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Editorial Comment

How much is too much?

... and how long is too long? These are the questions asked not only by consumers, but also food industry. EFSA has been asked several times since the initial inquiry by the Irish FSA in 2014 if VITAL reference doses were acceptable for precautionary allergen labeling. By now, three scientific committees in three European countries have established independently what they deem acceptable. Except, that the doses proposed differ by a factor no less than 100. And earlier this year, EFSA has funded the ThrAll project to establish minimum eliciting doses and develop robust analytical methods for food allergen detection in processed materials. The project is funded for four years, which could result in eliciting doses proposed by EFSA in 2022 or later. The question that needs to be asked is how long industry and consumer can reasonably be expected to wait for such important decisions to be made. So far it has been already four years, making it eight in 2022.

The other two items that the current issues of the Food Allergen Community Newsletter reports about are the US FDA (CDER and CBER) guidance for the labeling of pharmaceutical products concerning gluten content, and the ELISA kit study for lupine detection by Australia's NMI.

In addition, you will learn about three upcoming conferences: the 10th Workshop on Food Allergens Methodologies in Toronto, Canada (May 7-9), the 2nd MoniQA conference on food allergens and food fraud in Vienna (June 7-8) and the 2nd International Conference on Food Analysis in Melbourne, Australia (Nov 20-22).

Bert Popping  Editorial Board Member

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Featured Article

Food allergen reference dose – Quo vadis?

How safe is safe? How clean is clean? And whether to label: it contains or ‘may contain’? These are the questions that are being hotly debated at present. Why? Because three European member states committees have published food allergen reference doses, which not only do not match, but they actually differ substantially, in some cases as much as 100 times. The reason for the differences is that the reference doses are based on different levels of protection (based on the proportion of reactions to an eliciting dose in a sensitive population) and correspond to either the ED01 or the lower limit of the 95% confidence interval of the ED05. Furthermore, our understanding of these ED values is being challenged by more recent clinical studies (Hourihane et al., 2017).

Back in 2014, the **German enforcement authorities published reference doses (Waiblinger and Schulze, 2018)**, derived from VITAL 2.0, and, together with action values as well. These action values are concentrations above which enforcement authorities would assume the label is incorrect and will take action. This can be either to determine if an ingredient has been forgotten from the label, or, if it may be a cross-contamination.

The values appear acceptable to many food manufacturers, as well as allergic consumers. For the food industry, food allergen control requires the implementation of many different measures and factory- and product-dependent strategies. For example, they include ingredient segregation, proper identification of rework products as well as rework scheduling, production workflow, equipment design and sanitation procedures. Cleaning procedures are a critical point in the control of adventitious contamination of products with food allergens. In food production, ensuring production lines are 100% clean is a major challenge. Equipment assembled in production lines may include parts that favor the accumulation of residues or inaccessible sections, posing a challenge for an effective cleaning. In a zero-tolerance enforcement environment, implementing stricter sanitation

procedures and additional allergen control measures will result in a major burden for the food industry, with limited additional protection for allergic consumers. Therefore, acceptable allergen tolerance levels are crucial. They should be achievable for the industry with proper control measures, and, at the same time, should be low enough to prevent allergic consumers from experiencing severe and life-threatening reactions when exposed to low amounts allergens. Zero tolerance has not been demanded by advocacy groups of allergic consumers since this would restrict even further the choices of products they can safely purchase. For this purpose, the VITAL concept of risk management and recommendations for precautionary allergen labeling (PAL) was developed. German control authorities base their action values on this concept, except where VITAL 2.0 reference doses are so low that no current routine analytical method would be able to detect at those levels. One example for this scenario is egg, which has a very low reference dose of 0.03 mg protein. Here, the German authorities adopted the Limit of Detection of available egg detection systems (e.g. ELISA). At this point, it is important to mention that VITAL does not cover all regulated in Europe, and validated reference materials are lacking for most of them, impacting in turn on the accuracy of analytical results.

In 2016, a **Dutch scientific committee** chose not to adopt the same VITAL reference doses as Germany, instead, they set significantly lower reference doses for the allergens. How these can be practically monitored and enforced with current analytical tests is not discussed in their statement.

Most recently, the **Belgian scientific committee** of the Federal Agency set their own reference doses, which differ from the German as well as from the Dutch. In particular, reference doses for peanut, egg, and milk are about 10 times higher as those set by Germany (Table 1), and about 100 times as those set by the Dutch committee.

Table 1. Action limits proposed for peanut, milk and egg in Germany, Belgium and The Netherlands.

Allergen	Belgium		Germany		The Netherlands	
	Proposed Reference Dose (mg protein)	For a Serving Size of 100 g (mg/kg)	Proposed Reference Dose (mg protein)	For a Serving Size of 100 g (mg/kg)	Proposed Reference Dose (mg protein)	For a Serving Size of 100 g (mg/kg)
Peanut	1.1	11	0.2	2	0.015	0.15
Milk	1.2	12	0.1	1	0.016	0.16
Egg	0.3	3	0.03	0.3	0.0043	0.043

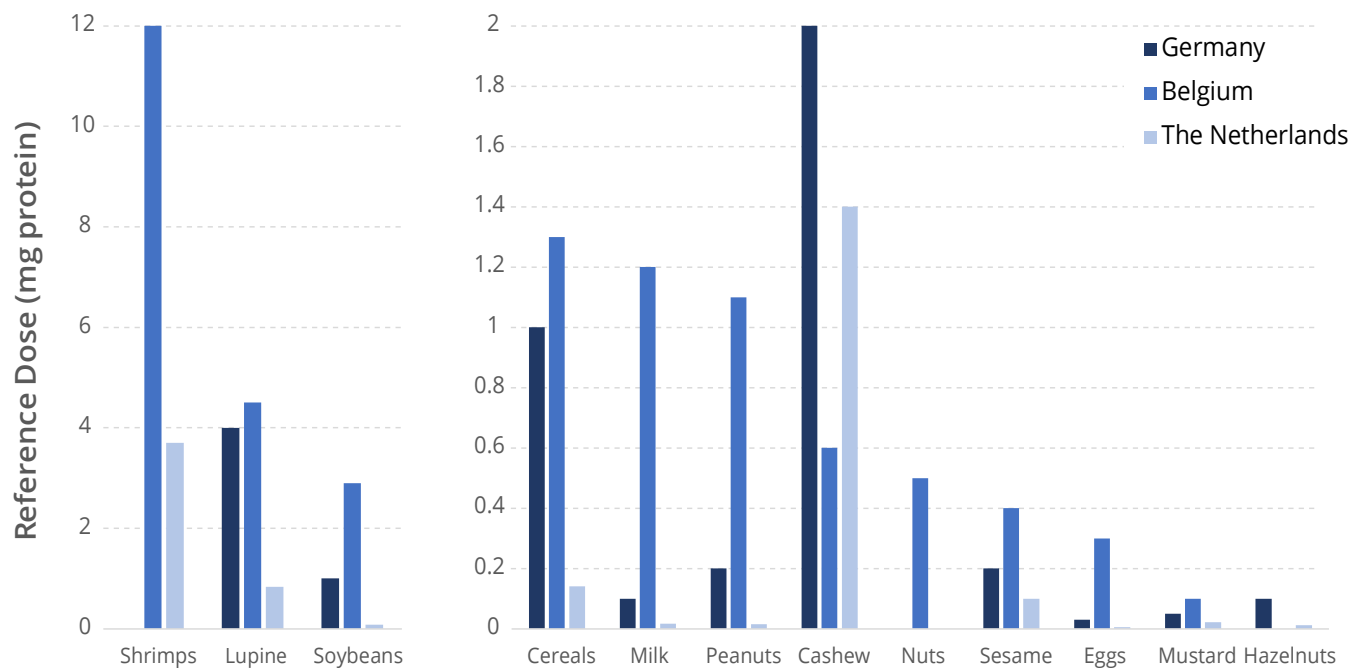


Figure 1. Proposed food allergen reference doses in Germany, Belgium and The Netherlands.

Figure 1 shows an overview over all references doses proposed by the committees of Germany, Belgium and The Netherlands.

Clearly, EFSA has not recommended Europe-wide reference doses and is unlikely to do so while the ThrAll project is still running (until about 2022), with the often-heard statement that no sufficient data to base a recommendation upon are available at the time. Because of lack of progress on this issue at EFSA level, individual countries are taking the lead, each with a different direction. This is generating a difficult and confusing environment for industry and consumers in the EU. So, the question is if over the coming years we will see different reference doses set by each European member states, of which at present, there are still 28.

What does this mean for the food manufacturer and 'may contain' labeling? Would the same product be labeled 'may contain' in the Dutch language? **Since Belgian products also require labeling in Dutch (flemish) language, would there**

be a Dutch label for Dutch citizens with 'may contain' and a Dutch label for Belgian citizens without? Are affected consumers in The Netherlands safer than those in Germany or are the affected Dutch consumer just restricted even more for choice without good reason?

What is clear is that all who have a vested interest in this area cannot wait for another four years or more to come up with harmonized reference doses. This situation poses increased complexity for the food industry especially with products on the market in several different EU countries which will lead to greater potential for forced errors and arguably product recalls, and it is definitely confusing and unhelpful for affected consumers who must decide every day what is an acceptable level of risk.

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News

The ThRAIL project

The ThRAIL project (Detection and quantification of allergens in foods and minimum eliciting doses in food allergic individuals) will seek to collate good quality data on the amounts of allergenic foods that can cause a reaction. These data are needed to help identify levels of allergens that can be considered as generally safe for the majority of food allergic consumers which in turn feed into a risk assessment process to identify whether foods which contain unintended allergens pose a risk of causing an allergic reaction and should carry a precautionary allergen label (PAL). A second objective is to develop methods that can be used to determine the levels of allergens in foods and check whether a food product contains unintended allergens, and if so, how much is present. These are needed because current test methods can be unreliable and may not be able to effectively quantify the presence of an allergen and yet have to be used to identify if foods require application of PAL. The results obtained using the current allergen test methodology may also form the basis of product recalls or withdrawals.

Funded by the European Food Safety Authority with additional co-funding from the UK Food Standards Agency (FSA) and the Federal Agency for the Safety of the Food Chain (FASFC) in Belgium, the project builds on the outputs of the recently completed EU-funded iFAAM project and nationally-funded projects in Belgium, France and Italy. Coordinated by the University of Manchester (professor Clare Mills, Dr Chiara Nitride) ThRAIL involves leading experts from across Europe including Dr Linda Monaci (CNR-ISPA, Bari, IT), Dr Nathalie Gillard (CER, BE), Dr Christof van Poucke (ILVO, BE) and Drs Olivier Tranquet (INRA-Nantes, FR) and Karine Adel-Patient (INRA-CEA Paris, FR)

Clare Mills | University of Manchester UK

Gluten in drug products

The Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research, (CBER), part of U.S. Food and Drug Administration, published in November of last year, a **Draft Guidance** for the pharmaceutical industry with information and recommendations on the labeling of gluten in interest of celiac patients. It is important to note that discussions and recommendations do not cover wheat hypersensitivity.

The guidance applies to human drugs products that pass the small intestine, specifically:

- Orally ingested drug products
- Topical drug products applied to or near the lips
- Drug products applied inside the mouth

The guidance neither applies to food nor dietary supplements nor cosmetics.

Among the recommendations, the guidance suggest a voluntary statement: "Contains no ingredient made from a gluten-containing grain (wheat, barley, or rye)". Such statement does not imply gluten-free, in part because it may be difficult to substantiate that a product is free of gluten.

The document, **Docket FDA-2017-D-6352**, was open for public comments for 60 days and it was closed in Feb 12. During this period the agency has received over 700 comments.

Carmen Diaz-Amigo [in](#) FOCOS GbR



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Scientific Publications

Lupine allergen detecting capability and cross-reactivity of related legumes by ELISA

Lupine belongs to the genus *Lupinus* and includes three species commonly consumed by humans. Figure 1 shows the three main lupine species, namely *Lupinus angustifolius* (Blue Lupine or Australian Sweet Lupine), *Lupinus albus* (White Lupine), and *Lupinus luteus* (Yellow Lupine). The *Lupinus* genus is closely related to other legumes, such as peanuts, soya, chickpeas, peas, lentils and beans. However, the consumption of lupine (and related legumes) can cause severe allergic reactions.



Figure 1. Three lupine species analysed in this study.

Due to the severity of lupine allergy, legume cross-reactivity and its abundance in processed food, the Australian and New Zealand Food Standards Code (Part 1.2 Labelling and other information requirements in the Australia New Zealand Food Standards Code) and the European Union (EU Regulation No. 1169/2011) made lupine a mandatory allergen, to be labeled on food products containing lupine. Therefore, reliable analytical detection methods are required for the analysis of food samples.

Enzyme-linked immunosorbent assay (ELISA) is the most widely used technique for the detection and identification of food allergens. The aim of this study was to investigate these three lupine species and 24 commercial food products consisting of related legumes using commercial available ELISA test kits for lupine quantification. Lupine quantification ELISA test kits have been assessed from five different manufacturers, two manufactures stating that their ELISA test kit does not detect all three lupine species. Therefore three ELISA test kits (ELISA Systems®, R-Biopharm® and Romer Labs®) were used for analysis of three lupine species and 24 commercial food products from related legumes.

The results showed that all three ELISA test kits could detect the lupine species, though with different sensitivities. Cross-reactivity varied for the ELISA test kits and all showed some cross-reactivity to related legume samples analyzed. Positive cross-reactivity for related legume samples ranged from 16-72%, and not detected ranged from 13-50%, respectively. Interestingly, the test kit cross-reactivity for soya was higher compared to peanut, although the clinical lupine cross-reactivity is highest for peanut. In detail, the three peanut products tested generated results ranging from not detected to just above the limit of quantification. In contrast, the results for the least processed soya products fall within the middle to upper end of the standard curve, with one even exceeding the standard range. This highlights that further research is required on comparing and determination of analytical detection methods with clinical relevant proteins.

Overall, the selection and interpretation of the results of ELISA test kits for lupine allergen analysis should consider the sample matrix, as the cross-reactivity of related legume samples.

**Martina Koeberl, Dean Clarke & James Roberts James
The National Measurement Institute of Australia**

Reference

- (1) Koeberl, M., Sharp, M. F., Tian, R., Buddhadasa, S., Clarke, D., & Roberts, J. (2018). Lupine allergen detecting capability and cross-reactivity of related legumes by ELISA. *Food Chemistry*, 256, 105-112.

Upcoming Events

10th Workshop on Food Allergen Methodologies

DoubleTree by Hilton Toronto Downtown

May 7-9, 2018
Toronto, Canada

2nd MoniQA Symposium

Food Fraud Prevention and
Effective Food Allergen Management

Austria Trend Eventhotel Pyramide

June 7-8, 2018
Vienna, Austria

2nd International Conference on Food Analysis (2nd ICFA) & Workshop

Tracy Centre

November 20-22, 2018
Melbourne, Australia

Conference Topics:

Food Allergens
Food Fraud
Food Safety & Food Trade in the Asia-Pacific Region
Hemp Food
PFOS
Honey



AOAC Food Allergen Community Newsletter

Contribute with articles, news items or suggestions.

Submission deadline for the 2nd issue of 2018: **July 20**

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