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Improving Allergy Risk Assessment Strategy for new food proteins

Dr. Kitty Verhoeckx
UMC Utrecht

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EUROPEAN COOPERATION
IN SCIENCE AND TECHNOLOGY

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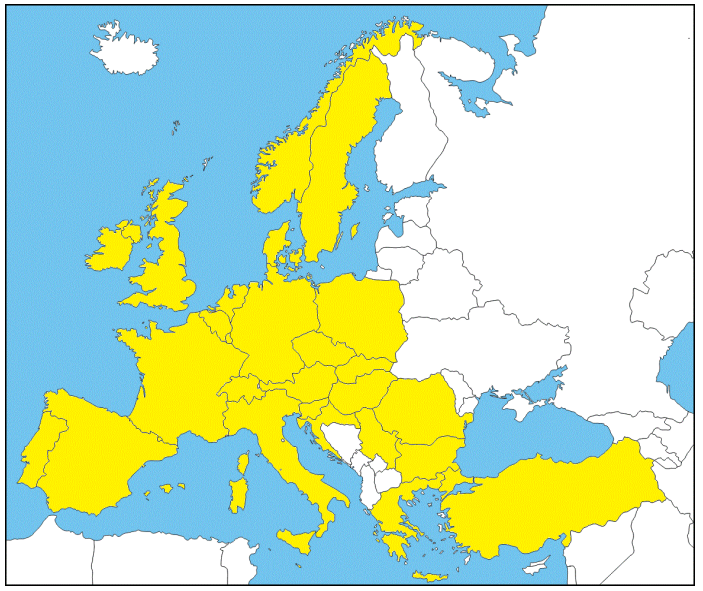
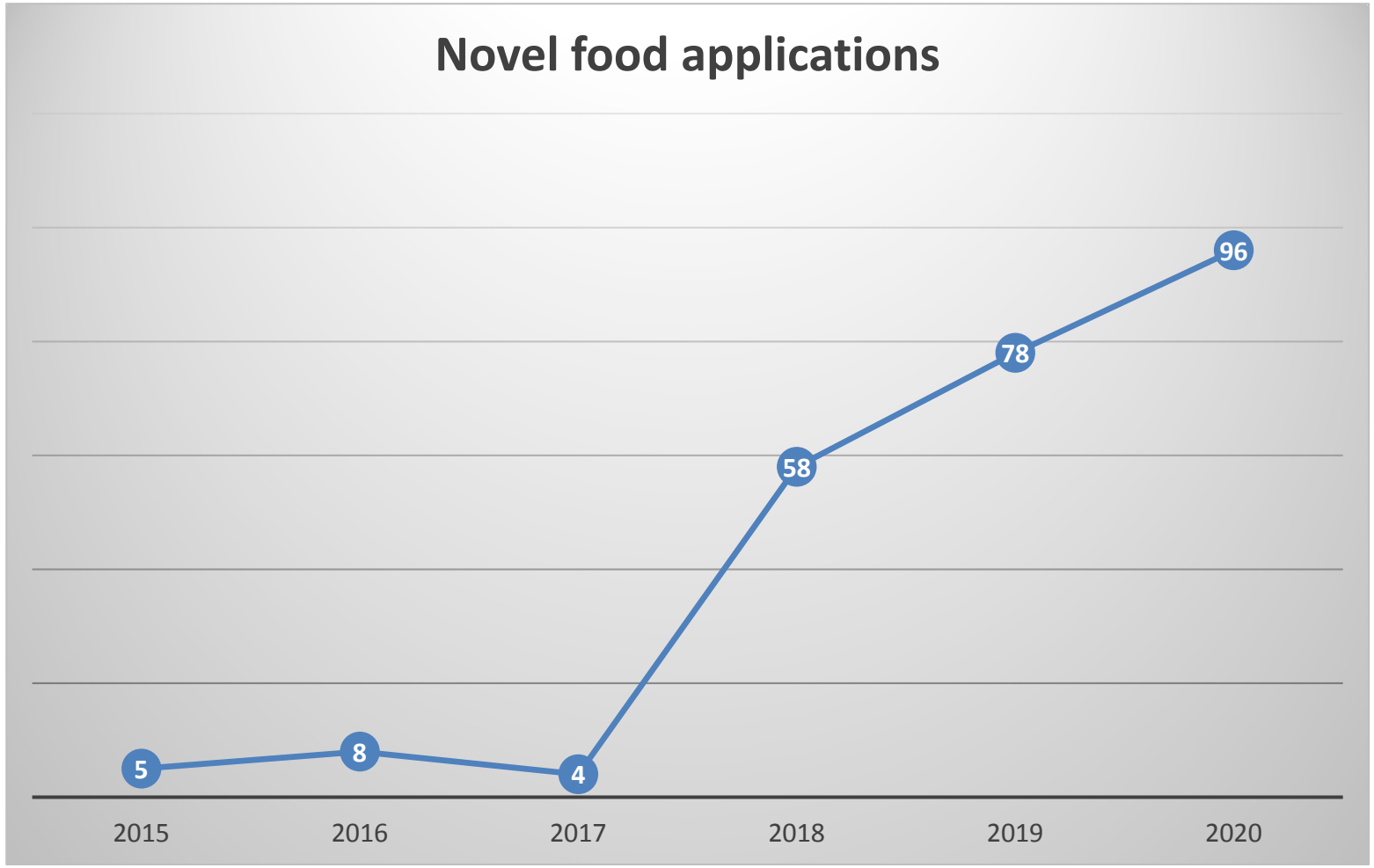


Aim:

To build an interdisciplinary European network of scientists with a broad range of expertise to discuss, with an out-of-the-box view, new ideas and more predictive models and approaches to improve the current allergenicity risk assessment strategy of novel foods

Novel food applications 2015-2020



http://registerofquestions.efsa.europa.eu/roqFrontend/login?7

Guidance novel foods 21 Sep 2016,

(amending EC regulation No 97/618 and 2015/2283)

- Regulation is in force since January 2018
- Default assumption for Novel Foods containing proteins is that such Novel Foods have allergenic potential
- Comprehensive literature review in order to retrieve available information on sensitization, and on case reports of allergic reactions and/or allergenicity studies (in vitro, in animals, in humans) of the Novel Food and/or its source(s).
- GMO guidance → individual proteins (digestion, homology, source of the gene, stability, IgE binding).

No validated methods for prediction sensitisation

efsa
European Food Safety Authority

Safety of rapeseed protein isolate

The Panel considers that the risk of sensitisation to rapeseed cannot be excluded and that it is likely that rapeseed trigger can allergic reactions in mustard allergic subjects.

efsa
European Food Safety Authority

Safety of 'Chia seed (*Salvia hispanica*) and ground whole Chia seed'

The Panel notes the cross-reactivity of sera from patients known to be allergic against peanuts and sesame and reiterates its previous opinion that it is not possible to predict the potential allergenicity of Chia using methodologies available to date.

Should we worry about novel foods?

- 87% of the Shrimp allergic patients had a positive DBPCFC to mealworm
  - Allergens involved: Tropomyosin and Arginine kinase
  - Reaction on first meal

- De novo sensitization/allergy to mealworm is also possible.
  - 2 out of 25 mealworm breeders had a positive DBPCFC to mealworm
  - 2 workers in production facility of mealworm flour food allergic to mealworm
  - Patients where not allergic to shrimp or any other food
  - Responsible allergen: Larval Cuticle protein, cockroach allergen like protein, early-staged encapsulation protein and troponin C
  - Route of sensitisation: lungs, skin and ingestion of multiple doses

Broekman et al: J Allergy Clin Immunol. 2016 doi: 10.1016/j.jaci.2016.01.005
Broekman et al: J Allergy Clin Immunol. 2017 doi: 10.1016/j.jaci.2017.01.035.
Nebbia, S., et al: Clin Exp Allergy, 2019 doi: 10.1111/cea.13461

Chair: Kitty Verhoeckx 

Vice Chair: René Crevel 

Working group 1
Physical chemical properties and Analysis


Karin Hoffmann-Sommergruber & Gabriel Mazzucchelli

Working group 2
In vitro methods


Erwin Roggen & Edyta Sienkiewicz-Szłapka

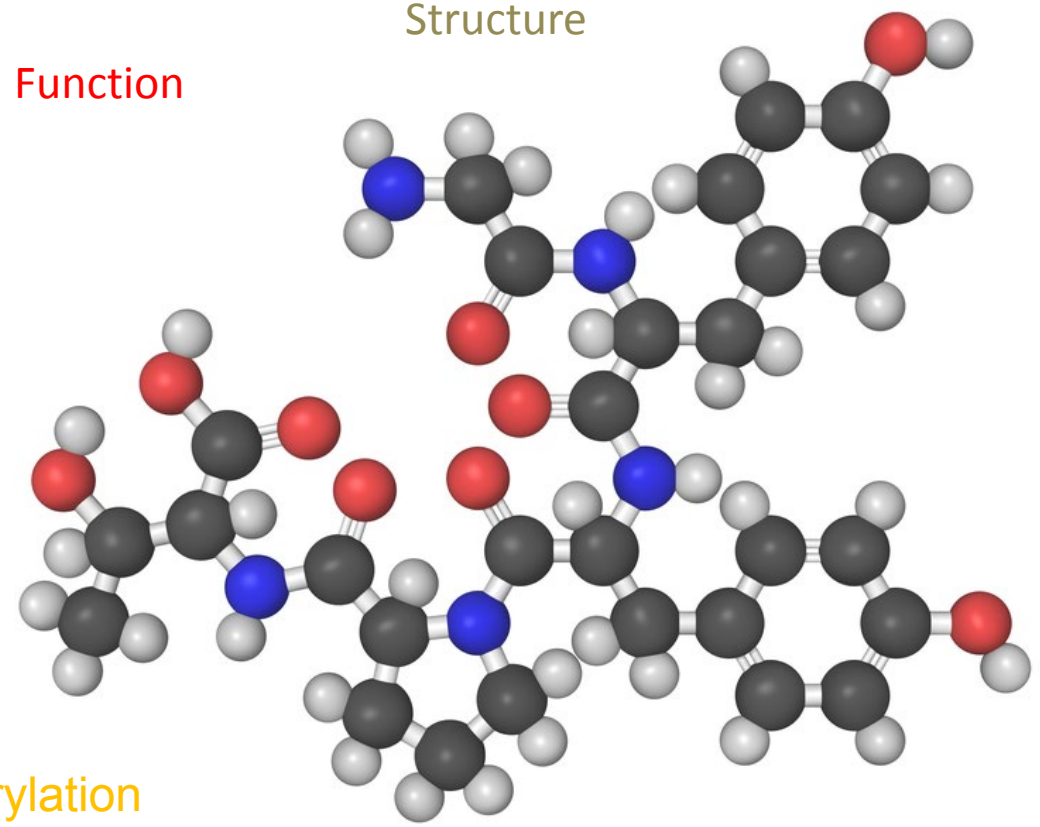
Working group 3
In vivo methods


Liam O'Mahony & Katrine Lindholm Bøgh

Working group 4
Risks assessment and clinical perspectives


Anne Constable & Ben Remington

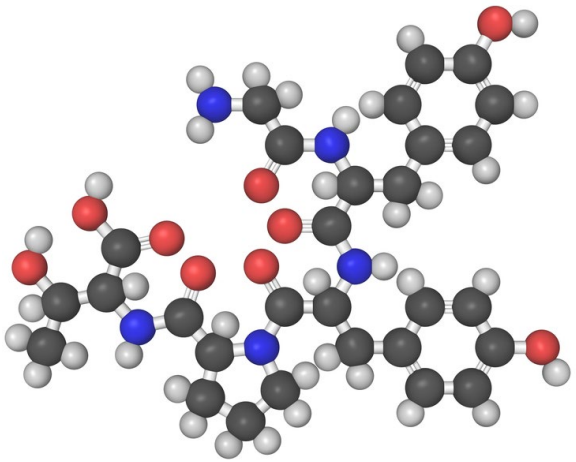
What makes a protein an allergen?



Costa et al, Clin Rev Allergy Immunol. 2020, doi: 10.1007/s12016-020-08810-9
Costa et al, Clin Rev Allergy Immunol. 2020, doi: 10.1007/s12016-020-08826-1

- **No single** distinct molecular parameter within one protein family (plant and animal) seems to be exclusively responsible for the allergenic potential at the site of elicitation.

- The integration of all the factors (proprieties) using a **multivariate statistical** approach could give a broader picture on how the complete set of properties impact protein allergenicity.



Verhoeckx *et al. Clin Transl Allergy,2020* doi: 10.1186/s13601-020-00318-x
Costa et al, Clin Rev Allergy Immunol. 2020, doi: 10.1007/s12016-020-08810-9
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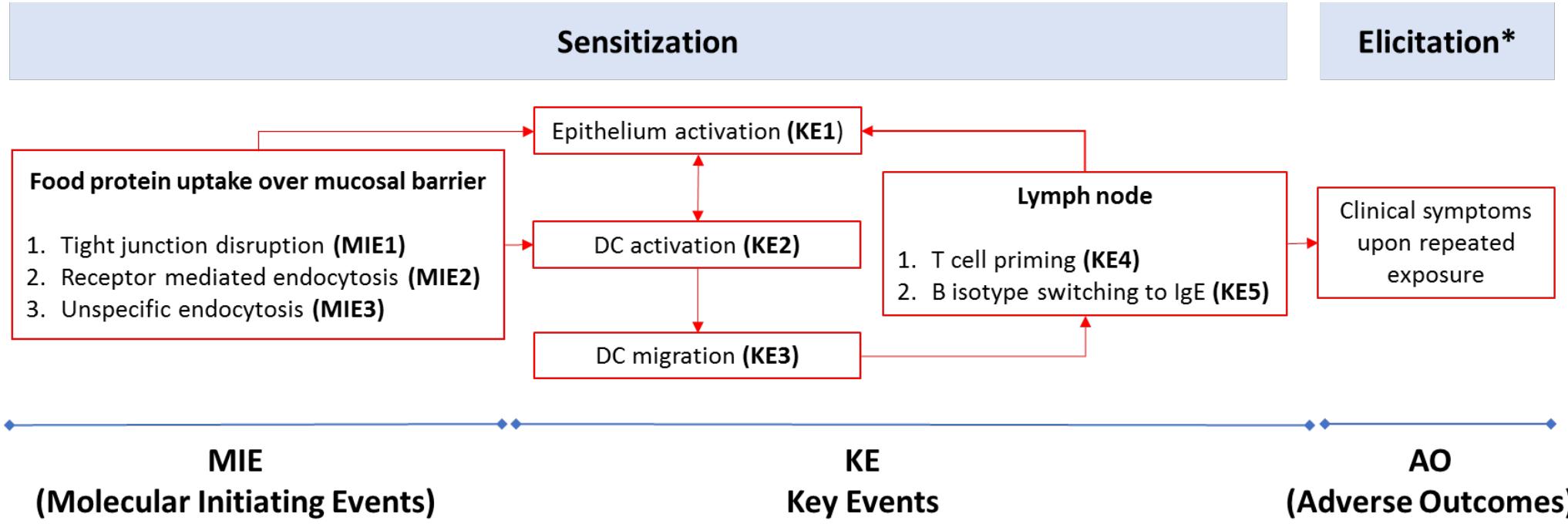
In vitro models based on Adverse Outcome Pathway (AOP): a framework on different levels



http:www.saaop .org/

Verhoeckx *et al. Clin Transl Allergy,2020* doi: 10.1186/s13601-020-00318-x
Van Bilsen et al, Clin Transl Allergy, 2017 May, doi: 10.1186/s13601-017-0152-0.
Lozano-Ojalvo et al, Trends in Food Science & Technology ,2019, doi: 10.1016/j.tifs.2019.01.014

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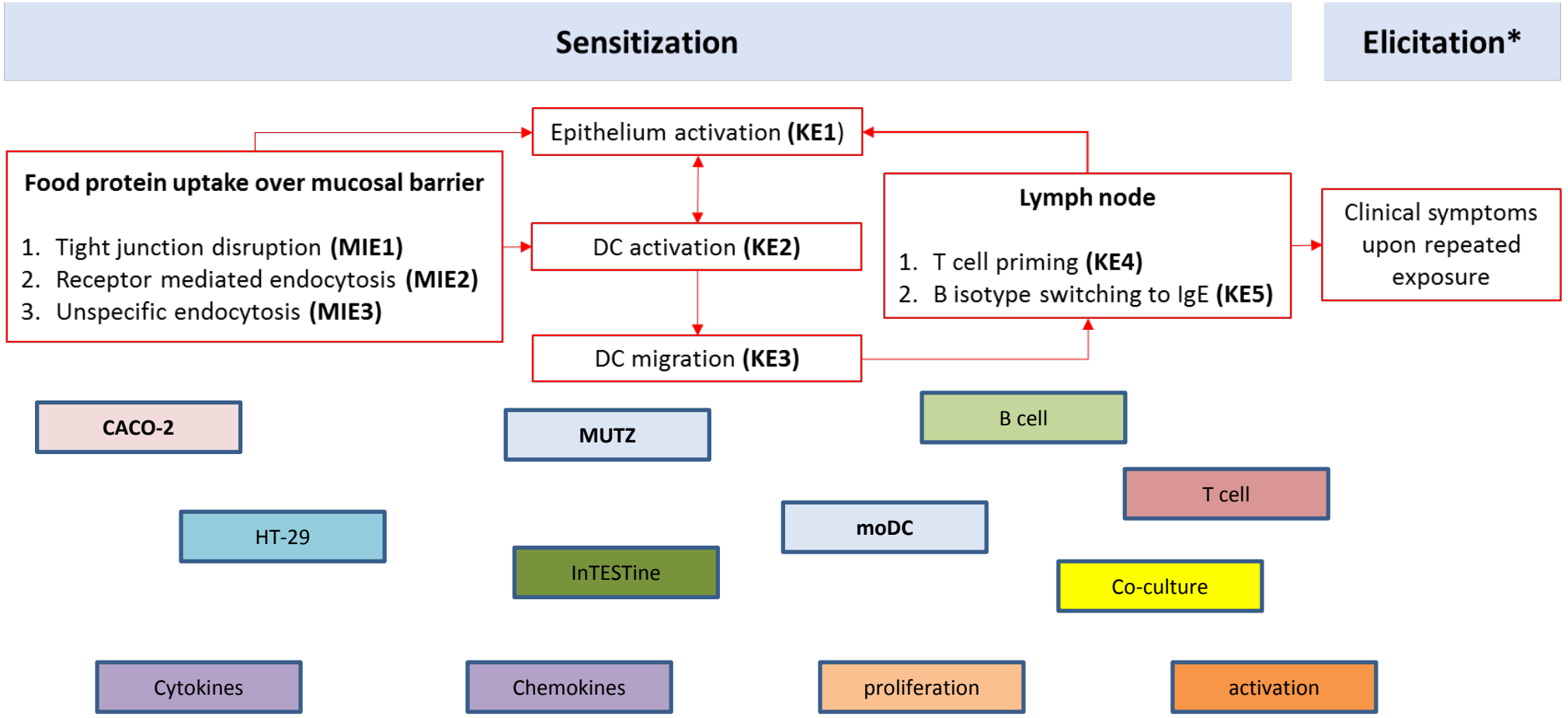

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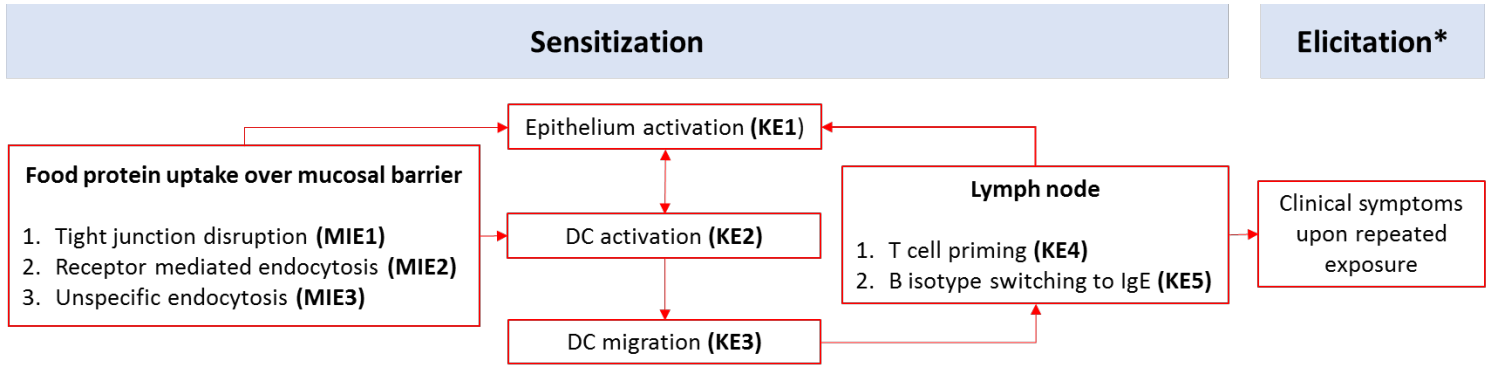
In vitro models based on Adverse Outcome Pathway (AOP): a framework on different levels

- In vitro methods should focus on the different events of the AOP for food allergy sensitization and initially, especially MIE 1-3 (food protein uptake over mucosal barrier) and KE1 (epithelium activation) using human epithelial cell models.



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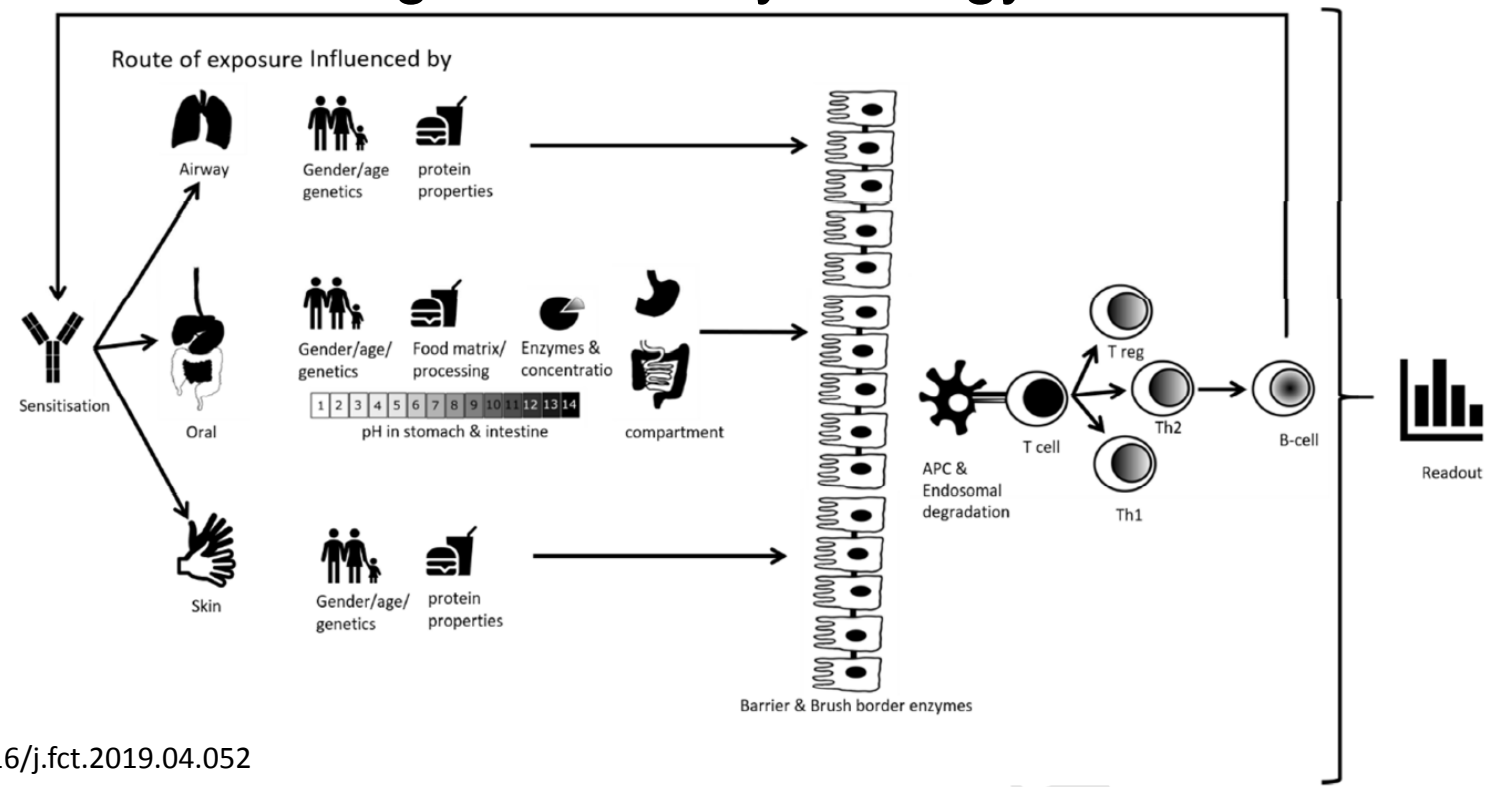
Lozano-Ojalvo et al, Trends in Food Science & Technology ,2019, doi: 10.1016/j.tifs.2019.01.014

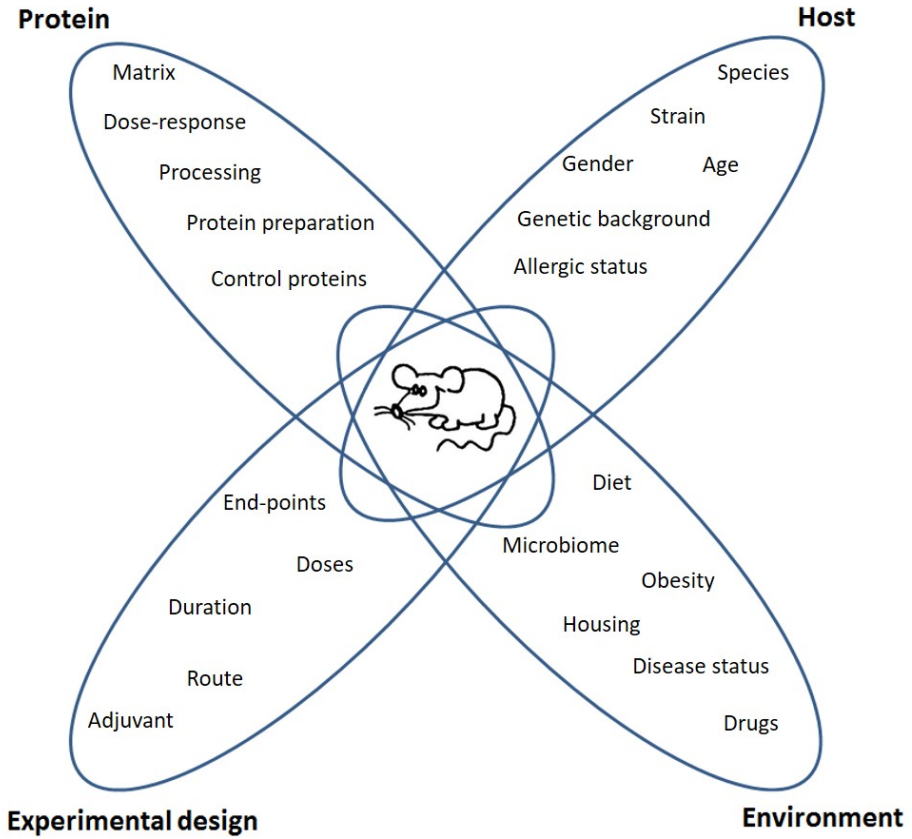
Relevance Protein digestion

- Protein digestion is relevant for allergenicity of some proteins, but not for all. Many other factors in addition to digestion in the stomach might play more pivotal roles and some of these factors may have a great impact on digestion and should be included in the digestion assay strategy.



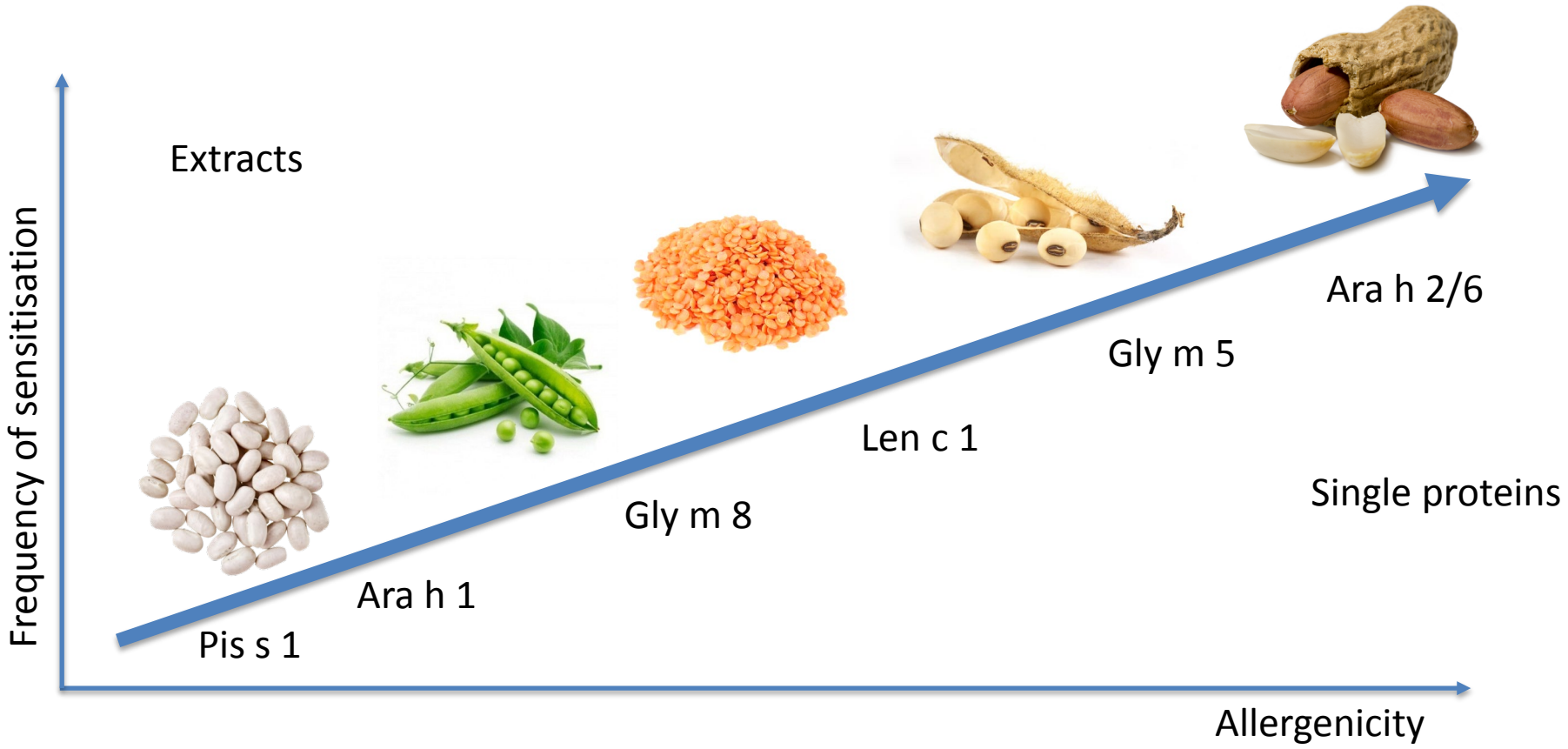
Verhoeckx *et al.* Food and Chemical Toxicology 2019, doi: 10.1016/j.fct.2019.04.052

- In vitro and in vivo methods including clear endpoint(s) need to be harmonised and validated for instance in ring trials using specified reference proteins/extracts



Verhoeckx *et al, Clin Transl Allergy,2020* doi: 10.1186/s13601-020-00318-x
Mazzucchelli et al,, Mol. Nutr. Food Res., 2018, doi: 10.1002/mnfr.20170 0278
Bøgh et al, Clinical and Translational Allergy, 2016, doi: 10.1186/s1360 1-016-0110-2

- The current general lack of systematic data to rank existing, known allergenic proteins according to their allergenic potency reflects a significant knowledge gap, which impairs the development and validation of potential methodologies.



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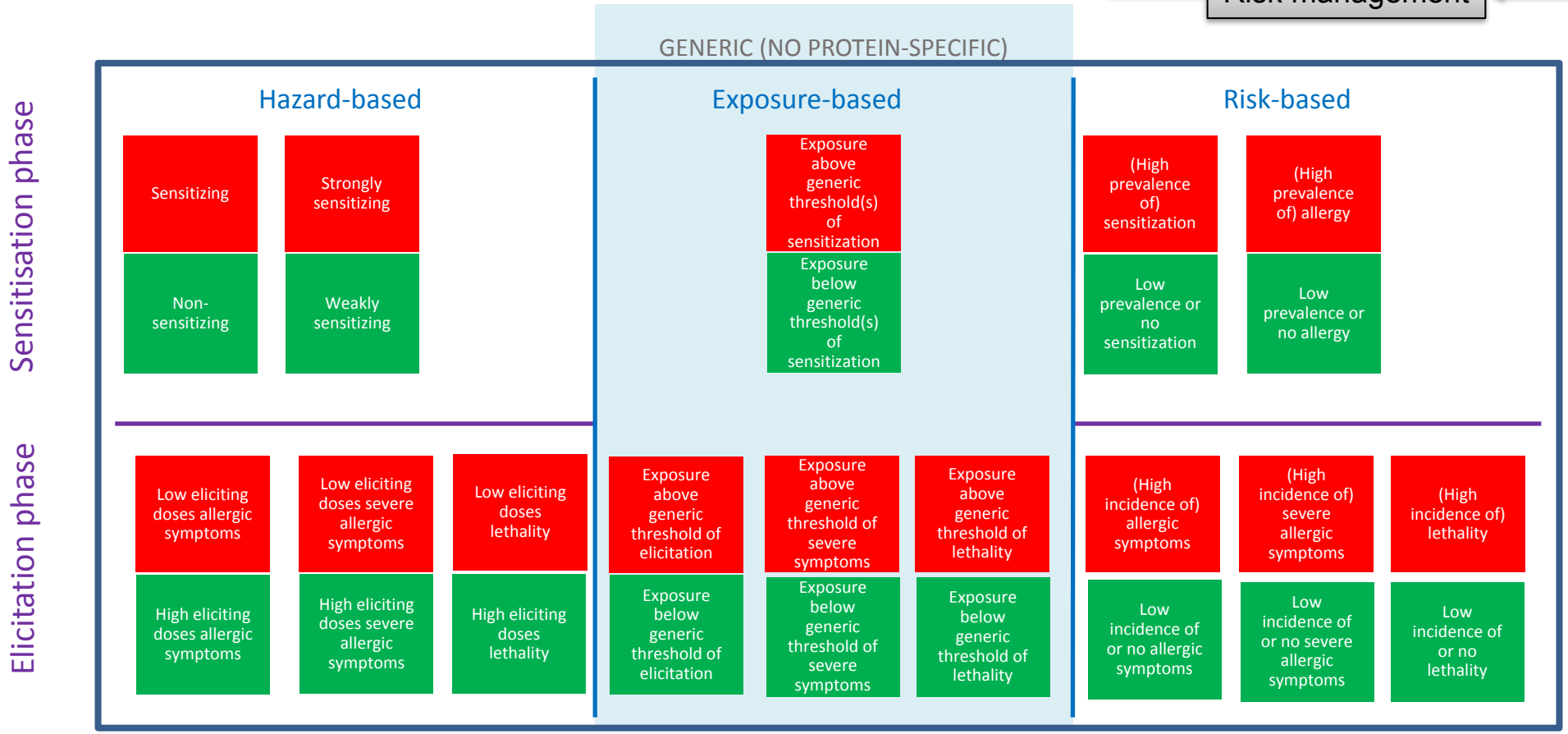
Working group 4
Risks assessment and clinical perspectives

What risk do we want to prevent?

Hazard | In combination with | Exposure | determine | Risk

Risk management



Houben et al, Food and Chemical Toxicology, 2019 doi: 10.1016/j.fct.2019.02.036

Decision has Implications for risk management and method development

Exposure above generic threshold(s) of sensitization

Exposure below generic threshold(s) of sensitization

Risk management

Criterion would require assurance that exposure can be managed and kept below the threshold

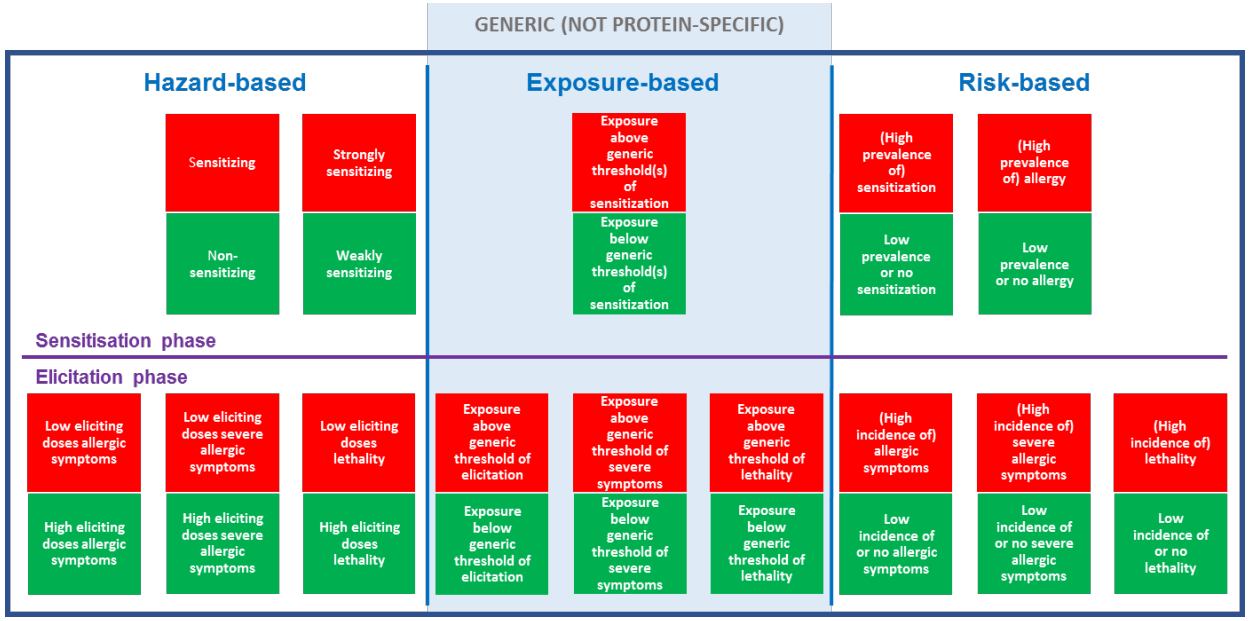
Methods

A threshold level of sensitisation is needed

Methods needed to assess and monitor exposure

What risk do we want to prevent?

- A clear outline of preferred decision-making criteria is needed from the risk management sector to help guide researchers during method development and ensure the applicability of newly developed methods to the risk management questions at hand.



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Take home messages

- **Decision-making criteria** for risk assessment
- **Ranking existing**, known allergenic proteins according to their allergenic potency
- Focus on **exposure**, **intrinsic protein properties** and **impact matrix/processing** on allergenicity
- **Multivariate statistics**/ in silico tools to find molecular patterns in protein characteristics to predict allergenicity
- AOP for food allergy sensitization focus on **food protein uptake** over mucosal barrier and **epithelium activation**
- **Clear endpoints** for In vitro and in vivo methods, **validation** for instance in ring trials using specified **reference proteins/extracts**

Acknowledgement

www.ImpARAS.eu

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Dr. Kitty Verhoeckx
Assistant professor UMCU
Dept. Dermatology & Allergology
@: K.C.M.Verhoeckx-2@umcutrecht.nl