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The changing food allergen landscape in Europe calls for harmonised food allergen monitoring: Position paper

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ABSTRACT

With the changing food allergen landscape in Europe, there is an increasing need for the monitoring of (non-) prepacked food products to improve the protection of consumers with food allergies. Although food allergy is a condition affecting up to 10 % of the consumers worldwide, a European harmonised approach for the management of precautionary allergen labelling, allergen reference doses, analytical methods or food product monitoring is not in place. This leads to limited food choices for consumers with food allergies but can also result in the occurrence of serious allergic incidents. The current state of non-harmonised and unregulated food allergen monitoring in Europe means risks and considerable costs for the individual consumer, but also for society in general. In this position paper, we argue for the introduction of harmonised guidelines for food allergen monitoring on the European level based on a discussion of the wide-ranging implications their lacking entails. We believe that there is a pressing need to update the European legislation on food allergens, including the introduction of harmonised monitoring programmes, which will lead to improved overall food safety, and better protection and options for consumers with food allergies.

1. Introduction

Most people can safely consume food and beverages of their choice without being concerned about the risk of a hypersensitive reaction. However, a small but significant minority of consumers, not limited by age or gender, must live with such a risk. With no cure available, the only sustainable way of managing a food allergy or intolerance is to avoid consumption of the offending food. For this reason, people with a food allergy or intolerance must have access to accurate and reliable information about the exact content of food products. This is provided for in EU Regulation 178/2002 article 8: “the protection of the consumers’ interests; Food law shall aim at the protection of the interests of consumers and shall provide a basis for consumers to make informed choices in relation to the foods they consume.” (European Commission,

2002)

Foods giving rise to hypersensitivity reactions, IgE-mediated, non-IgE-mediated intolerances and coeliac disease, in susceptible individuals may be present in food products for multiple reasons. These include, as an intentionally added ingredient, which has to be declared on the label, as an unintended contaminant, for which a label declaration is not currently subject to specific legislation as its presence is not confirmed, or fraudulent substitution in the supply chain (Gowland & Walker, 2015). Labelling mistakes concerning priority allergens can happen due to faults in the supply chain, during production, processing or packaging. When discovered, they have to be corrected without delay by the manufacturer of the respective product. Moreover, the undeclared or unintended allergen presence (UAP) in foods is a major cause of food allergy or intolerance incidents in sensitised consumers. To safeguard

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consumers with food allergies or intolerances, the prevalence of UAP should be monitored. The extensive use of precautionary allergen labelling (PAL) by food industry is a feasible solution to manage UAP and may be considered to be a less expensive alternative to the efficient control of food ingredients and manufacturing. However, the over-use and misuse of PAL is widely regarded (DunnGalvin et al., 2019) as sub-optimal for consumer choice, nutrition and safety.

Within the European Union, the protection of consumer health is regulated by the General Principles and Requirements of EU Food Law (Article 1 of Regulation (EC) No 178/2002 (European Commission, 2002)). More specifically, Regulation (EU) No 1169/2011 (European Commission, 2011) on the Provision of Food Information to Consumers, referred to as “FIC”, includes provisions to protect EU consumers with a food allergy or intolerance. Article 9.1(c) and Article 21 of FIC require the intentional use of any of the 14 priority allergens (Annex II, FIC) to be emphasised (unless its presence is clear from the name of the food) in the list of ingredients of prepacked foods. Where, for valid reasons, there is no list of ingredients a statement is required: ... ‘contains’ followed by the name of the Annex II substance. Member States may specify (Art. 44) how allergen information is otherwise made available to consumers of food that is non-prepacked or prepacked for direct sale (e.g. in food businesses such as restaurants and over-the-counter sales).

The Food Hygiene Regulation (EC) No 852/2004 (European Commission, 2004) ensures food safety throughout the food chain. In an amendment of the FIC Annex I, the management of food allergens by food businesses is laid down in Commission Regulation (EU) 2021/382 (European Commission, 2021).

The effectiveness of the EU legislation on priority allergen labelling depends on proper execution by the food industry, and monitoring and enforcement by food regulatory authorities. However, the appropriate application of UAP labelling is currently not regulated but addressed by industry-driven initiatives such as the Voluntary Incidental Trace Allergen Labelling (VITAL)[®] programme (Taylor et al., 2018). There is currently no EU-harmonised system guiding Member States and Associated Countries (MS; in this text considered together) on how they should monitor compliance with food regulations on food allergen labelling/declaration by food businesses. It could be argued that in view of the lack of systemised monitoring in the MS, the safety risks posed by the presence of the priority food allergens in food products is underestimated, especially in comparison to other, more attention-getting or perceived food safety risks. For example, despite the lack of any credible evidence of an actual risk for human health from food treated with ionising radiation, the respective EU legislation, Directive 1999/2/EC (European Commission, 1999), stipulates that the MS must annually return data on operational food irradiation facilities and surveys of irradiated food on the market to the EU Commission. The application of validated and accredited analytical methods for the detection of irradiated foods is harmonised at EU level for this purpose. This is in stark contrast to the situation concerning the priority food allergens that present an acknowledged food safety risk, and for which there is no coordinated approach at EU level to control compliance with the regulations.

International salience of allergen risk assessment has increased significantly from renewed activity by the Codex Alimentarius Commission. The Codex Committee on Food Labelling (CCFL) is currently reviewing allergen labelling in the General Standard for the Labelling of Packaged Foods (GSLPF) as well as developing guidance on the use of precautionary allergen labelling. The Codex Committee on Food Hygiene (CCFH) has developed a Code of Practice on Food Allergen Management for Food Business Operators, which was adopted in 2020. The General Principles of Food Hygiene (GPFH) was also updated in 2020 and includes information on the control of allergens. In view of the many scientific developments in the understanding of food allergens and their management and in response to the request from the CCFL and CCFH for scientific advice the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) convened a

series of expert meetings to provide scientific advice on this subject.

Five scientific reports by an expert working group of the FAO/WHO have now been published (WHO/FAO, 2022a, 2022b; WHO/FAO, 2023a, 2023b; WHO/FAO 2024) that collate and evaluate scientific information and data, which should be considered in a re-evaluation of food allergen management in the EU.

2. Current status and relevance of food allergen monitoring

We observe that food allergen monitoring is not harmonised across the MS and does not receive the same attention in terms of resources as compared to the method development and monitoring for other food safety hazards. This could be a result of a combination of factors, including underestimation of the societal impact of food allergens, the complexity of food allergen detection and quantification, and the absence of a clear legislative framework for UAP and ‘free from’ products.

Food allergy by its immunological mechanism poses unique acute safety risks for sensitised individuals. Food hypersensitivity generally poses chronic risks to quality of life and nutrition, particular coeliac disease which may also precipitate long-term major adverse health sequelae (Iversen & Sollid, 2023; Laurikka et al., 2022). These acute and chronic risks seem to be underestimated when compared to other food safety risks such as pesticides, natural toxins or chemical contaminants.

2.1. The societal impact of food allergy and food hypersensitivities

This chapter presents recent data on food allergy prevalence and discusses the possible reasons why food allergens are not receiving the attention of policy makers that is appropriate with regard to their societal impact.

The *prevalence* of a food allergy in the context of epidemiology refers to the proportion of a population with that food allergy at the moment of the investigation, whereas *incidence* describes the number of new cases per population in a specified period of time (Tang & Mullins, 2017). Food allergy is a global public health problem affecting more than two hundred million people, with underreporting likely in some regions (Manea et al., 2016; Sicherer & Sampson, 2018). An increase in the prevalence of food allergies, initially a characteristic of western countries, is now also observed in Asia, Africa, Central and South America (Loh & Tang, 2018; Sampath et al., 2021). The prevalence of hypersensitivity to priority allergens in European children and adults has been estimated repeatedly based on published studies and national databases, separated between self-reported and clinically confirmed cases (Grabenherr et al., 2020; Kummeling et al., 2009; Lyons et al., 2019; Nwaru et al., 2014; Panesar et al., 2013; Spolidoro et al., 2024). Similar surveys on food allergy prevalence are also available for countries in North America (Clarke et al., 2020; Gupta et al., 2019; Messina & Venter, 2020; Warren et al., 2020), Central and South America (da S. Correia et al., 2022; Gonçalves et al., 2016), Africa (Botha et al., 2019; Sánchez & Sánchez, 2019), Asia (Li et al., 2020; Luo et al., 2021; Ma et al., 2020; Mahesh et al., 2023) and Australia (Peters et al., 2021; Warren et al., 2020), the overall global prevalence has also been summarised (Jiang et al., 2020; Loh & Tang, 2018; Sampath et al., 2021; Sicherer & Sampson, 2018; Tang & Mullins, 2017).

These studies report higher food allergy prevalence in children than in adults, and considerably higher numbers of self-reported than clinically confirmed cases (Loh & Tang, 2018; Lyons et al., 2019, 2020; Nwaru et al., 2014; Sicherer & Sampson, 2018). Overall, the prevalence of confirmed food allergies ranges from more than 0.1 %–10 % in children and 0.1 % to about 5 % in adolescents and adults, including a considerable number of patients with multiple allergies (Jiang et al., 2020; Tang & Mullins, 2017). For Europe the prevalence, taking symptoms and IgE sensitisation to FA as criteria, is 3.5 and 2.4 % for children and adults respectively (Spolidoro et al., 2023). Whereas time trends indicate a possible stabilisation for the prioritised allergies in

developed countries (Campbell & Mehr, 2015; Loh & Tang, 2018; Spolidoro et al., 2024; Willits et al., 2018), there is a notable increase in food allergen prevalence in urban areas in developing countries, possibly due to changes in the diet, lifestyle and environmental exposure (Sampath et al., 2021). More than 160 foods have been identified as causing IgE-mediated food allergies (Sampath et al., 2021), with varying importance for different countries and world regions, but the majority of severe incidents are associated with the consumption of the priority allergens: cow's milk, hen's egg, peanut, tree nuts, soy, wheat, shellfish, finfish and sesame (Jiang et al., 2020; Spolidoro et al., 2024). Mustard, lupin, oats, celery and buckwheat may need to be considered at regional levels (WHO/FAO, 2022a). Moreover, there is an observable trend of increasing food allergy prevalence to so-called emerging allergens such as e.g., kiwi, celery, tomato and beef (Spolidoro et al., 2024). The prevalence of coeliac disease in the general population has been estimated globally to range from 0.5 % to 2 %, with an average of about 1 %. Higher values have occasionally been reported and coeliac disease is less common in countries where gluten-containing cereals are not the staple food and where genetic predisposing factors are low, e.g. in Japan and Vietnam. Coeliac disease is more common in females than in males. An increasing trend has been observed in some countries for instance in Sweden, but not in others (Catassi et al., 2022).

Food hypersensitivities generate significant costs for the allergic individual, but also at national and global level. Economic consequences include expenses for health care, special diets, food manufacturing and labelling, and trade restrictions. The Rapid Alert System for Food and Feed (RASFF) of the European Union lists the presence of un- or misdeclared food allergens as the most important category for notifications of import products over the past three years, with annually more than 200 events (European Union, 2023). These numbers have continuously increased since 2012 (Papapanagiotou, 2021), showing the effects of the implementation of Regulation (EU) No 1169/2011 (FIC) (European Commission, 2011) and compliance control at EU external borders: the RASFF rapid warning system.

On the national level, mislabelling of prioritised allergens on food products can lead to recalls from the market (Yue et al., 2023), which can be extremely costly, financially and reputationally, for the food businesses, including manufacturers and retailers. Many companies have therefore food allergen control plans in place for the management of cleaning procedures, equipment and premises design, and employee training (Gupta et al., 2017). The efforts of national and international food safety authorities to protect consumers with food allergies show results, but the costs involved are non-negligible, including the maintenance of official food surveillance activities by public funding. Patients with food allergies mean a considerable economic burden for health care systems (Bilaver et al., 2019). The direct medical costs per year vary between European countries and can reach up to EUR 3500 for an individual (Cappell et al., 2020; Makharia et al., 2022; Mills et al., 2007; Scott et al., 2019). The expenses are generally higher for young children than for adults (Patel et al., 2011). The socioeconomic burden of food allergy includes costs for schools and employers, carers, lost days at work, reduced abilities to work, quality of life and psychosocial well-being (Dierick et al., 2020; Fong et al., 2022). Food allergy can affect the physical and psychological health of the persons concerned and their families, apart from the financial burden that has been estimated to range between USD 1400 and 4000 per child and year (Bilaver et al., 2019; Shaker et al., 2017; Warren et al., 2020). Worries are mostly connected to potential exposure outside the home and negative effects on the social surroundings, which can lead to anxiety and humiliation (Golding et al., 2022; Lieberman et al., 2021; Polloni & Muraro, 2020). Moreover, self- or misdiagnosed food allergies as well as the widespread and virtually unregulated use of PAL can lead to nutritional deficiencies (Fiocchi et al., 2021; Sampath et al., 2021; Sicherer & Sampson, 2018). Consequently, mitigation strategies for improving the life quality of consumers with a food allergy and reducing the economic consequences have to address a multitude of factors. New therapeutic approaches,

improved diagnosis, adequate methodologies for the detection of allergens, improved regulatory monitoring, harmonisation of guidelines and the reduced use of PAL would be positive steps along the way. In this respect, the food industry-initiated VITAL® system and the introduction of clinically relevant reference doses of food allergens could be beneficial (Taylor et al., 2021).

2.2. Current organisation of food allergen monitoring in the EU member states and associated countries

To understand the current status of allergen monitoring in the EU, a survey was conducted amongst members of the European Network for Allergen Detection Laboratories (ENFADL) in 2023. They were requested to indicate whether a monitoring programme is in place in their respective country and if so, which allergens and how many samples are analysed yearly. In addition, members were asked to share their opinion on the added value and envisioned strategy of allergen monitoring. The metadata are presented in the [Supplemental Information Table S1](#). Results showed that from the 27 countries who received an invitation to participate on the survey, 19 responded. Eleven out of the 19 EU respondents indicated allergen monitoring programmes are performed in their countries (Fig. 1a). In the context of the ENFADL survey, monitoring was defined as laboratory-based analysis performed by official food safety laboratories. Most countries having a monitoring programme in place analysed more than 100 samples per year, some more than 500, as depicted in Fig. 1b. These values translate to an average of 15–100 samples per million inhabitants.

Respondents indicated that decisions on the choice of allergens included in monitoring are made based on risk assessment, which can differ between countries, for instance due to differences in diet. Still, the major allergens responsible for most of the severe allergic incidents (milk, egg, peanut, tree nuts and soy) are monitored in most countries, as presented in Fig. 1c. In addition, gluten is highly monitored given the legislative limit for gluten in 'gluten-free' food.

The reasons given for not having allergen monitoring programmes (8 out of 19 EU respondents) included: no priority for funding, lack of reference methods, too complex, perceived substantial compliance of food manufacturers with the labelling guidelines therefore limited number of incidences, and no legal requirement. Members without a monitoring programme indicated that their country only performs checks for allergen presence in cases of an identified unconformity or complaint, or that monitoring is applied following checks on the documentation in place, i.e. by evaluating conformity of the labels.

The respondents were also asked on the envisioned strategy of allergen monitoring. The consensus is that monitoring should be carried out across the food product value chain: from raw ingredients and processing locations, including equipment and production lines, to the finished product, retailers and web-based businesses, restaurants and over-the-counter sales. The allergens and samples considered as highly relevant for inclusion into monitoring programmes are summarised in [Table 1](#), showing the common consent among the survey respondents that monitoring should be balanced between priority and risk-based allergens in a wide range of food products.

An additionally important outcome of the survey is that there is consensus on the need to regulate the use of PAL, and to standardise and harmonise analytical methods for food allergen detection and reporting. Monitoring is considered as essential to gain overview of the allergenic ingredient concentrations in PAL-labelled products and to guide future monitoring programmes towards relevant allergenic ingredients and product types.

We would like to point out that not all invited ENFADL members responded to the survey and that the outcome is biased towards MS with an interest in allergen monitoring. It should also be noted that although food allergen monitoring activities are undertaken in almost 60 % of the respondent's countries, monitoring practices are not harmonised.

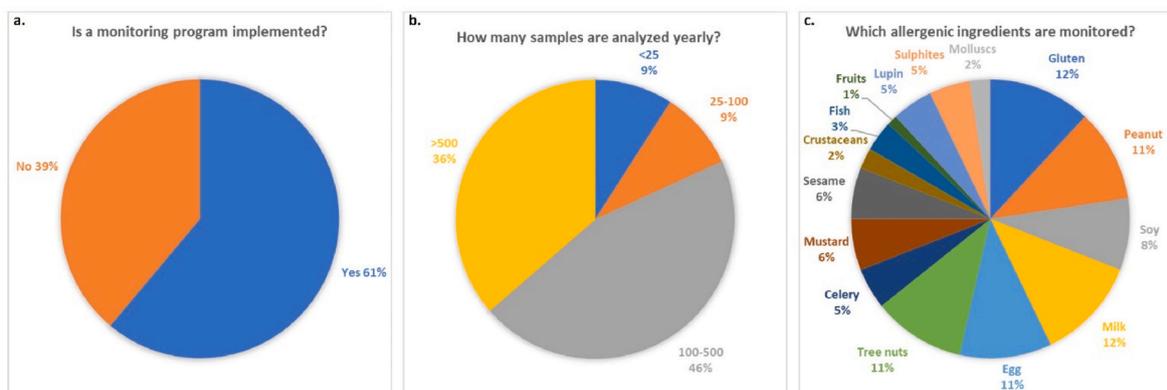


Fig. 1. Results of a survey on current food allergen monitoring programmes in the EU member states and associated countries (2023), sorted by a) implementation of a food allergen monitoring programme; b) number of yearly analysed samples in context of a monitoring programme; and c) specific allergenic ingredients analysed.

Table 1

Allergens and important food matrices identified by the survey respondents as important for existing or new food allergen monitoring programmes. The table is composed of replies of the respondents on the question how ideal monitoring would look like to their opinion, for which allergens and in what food matrices.

Allergens	Important food matrices
14 priority allergens	novel or specific foods
risk-based allergens:	prepackaged food products:
- Mentioned RASFF notifications	- With 'free from' labelling
- Evoking most severe reactions in patients	- Without PAL or ingredient labelling
- Identified as high on country-to country basis	- That are frequently contaminated or prone to cross-contact
new risks and emerging allergens	unpackaged food products

3. Codex risk assessment for application in food allergen monitoring

The recent Codex Alimentarius work and the five outputs of the ad-hoc Joint Expert Committee (JEC) (WHO, 2022a; 2022b; 2023a; 2023b, 2024) are described below. In these reports, the validation of the Codex Alimentarius priority allergen list and the determination of allergen-specific action levels are described. Furthermore, recommendations for precautionary allergen labelling and the establishment of exemptions are given. In addition, the fifth report describes threshold levels for specific allergens. All five reports are available in one place (FAO, 2024).

3.1. Summary FAO/WHO recommendations with respect to priority allergens, reference doses (RfD) and PAL and their meaning for EU monitoring plans

This chapter discusses the relevance of the new FAO/WHO food allergen risk assessments for the suggested harmonisation of food allergen monitoring in the EU.

3.1.1. Priority allergens

Eight (intentionally added) food allergens are defined by Codex Alimentarius in the General Standard for the Labelling of Pre-packaged Foods (GSLPF) (Codex Alimentarius, 2018). National and regional priority lists may differ from the GSLPF, for instance in the EU, 14 priority allergens are regulated (European Commission, 2011). The initial priority allergenic foods list approved by Codex and recognized internationally in subsequent years was established in 1999, when limited scientific and clinical information existed on allergenic foods. Later, in deviation from the GSLPF, the FAO/WHO JEC recommended to include sesame and to remove soy and sulphite from the priority list (Table 2).

Table 2

Food allergens prioritised for ingredient labelling or PAL.

Food allergen ^a	GSLPF	EU ^b (FIC)	FAO/WHO
Declared as	Ingredient	Ingredient	Ingredient and UAP
Celery	-	X	-
Crustaceans	x	X	x
Cereals containing gluten ^b	x	X	x
Egg	x	X	x
Fish	x	X	x
Lupin	-	X	-
Milk	x	X	x
Molluscs	-	X	-
Mustard	-	X	-
Peanut	x	X	x
Sesame	-	X	x
Soy	x	X	-
Sulphite	x	X	-
Tree nuts	x	X	x

^a Food allergens and products or derivatives thereof.

^b There are different interpretations of cereals containing gluten, nuts and molluscs in these jurisdictions.

3.1.2. Proposed reference doses and unintended allergen presence

To inform allergic consumers of possible UAP, the food industry introduced PAL for prepacked foods. The use of PAL is not specifically regulated by food law, although Article 36 of FIC deals with "voluntary food information", in which category PALs belong. The Allergen Bureau (Allergen Bureau, 2019a) has developed a quantitative risk assessment system based on proposed reference doses (RfDs) for selected allergens (Table 2). The system aims at helping food manufacturers to manage UAP in the food chain by assessing the impact of allergen carry-over and provides instructions for appropriate PAL labelling (Campbell & Mehr, 2015). An RfD is the eliciting amount in milligrams of protein (total protein from an allergenic food) below which only a given percentage of the population with that particular allergy will react with objective symptoms. Over the years, the proposed RfDs have been modified and additional RfDs were added in line with new data from recent clinical studies. However, the use of PALs by the food industry is not regulated or harmonised, neither with regard to the proposed threshold levels (Codex Alimentarius, 2008) nor a unified terminology on the label. It is not currently a legal requirement that food labelling should inform whether a quantitative risk assessment has been performed or indicate the actual allergen content. PALs are sometimes overused, and precautionary-labelled food products, for various reasons including intermittent cross contamination, often do not contain detectable amounts of the indicated allergen, which unnecessarily limits the choice for consumers with food allergies. The RfD values recommended by FAO/WHO JEC for the 8 priority allergens are based on the eliciting dose (EDp) values derived from clinical data as suggested by Remington

et al. (2020) and Houben et al. (2020). Taking into account consumer safety aspects such as reaction severity and frequency of fatal food anaphylaxis - next to observations regarding analytical limitations (especially method detection capability (sensitivity) and specificity, which will be covered in chapter 4) - the JEC, and recently also the Allergen Bureau VITAL 4.0® (Allergen Bureau, 2024), recommended to base the RfDs on allergen-specific ED05 values, the doses, where up to 5 % of the consumers allergic to a specific allergen are expected to show allergic symptoms (Allergen Bureau, 2024).

3.1.3. How to translate recommendations by JEC into a harmonised approach for UAP management in food in the EU

The JEC recommendations provide an important step towards regulated and harmonised UAP management in food products. Comparable to the development of the allergen priority list, the recommended RfDs need to be adopted by Codex, evaluated by The European Food Safety Authority (EFSA) and, if sufficient clinical data become available, supplemented with RfDs for allergens that are listed in the FIC. In a recent scientific opinion on allergenicity assessment of dietary proteins (Mullins et al., 2022) EFSA concluded: ‘establishing thresholds constitutes a critical first step to assessing the risk from allergens, as they are a characteristic of the hazard that allergenic foods present to the food-allergic population. Their establishment is, thus, essential to the evidence-based application of risk management and mitigation strategies, such as PAL (WHO/FAO, 2022b).’ From this we may conclude that EFSA is open to consider RfD as a limit for food allergen management after diligent evaluation of the underlying data. In addition, new EU legislation is required that presents a regulatory framework and guidance to food business operations (FBO) regarding the use of PALs, limiting it to cases where UAP could exceed the relevant RfD. As VITAL® is widely recognized by the food industry, the Allergen Bureau adopted the advice to introduce of RfDs based on ED05 instead of the currently used ED01 in order to align with JEC recommendations. The Food Safety Authorities of several EU Member States are in the process of evaluating the introduction of RfDs based on either ED01 or ED05 (Allergenconsultancy, 2024). We strongly recommend adopting an identical RfD approach across Europe, preferable for the allergens prioritised in FIC, but at least for the allergens prioritised by JEC. Guidance should also be considered for defining the transition point at which the allergen content in a food can no longer be labelled as PAL but has to be considered as an ingredient according to the FIC regulation (Fig. 2). Normally, a food allergen is listed as an ingredient on food products (European Commission, 2011) when it has been deliberately added. However, due to mishaps or for, presumably valid, economic reasons, e.g. shared equipment during manufacturing, UAP in concentrations exceeding 1–2 % of the total product mass might occur. If not correctly labelled, this may justify the

recall of a product. It is important to provide criteria on the basis of which Food Safety authorities (FSA) can decide whether PAL has been correctly applied or, perFIC, has been wrongly omitted, and whether a product should be withdrawn from the market despite a PAL. Harmonised upper limits for PAL would clarify the matter for food producers and FSA.

As a final step towards EU harmonisation the update on priority allergens, guidelines for RfD-based PAL labelling and ‘free from’ labelling could be developed that support the implementation of a common allergen monitoring strategy, which would help the MS to monitor compliance with allergen legislation. Adequate food monitoring, however, depends on the availability of suitable analytical methods and a methodological framework, which is subject in chapter 4 of this paper.

3.2. The added value of food monitoring

Monitoring, i.e. the strategic sampling of relevant foods and determination of target substance contents, is a means of inspecting adherence to regulations and thereby ensuring food safety for consumers. Moreover, sampling and analysis generates impartial data (albeit sometimes based on targeted sampling and hence not randomly representative) owned by the national food safety authorities (NFSA). This provides evidence instrumental in forming policy decisions on any further measures for the protection from harmful food constituents.

In the EU, there are several harmonised programmes for the monitoring of undesired substances in food, e.g., for pesticides, growth promoters and mycotoxins (European Commission a-c). Comparable programmes for the FIC priority food allergens, however, do not exist. As shown in the survey on monitoring practices performed in connection with this paper (see chapter 2.2), there are large differences between monitoring practices in the MS. Consequently, food safety for allergic consumers is currently not secured in the same way as it has been established for health risks caused by other undesired substances in food. To reach EU-wide conformity regarding the level of protection, the harmonisation of RfDs for PAL labelling is an essential precondition. Some countries, like Belgium and the Netherlands (Allergenconsultancy, 2024; SciCom, 2022) have already started to introduce RfDs according to the FAO/WHO report (WHO, 2022b).

Monitoring of food allergens is challengingly different to monitoring programmes for other compounds because the allergenic proteins are integral components of food in contrast to unintentional contaminants. Allergen monitoring has thus to differentiate between products containing allergens that are part of the recipe and specified on the ingredient list, products without the intended addition of certain allergens, which for different reasons (e.g. UAP) nevertheless are mentioned in a PAL statement, and products without any labelling of priority allergens. Four scenarios regarding the appropriateness of PAL labelling can be imagined: 1) no allergen labelling: correct; 2) no allergen labelling: incorrect; 3) PAL labelling: correct; 4) PAL labelling: incorrect (Blom et al., 2018). Monitoring of unlabelled products, scenarios 1 and 2, can help to map mislabelling by detecting food products that contain priority allergens without being identified on the packaging, which might require action by food authorities. Systematic monitoring can also help determining whether certain products are prone to contain UAP, which is useful information for a risk evaluation regarding the justified use of PAL. Monitoring of PAL-labelled products, scenarios 3 and 4, can help to indicate the distribution of allergenic ingredients in different food and assess the extent to which PAL is necessary or unnecessary.

A typical difficulty for successful monitoring originates from the varied consistency of the priority food allergens. Whereas liquid and also milk (in milk powder form) allergens could be homogeneously distributed in food products, granular allergens are more randomly distributed so that one product package could be free from the allergenic ingredient while the next package in the same batch could contain the allergenic ingredient in considerable amounts. Thus, sampling sizes, numbers and frequency have to be adapted to the objective of the monitoring exercise.

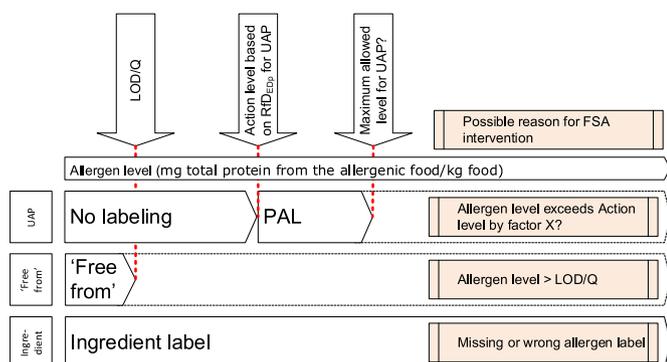


Fig. 2. Proposed decision scheme for food allergen labelling. On the left, the allergen presence is indicated: ‘UAP’, ‘free from’ or ‘ingredient’. On top, allergen levels are shown that should result in labelling as indicated below. On the right, possible reasons for FSA interventions are given, i.e. when monitoring results do not match allergen labelling.

Well-designed monitoring can help to map the distribution of the allergenic ingredients within a product batch and determine the occurrence levels. Allergen levels considerably above the RfD in PAL-labelled foods constitute a substantial risk for consumers with hypersensitivities, who do not expect high concentrations in such products. Monitoring of food labelled with PAL will thus increase the food safety for such consumers and extend the choice of suitable products. ILSI-Europe has produced 'Practical Guidance on the Application of Food Allergen Quantitative Risk Assessment (QRA)' that helps to address the issues raised above. It provides tools and approaches to help harmonise the data gathering process for food allergen risk assessments and therefore aid with their implementation. The Guidance aims to promote consistency in documentation, decision making and the application of allergen QRA (Remington et al., 2022).

4. Towards a framework for European food allergen monitoring, the minimum to achieve with the knowledge gaps and limitations in consideration

Multiple monitoring programs exist for safeguarding the safety of food in general, however none yet for monitoring allergenic ingredients. This chapter presents a brief overview of the minimum activities in terms of harmonised analytical methods, guidelines and standards required for allergen monitoring to provide sufficient protection to consumers allergic to the priority allergens. The FAO/WHO JEC observed that the RfDs can be implemented and monitored to some degree with the available analytical methods. However, there are still serious limitations, which will be also discussed.

4.1. Reference doses in relation to portion sizes (action levels)

The RfD, stating the threshold amount of an allergenic protein that is expected to not elicit a reaction in the great majority of consumers with the respective food allergy, provides guidance to food manufacturers, regulators, and healthcare professionals in assessing and managing allergenic risks from food. The RfDs are established probabilistically, based on allergen challenge tests, epidemiological studies, clinical studies and observed reactions in sensitive individuals. It is essential to note that RfD are subject to ongoing research and new allergens might enter the food market. As the RfDs are given in absolute protein amounts they need to be translated into concentrations to allow comparison with the results of analytical monitoring.

Thus:

$$\text{Action level (mg kg}^{-1}\text{)} = \frac{\text{RfD (mg protein of the allergenic ingredient)}}{\text{Ref consumption amount (kg)}}$$

Where: *Action level* is the critical concentration of mg protein from the allergenic ingredient per kg of food consumed; *RfD* is the reference dose; *Ref amount* is the reference amount of the food consumed.

The portion sizes of typical meals have to be factored in when risk assessments based on RfDs are performed (Benton, 2015). Holzhauser and colleagues have re-viewed the VITAL® 2.0 protein RfDs with regard to different portion sizes ("spoonful" 5 g, "scoopful" 50 g, "birthday cake" 250 g, and "beverage" 500 g) to estimate action levels (mg protein of the allergenic ingredient per kg diet) (Holzhauser et al., 2020). As portion sizes differ in several EU countries (Carruba et al., 2023), a harmonisation and standardisation might become a challenging task within the EU. However, standardisation and harmonisation are essential to avoid trade barriers. ILSI-Europe guidance recommends, rather than portion size, the use of data from National Food Consumption Surveys (Biro et al., 2018). The optimal percentile is currently considered to be the 75th percentile of the food consumption distribution (P75), in other words 75 % of the portions consumed are below this portion size. Although the P50 intake may be recommended as a Reference Amount of food intake for use in food allergen deterministic

risk assessment and calculation of Action Levels. If the p50 is not available, the mean would be a good alternative, as analyses of the intake data showed that the mean generally is between the p50 and p65.

4.2. Harmonised methods and reference materials applicable for food allergen monitoring

There are three main groups of methods used for qualitative and quantitative food allergens analysis: Liquid Chromatography coupled to Mass Spectrometry (LC-MS/MS), Immunoassays e.g. Enzyme Linked Immunosorbent Assays (ELISA) and Lateral flow devices, and quantitative Polymerase Chain Reactions (qPCR). LC-MS/MS is based on detection of peptides resulting from protease-digested proteins, Immunoassays detect proteins as such via sequences of amino acids (epitopes), and qPCR detects DNA from the allergenic source (Poms et al., 2004; van Hengel, 2007). No single method fits all purposes and therefore all three types of methods should be valued on their pros and cons and employed according to the research or monitoring question at hand. For reliable and broad monitoring, a sufficient combination of these approaches should be in place for at least the 14 priority allergens in a wide range of food matrices, which also argues for a new allergen European Union Reference Laboratory (EURL), or at least an allergen work program in an existing EURL.

For the allergen methods currently in use there are no harmonised EU criteria to gauge adequate analytical performance, there are, however, technical standards available, and new AOAC guidance on the validation of allergen ELISAs by test kit manufacturers has been released (separately, AOAC guidance for gluten ELISAs is expected) which are presented in Supplemental Table S2.

There are well known shortcomings: (1) a sufficiently low detection capability (LOD and LOQ), particularly at concentrations derived from ED01 data; (2) specificity, especially in discriminating species from the same family (e.g. cereals containing gluten) or larger phylogenetic groups such as fish and crustaceans; (3) method validation and sampling procedures; (4) recovery and detection of allergenic ingredients from specific matrices, such as thermally processed foods with high fat content and fermented foods; (5) availability of (certified) Reference Materials (CRM) for allergen quantification.; (6) availability of complete information for materials provided by manufacturers of some analytical kit (e.g. exact composition of calibrants and reagents).

4.3. Definition of units

To ensure comparable measurements of allergenic ingredients, the use of standardised reporting units particularly for reference materials is of utmost importance (Walker et al., 2016), however, several different units exist. As shown in 4.2, qPCR targets DNA base pair sequences, Immunoassays target protein epitope(s) and LC-MS/MS targets peptides in all methods specific for the allergenic ingredient. After measurement all results must be translated to a concentration expressed as recommended measurand, the mass of the total protein of the allergenic food ingredient per mass of food (O'Connor et al., 2017). Despite this many ELISAs report in terms of the commodity. There are no harmonised conversion factors or workflows to accomplish expression as the appropriate measurand.

4.4. Existing monitoring programs as example

To safeguard the safety of food in general, the European Commission (EC) has set a legal framework of procedures and limits, and has implemented an official control system. This system ensures that food businesses operate in compliance with safe manufacturing procedures, and that foods do not exceed the limits set for contaminants such as pesticides and natural toxins. The European Food Safety Authority (EFSA) assists the EC in setting safety limits and standards, including but not limited to Maximum Residue Limits (MRLs) for contaminants, or

RfDs for substances that are accepted as food or food additives. In accordance with Regulation (EU) No 2017/625 (European Commission, 2017), compliance of FBOs to the food law is investigated by official surveillance, monitoring and enforcement agencies e.g. NFSA. There is a multiannual control programme, of which the implementation is described for several years (Commission implementing regulation (EU) 2022/741 (European Commission, 2022)).

Another important initiative to support food safety is the designation of EURLs whose tasks are described in the EU regulation 2017/625 (European Commission, 2017). Approximately 50 EURLs cover animal and plant health, and topics related to safety of food and feed. For example, the EURL Mycotoxins and Plant Toxins is hosted by Wageningen Food Safety Research in the Netherlands, and the EURL Animal Proteins in Feeding stuffs is hosted by Centre Wallon de Recherches Agronomiques in Belgium. A network of accredited reference and expert laboratories, for instance National Reference Laboratories (NRLs), support or execute national food safety monitoring programmes and develop standardised testing methods. EURLs coordinate and support these tasks to ensure that food safety testing methods are consistently applied in all member states. An EURL's task is to arrange proficiency tests (PTs) for the NRLs who are obliged to participate and report accredited results. Where the NRL is not itself the Official Food Control Laboratory (OCL) the NRL cascades information and advice from the EURL to the OCLs in their respective MS. Consequentially, this system puts pressure on MS to implement and accredit methods within the work program of the EURLs. The EURLs also provide reference materials, an inventory of standardised methods, arrange meetings that address analytical challenges and occasionally provide hands on laboratory training for the NRLs.

4.5. EU tools to strengthen allergen control: reference laboratories, training and audits

A noteworthy EU initiative is The Better Training for Safer Food (BTSF) program, aiming at increasing awareness and facilitating the implementation and harmonisation of EU legislation. Different topics have been on the BTSF agenda since the program was inaugurated in 2006 but allergens have not been addressed yet.

To improve the EU regulatory control system and its credibility, EU has conducted recurring audits in diverse domains including food and feed safety. These audits, executed by The Directorate-General for Health and Food Safety (DG SANTE) tend to visit control authorities, laboratories and affiliated sites. During 2017 and 2018, the EU Commission carried out seven controls specifically on the provision of food information to consumers and nutrition and health claims made on foods. The specific reports can be accessed through the EC webpage (European Commission, 2024). These audits should be broadened to include scrutiny of the results obtained by analytical methods to support the establishment of an EURL/NRL-system for allergens.

Despite being an important food safety hazard, currently there is no EURL for food allergens and none of the EURLs have allergens on their work program. Instead, there is ENFADL which was established by the EU Commission in 2017. This network arranges annual meetings for MS and sets up PTs, but they do not have a mandate comparable with the EURLs, and as a consequence, the MS have no obligation, other than peer pressure and the desire to share and benefit from scientific information, to participate. Hence, implementation of analytical methods and official control for allergens lacks prioritisation and funding.

An important initiative to support EU regulatory control is the designation of European Union Reference Laboratories (EURLs) whose tasks are described in the EU regulation 2017/625 (European Commission, 2017). With regard to the national reference function, Belgium has voluntarily assigned a NRL for allergens, however, this is not embedded in a formally established EURL system. There is, therefore, a need of an EURL to formally recognise food allergens. Additionally, in the future, this laboratory could also consider to include alternative

proteins in its scope, such as lectins (Adamcová et al., 2021).

5. Conclusions, perspectives and recommendations

With the changing food allergen landscape in Europe, there is a need for food allergen monitoring to firstly better protect food allergic consumers, but secondly also reduce costs for the individuals and for society in general. The costs connected to food allergies are considerable for affected consumers, food producers and the society in general, taking into account also the expenses for providing health care systems and maintaining food authorities. Thus, solutions leading to a decrease in allergic incidents will be favourable for all parties concerned. Prerequisite for this desired development is the adherence to food safety guidance such as easily recognisable and correct labelling of food products. Implemented guidelines require compliance control, and therefore it is surprising to the authors that, although European standards for detection methods of important allergens in various food products have been developed, there is no harmonised approach regarding the performance of food monitoring for allergens in Europe. The new FAO/WHO reports on risk assessment of food allergens present a critical opportunity to harmonise food allergen monitoring across the EU. By consulting on the RfDs recommended by FAO and implementing new EU legislation to regulate PALs, we can establish a more harmonised and transparent allergen management system. This harmonised approach will not only protect allergic consumers but also foster industry-wide best practices, paving the way for a safer food market and is moreover essential to avoid trade barriers.

In moving towards a cohesive framework for European food allergen monitoring, the existing knowledge gaps and limitations to achieve a standardised and harmonised approach should be addressed. In the FAO/WHO reports the recommended RfDs can be a starting point to establish EU legislation on PAL and furthermore set criteria on for instance conversion factors and portion sizes. To start, detection of the allergenic ingredients across diverse food matrices can be executed by available techniques like LC-MS/MS, ELISA and qPCR. This will also give an opportunity to fill existing knowledge gaps.

Moreover, for a cohesive framework several points need attention, and recommendations are.

- Address the scientific basis for the EU-14 priority allergens as this is unclear, for instance by a review with the aid of the information, data and strategies as presented in the FAO/WHO food allergen reports.
- Address the voluntary and relatively uncontrolled use of PAL and related terminology by the food industry so that it becomes trustworthy for consumers again. For this, a change of legislation is needed to implement PAL. This could be addressed with the aid of information, data and strategies in the FAO/WHO food allergen reports and by fulfilling the obligations of the Commission set out in Article 36,3(a) of the FIC Regulation.
- Harmonise the methods of sampling and analysis of EU priority food allergens across MS. Moreover, these methods should be accessible by open access for all users.
- Implement an EU official control status for coordinating MS checks on the food allergen labelling and declaration requirement in the FIC Regulation. This could be addressed by complementary EU legislation mandating annual reporting under official controls of FIC labelling and declaration of food allergens.
- Assign a designating EURL is needed to assist on these points.

In conclusion, DG SANTE should be aware and act on the need to critically evaluate and update the legislation around food allergens, including monitoring programmes; ultimately guaranteeing food safety for all consumers, including the consumers with a food allergy.

CRedit authorship contribution statement

Nathalie G.E. Smits: Writing – review & editing, Writing – original draft, Supervision, Project administration, Funding acquisition, Conceptualization. **Nicolai Z. Ballin:** Writing – review & editing, Writing – original draft, Resources, Investigation, Formal analysis, Conceptualization. **Christine Bruggeman:** Writing – original draft, Resources, Conceptualization. **Christiane K. Fæste:** Writing – review & editing, Writing – original draft, Resources, Investigation, Formal analysis, Conceptualization. **Augusto A. Pastorelli:** Writing – review & editing, Writing – original draft, Resources, Investigation, Formal analysis, Conceptualization. **Christof van Poucke:** Writing – review & editing, Writing – original draft, Resources, Investigation, Formal analysis, Conceptualization. **Marleen M. Voorhuijzen-Harink:** Writing – review & editing, Writing – original draft, Resources, Investigation, Formal analysis, Data curation, Conceptualization. **Yvonne Westphal:** Writing – review & editing, Writing – original draft, Resources, Investigation, Formal analysis, Data curation, Conceptualization. **Michael Walker:** Writing – review & editing, Resources, Investigation, Formal analysis. **Matthias Winkel:** Writing – review & editing, Writing – original draft, Resources, Investigation, Formal analysis, Conceptualization. **Andries J. Koops:** Writing – original draft, Supervision, Resources, Investigation, Formal analysis, Conceptualization.

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

Data will be shared upon request after approval of participants

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Appendix A. Supplementary data

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References

- Adamcová, A., Laursen, K. H., & Ballin, N. Z. (2021). Lectin activity in commonly consumed plant-based foods: Calling for method harmonization and risk assessment. *Foods*, *10*(11), 2796.
- Allergen Bureau. (2019a). Allergen bureau releases VITAL program version 3.0 and all new allergen management resources. Retrieved 23.02.'24 from <https://allergenbureau.net/allergen-bureau-releases-vital-program-version-3-0-and-all-new-allergen-management-resources/>.
- Allergen Bureau. (2024). *VITAL 4.0 summary and FAQs*. Retrieved 13.09.'24 from [VITAL-4.0-Summary-and-FAQ_F1d.pdf](https://www.allergenbureau.net/vital-4-0-summary-and-faq-f1d.pdf).
- Allergenconsultancy. (2024). Nederlands allergenenbeleid aangepast en nieuwe referentiedossissen. <https://www.allergenconsultancy.nl/nieuws/nederlands-allergenenbeleid-aangepast-en-nieuwe-referentiedossissen>.
- Benton, D. (2015). Portion size: What we know and what we need to know. *Critical Reviews in Food Science and Nutrition*, *55*(7), 988–1004. <https://doi.org/10.1080/10408398.2012.679980>
- Bilaver, L. A., Chadha, A. S., Doshi, P., O'Dwyer, L., & Gupta, R. S. (2019). Economic burden of food allergy: A systematic review. *Annals of Allergy, Asthma, & Immunology*, *122*(4), 373–380. e371.
- Biro, S., Madsen, C. B., Kruijzinga, A. G., Crépet, A., Christensen, T., & Brockhoff, P. B. (2018). Food groups for allergen risk assessment: Combining food consumption data from different countries in Europe. *Food and Chemical Toxicology*, *118*, 371–381. <https://doi.org/10.1016/j.fct.2018.05.042>
- Blom, W. M., Michelsen-Huisman, A. D., van Os-Medendorp, H., van Duijn, G., Versluis, A., Castenmiller, J. J., Noteborn, H. P., Kruijzinga, A. G., Knulst, A. C., & Houben, G. F. (2018). Accidental food allergy reactions: Products and undeclared ingredients. *Journal of Allergy and Clinical Immunology*, *142*(3), 865–875.
- Botha, M., Basera, W., Facey-Thomas, H. E., Gaunt, B., Gray, C. L., Ramjith, J., Watkins, A., & Levin, M. E. (2019). Rural and urban food allergy prevalence from the South African Food Allergy (SAFFA) study. *Journal of Allergy and Clinical Immunology*, *143*(2), 662–668. e662.
- Campbell, D. E., & Mehr, S. (2015). Fifty years of allergy: 1965–2015. *Journal of Paediatrics and Child Health*, *51*(1), 91–93.
- Cappell, K., Taylor, A., Johnson, B. H., Gelwicks, S., Wang, S., Gerber, M., & Leffler, D. A. (2020). Healthcare resource utilization and costs in celiac disease: A US claims analysis. *Official Journal of the American College of Gastroenterology* | *ACG*, *115*(11), 1821–1829.
- Carruba, M. O., Ragni, M., Ruocco, C., Aliverti, S., Silano, M., Amico, A., Vaccaro, C. M., Marangoni, F., Valerio, A., & Poli, A. (2023). Role of portion size in the context of a Healthy, balanced diet: A case study of European countries. *International Journal of Environmental Research and Public Health*, *20*(6), 5230.
- Catassi, C., Verdu, E. F., Bai, J. C., & Lionetti, E. (2022). Coeliac disease. *The Lancet*, *399* (10344), 2413–2426. [https://doi.org/10.1016/S0140-6736\(22\)00794-2](https://doi.org/10.1016/S0140-6736(22)00794-2)
- Clarke, A. E., Elliott, S. J., Pierre, Y. S., Soller, L., La Vieille, S., & Ben-Shoshan, M. (2020). Temporal trends in prevalence of food allergy in Canada. *Journal of Allergy and Clinical Immunology: In Practice*, *8*(4), 1428–1430. e1425.
- Codex Alimentarius. (2008). Standard for foods for special dietary use for persons intolerant to gluten. *Codex Alimentarius international food standards, CXS*, 118–1979, 1–3.
- Codex Alimentarius. (2018). General standard for the labelling of prepackaged foods. *Codex Alimentarius international food standards, CXS*, 1–1985, 1–9.
- da, S., Correia, J. A., Antunes, A. A., Taborda-Barata, L., Boechat, J. L., & Sarinho, E. S. C. (2022). Prevalence of reported food allergies in Brazilian preschoolers living in a small Brazilian city. *Allergy, Asthma & Clinical Immunology*, *18*(1), 74.
- Dierick, B. J., van der Molen, T., Flokstra-de Blok, B. M., Muraro, A., Postma, M. J., Kocks, J. W., & van Boven, J. F. (2020). Burden and socioeconomics of asthma, allergic rhinitis, atopic dermatitis and food allergy. *Expert Review of Pharmacoeconomics & Outcomes Research*, *20*(5), 437–453.
- DunnGalvin, A., Roberts, G., Schnadt, S., Astley, S., Austin, M., Blom, W. M., Baumert, J., Chan, C. H., Crevel, R. W., & Grimshaw, K. E. (2019). Evidence-based approaches to the application of precautionary allergen labelling: Report from two iFAAM workshops. *Clinical and Experimental Allergy*, *49*(9), 1191–1200.
- European Commission. (2002). Commission Regulation (EC) No. 178/2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food. *Official Journal of the European Communities*, *L31*, 1–24.
- European Commission. (2004). Commission regulation (EC) No. 852/2004 on Hygiene of foodstuffs. *Official Journal of the European Communities*, *L139*, 1–54.
- European Commission. (2011). Commission Regulation (EU) No. 1169/2011 on the provision of food information to consumers. *Official Journal of the European Union*, *L304*, 18–63.
- European Commission. (2017). Commission Regulation (EC) No. 2017/625 on official controls and other official activities performed to ensure the application of food and feed law, rules on animal health and welfare, plant health and plant protection products. *Official Journal of the European Union*, *L95*, 1–142.
- European Commission. (2021). Commission regulation (EU) No. 2021/382 amending the annexes to regulation (EC) No. 852/2004. *Official Journal of the European Union*, *L74*, 3–6.
- European Commission. (2022). Regulation (EU) No. 2022/741 concerning a coordinated multianual control program of the Union for 2023, 2024 and 2025 to ensure compliance with maximum residue levels of pesticides and to assess the consumer exposure to pesticide residues in and on food of plant and animal origin. *Official Journal of the European Union*, *L137*, 12–24.
- European Union. (2023). In 2022 Annual report alert and cooperation network. <https://doi.org/10.2875/941288>
- FAO. (2024). Food allergen labeling: To exempt or not to exempt. Retrieved 16.05.2024 from <https://www.fao.org/food-safety/news/news-details/en/c/1679326/>.
- Fiocchi, A., Riso, D., DunnGalvin, A., Díaz, S. N. G., Monaci, L., Fierro, V., & Ansoategui, I. J. (2021). Food labeling issues for severe food allergic patients. *World Allergy Organization Journal*, *14*(10), Article 100598.
- Fong, A. T., Ahlstedt, S., Golding, M. A., & Protudjer, J. L. (2022). The economic burden of food allergy: What we know and what we need to learn. *Current Treatment Options in Allergy*, *9*(3), 169–186.
- Golding, M. A., Batac, A. L., Gunnarsson, N. V., Ahlstedt, S., Middelveld, R., & Protudjer, J. L. (2022). The burden of food allergy on children and teens: A systematic review. *Pediatric Allergy & Immunology*, *33*(3), Article e13743.
- Gonçalves, L., Guimarães, T., Silva, R., Cheik, M., de Ramos Napolis, A., e Silva, G. B., & Segundo, G. (2016). Prevalence of food allergy in infants and pre-schoolers in Brazil. *Allergologia et Immunopathologia*, *44*(6), 497–503.
- Gowland, M. H., & Walker, M. J. (2015). Food allergy, a summary of eight cases in the UK criminal and civil courts: Effective last resort for vulnerable consumers? *Journal of the Science of Food and Agriculture*, *95*(10), 1979–1990.
- Grabenhenrich, L., Trendelenburg, V., Bellach, J., Yürek, S., Reich, A., Fiandor, A., Rivero, D., Sigurdardottir, S., Clausen, M., & Papadopoulos, N. G. (2020). Frequency

- of food allergy in school-aged children in eight European countries—the EuroPrevall-iFAAM birth cohort. *Allergy*, 75(9), 2294–2308.
- Gupta, R. S., Taylor, S. L., Baumert, J. L., Kao, L. M., Schuster, E., & Smith, B. M. (2017). Economic factors impacting food allergen management: Perspectives from the food industry. *Journal of Food Protection*, 80(10), 1719–1725.
- Gupta, R. S., Warren, C. M., Smith, B. M., Jiang, J., Blumenstock, J. A., Davis, M. M., Schleimer, R. P., & Nadeau, K. C. (2019). Prevalence and severity of food allergies among US adults. *JAMA Network Open*, 2(1), Article e185630.
- Holzhauser, T., Johnson, P., Hindley, J. P., O'Connor, G., Chan, C. H., Costa, J., Faeste, C. K., Hirst, B. J., Lambertini, F., Miani, M., Robert, M., Röder, M., Ronsmans, S., Bugyi, Z., Tömösközi, S., & Flanagan, S. D. (2020). Are current analytical methods suitable to verify VITAL® 2.0/3.0 allergen reference doses for EU allergens in foods? *Food and Chemical Toxicology*, 145, Article 111709.
- Houben, G. F., Baumert, J. L., Blom, W. M., Kruizinga, A. G., Meima, M. Y., Remington, B. C., Wheeler, M. W., Westerhout, J., & Taylor, S. L. (2020). Full range of population Eliciting Dose values for 14 priority allergenic foods and recommendations for use in risk characterization. *Food and Chemical Toxicology*, 146, Article 111831.
- Iversen, R., & Sollid, L. M. (2023). The immunobiology and pathogenesis of celiac disease. *Annual Review of Pathology: Mechanisms of Disease*, 18(18), 47–70. <https://doi.org/10.1146/annurev-pathmechdis-031521-032634>, 2023.
- Jiang, J., Warren, C. M., Browning, R. L., Ciaccio, C. E., & Gupta, R. S. (2020). Food allergy epidemiology and racial and/or ethnic differences. *Journal of Food Allergy (USA)*, 2(1), 11–16.
- Kummeling, I., Mills, E., Clausen, M., Dubakiene, R., Pérez, C. F., Fernández-Rivas, M., Knulst, A., Kowalski, M., Lidholm, J., & Le, T. M. (2009). The EuroPrevall surveys on the prevalence of food allergies in children and adults: Background and study methodology. *Allergy*, 64(10), 1493–1497.
- Laurikka, P., Kivelä, L., Kurppa, K., & Kaukinen, K. (2022). Review article: Systemic consequences of coeliac disease. *Alimentary Pharmacology & Therapeutics*, 56(S1), S64–S72. <https://doi.org/10.1111/apt.16912>
- Li, J., Ogorodova, L. M., Mahesh, P. A., Wang, M. H., Fedorova, O. S., Leung, T. F., Fernandez-Rivas, M., Mills, E. C., Potts, J., & Kummeling, I. (2020). Comparative study of food allergies in children from China, India, and Russia: The EuroPrevall- INCO surveys. *Journal of Allergy and Clinical Immunology: In Practice*, 8(4), 1349–1358. e1316.
- Lieberman, J. A., Gupta, R. S., Knibb, R. C., Haselkorn, T., Tilles, S., Mack, D. P., & Pouessel, G. (2021). The global burden of illness of peanut allergy: A comprehensive literature review. *Allergy*, 76(5), 1367–1384.
- Loh, W., & Tang, M. L. (2018). The epidemiology of food allergy in the global context. *International Journal of Environmental Research and Public Health*, 15(9), 2043.
- Luo, W., Wang, D., Zhang, T., Zheng, P., Leng, D., Li, L., Liu, Y., Sun, B., & Zhang, X. D. (2021). Prevalence patterns of allergen sensitization by region, gender, age, and season among patients with allergic symptoms in mainland China: A four-year multicenter study. *Allergy*, 76(2), 589.
- Lyons, S. A., Burney, P. G., Ballmer-Weber, B. K., Fernandez-Rivas, M., Barreales, L., Clausen, M., Dubakiene, R., Fernandez-Perez, C., Fritsche, P., & Jedrzejczak-Czechowicz, M. (2019). Food allergy in adults: Substantial variation in prevalence and causative foods across Europe. *Journal of Allergy and Clinical Immunology: In Practice*, 7(6), 1920–1928. e1911.
- Lyons, S. A., Clausen, M., Knulst, A. C., Ballmer-Weber, B. K., Fernandez-Rivas, M., Barreales, L., Bieli, C., Dubakiene, R., Fernandez-Perez, C., & Jedrzejczak-Czechowicz, M. (2020). Prevalence of food sensitization and food allergy in children across Europe. *Journal of Allergy and Clinical Immunology: In Practice*, 8(8), 2736–2746. e2739.
- Ma, T., Wang, X., Zhuang, Y., Shi, H., Ning, H., Lan, T., Zhang, T., Kang, Z., SiQin, B., & Yang, B. (2020). Prevalence and risk factors for allergic rhinitis in adults and children living in different grassland regions of Inner Mongolia. *Allergy*, 75(1), 234–239.
- Mahesh, P. A., Moitra, S., Mabalirajan, U., Garg, M., Malamardi, S., Vedanthan, P. K., Christopher, D. J., Agrawal, A., & Krishna, M. T. (2023). Allergic diseases in India—Prevalence, risk factors and current challenges. *Clinical and Experimental Allergy*, 53(3), 276–294.
- Makharia, G. K., Singh, P., Catassi, C., Sanders, D. S., Leffler, D., Ali, R. A. R., & Bai, J. C. (2022). The global burden of coeliac disease: Opportunities and challenges. *Nature Reviews Gastroenterology & Hepatology*, 19(5), 313–327.
- Manea, I., Ailenei, E., & Deleanu, D. (2016). Overview of food allergy diagnosis. *Clujul Medical*, 89(1), 5.
- Messina, M., & Venter, C. (2020). Recent surveys on food allergy prevalence. *Nutrition Today*, 55(1), 22–29.
- Mills, E. C., Mackie, A., Burney, P., Beyer, K., Frewer, L., Madsen, C., Botjes, E., Crevel, R., & Van Ree, R. (2007). The prevalence, cost and basis of food allergy across Europe. *Allergy*, 62(7), 717–722.
- Mullins, E., Bresson, J. L., Dalmay, T., Dewhurst, I. C., Epstein, M. M., George Firbank, L., Guerche, P., Hejatk, J., & Naegeli, H. (2022). Scientific Opinion on development needs for the allergenicity and protein safety assessment of food and feed products derived from biotechnology. *EFSA Journal*, 20(1), Article e07044.
- Nwaru, B., Hickstein, L., Panesar, S., Roberts, G., Muraro, A., Sheikh, A., Allergy, E. F., & Group, A. G. (2014). Prevalence of common food allergies in Europe: A systematic review and meta-analysis. *Allergy*, 69(8), 992–1007.
- O'Connor, G., Haponiuk, M., & Ulberth, F. (2017). Joint DG SANTE and DG JRC Workshop- Harmonisation of Approaches for informing EU allergen labelling legislation. https://www.efanet.org/images/2017/Newsletters/2017-10_DG_Sante_DG_JRC_Workshop_report_Geel_June_2016.pdf.
- Panesar, S., Javad, S., De Silva, D., Nwaru, B., Hickstein, L., Muraro, A., Roberts, G., Worm, M., Bilò, M., & Cardona, V. (2013). The epidemiology of anaphylaxis in Europe: A systematic review. *Allergy*, 68(11), 1353–1361.
- Papapanagiotou, E. P. (2021). Serious alert and border rejection notifications on food in the EU RASFF. *Veterinary Sciences*, 8(11), 279.
- Patel, D. A., Holdford, D. A., Edwards, E., & Carroll, N. V. (2011). Estimating the economic burden of food-induced allergic reactions and anaphylaxis in the United States. *Journal of Allergy and Clinical Immunology*, 128(1), 110–115. e115.
- Peters, R. L., Krawiec, M., Koplin, J. J., & Santos, A. F. (2021). Update on food allergy. *Pediatric Allergy & Immunology*, 32(4), 647–657.
- Polloni, L., & Muraro, A. (2020). Anxiety and food allergy: A review of the last two decades. *Clinical and Experimental Allergy*, 50(4), 420–441.
- Poms, R., Klein, C., & Anklam, E. (2004). Methods for allergen analysis in food: A review. *Food Additives & Contaminants*, 21(1), 1–31.
- Remington, B. C., Baumert, J., Blom, M. W., Bucchini, L., Buck, N., Crevel, R., De Mooij, F., Flanagan, S., Stavropoulou, D. A., van den Dungen, M. W., van Ravenhorst, M., Wang, S., & Walker, M. (2022). *Practical guidance on the application of food allergen quantitative risk assessment*. ILSI Europe Report Series, Issue.
- Remington, B. C., Westerhout, J., Meima, M. Y., Blom, W. M., Kruizinga, A. G., Wheeler, M. W., Taylor, S. L., Houben, G. F., & Baumert, J. L. (2020). Updated population minimal eliciting dose distributions for use in risk assessment of 14 priority food allergens. *Food and Chemical Toxicology*, 139, Article 111259.
- Sampath, V., Abrams, E. M., Adlou, B., Akdis, C., Akdis, M., Brough, H. A., Chan, S., Chatchate, P., Chinthrajah, R. S., & Cocco, R. R. (2021). Food allergy across the globe. *Journal of Allergy and Clinical Immunology*, 148(6), 1347–1364.
- Sánchez, J., & Sánchez, A. (2019). Epidemiologic studies about food allergy and food sensitization in tropical countries. Results and limitations. *Allergologia et Immunopathologia*, 47(4), 401–408.
- SciCom. (2022). Opinion 08-2022 of the Scientific Committee established at the FASFC on reference doses for allergens. Retrieved 240524 from <https://scicom.favv-afsc.be/scientificcommittee/opinions/2022/documents/Opinion08-2022.pdf>.
- Scott, L. A., Berni, T. R., Berni, E. R., De Vries, J., & Currie, C. J. (2019). Evaluation of the healthcare resource use and the related financial costs of managing peanut allergy in the United Kingdom. *Expert Review of Clinical Immunology*, 15(8), 889–896.
- Shaker, M. S., Schwartz, J., & Ferguson, M. (2017). An update on the impact of food allergy on anxiety and quality of life. *Current Opinion in Pediatrics*, 29(4), 497–502.
- Sicherer, S. H., & Sampson, H. A. (2018). Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *Journal of Allergy and Clinical Immunology*, 141(1), 41–58.
- Spolidoro, G. C., Amera, Y. T., Ali, M. M., Nyassi, S., Lisik, D., Ioannidou, A., Rovner, G., Khaleva, E., Venter, C., van Ree, R., Worm, M., Vlieg-Boerstra, B., Sheikh, A., Muraro, A., Roberts, G., & Nwaru, B. I. (2023). Frequency of food allergy in Europe: An updated systematic review and meta-analysis. *Allergy*, 78(2), 351–368.
- Spolidoro, G. C., Nyassi, S., Lisik, D., Ioannidou, A., Ali, M. M., Amera, Y. T., Rovner, G., Khaleva, E., Venter, C., & van Ree, R. (2024). Food allergy outside the eight big foods in Europe: A systematic review and meta-analysis. *Clinical and Translational Allergy*, 14(2), Article e12338.
- Tang, M. L., & Mullins, R. J. (2017). Food allergy: Is prevalence increasing? *Internal Medicine Journal*, 47(3), 256–261.
- Taylor, S. B., Christensen, G., Grinter, K., Sherlock, R., & Warren, L. (2018). The allergen Bureau VITAL program. *Journal of AOAC International*, 101(1), 77–82.
- Taylor, S. L., Houben, G. F., Blom, W. M., Westerhout, J., Remington, B. C., Crevel, R. W., Brooke-Taylor, S., & Baumert, J. L. (2021). The population threshold for soy as an allergenic food—Why did the Reference Dose decrease in VITAL 3.0? *Trends in Food Science & Technology*, 112, 99–108.
- van Hengel, A. J. (2007). Food allergen detection methods and the challenge to protect food-allergic consumers. *Analytical and Bioanalytical Chemistry*, 389, 111–118.
- Walker, M., Burns, D., Elliott, C., Gowland, M., & Mills, E. C. (2016). Is food allergen analysis flawed? Health and supply chain risks and a proposed framework to address urgent analytical needs. *Analyst*, 141(1), 24–35.
- Warren, C. M., Jiang, J., & Gupta, R. S. (2020). Epidemiology and burden of food allergy. *Current Allergy and Asthma Reports*, 20, 1–9.
- WHO/FAO. (2022a). Risk assessment of food allergens - Part 1: Review and validation of Codex alimentarius priority allergen list through risk assessment. *Food Safety and Quality Series 14*, Issue <https://www.who.int/publications/i/item/9789240042391>.
- WHO/FAO. (2022b). Risk assessment of food allergens - Part 2: Review and establish threshold levels in foods for the priority allergens. *Food safety and quality series*, Issue <https://www.who.int/publications/i/item/9789240065420>.
- WHO/FAO. (2023a). Risk assessment of food allergens - Part 3: Review and establish precautionary labelling in foods of the priority allergens (food safety and quality series No. 16, issue).
- WHO/FAO. (2023b). Risk assessment of food allergens - part 5: Review and establish threshold levels for specific tree nuts (Brazil nut, macadamia nut or queensland nut, pine nut), soy, celery, lupin, mustard, buckwheat, and oats (food safety and quality series 23, issue).
- WHO/FAO. (2024). Risk assessment of food allergens - Part 4: Establishing exemptions from mandatory declaration for priority food allergens (food safety and quality series 17, issue).
- Willits, E. K., Park, M. A., Hartz, M. F., Schleck, C. D., Weaver, A. L., & Joshi, A. Y. (2018). *Food allergy: A comprehensive population-based cohort study*. Mayo clinic proceedings.
- Yue, S. R., Shrivastava, R., Campbell, K., & Walker, M. J. (2023). Food allergen recalls in the United Kingdom: A critical analysis of reported recalls from 2016 to 2021. *Food Control*, 144, Article 109375.