



Food Selection, Compatibility, and Testing Strategies

Shaping the Future of Pediatric Formulation Development

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Framing the Challenge...

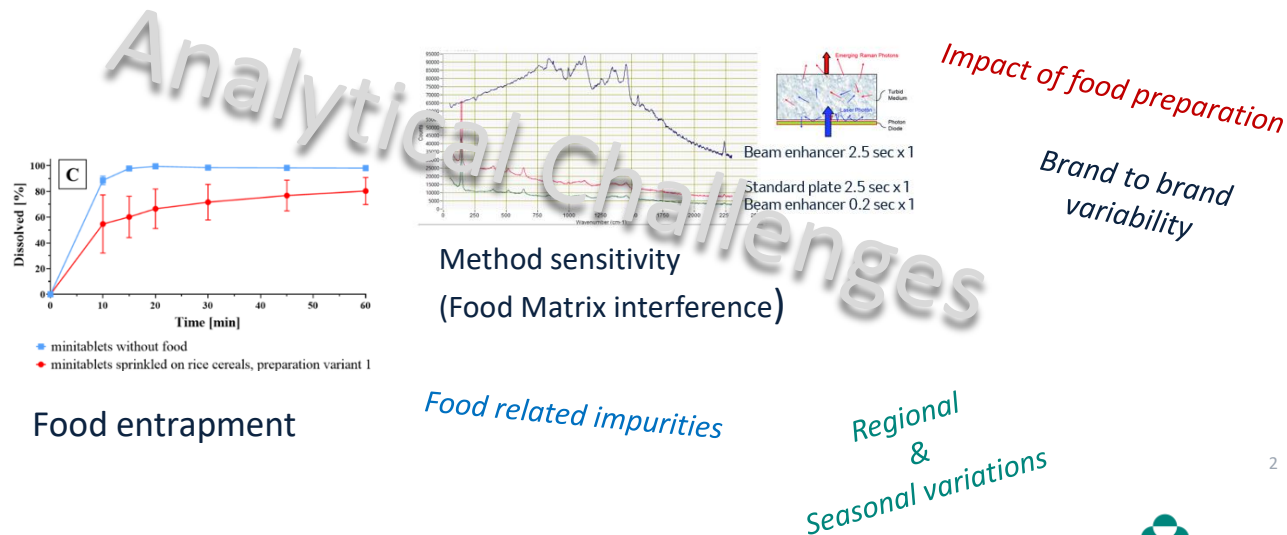
1. Why does food selection matter?

Caregivers need flexible and reliable options for administering medications in everyday settings



2. What makes robust testing of food-drug compatibility challenging?

How do we ensure meaningful assessment of compatibility and product quality in complex food matrices?



Principles for selecting food vehicles

Baseline Requirements based on patient population / TPP

Liquid dosing required?



Patient Compliance

Provide choices

Consider personal/regional preferences



Product Labeling



Define acceptable food vehicles, handling instructions and hold times

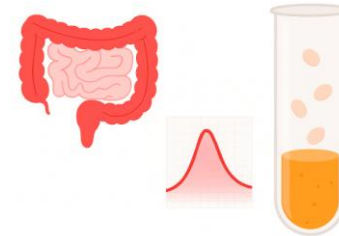


Identify foods to avoid to ensure safe and effective dosing

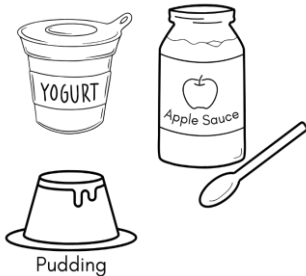
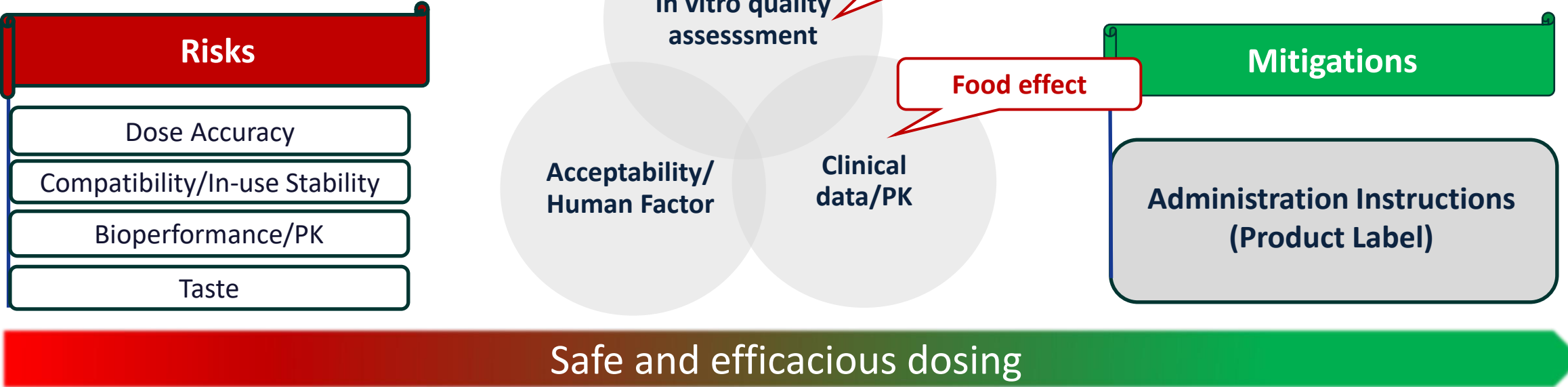


Product Performance

Compatibility with the drug product



Data to support food vehicle justification



*Improve patient compliance
(palatability & swallowability)*



Regulatory Guidance and Interpretation

**Use of Liquids and/or Soft Foods
as Vehicles for Drug
Administration: General
Considerations for Selection and
In Vitro Methods for Product
Quality Assessments**
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.



*How to translate regulatory
guidance into a meaningful
testing strategy?*

Conservative interpretation of FDA draft guidance:



PROBLEM STATEMENT

Reduce off-label use by providing clear and flexible administration instructions

THE SOLUTION

A science and risk-based framework, aligned with ICH Q9 principles, based on an understanding of food–drug product interactions



Supports general language in the product label

Examples from commercial labels:

Kalydeco® (ivacaftor)
Oral Granules



Caregiver should mix all granules into 1 teaspoon (5 mL) of age-appropriate soft food or liquid. Examples of soft foods....

[How to Take KALYDECO® \(ivacaftor\)](#)

Lamisil®
(terbinafine hydrochloride)
Oral Granules



Take Lamisil Oral Granules 1 time each day with pudding or other soft, non-acidic food such as mashed potatoes. Do not use applesauce or a fruit-based food.

[Lamisil Oral Granules: Package Insert - Drugs.com](#)

Science and Risk-based In-Food Stability Strategy

"It is understood that food and drinks are usually not standardized products and that the whole range of variability cannot be verified" (EMA Draft Guidance, 2013)

In-food stability risk assessment

Identify failure modes of the formulation & potential high-risk foods and conditions



- **Chemical and Physical Stability Risk**
- **Bioperformance**
- **Taste (in-food dissolution as benchmark)**



Food attribute-driven testing strategy

Focus on attributes most likely to impact product quality

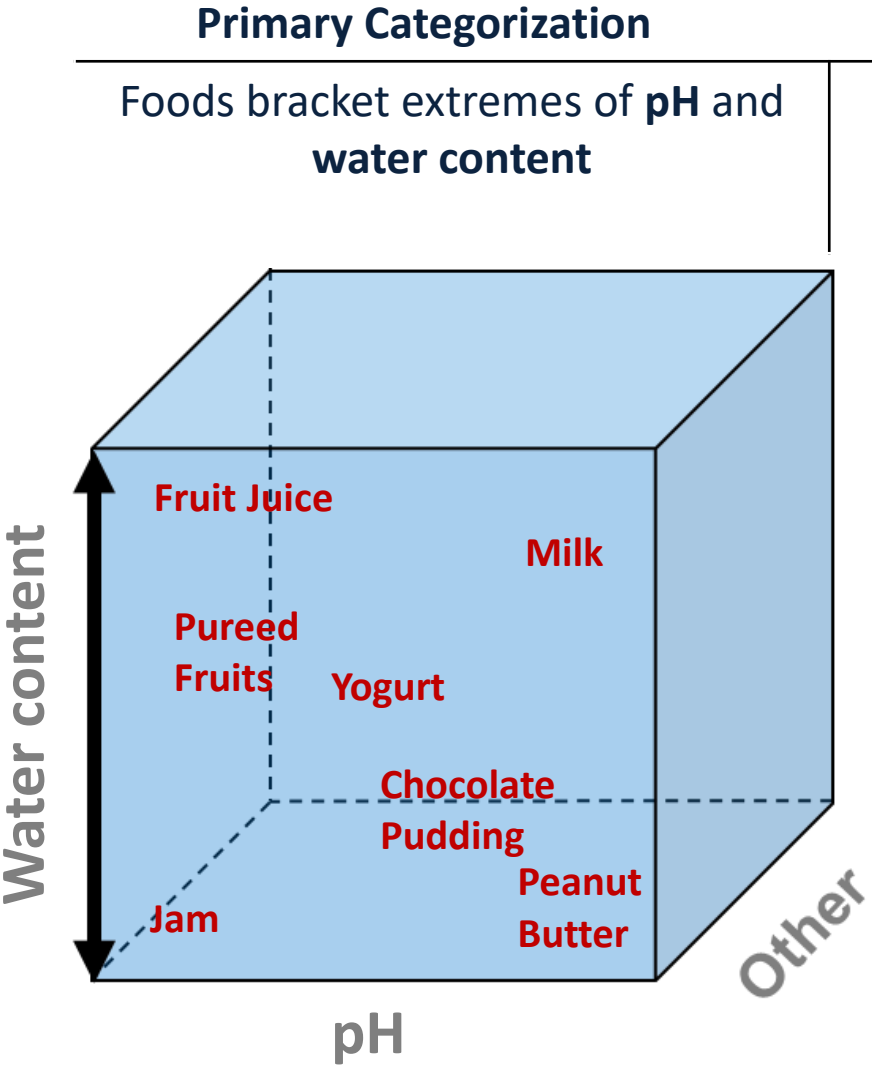
Food Selection Criteria for in-use study

- Span a broad range of relevant food properties
- Include high risk food matrices (worst case)
- Selected foods are commonly administered with pediatric drugs

Focus testing on high risk CQAs



Food Design Space Framework



Secondary Categorization

- Other pertinent food components and physicochemical attributes



High fat High protein



High Carbs

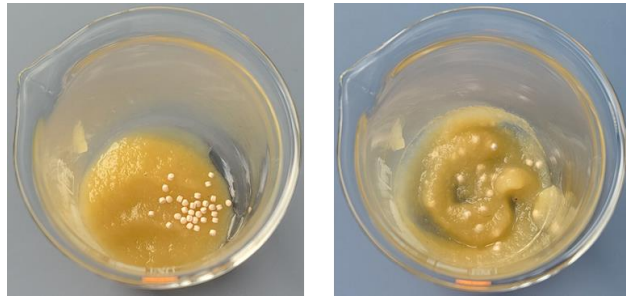
Examples of Relevant Food Attributes	
Water content	Measureable proxi associated with softening and tablet disintegration, → API dissolution required for all subsequent changes
pH	Optimum pH for all reactions e.g., pH-dependent coating
Fat	Depot for hydrophobic API/boost solubility
Proteins	Amine for condensation Protein binding (reversible)
Carbs	Adduct formation (reversible)
Preservatives	Reduction Reaction

- ❖ Framework for grouping foods based on physical and chemical properties
- ❖ Foods falling within defined brackets are deemed qualified



Designing in-use studies studies for labeling

Food In-use Study



Add

Mix + wait

Assessment window to support use time
2 hours (shorter if applicable)

Visual Examination



8 min Apple Sauce

60 min Jam

In-use & Labeling-Relevant Factors



Assessment Window

- Defines maximum hold time



Food vehicle characteristics

- Type
- Volume



Preparation variables

- Effect of Mixing
- Dispersibility & Dispersion time



Compatibility

- Device components
- Administration tools

Core analytical Design

- Dose bracketing
- Number of replicates
- Acceptance criteria
- Testing of aged product

CQAs to be tested



- Assay, (Degradation Products)
- Other CQAs as needed

Outcome: Label-Enabling Data



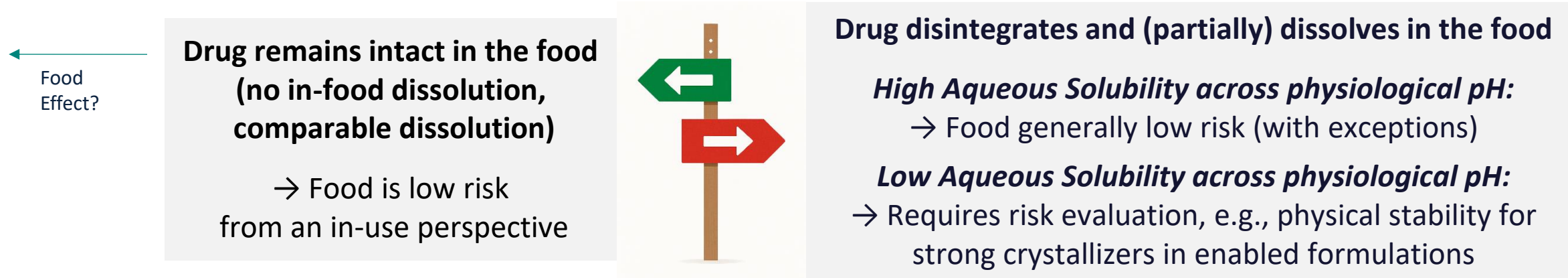
- Preparation instructions
- Acceptable Food Vehicles
- Maximum Hold Time

! API dissolution
required for all
reactions and
subsequent changes

Impact to Bioperformance

Considers **key biopharmaceutics risks** based on API physicochemical properties and formulation characteristics

Primary categorization: Physical integrity of the drug product in the food vehicle:



Final Decision

The final decision considers the food-in-use testing results and the totality of evidence, which may include

- Biopharmaceutics risk profile
 - PK and safety
 - Food Effect
- Relevant clinical experience (adult rBA study, pediatric trial)
- Risk mitigation using biopharmaceutic tools



Mavyret Oral Pellets Instructions for Use (AbbVie)

- ❖ Glecaprevir/Pibrentasvir 50 mg/20 mg film-coated 2mm oral pellets filled into Unit Dose Sachet
- ❖ Pediatric Patients 3 years of age and older

Dosing Description from drug.com:

2.5 Preparation and Administration of Oral Pellets

See MAVYRET oral pellets full Instructions for Use for details on the preparation and administration

- The oral pellets should be taken together, with food, once daily. In addition, the oral pellets for the total daily dose should be sprinkled on a small amount of soft food with a low water content that will stick to a spoon and should be swallowed without chewing (e.g., peanut butter, chocolate hazelnut spread, cream cheese, thick jam, or Greek yogurt)
- The entire mixture of food and oral granules should be swallowed within 15 minutes of preparation: the oral pellets should not be crushed or chewed.
- Liquids or foods that would drip or slide off the spoon are not recommended as the drug may dissolve quickly and become less effective.

<https://www.mavyret.com/content/dam/admpmavyret/documents/MAVYRET-Pediatric-Brochure.pdf>

STOP READ STEPS 1 - 5 before you get started!

1 Find the number of packets

The number of packets you need is on the pharmacy label.

Mix the day's packets together with food.

About 1-2 teaspoons of an acceptable food like the ones below

Remember, if you need help, you can always call! Call your healthcare provider, your pharmacist, or us: 877-MAVYRET (877-628-9738)

2 Choose the right food

USE THESE

IMPORTANT: If the pellets are chewed, or dissolve in the food, the medicine tastes bad and might not work.

NOT THESE

YES Choose soft foods that stick to the spoon

NO Watery, heated, frozen, or solid foods

3 Gather what you'll need

Container of soft food
MAVYRET pellets carton (packets inside)
Bowl
Teaspoon
Scissors

4 Prepare the dose

ADD the food to the bowl first

Be sure to get all of the pellets, and don't spill any - they're tiny!

TAP the packets above the bowl so pellets fall to the bottom

PINCH along the pellets so they don't spill

CUT along the line

POUR into the bowl of food

CHECK the packets for pellets

MIX thoroughly (don't crush, or it will taste bitter)

5 Give the medication

It's important that we take this right away.

Be careful not to chew the pellets.

You can always add more food to get every last pellet to get the full dose!

Make sure to follow medication with a snack or meal.

QUESTIONS AND SAFETY INFORMATION

How long can the pellets stay in the mixture?

- After 5 minutes, a bitter taste will be noticeable to the child.
- After 15 minutes, the medication will be less effective. Discard and call your healthcare provider.

What if my child missed a daily dose of the medication?

- Contact your healthcare provider. Do not give a double dose of MAVYRET.

What if my child is allergic to the recommended foods?

- Contact your healthcare provider. Do not mix with food that your child is allergic to.

What if my child has trouble swallowing or cannot finish the mixture?

- Contact your healthcare provider. Do not continue giving the mixture or give your child an additional dose of MAVYRET.

Can my child drink water after completing their dose?

- Yes. Drinking water after taking the medication will not change its effectiveness.

What if I need replacement packets?

- Contact your healthcare provider.

NEED HELP?

Call your healthcare provider, call your pharmacist, call us at 877-MAVYRET (877-628-9738) or visit www.mavyret.com

Please see additional Important Safety Information throughout the brochure, including Boxed Warning. Please see accompanying full Prescribing Information, including the Patient Information.

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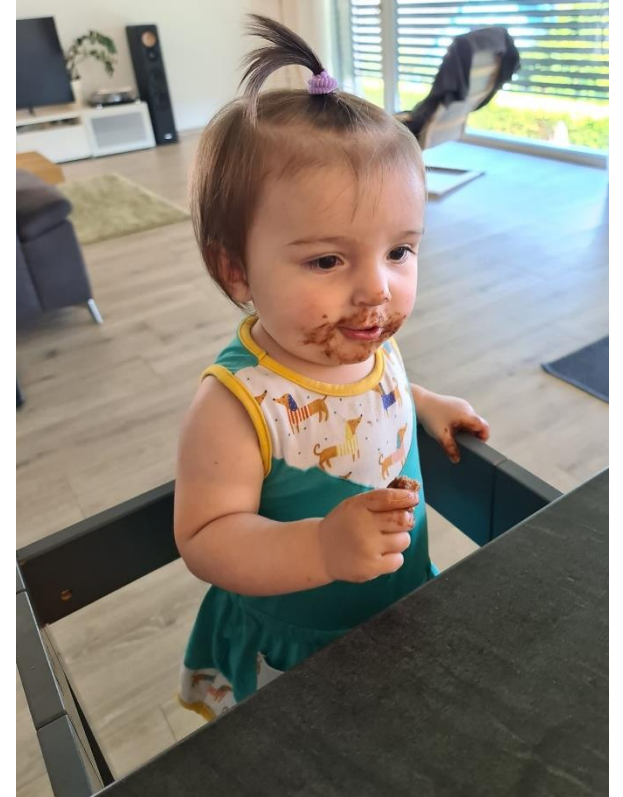
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Conclusion

A risk-based, scientifically sound framework for justifying food vehicles is proposed based on an understanding of food, drug product, and their potential interactions

The framework is intended to guide the development of clear label instructions on acceptable and unacceptable food types, thereby minimizing risks associated with off-label use



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