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‘VITAL 3.0’: New and updated proposals for reference doses of food allergens

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Appropriate food labelling, including the naming of all allergenic ingredients which the food contains, is of major significance for people suffering from allergies to certain foods. Manufacturers are obliged under EU law to name the 14 most significant substances or products which elicit allergies or intolerances in lists of ingredients for packaged foods. By contrast, there are no binding labelling regulations for traces of these allergenic substances which have unadvertently been included in the finished food product. This frequently leads to voluntary, precautionary information being provided by the manufacturer on the food label, such as ‘May contain traces of ...’ or ‘may contain...’. For people affected by allergies, on the one hand, this kind of precautionary information may lead to unnecessary restrictions in food selection, as it is ultimately left open as to whether the finished food product actually contains a significant amount of certain allergens. On the other hand, the possibility of problematic allergen quantities incidentally getting into the end product nevertheless cannot be ruled out for foods without precautionary labelling.

Concerning the current different ways of handling purely voluntary labelling for possible traces of allergens, the question of whether thresholds for allergenic substances may noticeably improve consumer protection for people affected is under discussion. The aim here would be for labelling of the product to be mandatory, in a manner yet to be determined, should this threshold be exceeded. However, general allergen information which is intended as being purely precautionary could then consistently be avoided for food products in which the thresholds for incidental allergen content have not been exceeded.

An important prerequisite for setting thresholds of this kind involves specific knowledge as to which allergen amounts are critical – presently known as reference doses. Proposals for reference doses which have been published in the past are currently being updated and expanded by a panel of experts (*‘VITAL Scientific Expert Panel’*, VSEP), using data from clinical studies and mathematical calculations for the most significant allergens. The values are to represent the current level of scientific knowledge as exactly and realistically as possible, in specifying the amounts of allergens that may cause consumers affected by allergies to expect a certain probability of an allergic reaction after consumption. Further updates to data and derivation methods may in principle facilitate further development and specification of the values with even more precision in the future.

The newly proposed reference doses were published in 2019 under the heading ‘VITAL 3.0’. This has resulted in new or updated values for some of the substances, compared to the previous recommendation ‘VITAL 2.0’ from 2011 (see table on page 8):

For **eggs, milk and shrimps**, reference doses have **increased**.

For **lupins, soya, wheat and sesame**, the values have **decreased**.

For **cashew nuts, celery, fish and walnuts**, values have been determined **for the first time**.

For **peanuts, hazel nuts and mustard**, reference doses remain **unchanged**.

VSEP scientists have derived a certain eliciting dose for each of the allergens investigated in 'VITAL 3.0', known as 'ED₀₁'. If the 'ED₀₁' value is not exceeded in food, it can therefore be deduced that 99% of people affected by each allergy are protected from developing objectively measurable allergic reactions. The VSEP has emphasised the possibility that, under certain circumstances, even more severe allergic reactions may occur for a small part of the remaining 1% or so of people affected by allergies. Another limitation is that the extent of allergic reactions cannot be predicted with certainty. In addition, other open questions and uncertainties must also be taken into account within the context of a possible threshold derivation.

1 Subject of the assessment

In this assessment, the reference doses newly published in 2019 by the VITAL (= *voluntary incidental trace allergen labelling*) *Scientific Expert Panel* (VSEP) for specific allergens in food (Allergen Bureau, 2019) will be discussed under the heading 'VITAL 3.0'.

With respect to the background to the current situation, 14 major substances or related products which elicit allergies or intolerances must be labelled in lists of ingredients on packaged foods, in accordance with Regulation (EU) No 1169/2011 on the provision of food information to consumers. By contrast, inadvertent inclusion and/or traces of these allergenic substances in foods is still not explicitly regulated. With regard to food labelling, this can sometimes lead to '*precautionary allergen labelling*' (PAL), often solely for the purposes of countering potential liability claims (e.g. 'May contain traces of ...' or 'May contain...'). On the one hand, PAL can lead to unnecessary restrictions in food selection for patients affected by allergies, but on the other hand, products which do not carry precautionary labelling of this kind may still exhibit problematic inclusions of allergens for this group of people (e.g. through incidental cross-contact) (Soon / Manning, 2017; Manning / Soon, 2017; Yeung / Robert, 2018; Dunngalvin, Roberts, Schnadt, *et al.*, 2019; FSAI, 2019).

The German Federal Institute for Risk Assessment (BfR) has repeatedly taken an extensive scientific stance on the topic in question in the past - including the VITAL concept:

New concept for the labelling of allergen traces in food. BfR Internet Opinion No. 038/2008 of 30 April 2008,

Thresholds for the labelling of allergens in foods. Transcript (2009) of an expert discussion as part of the 2008 BMEL conference 'Allergies: Better information, higher quality of life' on 15 October 2008 in Berlin.

https://www.bfr.bund.de/cm/350/schwellenwerte_zur_allergenkenzeichnung_von_lebensmitteln_tagungsband.pdf.

Improved labelling of allergens in foods for consumers: Threshold values cannot at present be determined reliably. BfR Internet Opinion No. 002/2010 of 29 July 2009.

How to deal with allergens requiring labelling under the circumstances outlined above, but have been inadvertently included in foods, is still under discussion. This includes considerations regarding the possible setting of thresholds for maximally tolerated quantities of such allergens for people affected by allergies and the question as to whether, in cases where respective thresholds are exceeded, voluntary (trace) labelling might be appropriate, or mandatory labelling would be required.

The reference doses for certain allergens in foods that have been published by the VSEP are the subject of part of this scientific discussion. The following is a scientific assessment by the BfR of these reference doses which were newly published in 2019 by the VSEP under the heading 'VITAL 3.0' and an opinion on the possible consequences which may result from labelling inadvertently included traces of allergens in food which require labelling.

2 Results

In 2019, the VSEP presented 'VITAL 3.0', setting out new 'reference doses' for certain allergens in foods requiring labelling and the reference doses being scientifically based on the use of clinical data for individual eliciting doses and applying various mathematical models.

The reference doses which have now been newly published represent a revision and continued development of the data published in this regard as 'VITAL 2.0' in 2011, i.e. the previous 'VITAL 2.0' has currently been replaced by 'VITAL 3.0' in 2019 (Allergen Bureau, 2019). This revision and continued development comprises both the further development of the mathematical methods and models used, and the involvement of a clinical data pool of findings obtained from studies on humans on individual eliciting doses for different allergens, which has significantly expanded in the interim. The BfR considers the principle of the method applied by the authors, which aims for 'quantifying risks' for certain populations with a probabilistic risk estimation, to be scientifically substantiated in principle and to be suitable and practical according to the latest knowledge. In their model on calculating reference doses for certain allergens, the authors of the VITAL 3.0 report focus especially on the calculation of the eliciting dose 'ED₀₁' (*minimal eliciting dose 01*). This means that if these calculated allergen doses are not exceeded, 99% of people affected by each allergy would be protected from objectively measurable allergic reactions. At the same time, the authors emphasise that there may be a possibility of more severe reactions occurring among a small part of the remaining 1% of people affected. The authors are therefore not aiming for 'zero tolerance' in the context of using the specified reference doses as a basis, but are naming a residual risk for consumers affected by allergies, from experiencing unwanted reactions due to undeclared incidental inclusions and/or traces of allergenic substances in foods.

Using the scientific basis of these reference doses as a starting point, specific thresholds for labelling food could, as far as possible, be derived by risk management. This depends on the extent to which the residual risk for consumers affected could be estimated as being low enough to be acceptable. The decision regarding the extent to which a residual risk would be accepted is not within the remit of the BfR, but does fall under the jurisdiction of risk management.

Other open questions involve the circumstance that a number of intrinsic and extrinsic co-factors may influence individual eliciting doses for allergic reactions, and the residual uncertainty that the actual extent of allergic reactions cannot be predicted with certainty when individual eliciting doses are reached. Moreover, according to various authors, more clinical 'single dose' studies should be carried out, especially in order to be able to identify patients who are particularly sensitive, and to avoid the possible effects of escalating test dosages. Open questions also remain with regards to non-homogeneously distributed allergens in ready-made foods (isolated allergens, present in larger particles).

If necessary, in view of the updated reference doses of certain allergens in 'VITAL 3.0', so-called internal assessment values from food monitoring authorities, which have been devel-

oped by food monitoring authorities' experts in the past (record of 74th ALTS (working group of experts active in the field of food hygiene and foods of animal origin) workshop, TOP 10, December 2014) should be discussed and/or revised, taking the data from VITAL into account.

The application of the 'VITAL' concept, originally native to Australia and New Zealand, is in principle voluntary for the food industry and manufacturers, and has so far only been applied in part in the above mentioned countries (Zurzolo *et al.*, 2017). According to available information, the entire concept - including the 'Action Levels' defined by VITAL as a specification for 'Precautionary Allergen Labelling' (PAL) - is currently not being applied on an official basis and as binding in any countries, and the international dissemination of the concept is unclear in practice (Yeung / Robert, 2018; FSAI, 2019; VITAL Science, 2019; Allergen Bureau, 10/2019). As part of the workshops carried out in 2016 and 2018 under the EU-mandated approach 'Integrated Approaches to Food Allergen and Allergy Risk Management' (iFAAM), it was explicitly noted that binding regulations with regards to PAL should be implemented as extensively across the EU as possible (DunnGalvin, Roberts, Schnadt, *et al.*, 2019; FSAI, 2019).

3 Rationale

3.1 'VITAL 3.0'

The VSEP has recently (in 2019) published reference doses for certain allergens requiring labelling in foods under the heading 'VITAL 3.0':

Allergen Bureau (2019).

Summary of the 2019 VITAL Scientific Expert Panel Recommendations.

http://allergenbureau.net/wp-content/uploads/2019/09/VSEP-2019-Summary-Recommendations_FINAL_Sept2019.pdf

The VSEP represents a collaboration between the *Allergen Bureau* (Australia and New Zealand), the *Food Allergy Research and Resource Programme* (FARRP) of the University of Nebraska (USA), and the *Netherlands Organisation for Applied Scientific Research* (TNO). A series of publications on the topic were published by the VSEP scientists involved throughout the course of the scientific discourse in recent years. Examples of such work include the work of Allen *et al.*, 2014, and Taylor *et al.*, 2014. The authors have derived reference doses for different known allergens using mathematical models, based on clinical studies of individual eliciting doses for allergic reactions caused by certain allergens. To this end, the authors presented a model for calculating the eliciting dose 'ED₀₁' ('*minimal eliciting dose 01*') for certain allergens. This means that if these calculated allergen doses are not exceeded, 99% of people affected by each allergy would be protected from objectively measurable allergic reactions. At the same time, the authors also emphasised that, depending on the circumstances, there may be a possibility of reactions, including in part more severe reactions, occurring among a small part of the remaining 1% of people affected. For allergens for which only a limited data situation was available, the authors determined the lower limit of the 95% confidence interval of the 'ED₀₅' ('*minimal eliciting dose 05*') as an alternative to 'ED₀₁'. In this case approx. 97-98% of patients affected could be viewed as being protected if the dose is not exceeded (Taylor *et al.*, 2014). In principle, this applies to both allergenic ingredients which have incorrectly not been declared, and unwanted inclusion of allergens, for example through cross-contact, in products which do not carry the relevant (warning) information.

The aim of these considerations is to derive scientifically-based 'reference doses' for certain allergens in foods requiring labelling, using clinical data on individual eliciting doses and suitable mathematical models. Based on the current level of scientific knowledge, the values regarding amounts of allergens that may cause consumers affected by allergies to expect a certain probability of an allergic reaction after consumption should therefore be delineated as exactly and realistically as possible. The sole consideration of the lowest possible eliciting doses (ever) measured, a concept that has previously been prevalent, has been significantly further developed and extended methodologically in favour of the new aim of 'quantifying risks' for certain populations using probabilistic risk estimations. Consequently, use of the reference doses according to Taylor and colleagues, 2014, does not involve aiming for 'zero tolerance', but rather specifying a residual risk. In their model, the authors therefore focus on calculating reference doses for certain allergies, especially the aforementioned eliciting dose 'ED₀₁'.

In a next step, specific thresholds for labelling food could, as far as possible, be derived from this scientific basis of reference doses by risk management. This depends on the extent to which the residual risk could be acceptable (Soon / Manning, 2017; Dubois *et al.*, 2018; DunnGalvin, Roberts, Schnadt *et al.*, 2019). According to DunnGalvin and colleagues, 2019, evidence-based quantifying of risks should also ensure that only such products which actually pose a risk (the magnitude of which is to be defined) for consumers affected by allergies carry '*precautionary allergen labelling*' (PAL) (DunnGalvin, Roberts, Regent, *et al.*, 2019; Roberts, 2019; Zurzolo *et al.*, 2017).

The reference doses which have now been newly published by the VSEP represent a revision and further development of the data in this regard which were published as 'VITAL 2.0' in 2011, i.e. the previous 'VITAL 2.0' is currently being replaced in 2019 by 'VITAL 3.0' (*Allergen Bureau*, 2019). This revision and continued development comprises both the further development of the mathematical methods and models used (see Wheeler *et al.*, 2019, for more on this), and the involvement of a clinical data pool of findings obtained from studies on humans on individual eliciting doses for different allergens, which has significantly been expanded in the interim (e.g. Westerhout *et al.*, 2019). This considerably expanded clinical data pool also in part concerns those allergens for which the database was previously described by the VSEP in 'VITAL 2.0' as still being insufficient with regards to viable statements and derivations. The reference doses published in 'VITAL 2.0' were stated as being based on three mathematical models ('Weibull, log-logistic, log-normal') for a clinical data pool which was in part limited. For 'VITAL 3.0' the '*stacked model averaging programme*' (Wheeler *et al.*, 2019) now includes five mathematical models ('Weibull distribution, log-logistic, log-normal (=log-Gaussian), log double-exponential (= log-Laplace), generalised Pareto') which, according to VSEP, result in a more exact depiction of distributions, and should provide a curve for each allergen. This would allow to derive the '*eliciting doses*' (ED) in a more exact and/or realistic manner. The reference doses determined essentially refer to the protein quantity of each allergen. Results show that three of the reference doses for known allergens remain unchanged (peanuts, hazel nuts, mustard), in 'VITAL 3.0, compared to 'VITAL 2.0'; the reference doses for three further allergens (eggs, milk, shrimp) have increased; reduced reference doses are now recommended for a further four allergens (lupins, soya, wheat, sesame); and reference doses for a further four allergens (cashew nuts, celery, fish, walnuts) can now be provided with regards to 'ED₀₁', which had previously been impossible due to insufficient data. According to VSEP, compared to the values from 'VITAL 2.0', the values which have since been derived in 'VITAL 3.0' for 'ED₀₁' generally result in a reduction of the proportion of patients who would have to suffer from a relevant risk of symptoms due to an existing allergy, as a result of unwanted cross-contact of allergens in (non-declared) foods. In addition to the

new values for 'ED₀₁', the values for 'ED₀₅' which have also been revised and further developed, are also provided in 'VITAL 3.0' as additional information for (Allergen Bureau, 2019).

As stated, the data used for 'VITAL 3.0' are based on published and non-published clinical studies which were carried out in Australia, the US and/or the European Union (VITAL Science, 2019) and have now provided a sufficient clinical data pool for the substances and/or foods listed as allergens (requiring labelling), which are eggs, hazel nuts, lupins, milk, mustard, peanuts, sesame, shrimp, soya, wheat, cashew nuts (and pistachio nuts), celery, fish and walnuts (and pecan nuts). According to VSEP, the data used for individual eliciting doses in adults originate from clinical studies which were carried out on a double-blind basis with a suitable control (placebo or verum-controlled) ('*double blind placebo-controlled food challenges*', DBPCFC), while studies for children and toddlers that were taken into account also included studies that, depending on the clinical situation, had not been carried out on a blind basis.

The following information is broken down for each individual allergen in 'VITAL 3.0' (see also table):

Peanuts

Data from 1306 individuals were entered into the calculation for peanuts, while only 744 such cases could be considered in 'VITAL 2.0'. 0.2 mg protein has now been identified as a reference dose for 'ED₀₁', and 2.1 mg protein for 'ED₀₅'. In relation to the reference dose 'ED₀₁' for peanuts, the value of 0.2 mg protein remains unchanged in comparison to 'VITAL 2.0'.

Hazel nuts

In 'VITAL 2.0' the reference dose for nuts and/or edible nuts in general was based on data obtained for hazel nuts. According to VSEP, the allergens of hazel nuts, cashew nuts and walnuts can be considered on a differentiated basis. 411 individual sets of data were considered for hazel nuts, while there were only 200 available previously. With regards to hazel nuts, 0.1 mg protein has now been identified as a reference dose for 'ED₀₁', and 3.5 mg protein identified for 'ED₀₅'. In relation to the reference dose 'ED₀₁', the value of 0.1 mg protein for hazel nuts remains unchanged in comparison to 'VITAL 2.0'.

Based on previous experiences, the VSEP recommends leaving the reference doses for nuts and/or edible nuts - except for walnuts, pecan nuts, cashew nuts and pistachio nuts – at 0.1 mg protein as before, based on the reference dose 'ED₀₁' for hazel nuts.

Mustard

The data situation remains unchanged in comparison to 'VITAL 2.0', with 33 individual sets of data. For mustard, 0.05 mg protein has now been derived as a reference dose for 'ED₀₁', and 0.4 mg protein for 'ED₀₅'. Concerning the reference dose 'ED₀₁' for mustard, the value of 0.05 mg protein remains unchanged in comparison to 'VITAL 2.0'.

Eggs

The available clinical data pool for eggs has improved, from previous 204 to current 431 individual sets of data. 0.2 mg protein has now been derived for eggs as the reference dose for 'ED₀₁' and 2.3 mg protein for 'ED₀₅'. In relation to the reference dose 'ED₀₁' for eggs in 'VITAL 2.0' (=0.03 mg Protein), an increased value of 0.2 mg protein is now recommended.

Milk

Previously, data from 344 individuals were available for milk and now, as stated, 450 individual sets of data have been entered into the calculation. 0.2 mg protein has now been derived for milk as reference dose 'ED₀₁', and 2.4 mg protein as 'ED₀₅'. In relation to the reference

dose 'ED₀₁' for milk in 'VITAL 2.0' (=0.1 mg protein), the recommended value has now increased to 0.2 mg protein.

Shrimp

The main allergen in crustaceans is the protein tropomyosine. Previously, data for 48 individuals were available for shrimp and now, as stated, 75 individual sets of data have been included in the derivation. Values of 25 mg protein and 280 mg protein are respectively considered as reference doses 'ED₀₁' and 'ED₀₅' for shrimp. In relation to the reference dose 'ED₀₁' for shrimp in 'VITAL 2.0' (=10 mg protein), an increased value of 25 mg protein has now been derived in 'VITAL 3.0'.

Lupins

Previously, data for 24 individuals were available for lupins and now, as stated, 25 individual sets of data have been included in the derivation. Based on current calculations for 'ED₀₁', a reduced value of 2.6 mg protein and a value of 15.3 mg for 'ED₀₅' have arisen as reference doses for lupins. In relation to the reference dose 'ED₀₁' for lupins in 'VITAL 2.0' (=4 mg protein), a reduced value of 2.6 mg protein is now recommended.

Soya

With regards to soya, data for 51 individuals were previously available and now, as stated, 87 individual sets of data have been considered in the derivation. VSEP have stated in 'VITAL 3.0' that the reference dose for soya must now be reduced, due to a previous data pool based on different soya products which was inconsistent in parts. Based on current calculations for 'ED₀₁', a reduced value of 0.5 mg protein has arisen for soya (soya drinks and soya flour) as a reference dose, and a value of 10 mg protein for 'ED₀₅'. In relation to the reference dose 'ED₀₁' for soya in 'VITAL 2.0' (=1 mg protein), a reduced value of 0.5 mg protein is now recommended.

Wheat

Previously, data for 40 individuals were available for wheat as an example of a cereal containing gluten and now, as stated, 99 individual sets of data are available for the derivation. Based on current calculations for 'ED₀₁' a reduced value of 0.7 mg has arisen as a reference dose for wheat, and a value of 6.1 mg as 'ED₀₅'. In relation to the reference dose 'ED₀₁' for wheat in 'VITAL 2.0' (=1 mg protein), a reduced value of 0.7 mg protein has now been derived.

Sesame

Previously, data for 21 individuals were available for sesame and now, as stated, 40 individual sets of data have been included in the derivation. Based on the current calculations for 'ED₀₁', a reduced value of 0.1 mg protein has now arisen as a reference dose for sesame. A value of 2.7 mg protein has been given as 'ED₀₅'. In relation to the reference dose 'ED₀₁' for sesame in 'VITAL 2.0' (=0.2 mg protein), a reduced value of 0.1 mg protein is now recommended in 'VITAL 3.0'.

Cashew nuts (and pistachio nuts)

The VSEP has now assessed the pool of data for cashew nuts as sufficient for being able to provide a value for 'ED₀₁' for this allergen, which was not the case in 'VITAL 2.0'. Previously, data for 35 individuals were available for cashew nuts and now, as stated, 245 individual sets of data are available for the calculation. Based on the current calculations for 'ED₀₁' a value of 0.05 mg protein has arisen as a reference dose for cashew nuts, and a value of 0.8 mg protein for 'ED₀₅'. In view of the potential for cross-reactions between cashew nuts and pistachio nuts, the VSEP have also recommended to transfer this new reference dose 'ED₀₁' of

0.05 mg protein for cashew nuts to pistachio nuts as the new reference dose 'ED₀₁' for pistachio nuts.

Celery

The data which now exist for celery have also been assessed by the VSEP as being sufficient for being able to provide an 'ED₀₁' value for this allergen, which was not the case in 'VITAL 2.0'. Previously, data for 39 individuals were available for celery and now, as stated, 82 individual sets of data are available for calculating the selected reference doses. 'ED₀₁' and 'ED₀₅' values of 0.05 mg and 1.3 mg protein, respectively, are now stated to be the new reference doses for celery.

Fish

The data situation for fish has now been assessed by the VSEP as being sufficient for being able to provide an 'ED₀₁' value for this allergen, which could not be done in 'VITAL 2.0'. Previously, data for 19 individuals were available for fish and now, as stated, 82 individual sets of data are available for calculating the selected reference doses. This has yielded 'ED₀₁' and 'ED₀₅' values of 1.3 mg protein and 12.1 mg protein as reference doses for fish.

Walnuts (and pecan nuts)

The data situation for walnuts has now been considered by the VSEP as sufficient to derive an 'ED₀₁', which was not the case with 'VITAL 2.0'. For walnuts, there were previous data for ~15 individuals; as stated, 74 individual data sets have since been made available for calculating the selected reference doses. A value of 0.03 mg protein has now arisen as 'ED₀₁' for walnuts, and a value of 0.8 mg protein for 'ED₀₅'. In view of the potential for cross-reactions between walnuts and pecan nuts, the VSEP recommends transferring the new reference dose 'ED₀₁' of 0.03 mg protein for walnuts to pecan nuts as the new reference dose 'ED₀₁' for pecan nuts. The VSEP has also issued the recommendation to set the reference dose 'ED₀₁' for tree nuts and/or edible nuts - except for walnuts, pecan nuts, cashew nuts and pistachio nuts - based on the value 'ED₀₁' for hazel nuts at 0.1 mg protein.

Table: Reference doses 'ED₀₁' and 'ED₀₅' ('minimal eliciting doses') according to 'VITAL 3.0', 2019, by the VITAL (= voluntary incidental trace allergen labelling) Scientific Expert Panel (VSEP), compared to 'ED₀₁' in accordance with 'VITAL 2.0'

Allergen	Reference doses VITAL 2.0, 2011 'ED ₀₁ ' (mg protein)	Reference doses VITAL 3.0, 2019 'ED ₀₁ ' (mg protein)	Reference doses VITAL 3.0, 2019 'ED ₀₅ ' (mg protein)
Egg	0.03	0.2	2.3
Hazel nuts	0.1	0.1	3.5
Lupins	4.0	2.6	15.3
Milk	0.1	0.2	2.4
Mustard	0.05	0.05	0.4
Peanuts	0.2	0.2	2.1
Sesame	0.2	0.1	2.7
Shrimp	10.0	25	280
Soya (soya 'milk', flour)	1.0 (soya flour)	0.5	10

Wheat	1.0	0.7	6.1
Cashew nuts		0.05	0.8
Celery		0.05	1.3
Fish		1.3	12.1
Walnuts		0.03	0.8

3.2 Open questions

Further open questions involve the possibility of a series of intrinsic and extrinsic co-factors (e.g. other medication, existing infections, etc.) being able to influence individual eliciting doses for allergic reactions. Another key point involves the residual uncertainty that the actual extent of allergic reactions when individual eliciting doses are reached cannot be predicted with certainty. Moreover, according to various authors, more clinical ‘single dose’ studies should be carried out, especially in order to be able to identify patients who are particularly sensitive, and to avoid the possible effects of escalating test dosages (Graham / Eigenmann, 2018; Dubois *et al.*, 2018). There is also an open question as to how to proceed with non-homogeneously distributed allergens (isolated allergens present in larger particles), e.g. if no peanut allergens could be detected in a pack of a food product, but a peanut is inadvertently contained in another pack of the same product (DunnGalvin, Roberts, Regent *et al.*, 2019; Roberts, 2019).

As part of the workshops carried out in 2016 and 2018 under the EU-mandated approach ‘*Integrated Approaches to Food Allergen and Allergy Risk Management*’ (iFAAM), it was explicitly noted that binding regulations with regards to ‘*precautionary allergen labelling*’ (PAL) should be implemented as extensively across the EU as possible (DunnGalvin, Roberts, Schnadt, *et al.*, 2019; FSAI, 2019).

3.3 Internal assessment values from food monitoring authorities

In accordance with Regulation (EU) No. 1169/2011 on the provision of food information, the 14 major substances or related products which elicit allergies or intolerances must be labelled in lists of ingredients on packaged foods. However, inadvertent inclusion and/or traces of these allergenic substances in foods is still not explicitly regulated. As well as concerning consumers affected by allergies, and the food industry, this problem also affects food monitoring authorities. To deal with the problem in a pragmatic manner, food monitoring authorities’ experts have developed their own internal assessment values, which were originally published within the record of the 74th ALTS (working group of experts active in the field of food hygiene and foods of animal origin) workshop (TOP 10) in December 2014. These assessment values are oriented along the above published reference doses for certain allergens named by Taylor *et al.*, 2014, but also take analytical feasibility into account as part of monitoring measures. The assessment values should therefore provide a proportionate guide as to which amount of a verified, but not labelled, allergenic ingredient in a food will require further measures to be taken. Regular updates of assessment values in accordance with the level of scientific knowledge are therefore explicitly viewed as necessary (Demmel *et al.*, 2015; Demmel *et al.*, 2016; see also: TOP 25 of the 76th ALTS workshop ‘Adjustment of Allergen Assessment Values’. In: 77th ALTS workshop on 20 and 22 June 2016, J. Verbr. Lebensm. 11 (2016): 359-367).

In view of the updated reference doses for certain allergens published in 'VITAL 3.0', it should be considered as to whether the above mentioned internal assessment values from food monitoring authorities should be discussed and/or revised.

Further information on the topic of allergies is available from the BfR website

A-Z index: Allergies: https://www.bfr.bund.de/en/a-z_index/allergies-129835.html



BfR "Opinions app"

4 References

- Allen KJ, Remington BC, Baumert JL, Crevel RW, Houben GF, Brooke-Taylor S, Kruizinga AG, Taylor SL (2014). Allergen reference doses for precautionary labeling (VITAL 2.0): clinical implications. *J Allergy Clin Immunol*, 133 (1): 156-64.
- Allergen Bureau (2019). Summary of the 2019 VITAL Scientific Expert Panel Recommendations. http://allergenbureau.net/wp-content/uploads/2019/09/VSEP-2019-Summary-Recommendations_FINAL_Sept2019.pdf
- Allergen Bureau (10/2019). Food Industry Guide to the Voluntary Incidental Trace Allergen Labelling (VITAL®) Program. Version 3.0, October 2019. http://allergenbureau.net/wp-content/uploads/2019/10/Food-Industry-Guide-to-the-Voluntary-Incidental-Trace-Allergen-Labelling-VITAL-Program-Version-3.0_Web.pdf
- ALTS (2014). ALTS-Beschlüsse der 74. Arbeitstagung Dezember 2014, Top 10. https://www.bvl.bund.de/SharedDocs/Downloads/01_Lebensmittel/ALS_ALTS/ALTS_Beschluesse_74_Arbeitstagung_Dez_2014.pdf?__blob=publicationFile&v=2
- Demmel A, Busch U, Waiblinger HU (2015). Existierende Aktionswerte. In: Busch, U.; Waiblinger, HU (Hrsg.). *Allergene in Lebensmitteln*. Behrs, Hamburg.
- Demmel A, Waiblinger HU, Busch U, (2016). Lebensmittelrechtliche Regelungen für Allergene in der EU. *Bundesgesundheitsblatt* 59 (7): 872-877.
- Dubois AEJ, Turner PJ, Hourihane J, Ballmer-Weber B, Beyer K, Chan CH, Gowland MH, O'Hagan S, Regent L, Remington B, Schnadt S, Stroheker T, Crevel RWR (2018). How does dose impact on the severity of food-induced allergic reactions, and can this improve risk assessment for allergenic foods? Report from an ILSI Europe Food Allergy Task Force Expert Group and Workshop. *Allergy*, 73 (7): 1383-1392.

DunnGalvin A, Roberts G, Schnadt S, Astley S, Austin M, Blom WM, Baumert J, Chan CH, Crevel RWR, Grimshaw KEC, Kruizinga AG, Regent L, Taylor S, Walker M, Mills ENC (2019). Evidence-based approaches to the application of precautionary allergen labelling: Report from two iFAAM workshops. *Clin Exp Allergy*, 49 (9): 1191-1200.

DunnGalvin A, Roberts G, Regent L, Austin M, Kenna F, Schnadt S, Sanchez-Sanz A, Hernandez P, Hjorth B, Fernandez-Rivas M, Taylor S, Baumert J, Sheikh A, Astley S, Crevel R, Mills C (2019). Understanding how consumers with food allergies make decisions based on precautionary labelling. *Clin Exp Allergy*, 49 (11): 1446-1454.

FSAI (2019). Food Safety Authority of Ireland: Report of the Scientific Committee of the Food Safety Authority of Ireland - Information required for the risk assessment of undeclared food allergens in Ireland. 2019, Dublin, Ireland.

Graham F, Eigenmann PA (2018). Clinical implications of food allergen thresholds. *Clin Exp Allergy*. 48: 632-640.

Manning L, Soon JM (2017). An alternative allergen risk management approach. *Crit Rev Food Sci Nutr*, 57 (18): 3873-3886.

Roberts G (2019). The uncertainties and anxieties around food allergy. *Clin Exp Allergy*, 49 (11): 1388-1389.

Soon JM, Manning L (2017). "May contain" Allergen statements: Facilitating or frustrating consumers? *J Consum Policy*, 40: 447-472.

Taylor SL, Baumert JL, Kruizinga AG, Remington BC, Crevel RW, Brooke-Taylor S, Allen KJ; Allergen Bureau of Australia & New Zealand, Houben G (2014). Establishment of Reference Doses for residues of allergenic foods: Report of the VITAL Expert Panel. *Food Chem Toxicol*, 63:9-17.

Westerhout J, Baumert JL, Blom WM, Allen KJ, Ballmer-Weber B, Crevel RWR, Dubois AEJ, Fernández-Rivas M, Greenhawt MJ, Hourihane JO, Koplin JJ, Kruizinga AG, Le TM, Sampson HA, Shreffler WG, Turner PJ, Taylor SL, Houben GF, Remington BC (2019). Deriving individual threshold doses from clinical food challenge data for population risk assessment of food allergens. *J Allergy Clin Immunol*, 144 (5): 1290-1309.

Wheeler MW, Westerhout J, Baumert JL, Remington BC (2019). Bayesian Stacked Parametric Survival with Frailty Components and Interval Censored Failure Times. August 2019. <http://arxiv.org/abs/1908.11334>

VITAL Science (2019). What is the VITAL science? <http://allergenbureau.net/vital/vital-science/>

Yeung J, Robert MC (2018). Challenges and Path Forward on Mandatory Allergen Labeling and Voluntary Precautionary Allergen Labeling for a Global Company. *J AOAC Int*, 101 (1): 70-76.

Zurzolo GA, Peters RL, Koplin JJ, de Courten M, Mathai ML, Tye-Din JA, Tang MLK, Campbell DE, Ponsonby AL, Prescott SL, Gurrin L, Dharmage SC, Allen KJ (2017). The practice and perception of precautionary allergen labelling by the Australasian food manufacturing industry. *Clin Exp Allergy*, 47: 961-968.

About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. It advises the German federal government and German federal states ("Laender") on questions of food, chemical and product safety. The BfR conducts its own research on topics that are closely linked to its assessment tasks.

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