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A Guide to Risk Assessment Using Food Allergen Reference Doses

A Data-Driven Approach

One of the most challenging problems the food industry experiences related to food allergens is answering the question, "How much is too much?" From a regulatory standpoint, there are not any defined thresholds below which food is considered safe in almost all cases. There is, however, more information that has historically been available to allow for informed decision-making and risk assessment. Most of this information is data-driven from clinical patients and is widely published.

Many companies are beginning to use VITAL 3.0 (Voluntary Incidental Trace Allergen Labeling version 3.0) published in Australia, which models human clinical data for probable reaction based on double-blinded placebo-controlled allergen challenge studies. You will notice that FARRP (Food Allergy Research and Resource Program) is also listed as co-authors of this document. The University of Nebraska was directly involved in providing the risk-based modeling used to derive these values. By collecting data generated from various double-blinded placebo-controlled human challenge studies that have taken place throughout the world, it can be statistically determined at what level allergic individuals are likely to begin to react. It should be noted that this does not in any way predict the severity of the reaction.

Reference Dose Table

Allergen	Number of Individuals	2019 VSEP Ref Dose (mg protein) [ED_{01}]*	2019 VSEP Ref Dose (mg protein) [ED_{05}]
Egg	431	0.2	2.3
Hazelnut	411	0.1	3.5
Lupin	25	2.6	15.3
Milk	450	0.2	2.4
Mustard	33	0.05	0.4
Peanut	1306	0.2	2.1
Sesame	40	0.1	2.7
Shrimp	75	25	280
Soy (Milk + Flour)	87	0.5	10.0
Wheat	99	0.7	6.1
Cashew	245	0.05	0.8
Celery	82	0.05	1.3
Fish (finfish)	82	1.3	12.1
Walnut	74	0.03	0.8

**The VITAL panel is recommending the ED01 doses are used as the VITAL 3.0 thresholds. However, these remain recommendations so companies have the option to use either ED01 or ED05 doses as guidelines to help develop and support their allergen control plans.*

If we were to take the VITAL reference dose and use milk as our allergen example, we could conclude the following:

The suggested 2019 reference dose is 2.4 mg of milk protein for the [ED_{05}] based on 450 patients. This means that 95% of the milk allergic patients will not react at levels below 2.4 mg of milk protein.

Some important things to remember:

Using the [ED_{05}]

- This is not a regulatory document but a guidance document for best practices.
- 2.4 mg is a value of protein per serving, so it must be converted to align with test kits.
  - Assuming a 100 g serving size (these will vary), a finished product must contain less than 24 ppm milk protein to be in compliance with this document. To convert this value into Veratox, 24 ppm milk protein is equal to 66.7 ppm Non-Fat Dry Milk. (NFDM contains 36% protein)
  - If the serving size is much larger, say 250 g, the finished product would need to be below 9.6 ppm Milk protein or 26.67 ppm on the NFDM Veratox scale.

Using the [ED_{01}]

- Let us say, for the sake of argument, a company wishes to be more conservative and use the [ED_{01}] scale instead of the [ED_{05}]. This would mean that 99% of the milk allergic patients will not react at levels below the value. In this case, the value is 0.2 mg of milk protein per serving.
  - Assuming a 100g serving size, a finished product must contain less than 2 ppm milk protein to be in compliance with this document. To convert this value into Veratox, 2 ppm milk protein is equal to 5.56 ppm Non-Fat Dry Milk. (NFDM contains 36% protein)
  - If the serving size is much larger, say 250 g, the finished product would need to be below 0.8 ppm Milk protein or 2.2 ppm on the NFDM Veratox scale.

This exercise can be carried out for any allergen and any test kit provided that the reporting scale is known. With this information, the user can be informed with a data-based risk assessment to determine if their test kit is sensitive to their desired range. Since different test kits express results on different scales (ppm food versus ppm protein versus ppm allergenic protein fraction), it is imperative to standardize the reporting scale to mg of protein when performing these calculations. Ultimately this means that whether a company chooses to use the [ED_{05}] or the [ED_{01}] as a guideline, they can calculate if a test method is sufficiently sensitive to be able to test to that standard.

The following is a tool to determine Veratox method alignment with VITAL 3.0 recommendations at various intervals and serving sizes.

Veratox Alignment

	Egg	Hazelnut	Milk	Mustard	Peanut	Sesame	Shrimp	Soy	Wheat	Cashew	Walnut
[ED_{05}] 100 g Serving	X	X	X	X	X	X	X	X	X	X	X
[ED_{05}] 250 g Serving	X	X	X	X	X	X	X	X	X	X	X
[ED_{01}] 100 g Serving	X	X	X		X	X	X	X	X		
[ED_{01}] 250 g Serving		X			X	X	X	X	X		

Allergen Bureau Reference

http://allergenbureau.net/vital-scientific-expert-panel-2019-summary-recommendations-the-new-allergen-reference-doses-for-vital-program-version-3-0/

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