# Food effects in paediatric medicines development for products co-administered with food

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# Current status

- Dosage form manipulations are often performed to improve the acceptability of medicines to children, such as using food to aid administration of unpalatable medicines
- These manipulations can affect the bioavailability/pharmacokinetics of a drug product

- There is no guidance on how the impact of manipulations is risk assessed from the laboratory to the patient
  - Current practice is for **each drug** to undergo clinical evaluation with a **range of foods or other manipulations** to understand the impact on therapeutic efficacy
    - This is costly and requires many studies in children
    - Most studies use a range of "Western" foods

**Children are at risk of sub-optimal therapy**

# Current regulatory view

*WHO*

*"Ideally, an integrative analysis of all data available in different age groups and in vitro, using modelling and simulation techniques, should be used to identify the effects of different covariates (i.e. age, size, weight, **food**, sex) on PK/PD. "*

*ICH E11*

*"When a medicinal product is studied in pediatric patients in one region, the intrinsic (e.g., pharmacogenetic) and extrinsic (e.g., **diet**) factors that could impact on the extrapolation of data to other regions should be considered."*

*FDA*

*"Potential drug- **food** or vehicle interactions should be considered, such as those that have been reported with apple juice (Abdel-Rahman, Reed et al. 2007), in these study designs."*

*EMA*

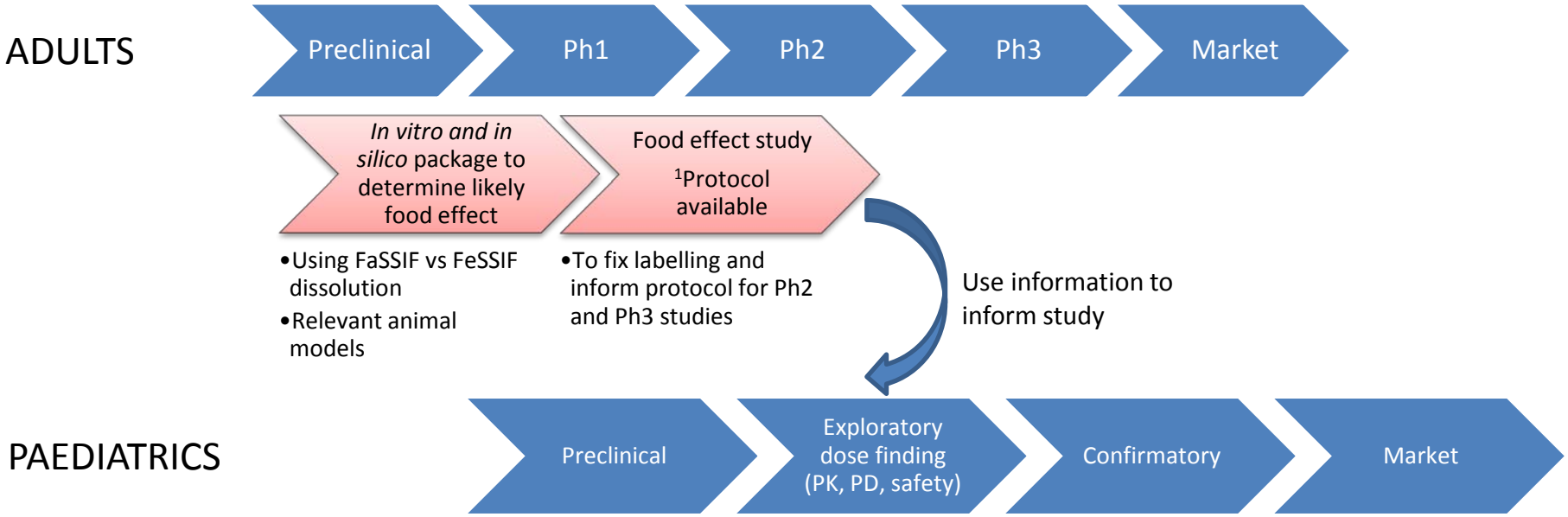
*"Mixing with food or drinks may affect the product performance and the pharmacokinetic behaviour. ……. Assessment of the impact on bioavailability of products mixed with food or drinks may be needed depending on information that is available from studies undertaken during the development of the product……."*

Food effect implications in drug delivery:

1. Variable pharmacokinetics → variable efficacy
2. Undesirable labelling restrictions

- Development processes are not defined for paediatric products which increases the time and costs of development
- Places additional barriers to the development of evidence based age appropriate paediatric medicines

# Parallel development of adult and paediatric products




**No guidance to support *in vitro* or *in silico* risk assessment to understand food effect**

**No clear protocol to undertake food effect study**

**Non-standardised development approach for paediatric products increases the relative cost and timelines to support labelling claims**

1. http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126833.pdf
*FDA Guidance for Industry. Food-Effect Bioavailability and Fed Bioequivalence Studies*

# Development pipelines

- Drugs most likely to be affected by a food effect are BCS II, III and IV
  - BCS II, III and IV are poorly soluble and/or poorly permeable drugs

- Regulatory guidelines do not provide sufficient information on assessment of food effects or other manipulations for paediatric products
  - Guidance mandates an adult fed effect study
  - Guidance for paediatric food substances is missing

- Extrapolation of food effects from adults does not always predict food effects in paediatric populations
  - In a review of 18 studies reported 11 showed the same pharmacokinetic result as that in adults in a food study; 5 showed different results to the adult study and 2 could not be compared. [1]

*1. Influence of Food on Paediatric Gastrointestinal Drug Absorption Following Oral Administration: A Review Hannah K. Batchelor Children 2015, 2(2), 244-271; doi:10.3390/children2020244*

# Aim of the session

- Develop a decision tree and best practice approach for which *in vitro / in vivo* studies should be conducted to de-risk co-administration of paediatric medicines with food
- How we will achieve this:
  - Bring together academic and industrial expertise in this area
  - Use two case studies to consider a theoretical plan of in vitro, in silico and clinical studies to ensure risks are minimised
  - Review case studies and proposals to seek consensus amongst experts present

# BACK-UP SLIDES