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The 50th percentile of the general population single eating occasion intake of food is optimal for the calculation of action levels for precautionary allergen labelling

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ABSTRACT

Lack of guidance regarding selection of food intake values for allergen risk assessment can lead to different outcomes for similar levels of allergens in food products. Several food consumption survey databases (United States, North-West Europe, and Netherlands) were analyzed to identify optimal food intake percentiles using a sensitivity analysis. Deterministic risk assessment scenarios using the 50th percentile up to the maximum intake per food group were compared with probabilistic risk assessment outcomes. The optimal intake percentile is the lowest percentile that results in a deterministic risk assessment outcome compliant with the predefined safety objective, i.e., the predefined risk of an objective allergic reaction at ED01, ED2.5, ED05 or ED10 doses of 14 allergenic foods. The P50 intake met these criteria in more than 99.9% of all 28,784 scenarios tested. The P50 is therefore recommended for deterministic allergen risk assessment and calculation of action levels for precautionary allergen labelling. In case a P50 value is not available, the mean is a good alternative, as analyses of the intake data showed that the mean generally is between the P50 and P65.

1. Introduction

Allergen cross-contact during the production of food may result in unintentional allergen presence (UAP), which is globally known as a major cause of accidental and unexpected allergic reactions (Michelsen-Huisman et al., 2018; Sheth et al., 2010; Zurzolo et al., 2019). Allergen risk assessment supports in assessing and managing the risk of possible UAP during food production and for establishing action levels for Precautionary Allergen Labelling (PAL) (Crevel et al., 2014; Houben et al., 2020; Remington et al., 2022). UAP risk in food products can be assessed by deterministic or probabilistic quantitative risk assessment methods. Probabilistic risk assessment is considered the most appropriate method for population food allergen risk assessment and risk management purposes (Madsen et al., 2009). However, for many purposes, deterministic risks assessment may provide adequate and sufficient information (Houben et al., 2020), provided that adequate hazard data and food intake figures are used. Houben et al. (2020) published full range population Eliciting Dose values for 14 priority allergenic foods and recommendations for use in risk characterization, which provides state of the art hazard characterization data for protein from these allergenic foods. Blom et al. (2020) showed that food intake information from the general population represents the intake levels of food allergic patients. In the framework of the EU funded iFAAM project a food intake database for allergen risk assessment was developed, comprising 3 North-western European countries (Denmark, Netherlands and France; Birot et al., 2018), and a sensitivity analysis method to establish the optimal food intake percentile for allergen risk assessment was presented (Blom et al., 2019). Using this sensitivity analysis, Blom et al. (2019) showed that the 50th percentile of the intake distribution of the single eating occasion of products in food groups was in compliance with the safety objective of the ED01 of the ED population distribution of allergenic foods in more than 99% of the investigated risk assessment scenarios. Compliance of all scenarios was reached with the 75th percentile. This point estimate was therefore suggested as the optimal

Abbreviations: ED, Eliciting Dose; LOAEL, lowest observed adverse effect level; RD, Reference Dose; PAL, Precautionary Allergen Labelling; LCI, Lower Confidence Interval; P50, 50% percentile of the food consumption distribution; RA, risk assessment; UAP, unintended allergen presence; US, United States America; NL, The Netherlands; NW EU, Northwest Europe.

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point estimate for use in deterministic allergen risk assessment in case the safety objective is the ED01, as it would be adequately conservative in the public health context. When selecting any other ED value as safety objective, the optimal percentile likely will also fall in the P50–P75 range, but the sensitivity analysis developed should be applied to determine the optimal point estimate for the respective safety level (Blom et al., 2019). The previous analysis was performed with one food consumption database and for one safety objective (the ED01). Since then, there have been various important developments that make it necessary to conduct a new sensitivity analysis to confirm or re-establish the optimal percentile of food intake for deterministic risk assessment or the elaboration of action levels for PAL. Recently, the FAO/WHO expert consultation recommended Reference Doses based on the ED05 of the population ED-distribution (FAO/WHO Expert Consultation, 2022; FAO/WHO Expert Consultation, 2021). In addition, we have made several significant improvements and expansions in the datasets for population allergen ED-distributions and those for food intake that both are input in the sensitivity analysis. First of all, an improved model averaging methodology removed subjectiveness in derivation of the population ED values. Second, the number of individual threshold data for allergenic foods doubled to 3440 individual datapoints and for more allergenic foods than previously. This resulted in updated population ED values for 14 allergenic foods (Houben et al., 2020; Remington et al., 2020; Wheeler et al., 2021). And third, new food intake datasets attuned to allergen risk assessment purposes were developed for the adult population of the United States, based on NHANES, and for the Netherlands based on the Dutch Food consumption database (DNFCS) (Meima et al., 2021). In addition, for the present study two food intake databases for children were generated based on NHANES, and the Dutch Food consumption database (DNFCS). The present study was conducted with the aim of establishing the optimal percentile of the food intake distribution for compliance with the ED05-based Reference Doses (RfD) recommended by the Ad Hoc FAO/WHO Experts Consultation. In addition, by analyzing scenarios for a broader range of safety objectives (i.e. a broader range of ED-values), regions (including food intake data from Europe and the US) and age ranges (including food intake data from children in addition to adults), the general applicability of the results was aimed to be strengthened.

2. Methods

2.1. Input parameters

2.1.1. Food intake data

In total 5 food intake datasets were used; 3 databases for adult populations and 2 databases for child populations. For the adult population (≥19 years) these were the food intake databasess from the United States (US) with 15227 adults and The Netherlands (NL) with 3819 adults (Meima et al., 2021). The third database was the combined food intake database for North-western Europe (NW EU) developed previously as part of the EU iFAAM (Integrated Approach to Food Allergen and Allergy Management) project combining national food consumption data from Denmark, Netherlands and France, with a total of 8472 adults (Birot et al., 2018). For the US child population the data was based on the NHANES 2003–2010 (https://www.cdc.gov/nchs/nhanes/) and for the NL child population based on the Dutch National Food Consumption Survey 2007–2010 (DNFCS) of the National Institute of Public Health and the Environment (https://www.rivm.nl/en). Both datasets for the child populations were prepared as previously described by Meima et al. (2021). Briefly, for both countries the food consumption surveys were each based on two nonconsecutive 24-hrs recalls per individual. Data from children aged 0–18 years for which both recall days are available were used for our analysis. This applied to 13833 children from the US national food consumption database and 1730 children from the Dutch national food consumption database.

Food items of a database were categorized into food groups based on similarity of food products as proposed by (Birot et al., 2017) and the adjustments presented in (Meima et al., 2021). When a food product within a food group was eaten multiple times during the non-consecutive sampling days by a single person, the highest of the multiple intake amounts was selected for the analysis. Food intake log-normal distributions were drawn for all food groups. This analysis was only performed if food intake data were available for ≥8 subjects for a food group. In case for a food group data was available for less than 8 individuals, this food group was not represented in a database (though a few data could be present in the national food consumption survey). This resulted in 50–55 food groups per database depending on the number of observations available for a food group (Supplement Table S1). The full food intake distribution was used for the probabilistic RA, whereas single percentiles (P50, P55, …up to P100) of the food intake distribution for each food group were used as input values for the food intake figure in the deterministic RA.

2.1.2. Food allergen contamination data

The deterministic and probabilistic quantitative risk assessments were performed assuming allergen concentrations in the food products ranging from 1 to 10,000 ppm (1, 3, 10, 30, 100, 300, 1000, 3000 and 10,000 mg protein of the allergenic source/kg food products). These levels were chosen to cover a wide range of concentrations known to be present in food products (Allen and Taylor, 2018) and to ensure that these cover allergenic protein intakes through the various food groups both below and above the ED values to be used in the analyses.

2.1.3. ED values for the food allergic population

The recently updated full population Eliciting Dose distributions for 14 allergic foods (Houben et al., 2020) were used. The full ED distribution was utilized when performing the probabilistic RA. For the deterministic RA, the ED01, ED2.5, ED05 and ED10 (in mg total protein of allergenic food) of the discrete and cumulative distributions were applied. These ED values have been derived for mustard, egg, milk, celery, walnut, cashew, peanut, wheat, sesame, lupin, hazelnut, fish, soy, and shrimp (Houben et al., 2020; Remington et al., 2020). The exact dose in mg protein of the allergenic food and the confidence interval at an ED value have been published by (Houben et al., 2020).

2.1.4. Risk assessment

2.1.4.1. Deterministic allergen risk assessment. The deterministic RA is captured in the following formula:

Exposure [amount of food consumed (in kg) X concentration of allergenic substance (in mg total protein from the allergenic food/kg food)] **≤ or > Eliciting Dose x** *)

*) EDx, i.e., the ED01, ED2.5, ED05 or ED10, in mg total protein from the allergenic food.

For each of the input parameters a point estimate is required. The exposure is calculated by multiplying the amount of food consumed by the concentration of the protein from the allergenic food. For the amount consumed, the various percentiles of the food intake distribution for food groups were applied (see section 2.1.1), and for the concentration the different levels presented in section 2.1.2. The exposure in mg total protein from the allergenic food is then compared with the various ED values (i.e., safety objectives) also in mg total protein from the allergenic food as described in section 2.1.3. The outcome of each risk assessment is a binary answer, either the exposure is at or below the applied ED (or it exceeds it; see Fig. 1).

2.1.4.2. Probabilistic allergen risk assessment. The quantitative probabilistic RA is performed as described in various publications (Spanjersberg et al., 2007; Blom et al., 2020; Meima et al., 2021). The quantitative probabilistic RA model uses the full intake distribution of food derived for a food group for the various country specific databases (section

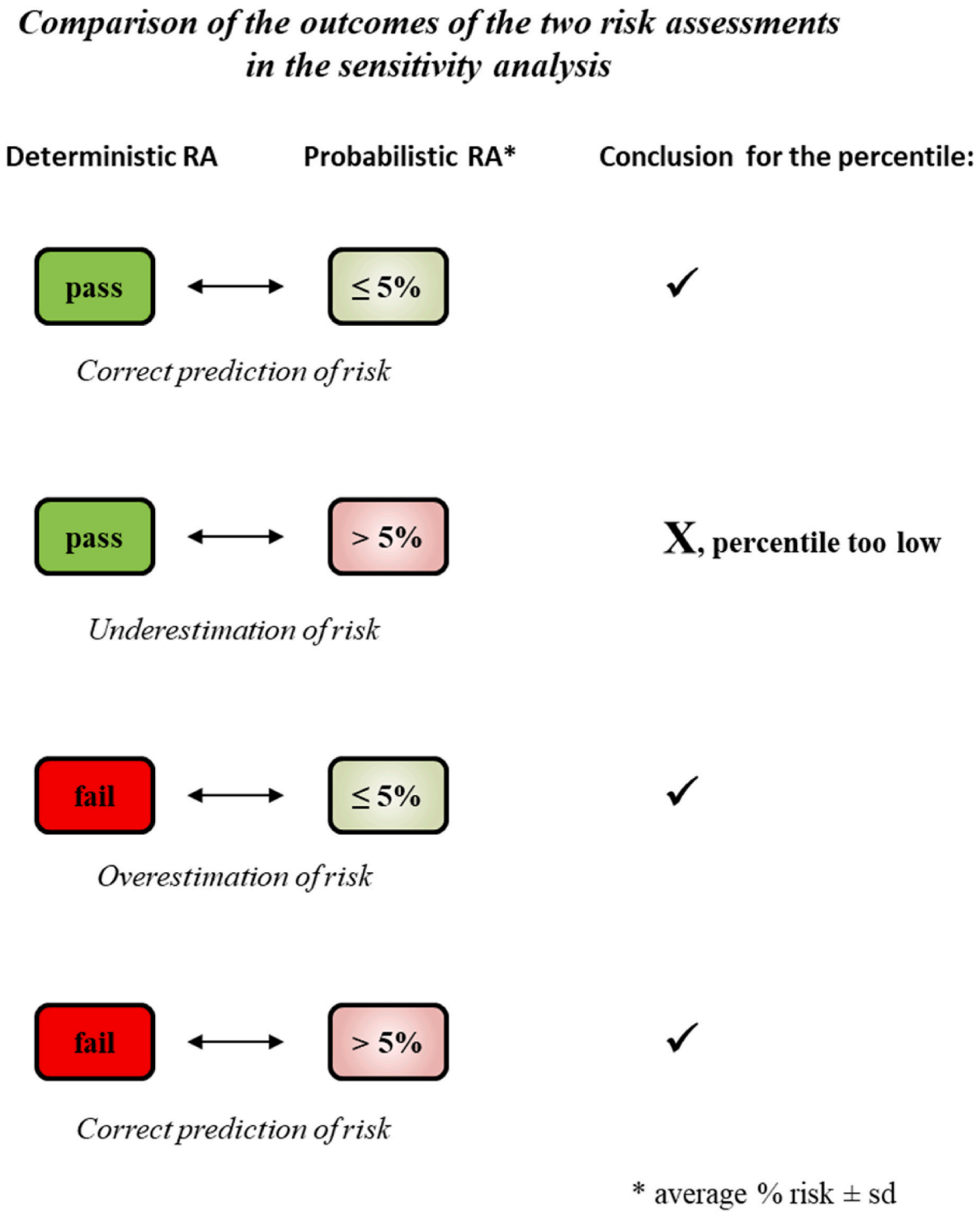

Fig. 1. Description of the possible outcomes in the sensitivity analysis to derive an optimal point estimate for allergen risk assessment (partly reproduced from Blom et al 2019**).** The deterministic RA and the probabilistic RA outcomes are compared in the sensitivity analysis. The formula and the input parameters for the deterministic RA are described in the Methods section. The outcome of a deterministic RA is a binary answer: if the amount of allergenic protein in the amount of food consumed is at or below the relevant ED value, a product is considered to comply with the safety objective of using the respective ED value ("pass"; green boxes). Conversely, if it exceeds that amount, the product does not comply ("fail"; red boxes). The cut-off for probabilistic RA is the estimated percentage of allergic responders and is either at or below (light green boxes) or above (light red boxes) the defined risk level at the ED values (based on using the ED05 in the example of the figure indicated as ≤5% and >5%. The outcomes of the two risk assessments are compared: Underestimation or overestimation of the risk by the deterministic RA occurs if too low or too high food intake values were used in the deterministic modelling. The comparison with the more sophisticated probabilistic modelling is thus used in the sensitivity analyses to derive the optimal food intake percentile for deterministic RA. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

2.1.1) combined with the concentration of protein from an allergenic food in the food product (section 2.1.2) and the model averaged population ED-distribution (section 2.1.3). These allergen threshold distributions were generated with model averaging methodology in which the individual threshold data were fitted into population threshold distributions for the respective allergic population, that was a weighted average of five parametric models (Weibull, LogNormal, LogLogistic, Generalized Pareto, and Log Double Exponential). In a Monte Carlo simulation of 100 runs of 10,000 iterations, these intake distributions of protein of an allergenic food were compared to the population threshold dose distribution for the respective allergenic foods (Houben et al., 2020; Remington et al., 2020; Wheeler et al., 2021).

The risk assessments are performed for allergic users of food products containing the relevant allergenic proteins. The resulting risk assessments provide an estimation of the percentage of expected allergic reactions in the allergic population eating such products.

2.1.5. Sensitivity analysis

The sensitivity analysis to establish the optimal percentile of the food consumption distribution for use in deterministic allergen risk assessment at a predefined safety objective has been described in detail in Blom et al. (2019).

Briefly, the analysis compares in multiple scenarios the outcome of the deterministic risk assessment with the outcome of the probabilistic risk assessment using the same underlying datasets for food intake (2.1.1), contamination (2.1.2) and population ED distribution (2.1.3). Deterministic RA scenarios are generated using the wide range of percentiles (the P50, P55, …up to P100) of the food intake distribution for each food group and the various concentrations and compared to the probabilistic RA outcomes for this food group. If the probabilistic RA predicts that the percentage of reactions in the allergic population exceeds the predefined safety objective, which is for instance 5% in case of using the ED05 of the population distribution, the outcomes of the deterministic RA for that food group should also indicate that this predefined percentage is exceeded. Vice versa, the deterministic RA outcome should indicate that the predefined percentage is not exceeded if the probabilistic RA estimated percentage of responders is at or below the predefined percentage. Conservatively, the deterministic RA outcome may indicate a risk, whereas the probabilistic risk assessment outcome is below the predefined risk level. Fig. 1 shows the possible outcomes in the deterministic RA that are compared to the probabilistic RA outcomes. The analysis identifies for a specific food group the lowest percentile of the food intake distribution for which the outcome in a deterministic risk assessment is in compliance with the predefined food safety objective as verified by the probabilistic risk assessment. In principle this lowest percentile can be different for various food groups. The overall optimal percentile of food intake is based on the results of all food groups.

2.2. Software

SAS 9.3, Copyright © 2002–2010 by SAS Institute Inc., Cary, NC, USA was used for statistical analysis of the demographics of the US and Netherlands intake data.

R version 3.5.2, Copyright © 2017 The R Foundation for Statistical Computing was used for the probabilistic risk assessment, making use of R packages DescTools (version 0.99.35), EnvStats (version 2.3.1), fitdistrplus (version 1.0–14), gplots (version 3.0.3), Hmisc (version 4.4-0), msm (version 1.6.8), MASS (version 7.3–51.4), plyr (version 1.8.6), Rmisc (version 1.5) and scales (version 0.4.1).

3. Results

3.1. Sensitivity analysis

In total, 28,784 deterministic risk assessments (scenarios) were performed for the 4 safety objectives (ED01, ED2.5, ED05 or ED10), using 5 food intake databases, and 14 allergenic foods. The result of each deterministic risk outcome was compared with the outcome of the probabilistic risk assessment (expressed in the % risk). This showed that for almost all scenarios (99.84%) the 50th percentile of a food group intake distribution was meeting the safety objective (Supplement Table S2). For 46 food group-allergen combinations (0.16% of all 28,784 tested scenarios) the sensitivity analysis suggested that a percentile of P55–P65 of the intake distribution was required to assure that the deterministic outcome was in accordance with the outcome of the probabilistic risk assessment. These 46 deviations did not occur for a specific food intake database or specifically for the discrete or the cumulative threshold dose datasets. Further, most deviations occurred for the ED01 and ED2.5 as safety objective and often the P55 of the intake distribution was sufficient.

3.2. Scenarios deviating from the 50th percentile

Deviations from the P50 occurred in various food groups and in all 5 country food intake databases (Fig. 2). The adults and children NL food intake databases were contributing for almost two-third of the deviations from the P50, and one-third concerned the US databases (Supplement Table S3). There was a difference between the discrete and cumulative datasets: for the discrete threshold dose dataset the food group *Mashed potato powder* almost completely caused the deviations (92%) for multiple allergenic foods (Supplement Figure S1A). For the cumulative threshold dataset, deviations scattered among food groups (18 different food groups) and country databases (Fig. 2 and Supplement Figure S1). Three food groups contributed most (55%) to the deviations: *Mashed potato powder* due to the NL-adult population (35%), *Alcoholic drinks>15%* for the NL adults and NL children databases (11%) and *Milk* powder & Cocoa powder (9%), most due to the US adults and US children databases.

A closer look at the *Mashed potato powder* food group for the NL-adult population showed that the intake distribution of this food group was based on a low number of observations, 9 subjects of which 1 subject consumed an extremely low quantity, 1.8 g compared to the range of 37–104 g consumed by the other 8 subjects in this food group (Supplement Figure S2). This one observation contributed significantly due to the low number of observations and resulted in an overall intake distribution that was an underestimation of the observed dataset. In contrast, in the NW EU database, 1209 datapoints were available for food group *Mashed potato powder* (mean 177 g) and the P50 resulted in an adequate deterministic risk assessment for this particular dataset. In other databases the number of observations were too low (NL-children, US-adults), or not present (US children) for generating the food group. The extreme low intake amount was removed from NL-adult population food group *Mashed potato powder* and the sensitivity analysis was repeated for food group *Mashed potato powder* for the NL-adult population which resulted in an optimal point estimate of P50 at all safety objectives chosen (Supplement heatmaps Figure S3).

The 30 other deviations were due to various combinations, i.e., not a particular database or food group was involved, however, they were almost solely the result of the cumulative peanut threshold dose distribution (Supplement Figure S1B; Table S3, S4), and mainly observed at the ED01 and ED02.5 as safety objectives (Table 1, Supplement Table S5, S6).

After adjusting the food group *Mashed potato powder* in the NL adults database, for 99.9% of all scenarios the 50th percentile of a food group intake distribution was meeting the safety objective (Table 1). When using the discrete dataset, the deterministic outcome was in accordance with the probabilistic risk assessment in about 100% (99.97%) of the scenarios, and for the cumulative dataset in 99.6%–100%. The analysis indicated that for just 0.1% of food group and allergen combinations a higher percentile (P55–P65) might apply. These remaining deviations occurred in almost all cases for scenarios of the ED01 and ED02.5 of the

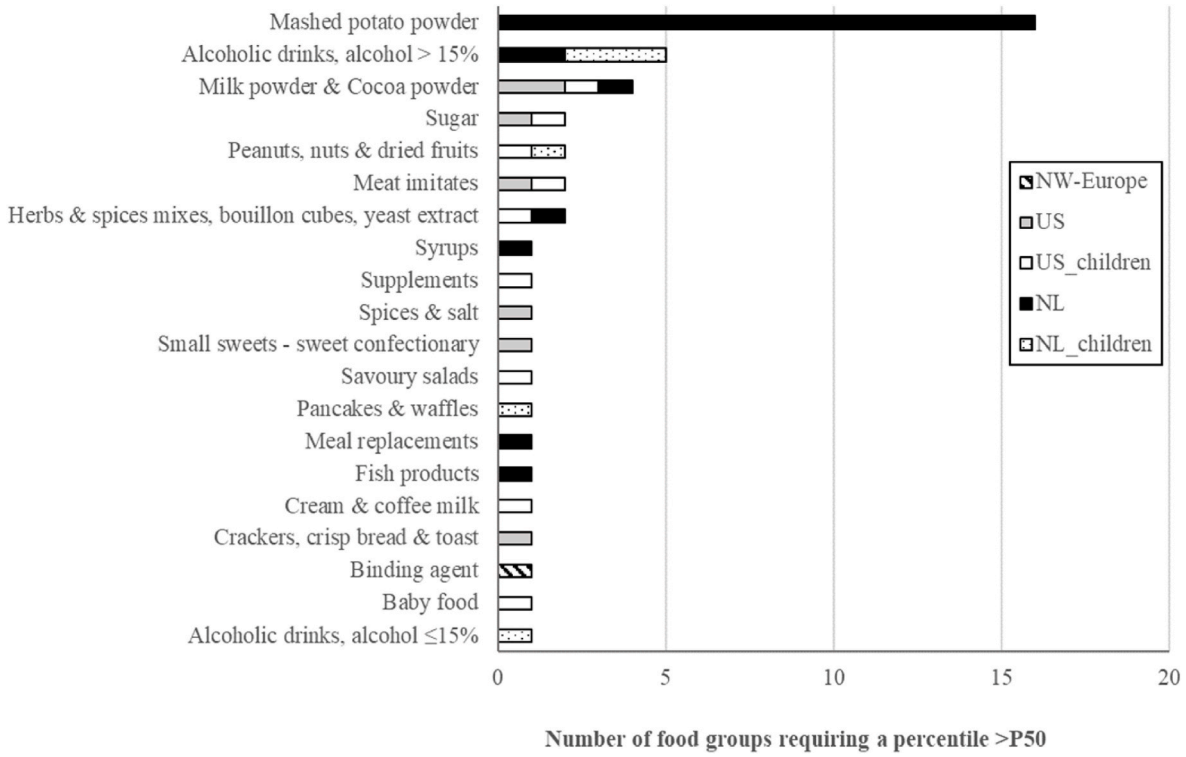

Fig. 2. Food groups (n = 46) for which the sensitivity analysis suggested a percentile above the 50th percentile of the food intake distribution. This was irrespective of the safety objective (ED01, ED2.5, ED05 or ED10) and the allergens. Note: these 46 cases represent only 0.16% of all 28,784 scenarios assessed; in 99.84% of all scenarios the 50th percentile resulted in an adequate deterministic risk assessment.

cumulative peanut distribution as the predefined safety objective. In many cases the P55 was sufficient. Overall, with the P65 of the distribution a conservative intake estimate will result in meeting all safety objectives.

Recently, the Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens (Part 2: Review and establish threshold levels in foods of the priority allergens) recommended Reference Doses based on the ED05 of the population ED distributions for 14 priority allergens (FAO/WHO Expert Consultation, 2022; FAO/WHO Expert Consultation, 2021; Houben et al., 2020; Remington et al., 2020). At the ED05, only 2 deviating scenarios were present (0.03% out of 7196 risk assessments): *Alcoholic drinks, alcohol <15%* for the NL children database, and *Baby food* for US children database. In both cases the P55 was sufficient for meeting the safety objective, indicating that the best value for intake was between the P50–P55. The methodology used for the sensitivity analysis applies a strict cut off based on the upper confidence interval of the probabilistic risk assessment (the 2.5 and 97.5 percentiles of the estimated risk) in deciding whether the deterministic risk assessment complies with the outcome of the probabilistic assessment. In both cases the estimated risk was just above the upper limit of 6.7%, which were 6.9% and 7.3% for food group *Alcoholic drinks, alcohol< 15%* (NL children) and *Baby food* (US children) respectively.

3.3. Mean intake compared to the P50–P65 percentile

The outcomes of our analyses show that the P50–P65 of the population distribution of the single eating occasion intake of foods within a food group lead to a deterministic risk assessment that is in compliance with the safety objective intended when using low ED values (ED01-ED10) as reference dose. However, such P-values often are not publicly available. The mean of the population distribution of the single eating occasion intake of food was investigated as alternative. The mean generally (99.2% of all food groups) was above the P50. In 2 cases (0.8%) the mean intake was just below the P50, but this was a small difference of 3% and 5% of the intake. Approx. 60% of the mean intakes was below the P65, and 40% was above the P65. Overall, the mean intake was sufficiently conservative, i.e., the mean intake was in above the P50 intake and thus would result in a higher risk estimate (Supplement Figure S4 for details per food intake database).

4. Discussion

The sensitivity analysis performed in this study shows that the 50th percentile of the general population distribution of the single eating occasion intake of foods in almost all scenarios (>99.9%) resulted in a deterministic risk assessment outcome in compliance with the safety objectives ED01- ED10, without being over-conservative. Deviations of this P50 occurred mostly at low ED values (ED01 and ED02.5), and in these cases the P55–P65 was sufficient. In part of the few scenarios in which a slightly higher percentile was suggested, an outlier in the food intake survey data was found to cause this deviation. For the ED05, the P50 was sufficient in 99.97% of the scenarios. At the ED05, 2 deviating scenarios suggested that the P50 would be insufficient but using the P50 only resulted in a negligible exceedance of the risk tolerated by the safety objective (0.2% and 0.6% above the set upper limit).

The Ad hoc Joint FAO/WHO Expert Consultation on Risk Assessment of Food Allergens (Part 2: Review and establish threshold levels in foods of the priority allergens) recommended reference doses based on the ED05 (FAO/WHO Expert Consultation, 2022). Here we show that the P50 of the intake distribution is sufficient for use as the reference amount in calculation of action levels for precautionary allergen labelling. If the P50 is not available, the mean would be a good alternative, as analyses of the intake data showed that the mean is generally between the P50 and P65, or occasionally above the P65 of the distribution. Our analyses provide the science-based substantiation of the adequacy of the P50 or mean for ED05-compliant calculation of action levels for PAL.

The sensitivity analysis shows that the few scenarios that demanded an intake based on the P55–P65 percentile mostly occurred for the safety

Table 1
The percentage of product and allergen combinations at each percentile of the food intake distribution for which the deterministic RA outcome is in compliance with the probabilistic RA. Results are shown per safety objective (ED value) for the discrete dataset (A) and the cumulative dataset (B).

1A. Safety objective based on the discrete dataset	**Food intake database**				
	NW EU	**United States (US)**		**Netherlands (NL)**	
	adults	**adults**	**children**	**adults**	**children**
	n = 728	n = 742	n = 728	n = 714	n = 686
ED01_discrete					
P50	100%	100%	100%	100%	99.9%
P55					99.9%
P60					100%
ED02.5_discrete					
P50	100%	100%	100%	100%	100%
ED05_discrete					
P50	100%	100%	100%	100%	100%
ED10_discrete					
P50	100%	100%	100%	100%	100%

1B. Safety objective based on the cumulative dataset	**Food intake database**				
	NW EU	**United States (US)**		**Netherlands (NL)**	
	adults	**adults**	**children**	**adults**	**children**
	n = 728	n = 742	n = 728	n = 714	n = 686
ED01_cumulative					
P50	100%	99.6%	99.3%	99.3%	99.7%
P55		99.7%	100%	99.9%	99.9%
P60		100.0%		99.9%	100%
P65				100%	
ED02.5_cumulative					
P50	99.9%	99.5%	99.6%	99.7%	99.7%
P55	99.9%	100%	100%	99.9%	100%
P60	99.9%			100%	
P65	100%				
ED05_ cumulative					
P50	100%	100%	99.9%	100%	99.9%
P55			100%		100%
ED10_ cumulative					
P50	100%	100%	100%	100%	100%

objectives at the ED01 and ED02.5. Previously Blom et al. (2019) similarly found that over 99% of the scenarios were meeting the safety objective compliant with the ED01, but some scenarios needed a higher percentile. They recommended the P75 as a conservative choice to cover 100% of the scenarios. The present analysis using updated methodology and improved datasets indicates that this P75 was unnecessarily conservative.

The analysis shows that the distributions fitted on the intake data should be checked for number of subjects, distribution, and potential outliers. A defined minimum standard for the number of subjects for generating the intake distribution does not exist, however a number of ≥8 subjects generally seems sufficient for fitting data and perform adequate risk assessment (Blom et al., 2020; Meima et al., 2021). Generally, a sufficient number of users will be present for a food group (i.e., the median number in the present study was 1252 subjects per food group) and a potential outlier at the low or high end of the distribution hardly influences the overall fitting. However, when a low number of subjects is present, a potential extreme outlier can be expected to have a relatively large impact on the fitted distribution (resulting either under or overestimating the risk). This occurred in the present study for food group mashed potato powder. Removing the outlier resulted in a fitting that represented the intake data well.

Our current analysis covered databases of various countries and subpopulations, suggesting a generic adequacy of the P50 value of the food group intake for use in deterministic risk assessment at low ED levels (up to ED10). However, this P50 value should be selected from country- or region-specific food intake data. The quantity of food that is eaten for a specific food group can be highly variable between countries or continents (Meima et al., 2021; Birot et al., 2018), indicating that food intake amounts cannot extrapolated from country to country without prior verification research. A systematic comparison of US and NL food databases concluded that food intake data from the US and The Netherlands showed large differences in 20% of the food groups (Meima et al., 2021).

Important when selecting the P50 or mean intake value from a database is to realize that the intake figure should be based on the single eating occasion food intake amounts. A food allergic reaction usually develops within 10–30 min after the intake of the allergenic food, which means that within or shortly after the meal occasion the reaction may evolve. Most food consumption databases are set up for providing nutritionally or toxicologically related information, providing for example the amount eaten of a product during a day. The European Food Safety Authority (EFSA) Comprehensive European Food Consumption Database (https://www.efsa.europa.eu/en/data-report/food-consumption-data) contains summary food intake data per country and though this database is developed for evaluation of risks related to possible hazards in food, the data are not one to one applicable for allergen risk assessment. The "acute data for consumers only" appears most comparable to a highest eating occasion but sums up the intakes of a single day. This indicates that these data represent an overestimation of the intake for products that can be consumed on several occasions for one day, such as bread or drinks. Such data is not suitable for accurate food allergen risk assessment or as a basis for action level calculations and risk management decisions such as those related to the application of PAL.

Food consumption patterns are dynamic and changes can occur in alimentary habits in the population, e.g. adolescents are shown to eat more of specific food groups (Diethelm et al., 2012) or consumption of particular food categories can increase (or decrease) over time, e.g. vegetable consumption increased in the Netherlands population over a 4-year time range (https://www.wateetnederland.nl/resultaten/veranderingen/verandering-consumptie-groente-en-fruit? =). It is uncertain whether these changing alimentary habits will actually result in significant changes in the overall amount eaten at a single meal occasion (which is the input for the food intake value for food allergen risk assessment). The food consumption surveys used in the present study are for the general population and cover various countries/geographical regions, a wide range of ages and many eating habits, including those of adolescents, or differing trends. Further, studies on alimentary habits show that the effect is often on the frequency of consumption (how often a food product or category is consumed) rather than the intake at single eating occasions. For example an increased vegetable intake was observed in the Netherlands from 135 g/day in 2012–2016 to 163 g/day in 2019–2021, but this consumption is the sum of 4 eating occasions and it is therefore unclear if this increase was caused by an increased number of eating occasions or that this increase was spread over the one or multiple meal occasions. Based on the present study accounting wide variations in alimentary habits in several countries it is likely that the P50 of the food intake distribution still is the optimal point estimate in more than 99.9% of the scenarios also with changing eating habits. Yet, it should be realised that with the P50 still being the optimal point estimate it may in theory be possible that the overall intake distribution slightly changes with changing alimentary habits and results in a different amount at the P50 of the distribution (gram food product). Previous studies however showed that considerable differences in the food intake at the eating occasion are needed before a significant effect is observed for the percentage risk for the allergic population (Blom et al., 2020; Meima et al., 2021).

Food product compositions often change which may lead to dietary changes. For example the current vegan trend leads products containing only plant-based ingredients (Košiciarová et al., 2022). New ingredients are developed that may give rise to new food safety issues, including for the allergic population e.g. the potential allergenicity of ingredients

based on insect proteins (Broekman et al., 2017) and the development of food crops in which genes of food allergens are transferred (). This means that for a risk assessment the potential hazard of the ingredient should be investigated. However the food products containing these novel ingredients are usually variations of existing food products and replace a similar product in the diet, e.g. a vegan cheese replaces the dairy based cheese, an almond drink that is an alternative for a similar dairy product. We previously showed that intakes of alternative products replacing traditional products are comparable to the intakes of food items of the same food group (Blom et al., 2020). Therefore, it is unlikely that such replacements would affect the outcome of sensitivity analyses as conducted and the P50 would remain the optimal point estimate of intake.

To conclude, the present study shows that the 50th percentile or mean of the general population single eating occasion intake of food together with recently FAO-WHO recommended Reference Doses provide risk assessors and managers optimal standardized data for a harmonized calculation of action levels for precautionary allergen labelling.

CRediT authorship contribution statement

W. Marty Blom: Conceptualization, Investigation, Methodology, Data curation, Writing – original draft, Project administration, Funding acquisition. **Joost Westerhout:** Investigation, Methodology, Data curation, Software, Writing – review & editing, Visualization. **Geert F. Houben:** Conceptualization, Methodology, Investigation, Funding acquisition, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Data availability

The data that has been used is confidential.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fct.2023.113953.

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