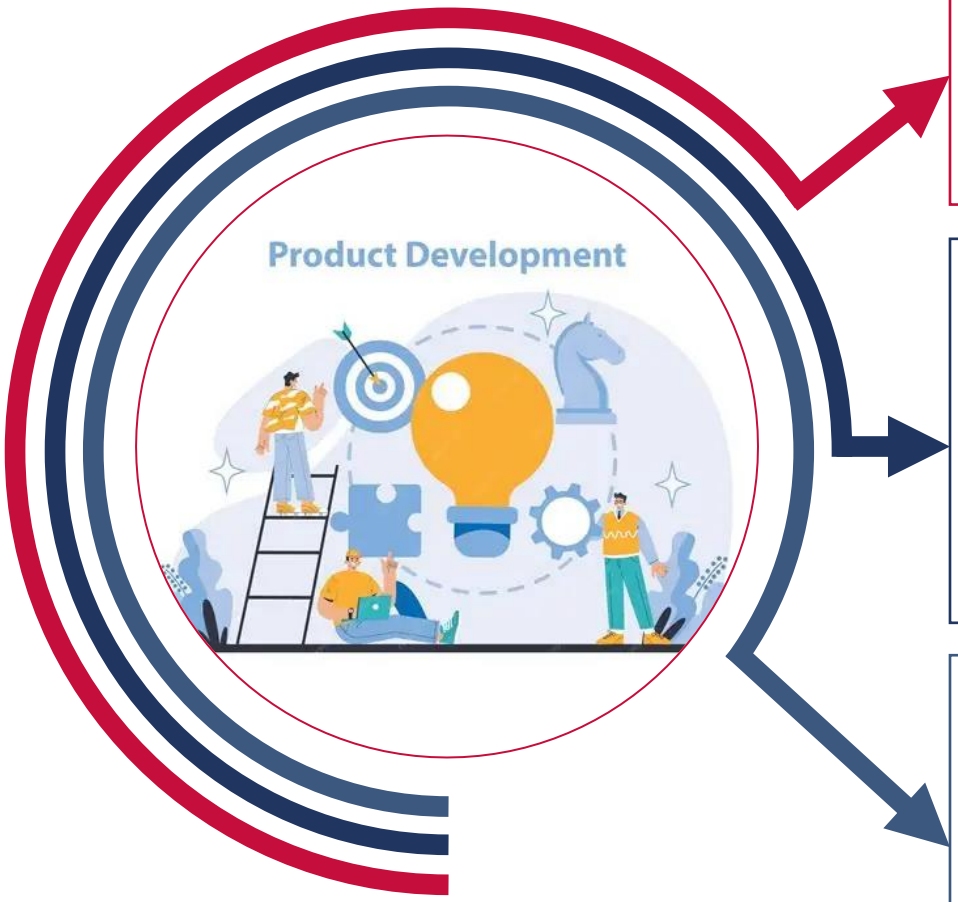
Model-Informed Drug Development

Expanded use of efficacy extrapolation

Decentralized Trials, Digital Endpoints, and Patient-Centric Innovations

What Remains Unsolved

Remaining Challenges



Regulatory

- Complex and evolving global requirements
- Persistent differences across regions on timing, sequencing, and data expectations
- Once pediatric commitments are set, modifications are slow and complex, even when science or guidelines evolve

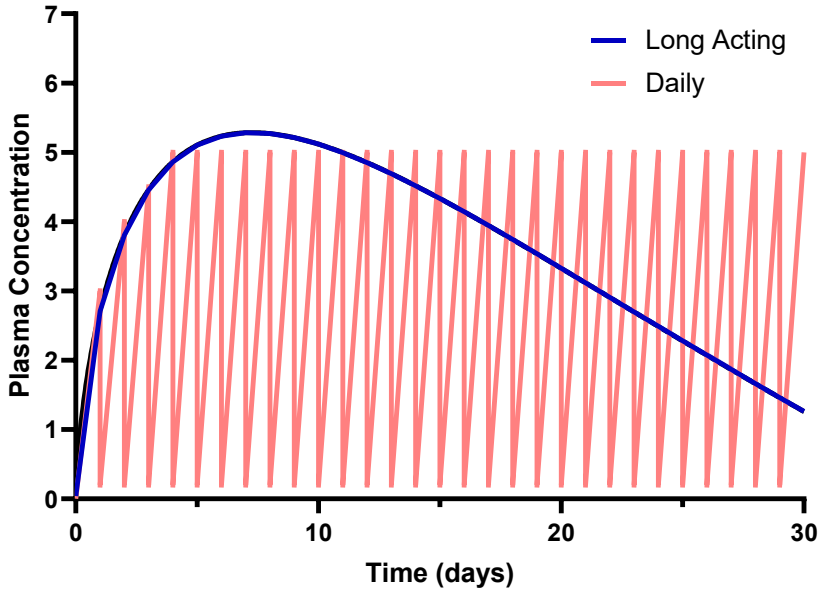
Scientific/technical

- Neonates remain the most underserved population
- Novel dosage forms
- Safety of excipients and novel excipients

Operational

- Enrollment challenges
- Lengthy, often sequential trials
- Inability to extrapolate efficacy and safety for many diseases

Advancing Long-Acting PK Control - Without Fully Understanding Pediatric Acceptability



With advancements in long-acting therapies formulations becoming more complex

- Platform diversification beyond “classic depots”
- Shift from oil-based depots → advanced platforms

Move toward ultra-long duration and steady PK

- Extend duration from monthly → quarterly → annual

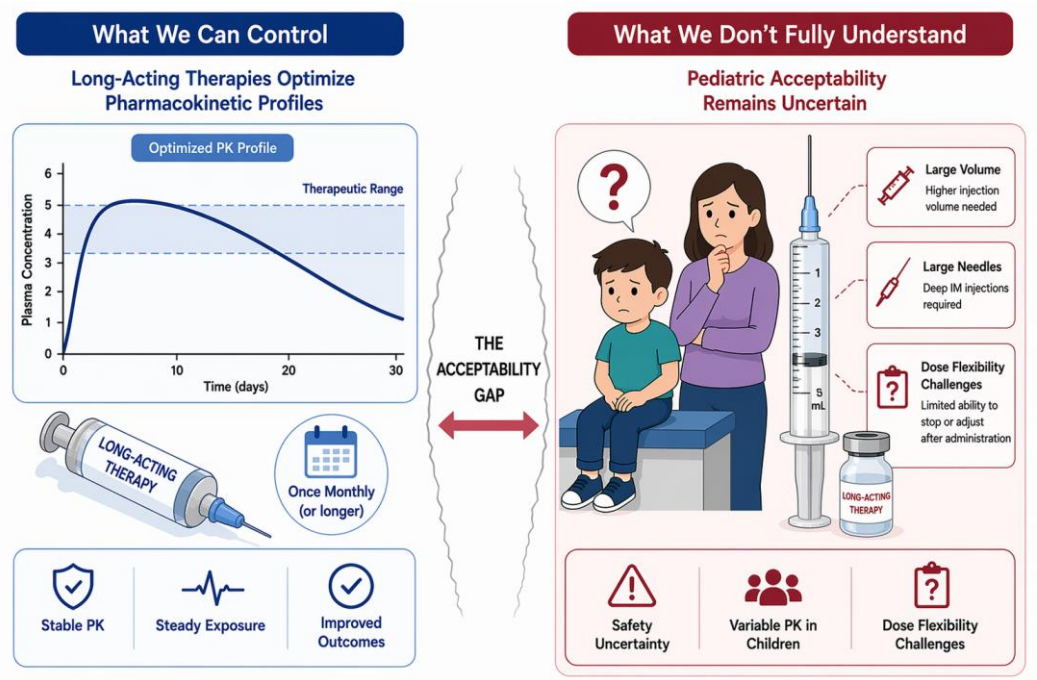
Patient-centric design as primary driver

- Reducing dosing frequency to improve adherence
- Strong uptake in chronic diseases (HIV, diabetes, CNS)
- Preventive therapies

Why pediatrics may benefit disproportionately:

- Reduces daily dosing burden on caregivers
- Improves adherence in chronic conditions
- Enables consistent exposure → better outcomes

Acceptability: A Critical Gap in Translating Long-Acting Therapies to Pediatrics



Injection volume & needle burden

- Many LAIs require large volumes/multiple injections
- Deep IM injections→ problematic in pediatrics
- Lower gage needles

Safety & excipient considerations

- Long exposure to polymers
- Organic solvents
- Limited long-term safety data in children

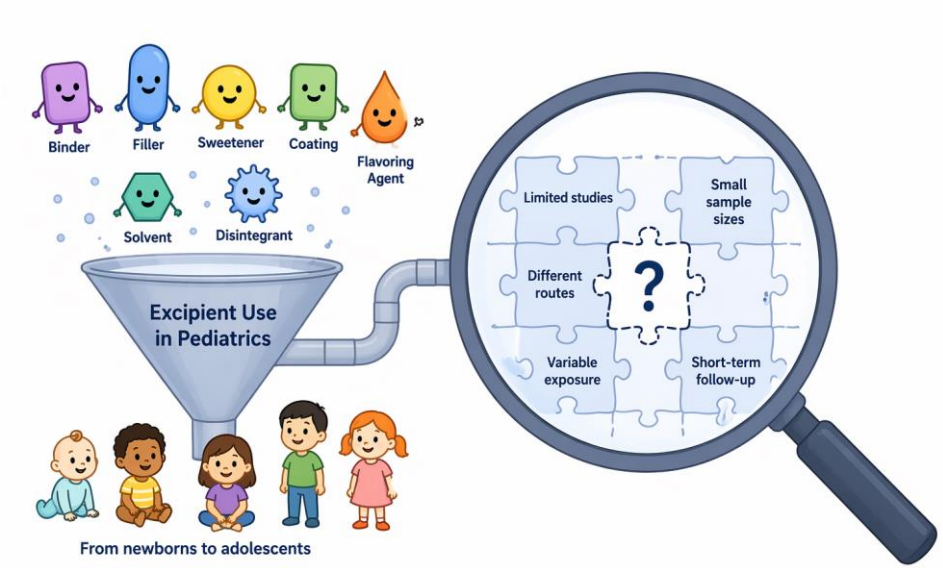
PK/PD/local tolerability complexity amplified in children

- Growth and maturation
- Changing body composition
- Immature metabolic pathways
- PK dependence on depo structure

What will it take to translate PK-optimized therapies into real-world pediatric use?

Excipients: Critical Enabler, Persistent Gap

Innovation is advancing, but translation and safety understanding remain limiting factors



Innovation depends on excipients

- Novel age-appropriate formulations rely on novel excipients
- Despite progress in identifying potential bitter blockers, but the field's translation into real-world drug products remains limited[1]

Formulation trade-offs persist

- Balancing acceptability with technical complexity (e.g., flavoring agents)

Safety data remains insufficient

- Need for more safety information on commonly used excipients in various routes of delivery and the youngest patients
  - 50 studies (pre-clinical and clinical) were published[2] on pediatric excipient safety with focus on excipients *already* suspected to pose risk

How do we pool available proprietary (and public) data to share for greater benefit and accelerate safe excipient use in pediatrics?

[1] European Journal of Pharmaceutics and Biopharmaceutics 158 (2021) 35-51
[2] Literature search results (2019 thru June 2026) New Clinical and Preclinical Studies on Pediatric Excipient Safety in PubMed/MEDLINE, Embase, Web of Science, and Scopus

Remaining Operational Challenges in Pediatric Clinical Trials

Access & Recruitment Constraints

- Small, heterogeneous populations limit enrollment speed
- Concentration of patients in few specialized centers
- High competition across trials for eligible participants
- Strong reliance on caregiver availability and engagement

Complex Study Design & Ethical Requirements

- Multiple cohorts (age, weight, developmental stage) increase complexity
- Sampling and endpoint selection constrained in children
- Added layers of consent + assent + re-consent
- More stringent ethical scrutiny → longer startup timelines

Execution & Site Limitations

- Limited number of sites with pediatric trial expertise
- Need for specialized infrastructure and trained staff
- Higher operational burden to support families and retention
- Variability in capabilities across regions impacts global rollout

Patient & Caregiver Burden

- Travel, time, and scheduling conflicts with school/work
- Emotional and logistical strain on families
- Adherence and retention challenges, especially in long studies
- Limited adoption of decentralized solutions tailored to pediatrics

Where should we focus to meaningfully accelerate pediatric study delivery?

Where Do We Go Next?

Strong foundation in place - now we must move beyond incremental progress to truly innovate

Achieving this will require us to stay aligned on our goals and **work together** to unlock the next frontier