Center for Drug Evaluation and Research

# of Excipients for Pediatric Population

Assessment, Inactive Ingredient Database, and ELSA Tool

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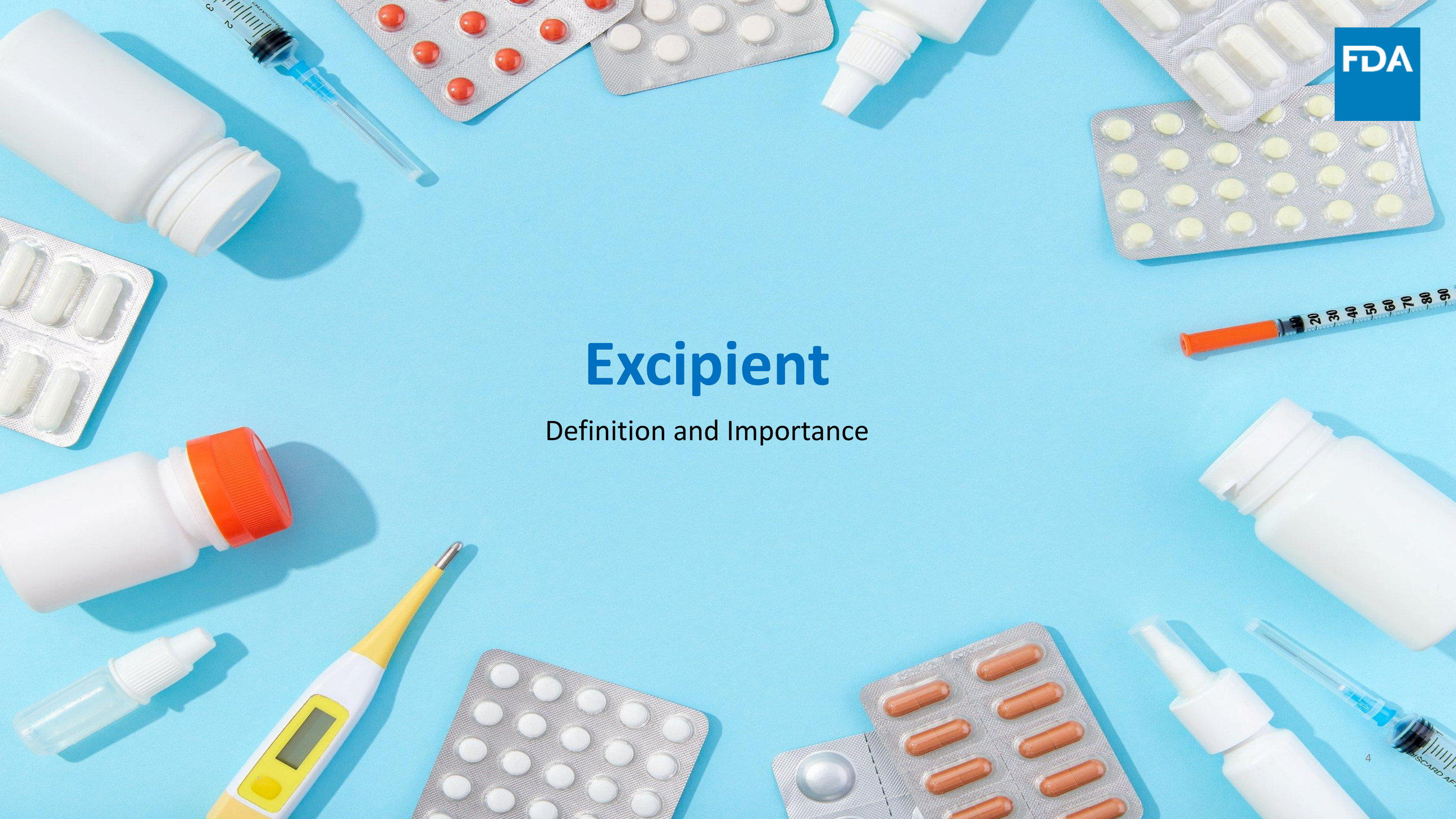
Day 2, Session 2B: Formulation and Analytical Aspects of a Pediatric Dosage Form - Excipients for Pediatric Formulation - Thursday, June 25, 2026

Disclaimer

This presentation reflects the views of the presenter and should not be construed to represent FDA's views or policies

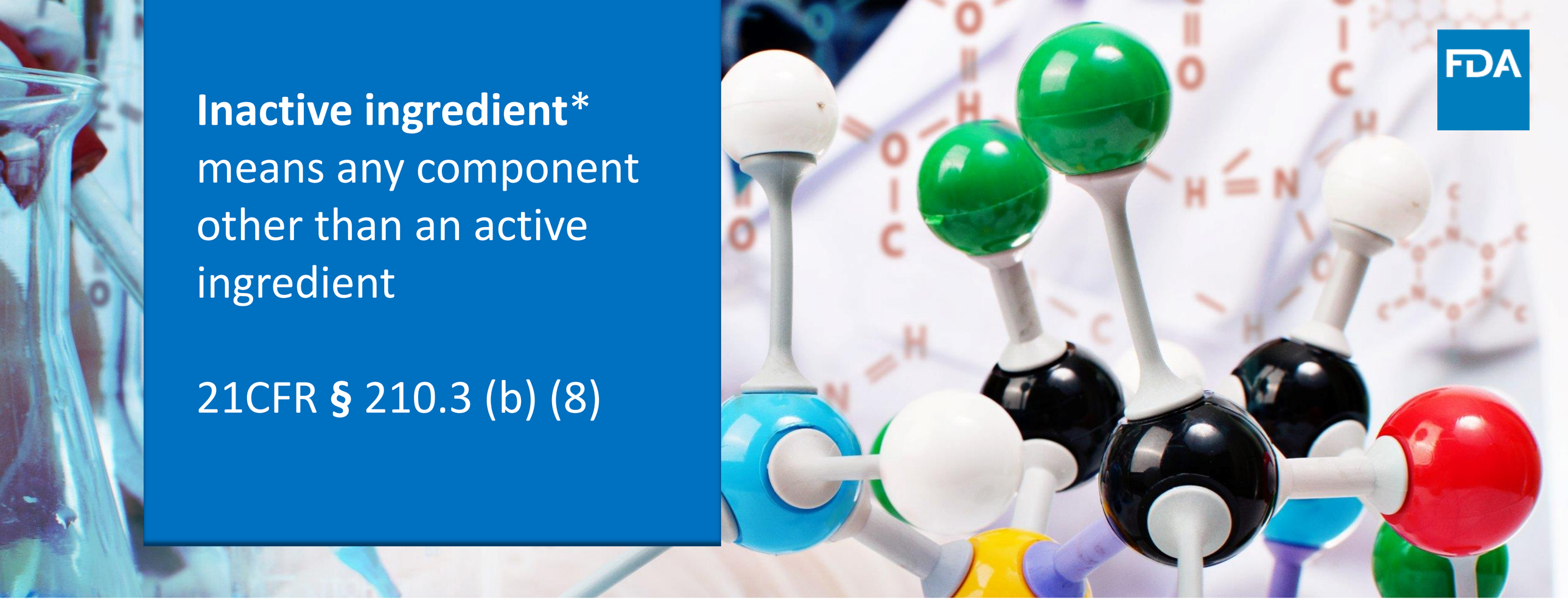
Agenda

1. What are excipients and why do they matter?
2. Excipient safety for pediatric population
3. Innovator and generic drug products – Key assessment and regulatory framework
4. The FDA Inactive Ingredient Database
5. Using ELSA AI tool to support excipient review
6. Key takeaways & resources



Excipient

Definition and Importance



Inactive ingredient* means any component other than an active ingredient

21CFR **§** 210.3 (b) (8)

FDA Code of Federal Regulations

*Referred to as excipient interchangeably throughout the presentation

Excipients – More than Inactive Ingredients

Examples of excipients:

Fillers, binders, extenders, diluents, wetting agents, solvents, emulsifiers, preservatives, flavors, absorption enhancers, sustained-release matrices, and coloring agents

Some critical functions of excipients:

- Drug delivery
- Ensure stability
- Improve palatability

Not truly "inactive"

Not all excipients are inert; some have shown to be toxic

Clinical Impact

Influence drug absorption, stability, tolerability, and patient safety

Particularly vulnerable populations – **pediatric populations**

Why Excipient Safety Matters

Serious adverse events over the course of history

1937 Diethylene Glycol
Mass deaths due to toxic excipient in Sulfanilamide elixir

1980s Benzyl Alcohol
“Gasping syndrome” and deaths in neonates

Polyethylene Glycol
Accumulation causing lactic acidosis and CNS depression

Pediatric population(s)/pediatric patient(s) defined as the pediatric age group, from birth to 16 years, including age groups often called neonate, infants, children and adolescents
21 CFR **§** 201.57 (c)(9) (iv) (A)

- Neonates: birth through 27 days (corrected gestational age)
- Infants: 29 days to 23 months
- Children: 2 years to 11 years
- Adolescents: 12 years to younger than 17 years

Through federal laws, pediatric research, and child-focused initiatives, the FDA supports the development and availability of drugs, biologics, and medical devices for children.

FDA Code of Federal Regulations

Pediatric Formulation Considerations

Age and physiological differences

Dosing of the active pharmaceutical ingredient

Excipient acceptability

Dosage form selection and taste preferences

Bioavailability and bioequivalence considerations

Innovator and Generic Drug Products

Assessment and Regulatory Considerations

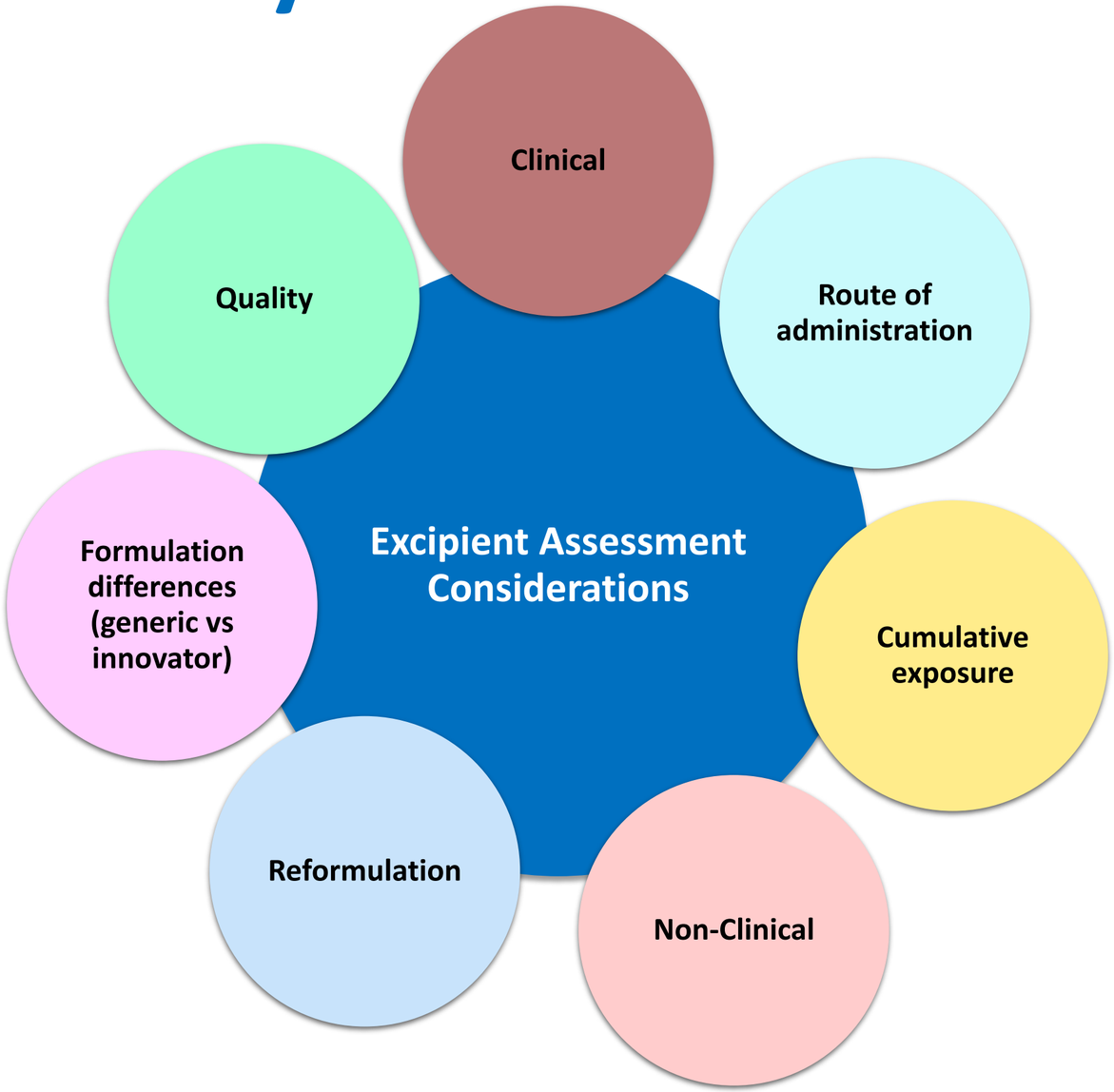
Core Assessment and Regulatory Framework

Innovator New Drug Application (NDA)	Generic Abbreviated New Drug Application (ANDA)
APPROVAL BASIS Safety & efficacy data	**APPROVAL BASIS** Reliance on RLD's safety and efficacy findings – "Sameness" + Establish BE
PEDIATRIC STUDIES **PREA/BPCA as applicable**	**PEDIATRIC STUDIES** **None**
EXCIPIENT FLEXIBILITY **Broad-Sponsor selects excipients**	**EXCIPIENT FLEXIBILITY** **Q1/Q2 the same for certain drug products; otherwise, some limited flexibility – must not affect BE, safety and/or efficacy***
FORMULATION Age appropriate for target pediatric group	**FORMULATION** Assess the proposed levels of **All** excipients for the **youngest** age group specified in the RLD labeling
NOVEL EXCIPIENTS **Allowable**	**NOVEL EXCIPIENTS** **Generally, not permitted**
LABELING Sponsor-developed; may include excipient information relevant to significant safety concerns	**LABELING** Match RLD/RS labeling with certain limited exceptions
REGULATORY PATHWAY(S) 505(b)(1) 505(b)(2)	**REGULATORY PATHWAY(S)** 505(j)

*Excipients are qualified during NDA development (Phase 3 clinical trials); ANDAs for generics lack Phase 3 clinical safety and efficacy data.

NDA – New Drug Application
ANDA – Abbreviated New Drug Application
PREA – Pediatric Research Equity Act of 2003
BPCA - Best Pharmaceuticals for Children Act
RLD – Reference-listed drug product
RS – Reference Standard
BE – Bioequivalence

Critical Considerations for Excipient Assessment – Lifecycle

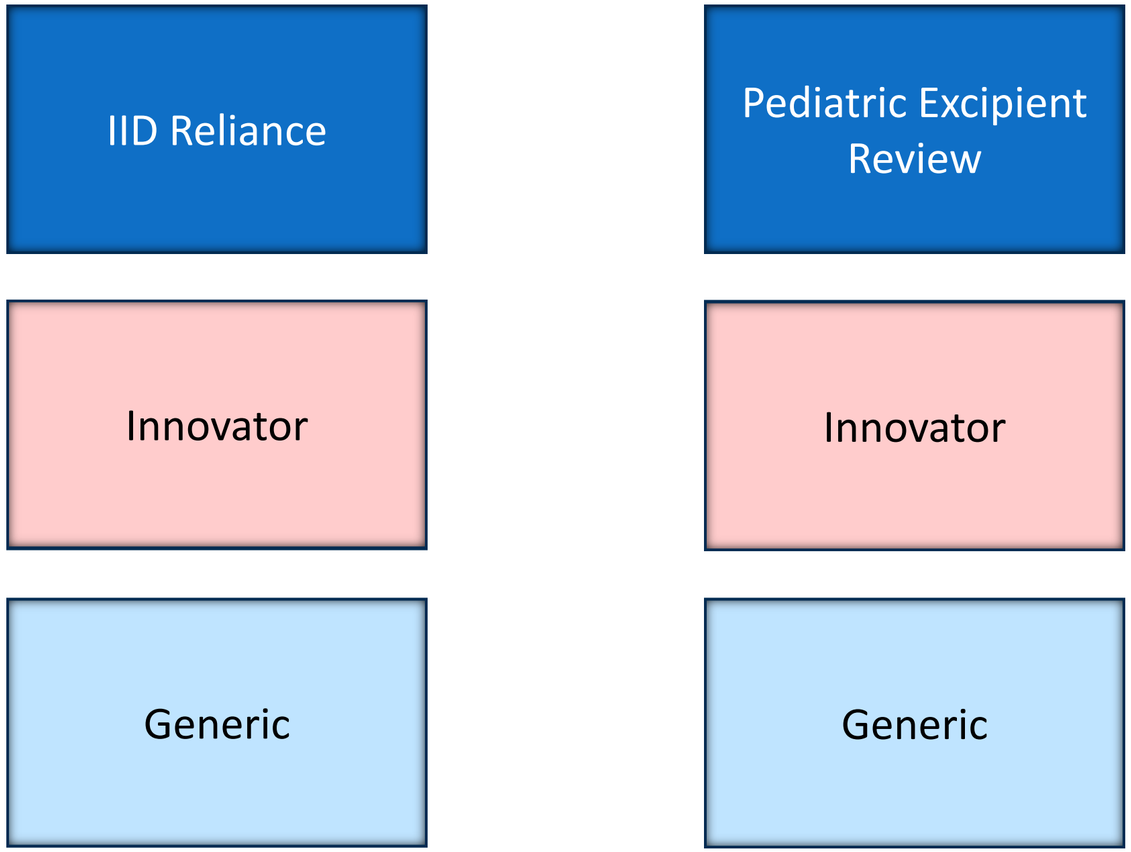


Post-marketing surveillance is a part of the life cycle of a drug product

Inactive Ingredient Database

Approved Drug Products

FDA IID Utilization in Assessment Process



Inactive Ingredient Search for Approved Drug Products

[About this Database] | [Most Recent Changes to the Database] | [Ingredients Database Download]

Search and Browse by Inactive Ingredient

Presentation last modified: 13h ago

Search for Inactive Ingredient Name*: Search for Inactive Ingredient Name

Submit Clear

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z 0-9

About this Database | Back to Search Page

Guidances | CFR

Search Results for: Benzyl alcohol

Show 30 rows CSV Excel

Filter: oral

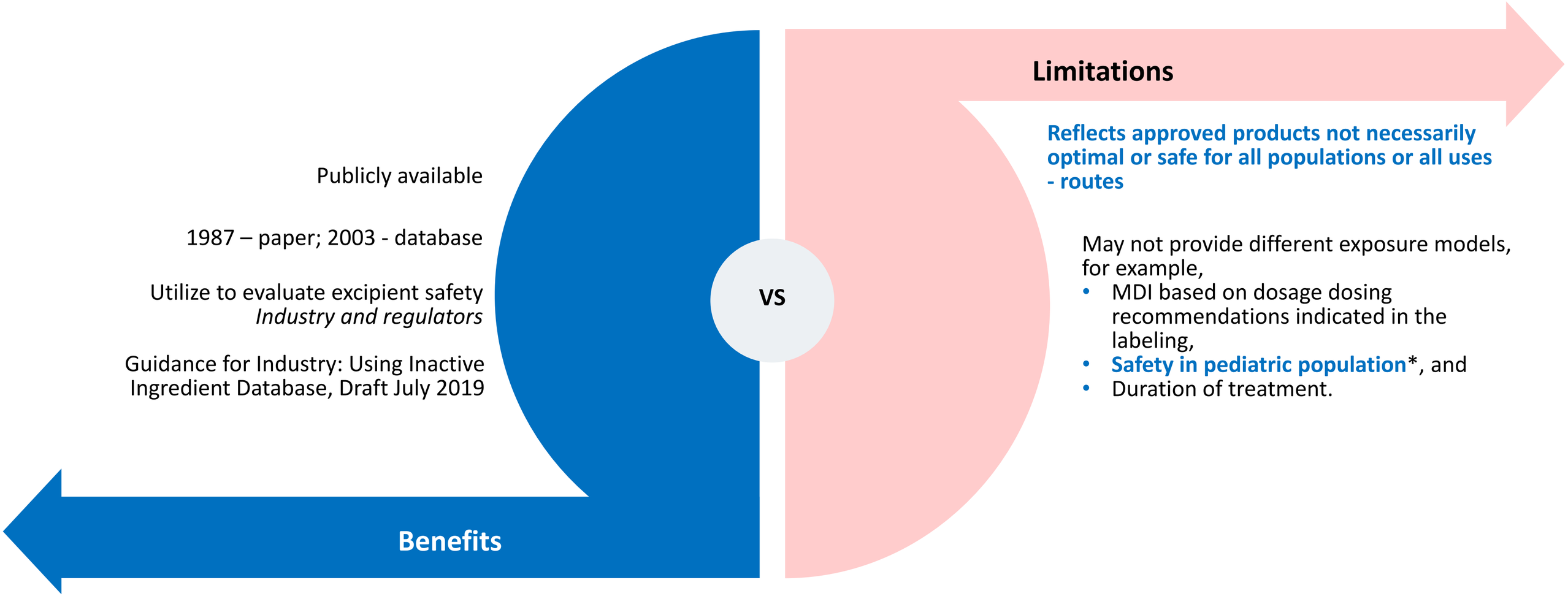
Inactive Ingredient	Route	Dosage Form	CAS Number	UNII	Maximum Potency per unit dose	Maximum Daily Exposure (MDE)	Record Updated
BENZYL ALCOHOL	ORAL	CAPSULE	100516	LKG8494WBH		450mg	
BENZYL ALCOHOL	ORAL	CAPSULE, EXTENDED RELEASE	100516	LKG8494WBH	1.23mg		
BENZYL ALCOHOL	ORAL	SOLUTION	100516	LKG8494WBH		360mg	
BENZYL ALCOHOL	ORAL	SUSPENSION	100516	LKG8494WBH		100mg	
BENZYL ALCOHOL	ORAL	TABLET	100516	LKG8494WBH	1.06mg		
BENZYL ALCOHOL	ORAL	TABLET, DELAYED RELEASE	100516	LKG8494WBH	2.31mg		

Showing 1 to 6 of 6 entries (filtered from 51 total entries)

Previous 1 Next

FDA IID

As per current draft guidance document



IID – Inactive Ingredient Database
MDE – Maximum Daily Exposure
* Very rare; if all (factors must be considered)

CAS – Chemical Abstract Service
UNII – Assigned by GSRS, a unique alphanumeric code that identifies a substance based on ,molecular structured and/or descriptive information

IID Considerations – Pediatric Specific

Resources - Tools and Databases

- Support regulatory review of drug products with pediatric indications
- Improve safety evaluation for vulnerable populations
- MDI and MDE calculations for individual ages (newborn to adolescents)
- Multiple dosage forms

IID Considerations – Pediatric Specific

Resources - Tools and Databases

Potential benefits for innovator and generic drug products:

- Align with regulatory mandates for pediatric patients
- Fill potential pediatric excipient safety data gaps
- Support pediatric drug research, development, and approval
- Support the development of age-appropriate pediatric formulations
- Provide useful information to patients, caregivers, and physicians
- Facilitate cumulative exposure assessments/risk management across multiple drug exposures

Hypothetical Scenario # 1

Potential Drug product (Drug X)

Oral: Tablet; Chewable

Dose: 4 mg

MDD = 4 mg/day (once daily)

Duration: Chronic

Population: Adults and Pediatrics (Youngest pediatric age group: 2 years old and older)

Drug X	MDE value Based on Current IID*
Hydroxypropyl Cellulose	1050 mg
Microcrystalline Cellulose	1725 mg
Magnesium Stearate	127 mg
Aspartame	195 mg

Is it acceptable for pediatric populations?

* - Actual values in FDA's IID as of 5/19/2026

Hypothetical Scenario # 2

Weight-based considerations

Potential Drug Product Y

Oral: Suspension

Maximum Dose: 10 mL twice a day

Excipient Z– 5 mg/mL

MDD = 100 mg/day

Threshold/MDE for Excipient Z: 25 mg/kg per day*

Duration: Chronic

Population: Adults and Pediatrics (Youngest age group: Neonates)

Patient	MDE	Assessment
Child	6.7 mg/kg/day	
Infant	20 mg/kg/day	
Neonate	50 mg/kg/day	

* Hypothetical threshold – not meant to align with other regulators or regulatory initiatives

ELSA

Artificial Intelligence Tool

ELSA

ELSA is a generative AI-based chat tool designed to internally assist FDA staff with core functions

Usage Capabilities:

- Data Analysis Support
- Research and information synthesis
- Regulatory guidance research
- Document drafting assistance
- Process clarification and workflow guidance
- Training and educational support
- Secure web access

What it is not used for:

- Final regulatory decisions
- Confidential or sensitive information
- Real-time regulatory updates
- Legal advice or official interpretations
- External communications
- Emergency or time-crucial decisions

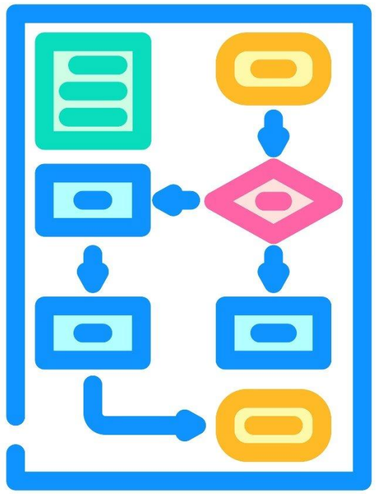
Secure government cloud environment

June 2, 2025

ELSA Review Features

Chat box

Use this feature for individual MDD and MDE calculations and quick consultations on specific questions



Agents

Use this feature to perform batch MDD and MDE calculations, organize large-scale review projects, and maintain structured workflows

ELSA Considerations

Several factors are critical to success when using ELSA, including:

- Prompt specificity
- Ability to read approved drug labels
- Document format compatibility
- Considerations for specific age or body weight information
- Understanding the time requirements for different run types (chat versus workspace)
- Verify results – potential hallucinations

Example of Successful ELSA Run - MDD and MDE Calculations

PROMPT

Please calculate the maximum daily dose of **Drug X** oral suspension for the youngest protease inhibitor-naive children using the attached label document and body weight of 5.6 kg. Then please calculate the maximum daily exposure of **Propylene Glycol** based on the calculated the maximum daily dose of **Drug X** oral suspension and Quantity in Table 1 in the attached description-and-composition

ELSA OUTPUT

MAXIMUM DAILY DOSE CALCULATION: from "**DRUG X**" LABEL:

Dosing Requirements
From the **Drug X** prescribing information:

Weight: 5.6 kg (<11 kg weight category)

Dosing regimen: 45 mg/kg twice daily with **Drug X** (required for youngest children)

Concentration: 50 mg/mL **Drug X**

Drug X Oral Suspension Calculation
Single dose: 45 mg/kg × 5.6 kg = **252 mg Daily dose**: 252 mg × 2 = **504 mg per day Volume per dose**: 252 mg ÷ 50 mg/mL = **5.04 mL Total daily volume**: 5.04 mL × 2 = **10.08 mL per day**

Propylene Glycol Exposure Calculation
Composition Data (from Table 1)
From the description-and-composition document:
Propylene glycol: 10.2 mg/mL
Function: Solubilizer
Propylene Glycol Exposure Calculation
Propylene glycol per dose: 10.2 mg/mL × 5.04 mL = **51.41 mg Daily propylene glycol exposure**: 51.41 mg × 2 doses = **102.82 mg per day**
Weight-normalized exposure: 102.82 mg ÷ 5.6 kg = **18.36 mg/kg/day**

ELSA OUTPUT – FINAL ANSWER

Final Answer
For the youngest protease inhibitor-naive children weighing 5.6 kg:

Maximum Daily Dose of Drug X Oral Suspension:
- **504 mg per day** (252 mg twice daily)
- **10.08 mL per day** (5.04 mL twice daily)

Maximum Daily Propylene Glycol Exposure:
- **102.82 mg per day** (51.41 mg per dose)
- **18.36 mg/kg/day** (weight-normalized)

This calculation is based on:

- ***Drug X*** dosing: 45 mg/kg twice daily with ***Drug Y***
- Propylene glycol concentration: 10.2 mg/mL (from composition table)
- Patient weight: 5.6 kg
- Total daily volume: 10.08 mL

Note: Analyzed 4 total documents: Drug X labeling, body weight chart for boys 2 years and older, body weight chart for boys below 2 years old and description and composition document

Takeaways

- Excipients are not truly “inactive” – their safety must be rigorously evaluated
- The lifecycle of a drug product indicated for a pediatric population is dependent upon both the innovator and generic drug products
- There are limitations to the current publicly available IID as it relates to the pediatric population
- A pediatric IID can be a beneficial resource and align with regulatory mandates
- ELSA can be a meaningful tool to support excipient review workflows for innovator and generic drug products when used responsibly, with appropriate human verification and oversight

Resources

- Guidance for Industry: E11 Clinical Investigation of Medicinal Products in the Pediatric Population, ICH, December 2000 (Final). Link
- Guidance for Industry: Pediatric Information Incorporated Into Human Prescription Drug and Biological Products Labeling Good Review Practice, FDA, March 2019 (Final). Link
- Guidance for Industry: Acceptability of Draft Labeling to Support Abbreviated New Drug Application Approval, October 2015 (Draft). Link
- Guidance for Industry: Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients, FDA, May 2005 (Final). Link
- Guidance for Industry: Using the Inactive Ingredient Database, FDA, July 2019 (Draft). Link
- Guidance for Industry: General Clinical Pharmacology Considerations for Pediatric Studies of Drugs, Including Biological Products, FDA, September 2022 (Draft) Link
- Guidance for Industry: Pediatric Drug Development: Regulatory Considerations – Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act, FDA, May 2023 (Draft, Level 1 Guidance), Link
- Guidance for Industry: Pediatric Drug Development Under the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act: Scientific Considerations, May 2023 (Draft, Level 1 Guidance). Link
- Product-Specific Guidances for Generic Drug Development. Link

Thank You