## Allergen Bureau

The recommendations of the FAO/WHO Ad Hoc Expert Consultation on Food Allergens and their application in VITAL

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## Provide scientific/risk assessment advice to Codex Committees:

### CCFL

- Standards & Guidelines for Allergen Labelling;
  CCFH
  - Code of Practice (CoP) on Food Allergen Management for Food Business Operators;
  - General Principles of Food Hygiene.

The FAO/WHO Expert Consultation provides Risk Assessment Advice in response to Codex requests.

Codex makes Risk Management Decisions & Develops Standards.



#### Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens Meetings

- 1 Review Codex priority allergen list
  30 November 11 December 2020
- 4 Mandatory allergen declaration exemptions
  14 18 November 2022
- 2 Threshold levels for priority allergens
  15 March 2 April 2021 & 15 March 2021
- 5 Threshold levels for non-priority allergens
  20 March 2023
- 3 Precautionary labelling for priority allergens
  18 29 October 2021

# VSEP are also members of the FAO/WHO Expert Panel

- Steve Taylor, Chair FARRP
- Joe Baumert FARRP
- Rene Crevel René Crevel Consulting
- Geert Houben TNO
- Simon Brooke-Taylor Brooke-Taylor & Co.
- Paul Turner Imperial College/University of Sydney
- [Ben Remington Remington Consulting Group/FDA]

## Meeting 1 -Codex priority allergen list

- only foods or ingredients that cause immune-mediated hypersensitivities (e.g. IgE-mediated food allergies and coeliac disease).
- key criteria considered by Expert Panel for inclusion:
  - prevalence
  - severity
  - potency



## **Priority Allergen Recommendations**

- Cereals containing gluten (i.e., wheat, rye, barley species and strains)
- Fish & Crustacea,
- Eggs,
- Milk,
- Peanuts,
- Sesame,
- Specific tree nuts

(almond, cashew, hazelnut, pecan, pistachio, walnut)



## **Non-Priority Allergens**

#### Possible regional significance

- buckwheat
- celery
- lupin
- mustard
- oats
- soybean
- tree nuts (Brazil nut, macadamia, pine nuts)

#### Emerging watch-list

- pulses
- insects
- kiwi fruit



#### Systematic review to identify the predominant causes of food anaphylaxis



Graphical abstract from Conrado et al, Global patterns in anaphylaxis due to specific foods: A systematic review. Food allergy and gastrointestinal disease J Allergy Clin



## Meeting 4 – Allergen Labelling Exemptions

- Developed pro-forma process & flow-chart for exemption decisions;
- Tested & effective against existing allergen exemptions;
- Worst-case exposure estimates for exiting exemptions @ RfD/30;
- Confirmed suitable methods of analysis are available for allergen protein at RfD/30.

# Meeting 2 - Threshold levels for priority allergens

Safety objective\*:

"to minimise, to a point where further refinement does not meaningfully reduce health impact, the probability of any clinically relevant objective allergic response, as defined by dose distribution modelling of minimum eliciting doses (MEDs) and supported by data regarding severity of symptoms in the likely range of envisioned Reference Doses (RfD)"

\*Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens - Final Report Meeting 2



# Threshold levels for priority allergens

#### Approaches considered:

- Analytical-based,
- No Observed Adverse Effect Level [NOAEL] + Uncertainty Factor [UF],
- Benchmark Dose with or without a Margin of Exposure,
- Probabilistic Hazard Assessment.

#### Chosen approach:

Benchmark Dose (without a Margin of Exposure) and the Probabilistic Hazard Assessment approach selected as most closely aligning with the objective. Same methodology as VITAL 3.0.





Dose distribution modelling for peanut (expressed as discrete dose of mg peanut protein) utilizing Bayesian Stacked Parametric Survival methods with Frailty Components and Interval Censored Failure).

Five different parametric distributions are modelled, weighted and combined into a single dose distribution.

The predicted Stacked Model Averaging distribution estimate (red line) is presented with its corresponding 95% posterior predicted failure times (dashed red lines).

from Remington et al. Food and Chemical Toxicology 139 (2020) 111259  $\ensuremath{\mathsf{111259}}$ 

Discrete dose of protein (mg)

# Threshold levels for priority allergens

Reference doses (RfD) determined by dose-distribution modelling of results from DBPC challenge studies.

Clinical data indicated up to 5% of reactions at both ED01 and ED05 could be classed as anaphylaxis, although none were severe, based on the WAO definition.

Fatal food anaphylaxis is very rare (1per100000 person-years in allergic population) & no fatal reactions are documented following exposure to doses at or below ED01 nor ED05.



## Hierarchy of risks faced by people susceptible to IgE-mediated food allergy, proportionate to their estimated occurrence for peanut in peanut-allergic individuals. Turner *et al,* 2021



# Risk Assessment Objective for PAL

"To minimise, to a point where further refinement does not meaningfully reduce health impact, the probability of any clinically relevant objective allergic response following exposure to unintended presence of allergens"



# Threshold levels for priority allergens

Agreed safety objective [slide 10] would be met by starting the definition of RfD at the ED05.

Recommendations further simplified by rounding ED05 values down to one significant figure.

Foods with close ED05 values grouped together and a single value derived for the RfD, further rounding down the value, if necessary.



Proportion of peanut-allergic individuals expected to have subjective or objective symptoms following exposure to an  $ED_{05}$  or  $ED_{01}$  amount of peanut. Turner *et al,* 2



- Objective symptoms
- Anaphylaxis



### **FAO/WHO Panel Reference Doses**

	RfD Recommendation (mg total protein from the allergenic source)	VITAL 3.0 (ED01 based RfD, mg total protein)
Walnut (& Pecan), Cashew (& Pistachio), Almond	1.0	0.03 0.05 0.1 (hazelnut)
Egg, Milk, Peanut, Sesame	2.0	0.2 0.1
Hazelnut	3.0	0.1
Wheat <i>,</i> Fish	5.0	0.7 1.3
Shrimp	200	25

## **VSEP Threshold levels for non-priority allergens**

VSEP met Feb/March to review & update 2019 ED05 recommendations for nonpriority allergens "provisional recommendations" for VITAL, pending the outcome of the FAO/WHO expert group recommendations for the allergens on the "regional significance list".







# VITAL Threshold levels for

3rd FAO/WHO Expert Panel Report:

"If an RfD is not established for a particular priority allergenic food, an estimated RfD can be used providing it is determined following the guiding principles elaborated by Meeting 2 of the FAO/WHO consultation."

Addressed by Meeting #5

- 20 March 2023

## FAO/WHO levels for nonpriority allergens Virtual Meeting #5 - 20 March 2023

- Generally, data insufficient to support risk assessment principles from Meeting 2;
- Where data adequacy allows (i.e. prevalence severity & potency) recommend "provisional RfD" for allergen based on limited risk assessment [keep under review];
- Where data not adequate for risk assessment, recommend "Risk Management value", to provide a basis for quantitative risk assessment & to minimize adoption of zero tolerance approaches for PAL.



Non-Priority Allergens	VSEP	FAO/WHO Panel	
	Provisional RfD	Provisional RfD	Risk Mgt value
Celery	1.0	1.0	
Lupin	15.0		10
Soy	10.0	10.0	
Mustard	0.5		1.0
Brazil nut, macadamia, pine nuts	<b>1.0</b> group with most potent tree nuts)	1.0	
Buckwheat			10
Oats		No oat-specific value recommended, manage cross- contamination of oats	
Molluscs	20 additional Uncertainty Factor of 10 to crustaceans RfD.		



## Meeting 3 – Recommendations for PAL (part 1)

- Use RfDs from 2<sup>nd</sup> meeting [& provisional RfDs & RM values from 5<sup>th</sup> meeting]
- PAL only when Unintended Allergen Presence (UAP) exceeds RfD
- Compliance with existing Codex codes of practice, good allergen management and allergen control programs all prerequisites for PAL



### Meeting 3 – Recommendations for PAL (part 2)

Presentation of PAL: simple, clear, unambiguous, not false or misleading

e.g. "Not suitable for....".

Actual wording a risk management decision for Codex Use PAL only where Allergen Risk Assessment concludes UAP not preventable & exposure may be above RfD.

Label to indicate when an Allergen Risk Assessment has been undertaken.

Similar to Vital Standard



VITAL The Future?	RfD / RM value (mg total protein from allergenic source)
Walnut (& Pecan), Cashew (& Pistachio), Almond, Brazil nut, Macadamia, Pine nuts Celery, Mustard	1.0
Egg, Milk, Peanut, Sesame	2.0
Hazelnut	3.0
Wheat, Finfish	5.0
Soy, Lupin, [Buckwheat]	10.0
Molluscs	20
Shrimp	200

## Thank You for Listening

#### References

Remington BC, Westerhout J, Meima MY, Blom WM, Kruizinga AG, Wheeler MW, Taylor SL, Houben GF, Baumert JL. Updated population minimal eliciting dose distributions for use in risk assessment of 14 priority food allergens. Food Chem Toxicol. 2020 May;139:111259. doi: 10.1016/j.fct.2020.111259. Epub 2020 Mar 13. PMID: 32179163; PMCID: PMC7748293.

Umasunthar, T., Leonardi-Bee, J., Hodes, M., Turner, P. J., Gore, C., Habibi, P., Warner, J. O., & Boyle, R. J. 2013. Incidence of fatal food anaphylaxis in people with food allergy: a systematic review and metaanalysis. Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology, 43(12), 1333–1341. https://doi.org/10.1111/cea.12211

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