Case studies: application of non-animal approaches to assess food ingredients

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2020 Summer Meeting

Introduction

- Overview of food ingredients safety dossiers submitted to EFSA or FDA

- Non-animal approaches (NAMs) were used:
  - **Successfully** – with newly generated *in vivo* data adding little to the WoE approach
  - **Unsuccessfully** – additional data required (not necessarily animal data)

efsa
European Food Safety Authority

FDA
GRAS GENERALLY RECOGNIZED AS SAFE

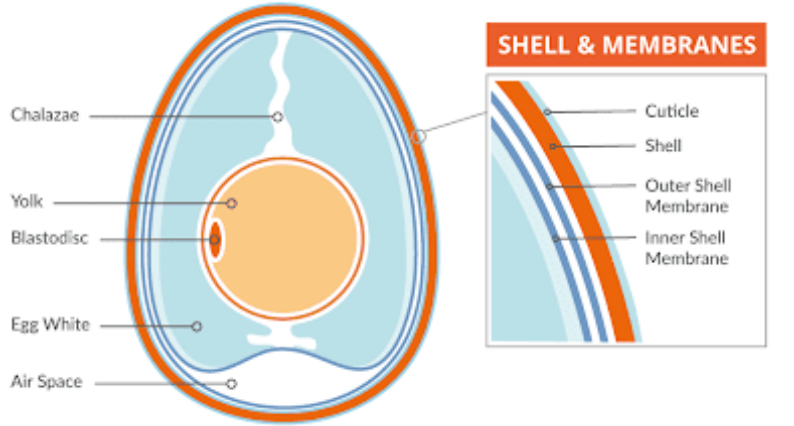
Unilever

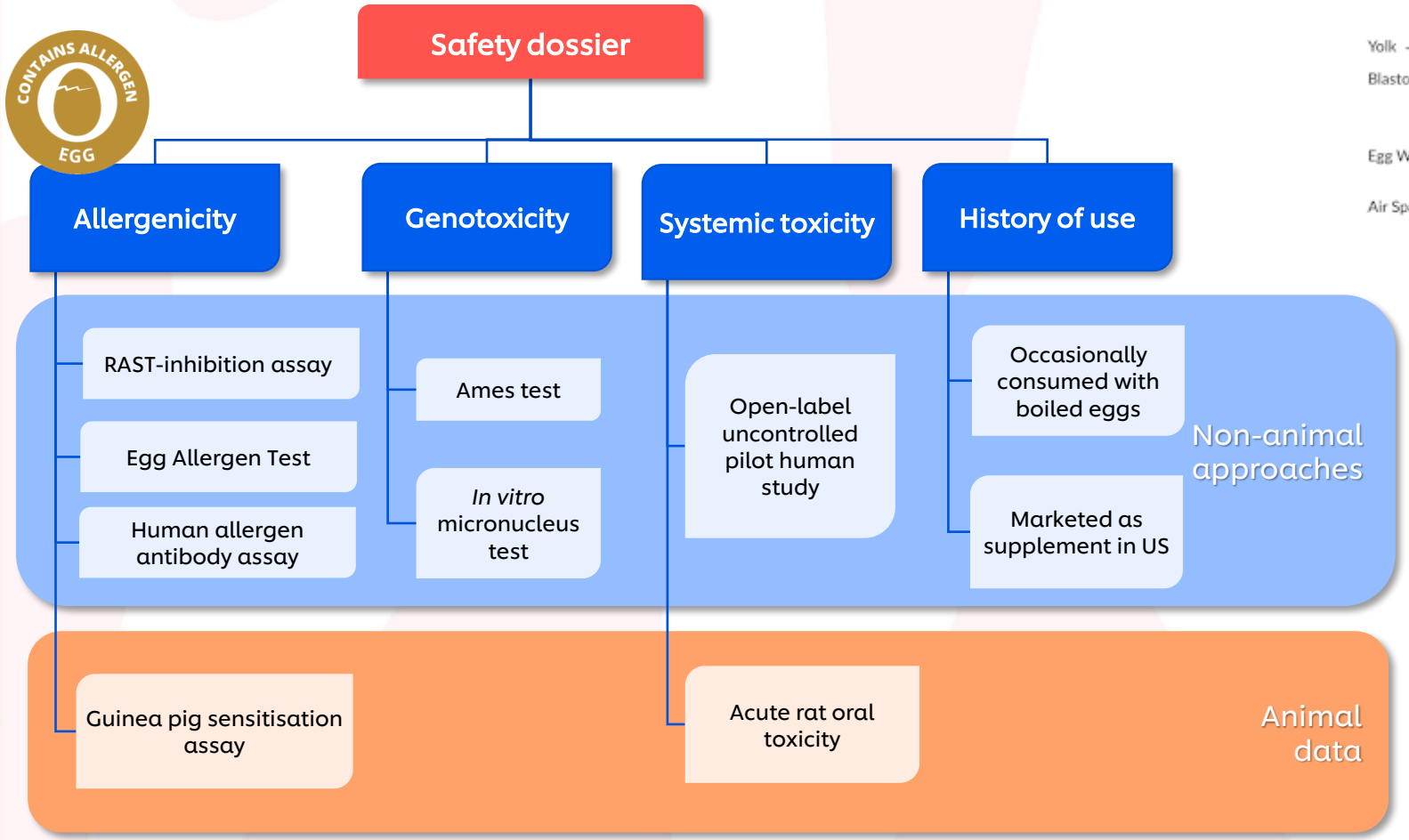
Egg membrane hydrolysate

New Dietary Ingredients (NDI) Notification (2009)

Novel Food Submission (2016)

- **Identity of the food:** a protein-based powder. Its main constituents are elastin, collagen and glycosaminoglycans derived from chicken eggs.
- **Proposed use:** food supplement.





Key points

- A full toxicological assessment was not provided by the applicant and not deemed necessary by EFSA.

Ingredient-specific in vivo data added little to the weight of evidence approach.

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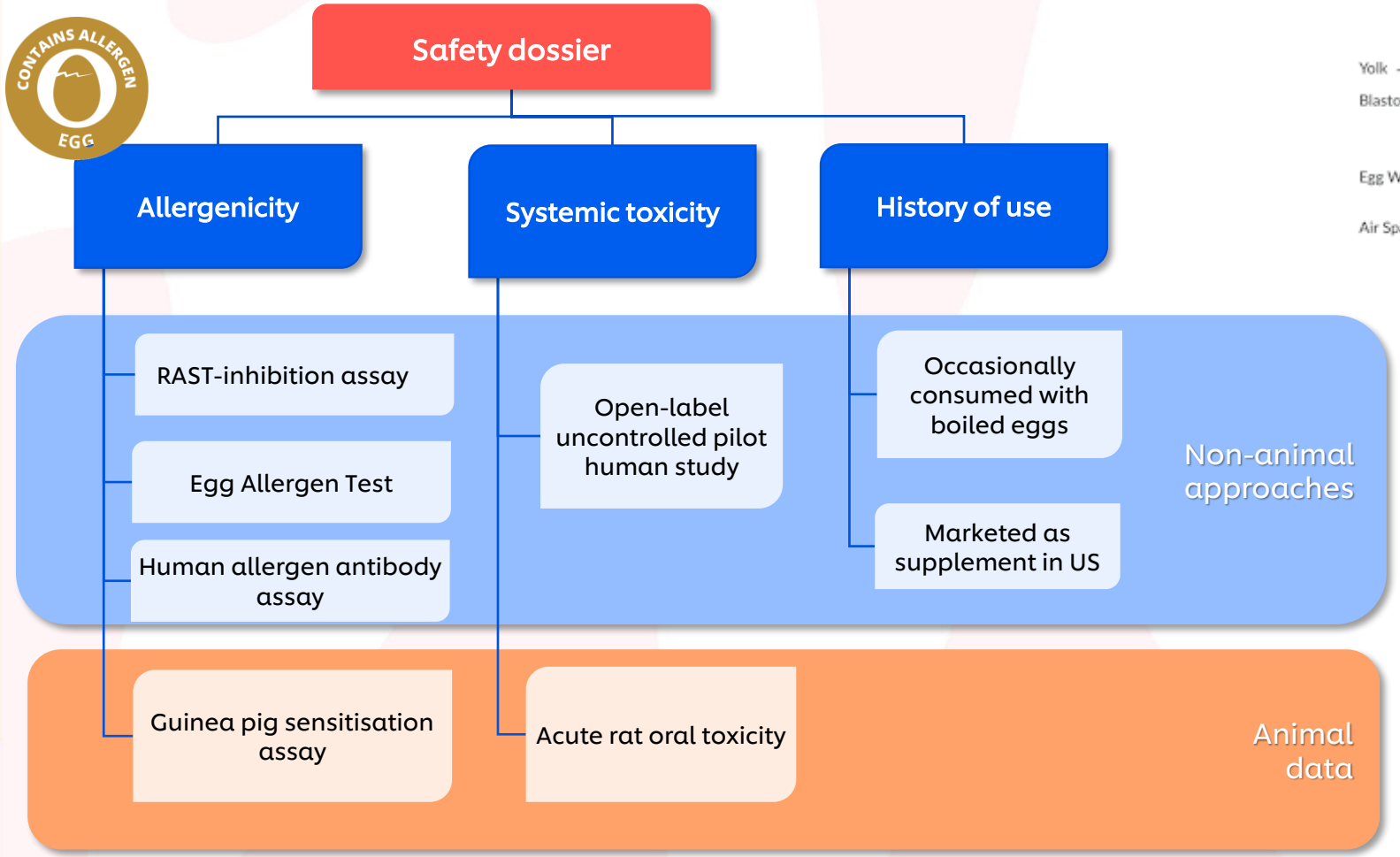

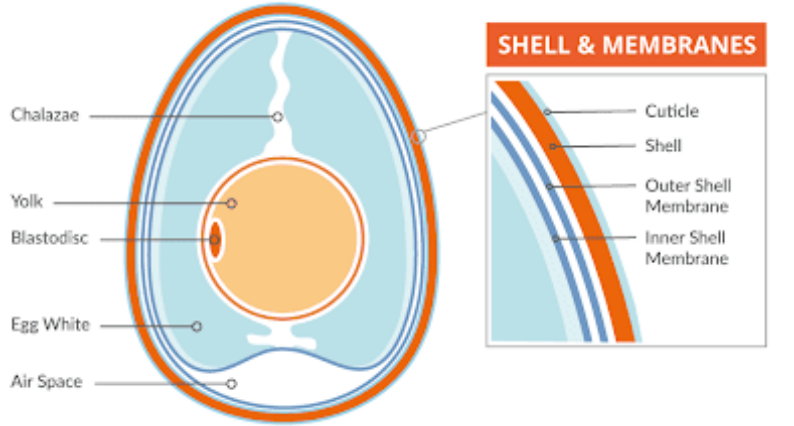

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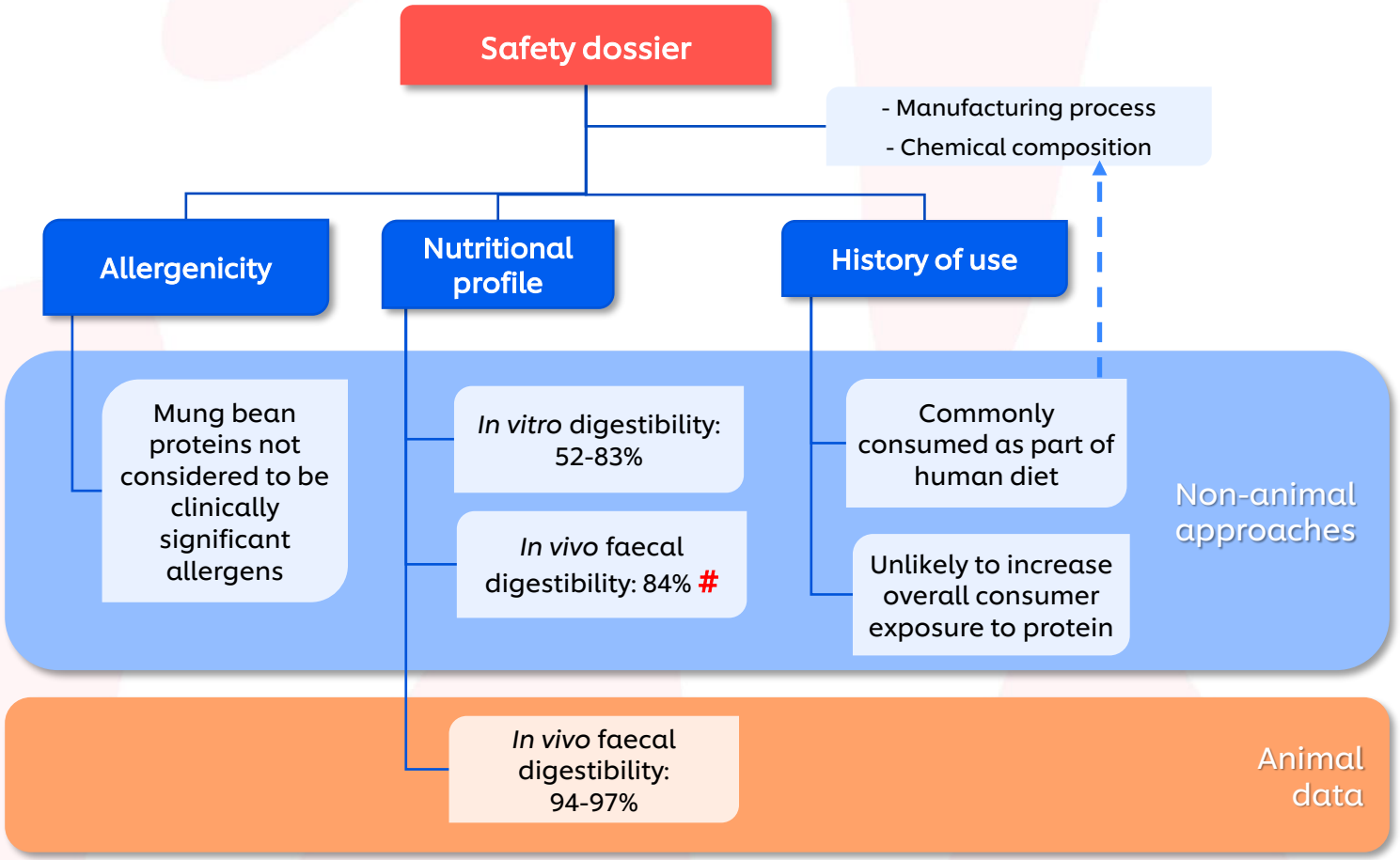
Mung bean protein isolate

GRAS Notification (2016)

- **Identity of the food:** powder from mung beans (*Vigna radiata*) (>80% protein)
- **Proposed use:** direct protein replacement of animal- or vegetable-based protein.



existing *in vivo* data, not generated for the intended assessment

Key points

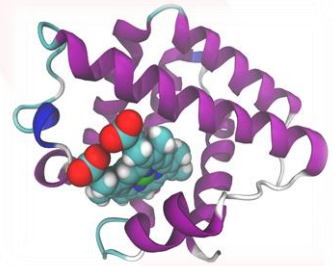
- The applicant stated that product-specific *in vivo* toxicity studies were not necessary for the safety assessment.
- No additional toxicological data requested by FDA.

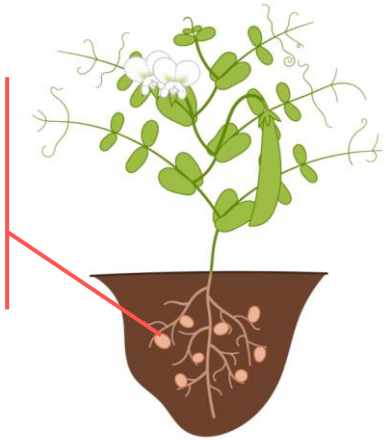
Ingredient-specific in vivo data did not provide any additional information

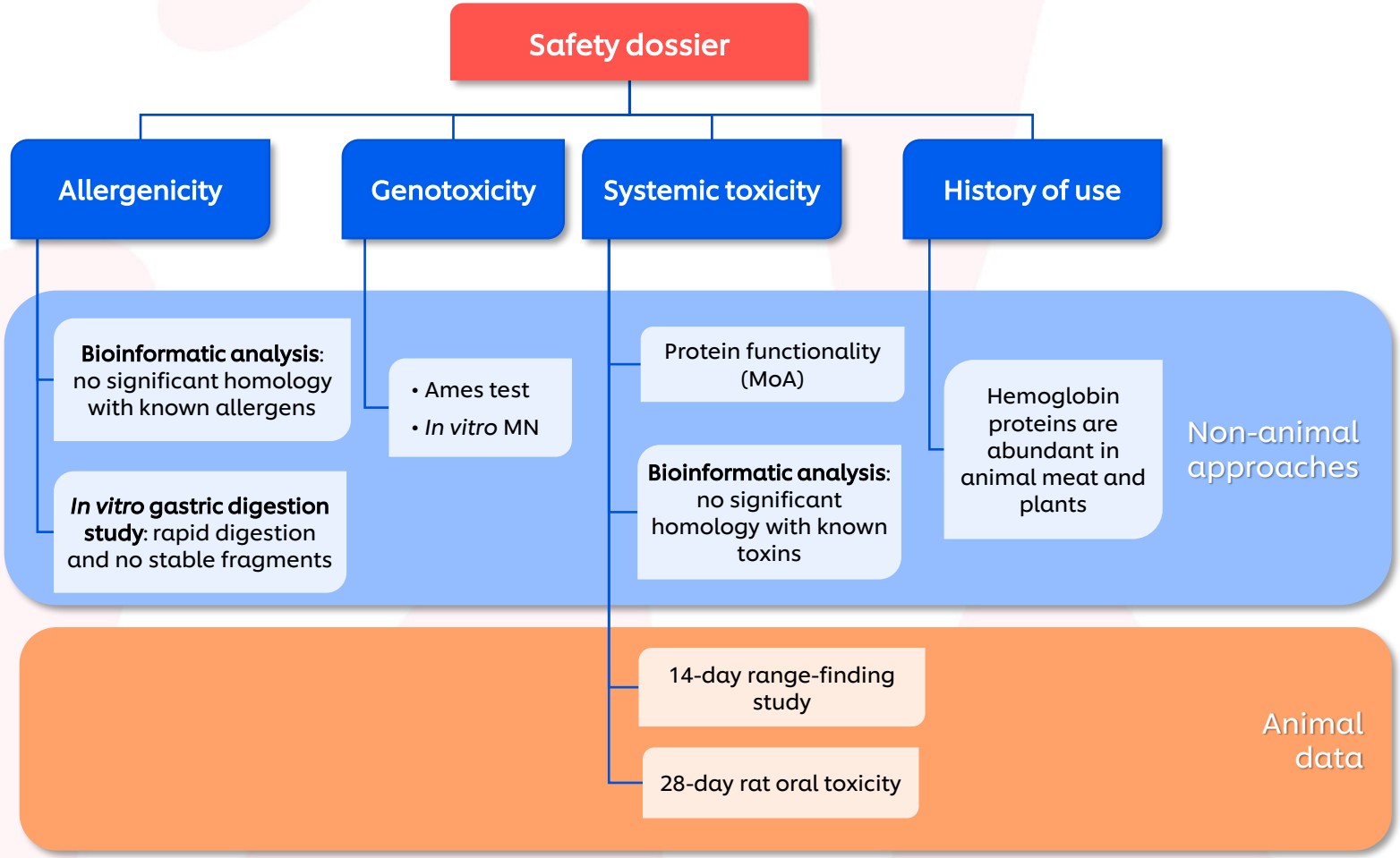
Soy leghemoglobin

GRAS Notification (2017)

- **Identity of the food:** leghemoglobin from soy (*Glycine max*) expressed in yeast (*Pichia pastoris*).
- **Proposed use:** food ingredient in meat-replacement products as iron source.







Key points

- The history of consumption of hemoglobin proteins in food together with the NAM data provided clear evidence to make a determination of safety.

Conclusion could have been based on comparison with other haemoglobin/overall protein intake rather than NOAEL from in vivo tox study.

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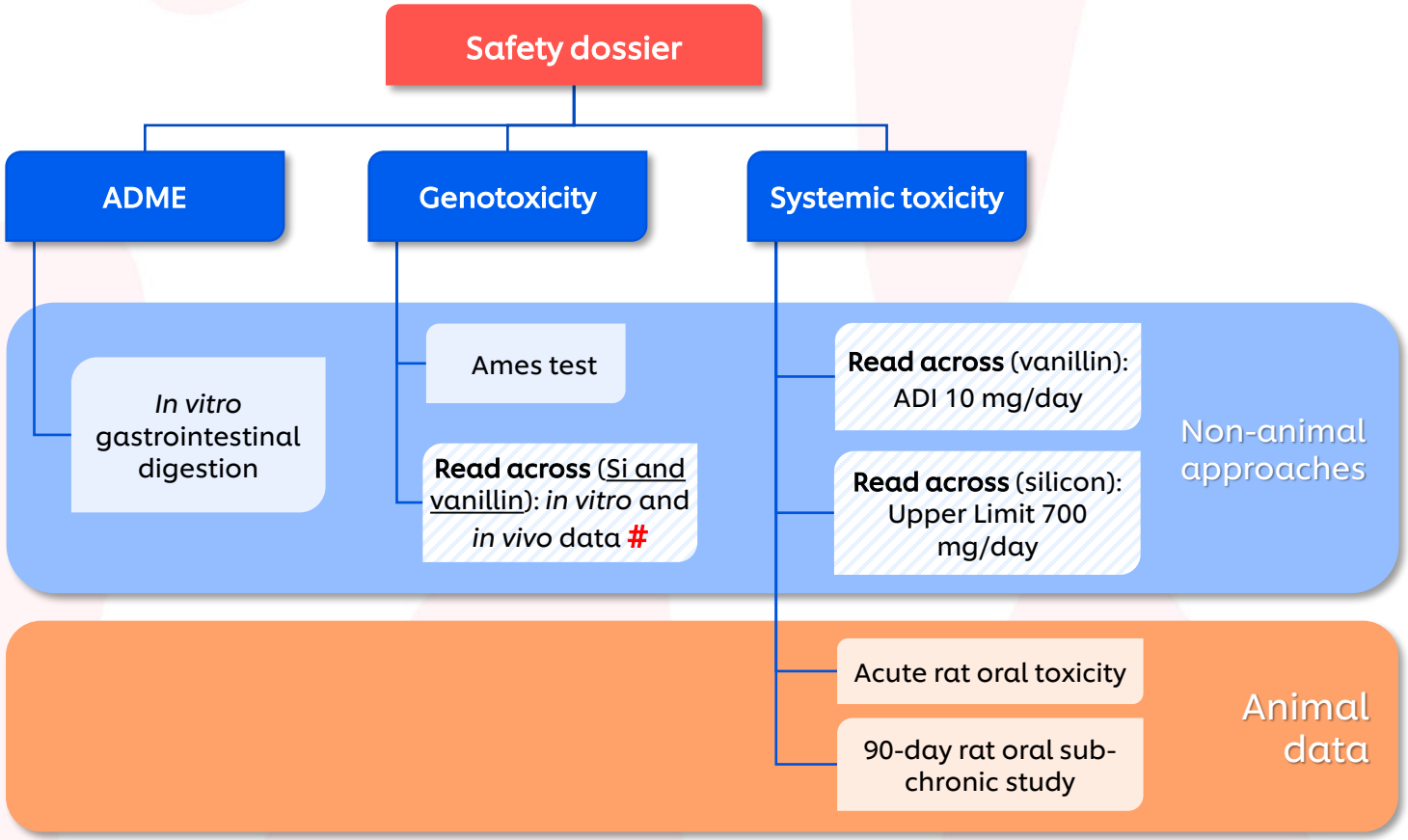
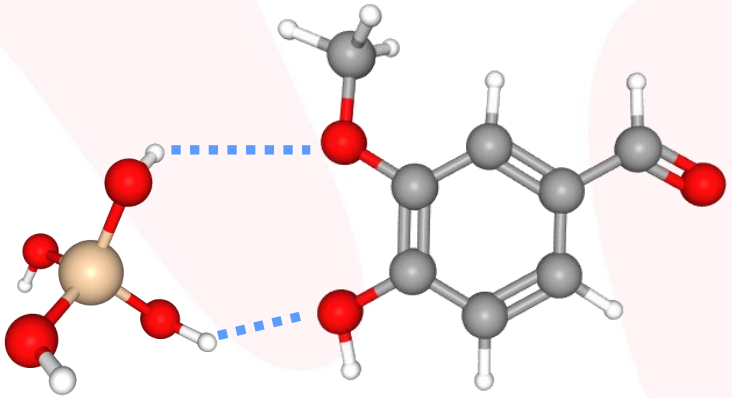
Orthosilicic Acid – Vanillin Complex (OSA-VC)

Novel Food Submission (2014)

efsa European Food Safety Authority

- **Identity of the food:** complex composed of orthosilicic acid [$Si(OH)_4$] and vanillin linked by weak hydrogen bonds.
- **Proposed use:** food supplement as a source of silicon (Si).





Key points

- *In vivo/vitro* studies on OSA-VC had severe limitations due to the technical difficulties with the solubility and dosing of the substance.
- Nevertheless, no additional toxicological data were required for the complex by EFSA

Ingredient-specific in vivo study could be considered unnecessary

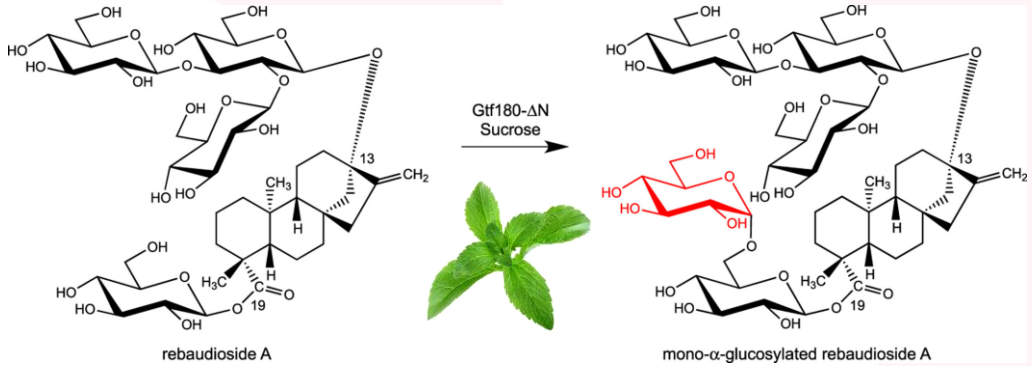
existing *in vivo* data, not generated for the intended assessment

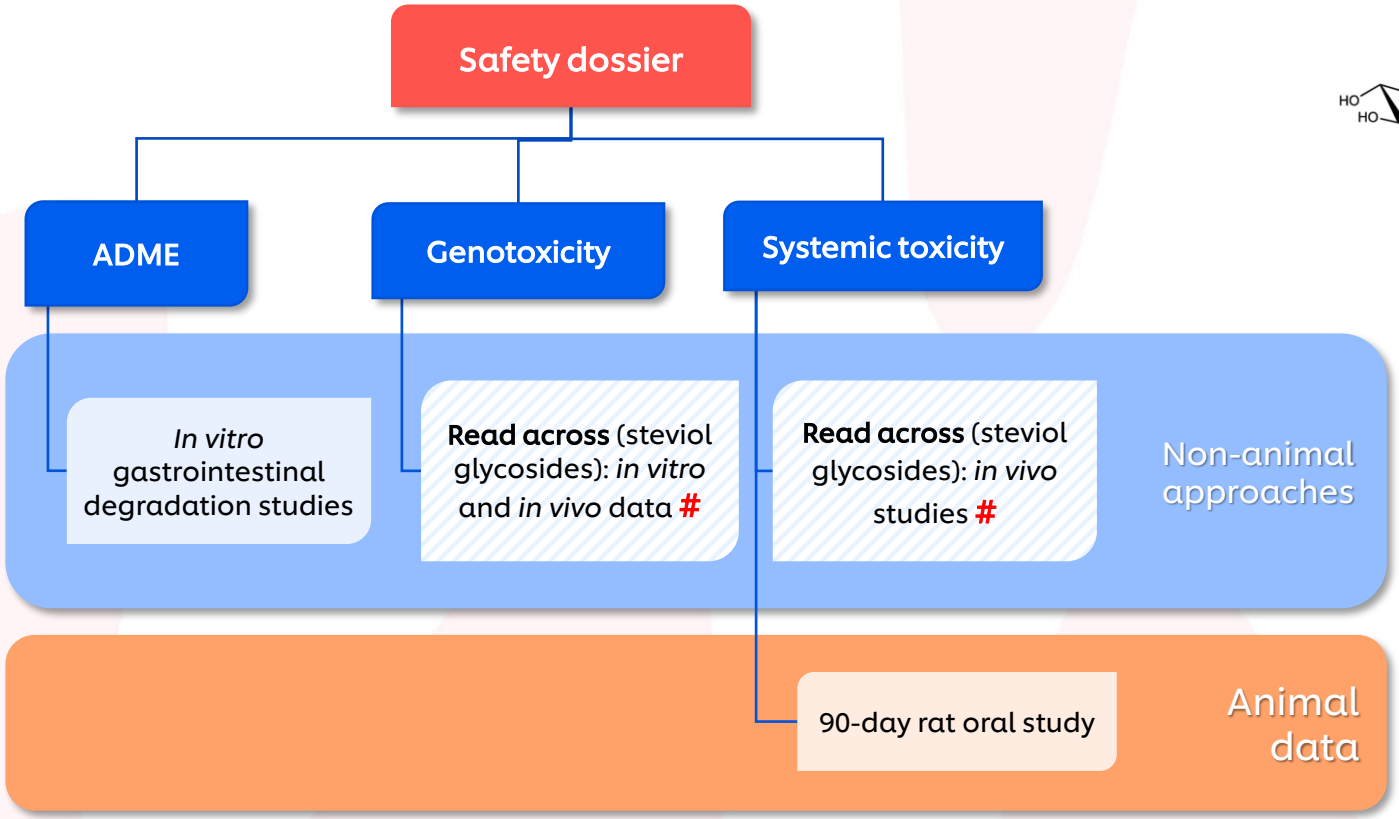
Unilever

Glucosylated steviol glycosides

GRAS Notification (2016) ✓ | Food Additive Application (2018) ✗

- **Identity of the food:** mixture of glucosylated steviol glycosides, containing 1–20 additional glucose units bound to the parent steviol glycoside
- **Proposed use:** sweetener





existing *in vivo* data, not generated for the intended assessment

Key points

- EFSA rejected the *read-across* approach because the common metabolic pathway could not be proved
  - Complete hydrolysis was not demonstrated in one study
  - Full study data from (incl. test material characterisation) were not provided by the applicant

Read-across needs to be properly substantiated

Ingredient-specific in vivo study can be considered unnecessary

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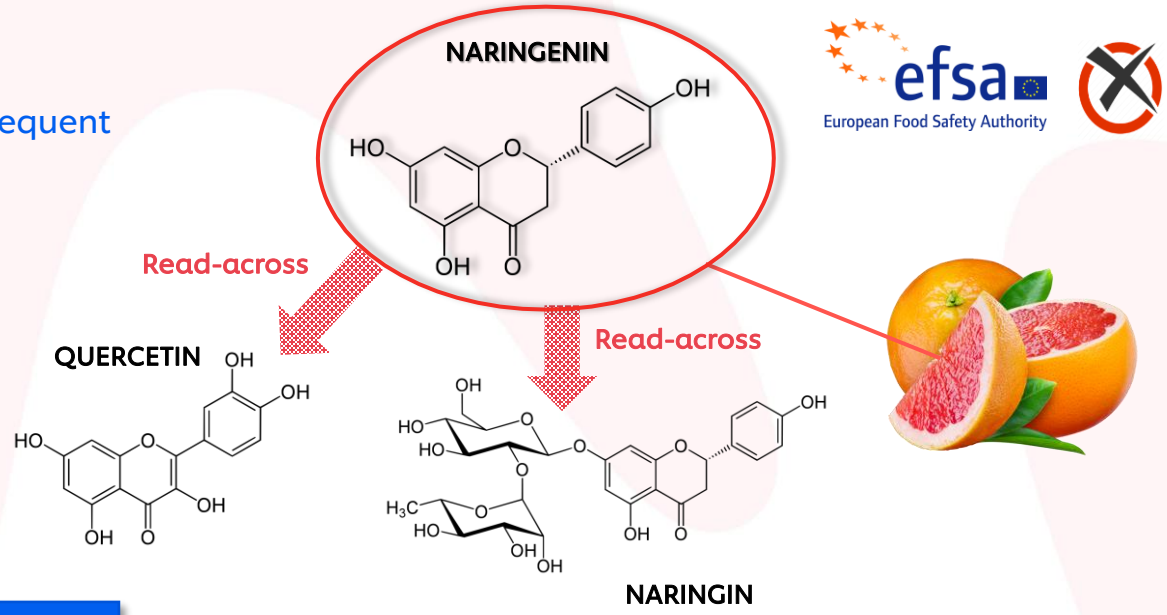
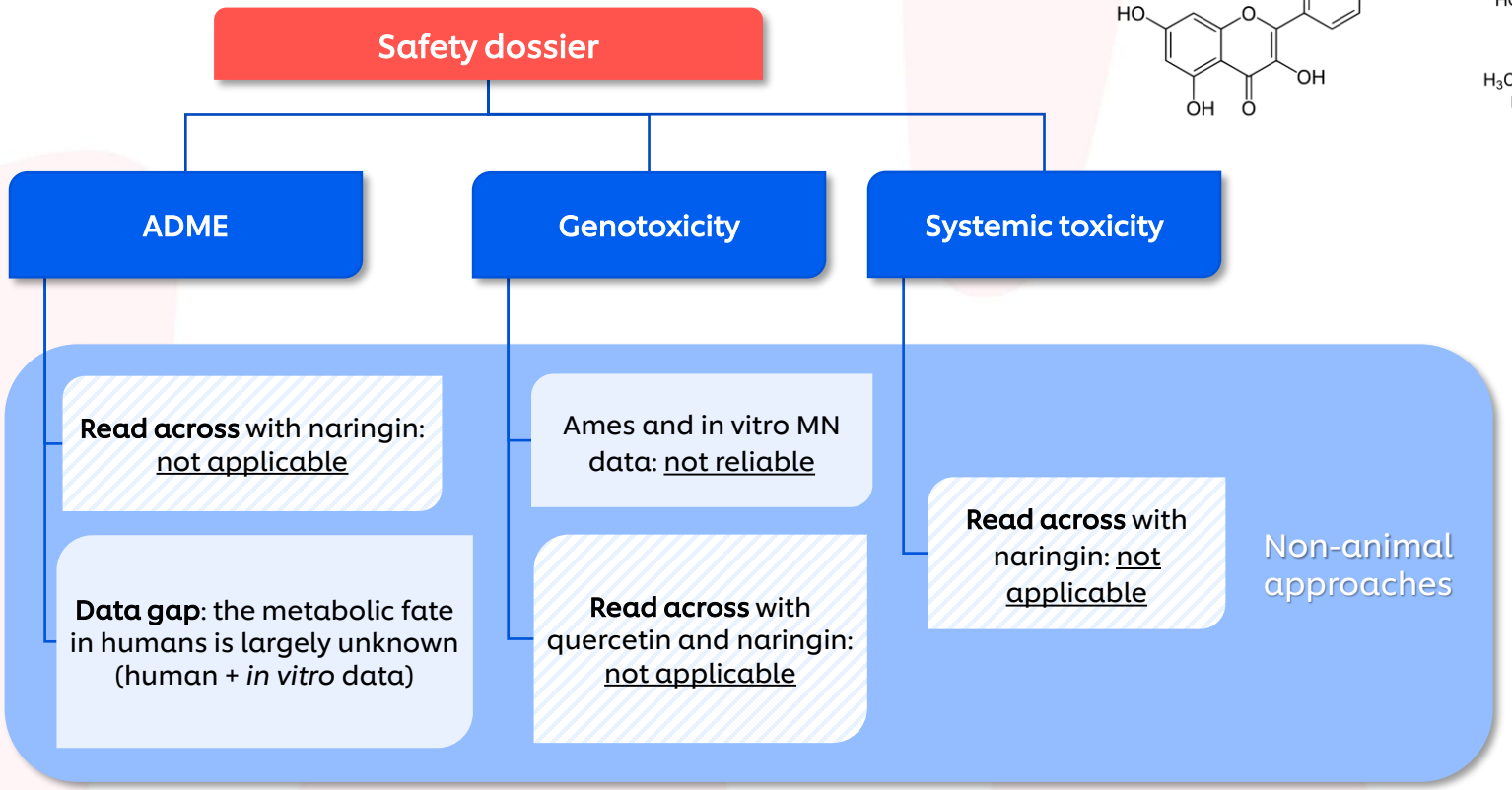
Naringenin

Flavorings Submission (2017)

- **Identity of the food ingredient**: obtained via extraction and subsequent hydrolysis of *naringin* from grapefruits.
- **Proposed use:** flavouring substance





Key points

- Read-across between naringenin and naringin or quercetin was considered not applicable
- EFSA could not reach a conclusion as to the safety of naringenin since the available data on genotoxicity are not adequate.

Read-across needs to be properly substantiated

Conclusions

- Food ingredient safety assessment requires a different and more flexible approach with respect to that traditionally used for chemical entities.
- A case-by-case approach is needed which must be adapted to take account of the characteristics of the individual novel food
- As the occurrence of completely new chemical entities is unlikely to happen in the food space, this provides a unique opportunity for the use of non-animal methods in RA:
  - Chemical composition/characterisation
  - ADME
  - Exposure estimates
  - History of use
  - Read-across
  - Existing *in vivo* data
- Joint effort from regulators and industries in being more open and confident in generating, considering and accepting non-animal approaches for food risk assessment and management.

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Acknowledgment

Innovation Through Collaboration

IFSH | INSTITUTE FOR FOOD SAFETY AND HEALTH

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