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Food allergies: some epidemiological data

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Analysis and critical comparison of food allergen recalls

/interview
ELISA kits... quantitative or not?

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Maurizio Paleologo

Founder and Chief Executive Officer of Affidia. He has about 30 years of experience in the field of food diagnostics. He was founder and director of Tecna, a company focused on food chemical contaminants detection.

The impact of food allergies on human health is a growing concern. We present here both a review of prevalence data and an analysis of food product recalls. The first paper demonstrates how difficult epidemiologists' work is in this area. The second introduces the world of food manufacturing, a complex industry where allergen sources are difficult to detect in the "nesting doll" combination of ingredients. We interviewed food safety managers both in the food production industry and in the mass catering business, as well as senior leadership from test kit manufacturers and service laboratories. Large industries are generally doing well in this area, while the restaurant and catering businesses, as several fatality cases remind us, still have more to do. Of equal concern, however, are the shocking studies revealing that excessive Precautionary Allergen Labeling, PAL, has created a paradox where patients with food allergies disregard "may contain" label information. In the US, as Dr. Sayler reports, the FDA discourages the use of PAL but even in the US there are no allergen thresholds.
Dr. Varallo reports that we face a "puzzle" because the list of allergens required to be labeled differs from country to country while the EU, the US, and the majority of countries still have not established allergen thresholds that would allow food industries to reduce PAL.
There are now a large choice of quantitative test methods and, just as important, operators have the necessary experience to control raw materials and prevent cross-contamination in the production process. It is time for authorities to issue action levels in order to stop a "blind" run to the detection of trace amounts of allergens so low that not one person in a million would be affected. If not, in the next years nothing will change in the number of people who suffer and sometimes die. Moreover, the international food product trade will face a growing jungle of different rules. For example, not only is the list of regulated allergens different from country to country, but the thresholds to achieve compliance may be as low as zero to 10 ppm.
Another issue is the analytical methods used in the food production industry and the urgent need to align the results of the different ELISA kits. Government agencies should create and enforce regulations and standards requiring test kit manufacturers to use identical calibration materials and methods and to clearly report results in a standardized milligram of allergenic protein/kg of tested food in order to receive accreditation. Of course, calibration is not the only problem, as we learn from Dr. Senyuva's contribution to this journal, but we believe that large differences in allergen quantification due to the use of different ELISA kits is unacceptable and avoidable.
A lot of work has already been done to establish the reasonable minimum immunoassay performance for the main targets, especially by AOAC. Meanwhile, MoniQA and other groups (as Dr. Poms writes) are doing excellent work to make Certified References Materials available. Unfortunately, we are afraid that this process will move very slowly. The EFSA has clearly stated that politicians, rather than scientists, should make the decision to abandon the "zero threshold" policy and how to do it. There are fears that this will result in booming LCMS sales because the priority will be obtaining a confirmatory method, and it is clear which technology will get this role.
I apologize to proficiency test providers. I had planned to include their important work but, due to space and time limitations, we must postpone reports of their activities and interviews until our next issue or we may post it on our website.
Last but not least, we also introduce *Food Test Compass*, an on-line meta-catalogue of commercially available test kits. Soon it will be possible to get comprehensive test kit information online in minutes without tedious searches. Moreover, this site will include end-user opinions about test devices and services to identify common problems and improve products.
I want to thank all the scientists, industrial experts, and managers that have been so kind to report their experiences and research to us and... I invite you all to follow us online!

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Food Allergens: why are allergic consumers still not protected enough?

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/focus on

Food allergies: some epidemiological data

Do we know how many people suffer from food allergies?

Sara Moraca

Sara Moraca is a PhD Scholar at University of Bologna and a scientific journalist. She collaborates as expert of science communication with newspapers, magazines, universities and institutions.

The socio-economic impact of food allergies

Allergy-related health loss is estimated to be of the same order of magnitude as prostate cancer or rheumatoid arthritis and it may be more severe than that of heart disease, skin cancer, or Parkinson's disease (Houben 2019). Patients and their families may also face additional costs and public health care systems pay the costs for related emergencies and hospitalizations. FAIRHealth (www.fairhealth.com), an American organization that studies the insurance market, reports that the annual per person cost of a milk allergy was about 2000 US dollars (only for medical services). A 2013 study (Gupta et al. 2013) reports that the total annual cost of food allergies affecting the child population is around US $25 billion in the US.

What is the prevalence of food allergies?

_ An Italian overview

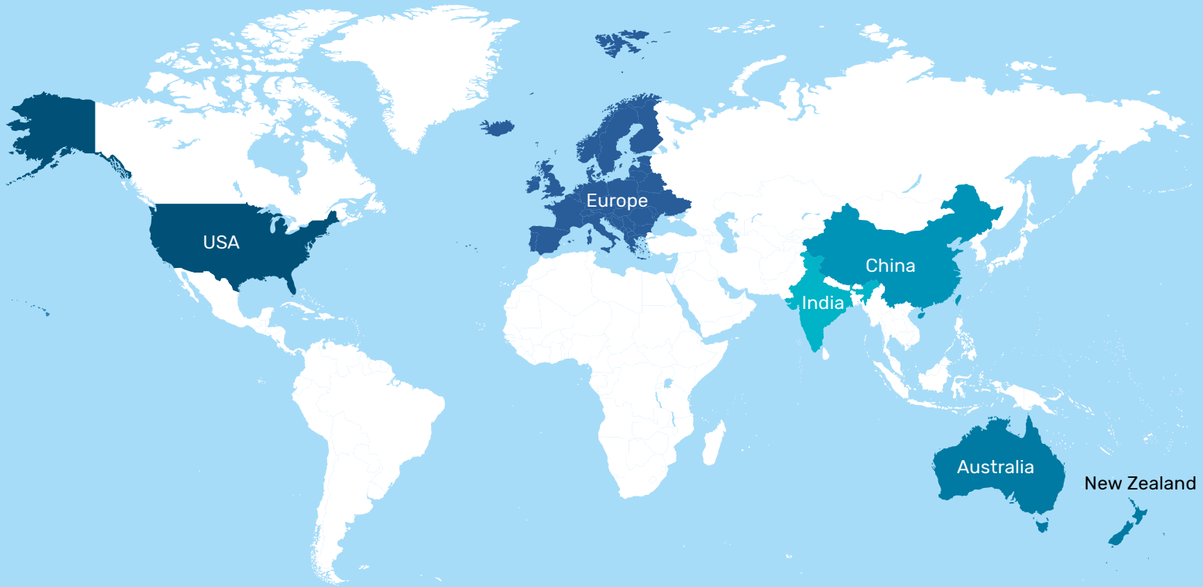
Food allergy organisations like *Food Allergy Italia APS* (FAI) and *Federasma e Allergie Onlus – Federazione Italiana Pazienti*, member of EFA - European Federation of Allergy and Airways Diseases Patients' Associations, tell us that there is no national allergy register or an Observatory on this issue. The diagnosis of this condition is not easy. "With the Skin Prick Test (SPT), which is the most economical method, false negatives are quite rare, while false positives are less so," explains dr Patrizia Restani, professor of Food Chemistry at University of Milan. "Obviously, the positive case is certainly a sensitized subject, but it is not said to be allergic. The same can be said for circulating IgE: even in this case values above the thresholds can be considered an indication, but not a certainty. It is clear that with both indications it is often possible to identify the food involved. But the only test that clarifies all doubts is that of triggering the allergy after having swallowed increasing doses of allergenic protein (Double-Blind Placebo-Controlled Food Challenges [DBPCFC]). This is an expensive and delicate test performed in the hospital only undergone by a small portion of suspected allergy subjects." So, it is clear that the prevalence data must be read very carefully. "The estimated prevalence on the basis of the triggering tests is completely different from that which appears from the results of the SPT. The method used to define a prevalence in a certain population is not always reported in the literature, hence the great variability of the data" explains professor Restani.

"The method used to define a prevalence in a certain population is not always reported in the literature, hence the great variability of the data" explains professor Restani.

Under this important premise, according to the *Food Allergy Italia* (FAI) and *Federasma e Allergie Onlus* associations, food allergies in Italy range from six percent to eight percent in children and from two percent to four percent in adults. Approximately two million italians suffer from some form of food allergy. Food allergies in children, according to a 2003 paper (Sabra et al.) have an average prevalence value of five percent. According to professor Restani, from the data published so far it would be correct to assume that, in the adult population, the prevalence of a true food allergy was lower than one percent. However, in the most prudent of hypotheses, we speak - only in Italy - of some hundreds of thousands of subjects, mainly children, but not only children.

_ What happens in other countries?

Some reliable data derived from the EuroPrevall study, carried out in 19 European countries, investigated allergies to milk (Cow's Milk Allergy, CMA). According to this study, milk aller-



PREVALENCE OF FOOD ALLERGIES (ADULT POPULATION) IN DIFFERENT PARTS OF THE WORLD.

USA 3,6%	Europe 3%	Australia and New Zealand 2%	China (rural) 1,4%	India 1,2%
(Acker et al. 2017)	(Burney et al. 2010)	(ASCIA 2019)	(ILSI 2011)	(Mahesh 2016)

gy prevalence is 0.54% in the first years of life. This estimate, which was confirmed by a DBPCFC trigger test, is valid in all European countries, except Greece and Italy, where prevalence is lower (Werfel et al. 2015).
The overall prevalence of food allergies both in Italy and in Europe is five percent in children under three years and three percent in adults (Burney et al. 2010). "It is estimated by the EAACI (European Academy of Allergists and Clinical Immunologists)," says lawyer Marcia Podestà of *Food Allergy Italia*, "there are about 17 million people with food allergies in Europe".
A 2014 meta-analysis found that the prevalence in the European adult population as measured by food challenges is at least 2.1% (Nwaru 2014). In the US, on the other hand, there would be around 30 million people with food allergies, of which 26 million are adults (11% prevalence) (Gupta et al. 2019). The same study also found that in the US the prevalence in subjects under 18 is eight percent. Previously, other studies have reported a much lower prevalence, more similar to the European prevalence, of five percent in children under three years and four percent in adults (Boyce et al. 2010). A more recent study reports a food allergy and intolerance prevalence of 3.6% in the adult population of the US (Acker et al. 2017).

"In part, it is true that prevalence has increased, but there are various reasons to be examined" says professor Restani.

According to the World Allergy Organization (WAO), which brings together numerous clinical immunology organizations, at least 240 million people suffer from food allergies worldwide, or more than three percent of the global population (WAO 2013). In Australia, the percentage of children at one year of age with a food allergy (positive response to triggering) was over 10%, much higher than the prevalence found in Europe and the US (Osborne 2011). However, the Australian Society of Clinical Immunology and Allergy reports a prevalence of 4-8% in children and just 2% in adults (ASCIA 2019). In South India, the adult prevalence is 1.2% (Mahesh 2016).
The EuroPrevall study showed that, among children, milk allergies were 10 times more frequent in Holland than in Greece, a country where even egg and peanut allergies were rare compared to what was observed in UK and Germany. Even in adulthood, allergies to hazelnuts, celery, and apples, are frequent in central northern Europe, while in Italy, France, Greece and Spain, peach and melon allergies are more frequent. In China, similarly, peanut allergies are rare, while seafood allergies are not. Half of the serious allergic reactions in China, according to a Chinese study, are triggered by crab or shrimp consumption (ILSI 2011).
These data introduce the issue of the variability of allergy pathology in various geographical areas. Do these strong differences really exist? In this regard, professor Restani explains, "They exist, of course, even if the reasons are not fully understood. The most glaring example is the peanut allergy which in Anglo-Saxon countries has very high incidence rates and which is not the case in Italy and in other Mediterranean countries. Worldwide, however, a significant percentage of children are allergic to milk and eggs; more than 90% lose this trait around the age of 10, but the few adults who maintain these allergies generally have very severe reactions."

_ The trend

We are, therefore, faced with a phenomenon that is difficult to quantify, with differences between age classes and between various geographical areas. Several sources report a trend towards an increased prevalence of food allergies, but there are varying opinions about this. "In part, it is true that prevalence has increased, but there are various reasons to be examined," says professor Restani. "First of all, the diagnostics available today allow us to detect more cases. Then there is also the spread of inadequately performed diagnoses, even outside medical contexts, which creates in the population wrong impressions." In the United States, the Centers for Disease Control and Prevention (CDC) reported that there was a 50% increase in the prevalence of food allergies between 1997-1999 and 2009-2011 in children (Jackson 2013).
Economic development brings with it an increase in prevalence, a phenomenon first observed in Hong Kong and Singapore (Crevel 2014). In cross-sectional studies of infants up to 2 years old in Chongqing, China, challenge-verified food allergies rose from 3.5% to 7.7% between 1999 and 2009 (Hu et al. 2010). Some studies of groups involved in the EuroPrevall project found that rural Chinese populations were less subject to food allergies than the inhabitants of Beijing. Among those who grew up or who were even born in rural areas of China, allergy prevalence was lower than that found among those born and raised in Hong Kong. In these childhood population studies, most of the data were obtained by SPT or serological analysis (IgE) but, as expected, when exposed to triggering (DBPCFC), the actual prevalence decreased from 2.8 to 1.4% (ILSI, 2011).
From a UK study, cases of anaphylaxis from food or non-food causes have significantly increased between 1998 and 2012, though there has not been an increase in fatal cases (Turner 2014). Further, data from the United States indicate an increase in cases of food anaphylaxis; between 2007 and 2016, the number of cases reported to insurance companies increased by 377%. The growth was due to a significant increase in cases of peanut and tree nut reactions (FAIR Health 2017).

Economic development brings with it an increase in prevalence, a phenomenon first observed in Hong Kong and Singapore.

Anaphylaxis and number of deaths

The number of deaths from anaphylaxis in Italy appears to be relatively low. "The only data we have, from Società Italiana di Allergologia, Asma e Immunologia Clinica (SIAAIC), is that there are about 40 cases of death from anaphylactic shock in Italy every year," says Mrs Frateiacci, representative of *Federasma and Allergie Onlus*: "most of which are due to insect bites, though some are reactions to drugs and some are due to food allergies. In the end we certainly have the cases reported by the press. On this basis we can talk about at least 4 cases of food allergy-related deaths per year in Italy. Unfortunately, there is currently no national standardized coding system and deaths from anaphylaxis are almost always recorded as deaths from cardiac arrest. But it must also be said that the cases of food anaphylaxis are hundreds per year. Fortunately, only a small part of these cases result in a fatal outcome".
"In 2018, in Italy," professor Restani explains to Affidia, "only two cases of death due to an allergic reaction to food (both to milk in adult subjects) have been reported by media". Clear historical data are missing in Italy. An analysis of the cases of hospitalization and fatal outcomes due to anaphylactic shock in the UK reports a clearer picture (Turner et al. 2015). According to these studies, there are approximately 30 fatal cases in the UK annually, compared to some thousands of annual admissions to the hospital system due to symptoms of anaphylaxis. The cases of

anaphylaxis related to food allergies comprised only a fraction of these 30 cases. The fatal cases, in 20 years of observation, were 124, an average of about six a year, or about 20% of the annual fatal anaphylaxis cases. Most of these were caused by peanuts and tree nuts but among the younger subjects, 20% of the cases were due to milk. Considering that the number of inhabitants in Italy and the United Kingdom is similar (59 and 63 million, respectively), deaths due to anaphylaxis from food allergens appears to be a little more common in the UK.

A study conducted between 2007 and 2015 in Europe reports that in patients under 18 admitted for anaphylactic shock, the majority (66%) had a reaction to food, but notes that such food anaphylaxis is largely prevalent in the early years of life and then becomes less frequent, especially compared to anaphylactic reactions due to drugs or insect bites, in adulthood (Grabenhenrich et al. 2016). In anaphylaxis cases due to food, the majority were due to milk or egg reactions in children up to two years and to nuts in children between two and six years of age, potentially indicating that the reaction to nuts was growing (Grabenhenrich et al. 2016).

According to data published in 2003, but also mentioned on the FDA website, every year in the US there are 30,000 emergency room visit, 2000 hospitalizations and 150 deaths from food allergies (Sampson 2003, FDA 2019).

If there are about 10 cases per year on average in Italy and the UK, there may be no more than 35 in all of Europe. The EU has 513 million inhabitants, while the US has 327; the approximately 150 annual fatal food anaphylaxis cases in the US is surprising. This is the equivalent of one food-related anaphylaxis death in every 2 million inhabitants in the US and one in every 14 million in Europe. Geographic, genetic, and dietary variation certainly play a role but perhaps in Europe the allergen risk is managed in a more effective manner.

Are there more cases of fatalities in restaurants?

While there may be a common impression that most food-related anaphylactic reactions come outside the home, data from the UK show that 27% of fatal anaphylactic reactions were the result of meals eaten at home and only 20% were due to restaurant meals (Turner 2014).

We have evidence from talks with our members," says the lawyer Podestà, "that serious reactions are frequent even after meals eaten at home by consuming food with incorrect or inaccurate labels". Mrs. Frateiacci confirms this and states that when this happens, families have difficulty demonstrating that the allergic reaction was caused by packaged or loose food (as is likely), or by a domestic accident (unlikely because the vast majority of those who suffer from allergies are aware of the risks to which they are exposed) and therefore, if the reactions are not very serious, it is difficult to report these events to the competent authorities.

"We have evidence from talks with our members" says the lawyer Podestà, "that serious reactions are frequent even after meals eaten at home by consuming food with incorrect or inaccurate labels".

Turner's study also sheds light on responsibilities in the case of the school-age population. Most of the school-age cases originated from the consumption of food in a "catering establishment," a quarter of which were "take away outlets." Cases related to the consumption of "pre-packaged food" are less frequent (27%). Fatal events occurred in schools in only 17% of cases.

However, there is no lack of studies in the literature that demonstrate the presence of allergens at concentrations higher than the doses considered dangerous not only in artisanal foods but especially in bakery items and industrial products (Trendelenburg et al. 2015, Remington et al. 2015, Decastelli et al. 2012, Michelsen-Huisman 2018, Blom 2018)

As you will see from the interview with dr. Gozzi of CAMST *(page 40)*, large European collective catering companies are strongly committed to risk reduction, an operation that requires above all a strong commitment to training. "What is lacking, to reduce the cases of anaphylaxis that arise from meals eaten or food taken in public establishments like restaurants or takeaways," explains the lawyer Podestà, "is the obligation to carry out adequate staff training."

But then, are industries wrong, too?

In this edition of *Affidia*, you will find *(page 36)* evidence of the commitment of some food industries to reduce the risk of allergens undeclared presence. From the article by dr. Luca Bucchini *(page 10)*, you will understand the errors that are still committed on an industrial level, observed through the recall statistics. Certainly, accidents can happen, very often due to labeling errors, but according to many observers, medium and large industries are prepared to prevent mistakes and their commitment not to abuse the precautionary labeling is also clear.

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Analysis and critical comparison of food allergen recalls

European Union, USA, Canada, Hong Kong, Australia, and New Zealand: an update

Luca Bucchini

Luca Bucchini is a food risk scientist, and an expert in food and food supplement regulation. After public health and food risk assessment studies at Johns Hopkins, in the US, he co-founded the Rome-based food consultancy Hylobates. He is a vice-chair of ESSNA, the European Sports and Specialist Nutrition Alliances, and a director of EuroFIR., the non-profit food composition organisation.

Abstract

As part of an EU-funded project (FP7) to develop "Integrated approaches to food allergen and allergy management", a database was constructed from publicly available information on allergen recalls between 2011 and 2014 in Europe, North America, Hong Kong, Australia and New Zealand. A new dataset including data up to 2016 is analysed in the present article. The analysis provides new evidence of the most prevalent allergens causing recalls, of the associated foods, and of the proximate causes of the recalls. Data indicate that the risks from food allergens in the food supply have not been reduced and that further improvements in risk management are required. Milk, followed by cereals containing gluten, is the food allergen triggering the most recalls globally, although local patterns exist. In general, as expected, the complexity of the food is associated with more recalls due to allergens. "Prepared dishes and snacks" and "Cereals and bakery products" are the food categories that are reported most frequently. Food allergens that represent a greater risk for different food types are identified. Overall, food recall data provide useful information for risk assessment and management.

Introduction

Despite regulatory differences across the world, most countries require the food industry to take appropriate measures to protect vulnerable consumers from potential exposure to allergens. As noted by Bucchini et al. (2016), the food industry is required to take precautions to minimise the risk of cross-contact, an aspect of Good Manufacturing Practice (GMP), but this should also involve specific allergen control measures (Taylor et al. 2006).

Allergen recalls provide information on failures to implement adequate measures. Allergen recall information is publicly available in the USA, Canada, Australia, New Zealand, Ireland, and the UK; in 2016, we published an analysis of allergen recall data. This is an updated analysis. As in the previous paper, we provide insights into the recall prevalence for different food types, prevalence of different allergens, and causes of recalls, examining as well any differences between geographical regions of the world.

Materials & methods

_ Data sources

As explained in a previous study (Bucchini et al. 2016), data sources were comprised of the food allergen alerts publicly available from:

- the Rapid Alert System for Food and Feed (RASFF) of the European Commission,
- the UK Food Standards Agency (FSA),
- the Food Safety Authority of Ireland (FSAI),
- the US Food & Drug Administration (FDA),
- the US Department of Agriculture Food Safety and Inspection Service (USDA FSIS),
- the Canadian Food Inspection Agency (CFIA),
- the Australia and New Zealand Food Standards (FSANZ), and
- the Hong Kong Centre of Food Safety (CFA).

These sources were searched for food allergen alerts occurring between January 2011 and December 2016. This extends the previous database from 2014 to 2016.

_ Design of database and selection of fields

Allergen categories identified in Regulation (EU) No 1169/2011 (i.e. celery, cereals, crustaceans, eggs, fish, lupin, milk, molluscs, mustard, nuts, peanuts, sesame, soybeans, sulphur dioxide and sulphites) were used to code the allergens found in the food products.

The cause of each food alert was classified according to a coding vocabulary developed by using terms from RASFF alerts and in the FSA recalls and then by including new terms that were encountered during the course of data entry in an effort to reconcile them with terms used by other food safety authorities. Further details are provided in the original publication.

More recent data from the RASFF show growing alert numbers, with 2018 proving to be a record year for the European Union. The presence of food allergens in the food supply remains problematic.

Results and discussion

_ Total numbers of non-compliancy in allergen recalls

Trends in total number of recall events found in the database from all sources is given in *Fig. 1* by year and authority (each one is a product/allergen combination, the number of recalls is smaller because one alert can involve multiple allergens.

There were no evident trends in the recorded numbers of recalls over the 6-year period. However, with the exception of Canada, the average number of recalls is higher in the last two years (2015-2016) than in the previous years. For Canada, recorded food allergen alerts were significantly higher in 2014 than in the previous and subsequent years. More recent data from the RASFF show growing alert numbers (149 in 2018; 114 in 2017) (EC 2018, EC 2019), with 2018 proving to be a record year for the European Union. The presence of food allergens in the food supply remains problematic.

_ Allergens responsible for product recalls

Allergen-related food recalls have been sorted by allergen to analyse and compare the data for each authority included in this database. Food alerts by allergen are shown in *Fig. 2*. The most undeclared allergen in the dataset is "milk and milk products" (26.4%), followed by "cereals containing gluten and products thereof" (13.1%), "egg and products thereof" (11.7%), and soybeans (11.1%).

Milk and milk products are the most undeclared food allergies reported by several of the authorities (CFIA: 30%, FSAI: 22%, RASFF: 24%, and FDA: 25%). However, in the US, according to FDA data for the period between 2014 and 2016, there is a significant increase in allergen recalls related to peanuts (24%) which is very close to the number of recalls related to milk. For USDA-FSIS, 19% of the recalls are due to undeclared milk but most of the recalls until 2016 are related to soybeans (35%).

"Cereals containing gluten" are associated with 20% of the recalls in EU-based datasets (RASFF, FSA, FSAI) and were the most undeclared allergen according to FSA data (24%). In Australia/New Zealand (34%) and Hong Kong (35%), the most undeclared allergen is "nuts and products thereof" where they represent the highest number of food allergen recalls while this accounted for only 3%-13% of alerts in other regions. While peanuts account for 24% of the FDA recalls, peanut-related recalls only account for 0% to 7% of recalls reported by other authorities. "Eggs and products thereof" were linked to 15% of the alerts in Canada but only account for 5%-13% of recalls in the other reporting areas. "Celery" was only mentioned in 2%-4% of recalls in EU databases (RASFF, FSA, & FSAI) and is not listed as an allergen by other authorities. "Sesame" accounted for 1%-4% of alerts. As previously noted, soybeans were associated with 35% of the USDA-FSIS alerts but only accounted for between 6% and 14% in other regions (the highest level is 14% in the FDA and the lowest numbers were observed in UK and Hong Kong). It should be noted that soybeans are used more often in the US as an ingredient in several composite foods. Sulphite-related recalls were mainly reported in Europe (15% UK, 11% Ireland, and 13% RASFF) while Canada, the US, and Australia/New Zealand reported lower numbers (1%-9%).

Fig. 1: Total number of allergen/product non-compliancy in recalls, by source (2011-2016).

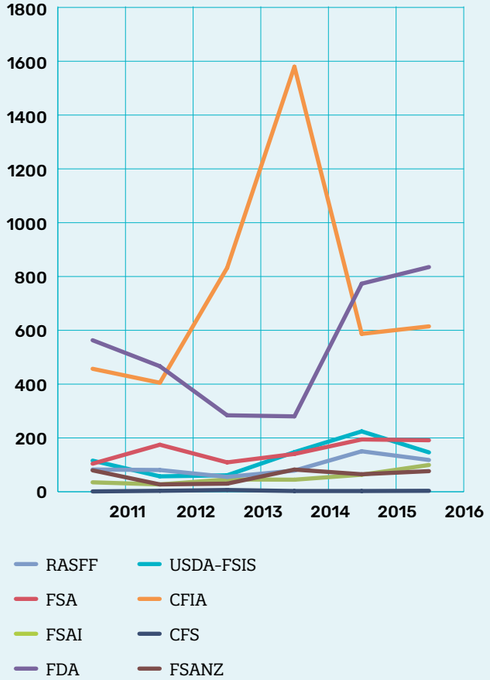
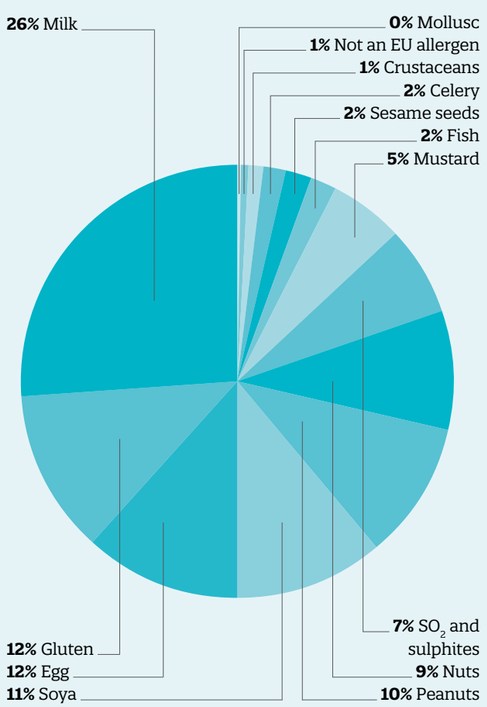


Fig. 2: Food alert per allergen recorded by all authorities (2011-2016).



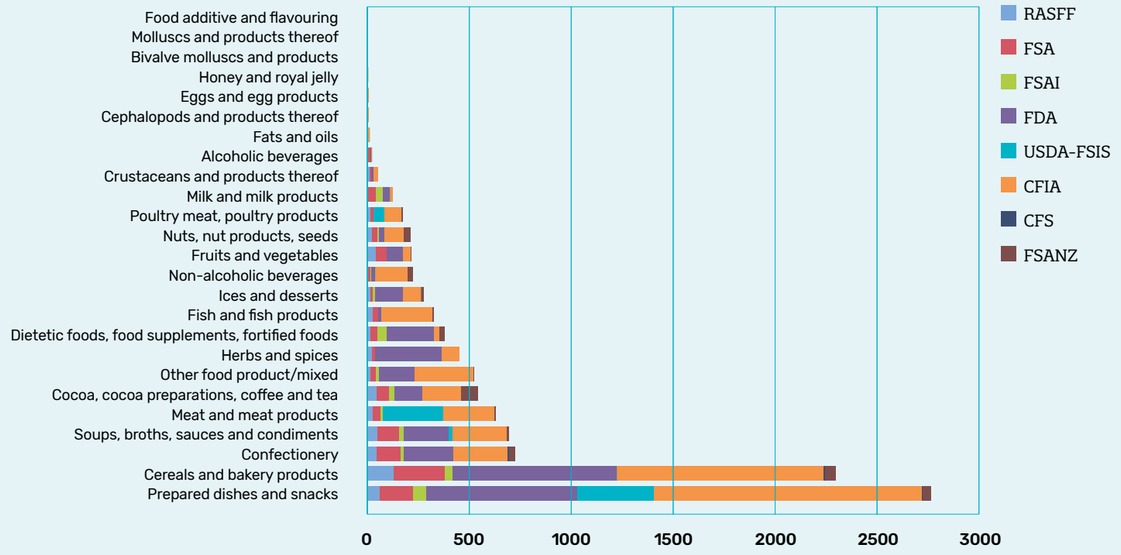


Fig. 3: Alerts by RASFF food categories and source (2011-2016).

_ Food categories

Allergen alerts by food category (RASFF categories) are shown in *Fig. 3*. "Prepared dishes and snacks" and "Cereals and bakery products" are the food categories that have been reported most frequently (25.9% and 21.5% respectively), followed by "Confectionery" and "Soups, broths, sauces and condiments" (6.8% and 6.5% of recalls, respectively). These results could be explained by the fact that these categories involve multiple ingredients enhancing possible cross-contact contamination. "Meat and meat products" make up 5.9% of the total recalls, followed by "Cocoa and cocoa preparations, coffee and tea" (5.1%). Other food categories such as "Dietetic foods, food supplements, fortified foods", "Herbs and spices", "Ices and Desserts", and "Fish products" account for about 3% to 4% but the 10 remaining categories do not even reach one percent.

_ Food allergen occurrence by food category

Milk was the most common allergen to cause a recall in most food categories:

– "Cereals and bakery products" (31%)
– "Cocoa and cocoa preparations, coffee and tea" (54%)
– "Confectionery" (44%)
– "Prepared dishes and snacks" (21%)
– "Dietetic foods, food supplement and fortified food" (37%)
– "Soups, broths, sauces and condiments" (17%)
– "Egg and egg products" (83%)
– "Fats and oils" (85%)
– "Ices and desserts" (33%)
– "Milk and products thereof" (31%)

In general, the complexity of the food is associated with more allergen recalls. "Prepared dishes and snacks" and "Cereals and bakery products" are the food categories that are reported most frequently.

– "Meat and meat products (other than poultry)" (17%, though soy [27%] was a more common cause of recalls)
– "Poultry meat and poultry meat product" (26%)
– "Non-alcoholic beverages" (71%)
– "Nuts, nut products and seeds" (13%, though 33% of recalls were related to peanuts [33%] and nuts [29%])
– "Other food product/mixed" (27%)

Nuts were a large contributor to food recalls in the following food categories:
– "Cocoa and cocoa preparations, coffee and tea" (26% [nuts])
– "Herbs and spices" (72% [peanuts])
– "Ices and desserts" (20% [nuts])
– "Milk and products thereof" (17% [peanuts] and 15% [nuts]).
– "Molluscs and products thereof" (38% [peanuts])
– "Nuts, nut products and seeds" (33% [peanuts] and 29% [nuts]).
– "Other food product/mixed" (18%)

Cereals containing gluten were a frequent cause of alerts in several food categories:
– "Cereals and bakery products" (21%)
– "Food additives and flavourings" (cereals containing gluten and sesame were the only allergens that provoked alerts in this food category)
– "Molluscs and products thereof" (15%)
– "Prepared dishes and snacks" (12%)
– "Soups, broths, sauces and condiments" (13%)
– "Alcoholic beverages"

Likewise, eggs constituted a significant contribution to food alerts in a number of food categories:
– "Fish and fish products" (70%)
– "Cereals and bakery products" (13%)
– "Crustaceans and products thereof" (12%)
– "Molluscs and products thereof" (15%)
– "Prepared dishes and snacks" (16%)

Sulphur dioxide makes several appearances on the recall lists:
– "Crustaceans and products thereof" (35%)
– "Fruits and vegetables" (63%)
– "Other food product/mixed" (17%)
– "Wine"
– "Alcoholic beverages"

Soy is also responsible for a number of recalls:
– "Dietetic foods, food supplement and fortified food" (23%)
– "Meat and meat products (other than poultry)" (27%)
– "Poultry meat and poultry meat product" (23%)
– "Prepared dishes and snacks" (13%)
– "Soups, broths, sauces and condiments" (15%)

The categories "Molluscs and products thereof" and "Crustaceans and products thereof" were also associated with recalls related to the presence of crustaceans (15%) and mustard (31%), respectively. As expected, milk is the most common allergen in a number of food categories. While some food categories are affected only by one or very few allergen contaminations or undeclared allergens, other food categories are susceptible to a wide range of allergen contamination. These food categories, therefore, present a higher allergen risk for consumers with food allergies.

Case study. Supply chain almond contamination case: evidence in the database

In 2015, the UK FSA announced several recalls due to alleged contamination of cumin with almond. It was eventually shown that Mahaleb, an aromatic spice made from the seeds of a species of cherry, *Prunus mahaleb*, was responsible for the false positive results (though contamination of chili pepper with almond appeared to be an accurate finding). The contamination originated in a Turkish food establishment. Cross-reactivity is responsible for the reactions. Mahaleb is not a food allergen according to EU law, although the clinical relevance of analytical cross-reactivity has not been established (Walker et al. 2018). We have examined how this incident appeared in food recall databases.

From the analysis performed on the RASFF data system, the trend of the number of recalls clearly shows an increase (+466%) in the number of almond-caused recalls in 2015. The food categories involved were mainly "Herbs and spices" (41%) followed by "Prepared food, dishes and snacks" (12%) and "Other food product/mixed". In addition, it could be noted that in the first two months of the year, recalls involved only "Herbs and spices", while other food categories were involved after April.

From the analysis performed on the FSA database the scenario does not seem as clear as it is for the RASFF database. However, taking a closer look at the recalls involved, 11 out of 15 recalls were announced in February and involved "Other food product/mixed", specifically "Spicy fajitas and enchiladas" and "Soups, broths and condiments" (only chili dressing involved). In April and June two recalls involved "Herbs and spices" but the April recall was related to paprika while only the June recall was related to ground cumin.

Regarding the FSAI, the situation seems similar to the one shown for FSA. In summary, such incidents translate rapidly to spikes in recalls and alerts that can be observed in food recall databases.

Causes of allergen recalls

In Bucchini et al. (2016), we propose a coding of "Causes" to provide a consistent approach. "Not indicated on the label" is an explanation of the recall encompassing several causes including "Labeling error", "Unauthorised", and "Allergic reaction". From the analysis of the causes that led to the recalls *(Table 1)*, "Not indicated on label" is the most used recall cause (78% of total recalls), although it is the least specific explanation and gives no clue as to the real reason for the recall. "Unauthorised" relates only to sulphites and represents just 6% of recalled products."

Cause	RASFF	FSA	FSAI	FDA	USDA	CFIA	CFS	FSANZ	Total
Allergic reaction	1	0	2	50	7	121	0	0	**181**
False label claim	19	51	27	19	2	19	0	14	**151**
Labeling error	6	44	54	66	3	7	0	14	**194**
Not indicated on label	405	393	132	2474	700	3952	16	311	**8383**
Packaging error	2	83	28	75	15	3	1	7	**214**
Unauthorised	44	150	4	64	0	365	0	0	**627**
Unintended presence	86	76	20	270	1	3	0	14	**470**
Wrong allergen advice	0	202	40	127	0	0	0	0	**369**
Wrong label	0	14	5	56	21	3	0	0	**99**
TOTAL	**563**	**1013**	**312**	**3201**	**749**	**4473**	**17**	**360**	**2239**

Table 1: Alerts and recalls in the dataset, by cause and source.

Conclusions and recommendations

Data show that the risks of food allergens in the food supply have not been eliminated. The nature of the contamination may prevent a complete resolution of the issue though authorities remain vigilant with reports of recalls continuing across countries. Generally, milk, followed by cereals containing gluten, is the food allergen triggering most recalls. Local patterns exist, such as soybean- and peanut-related recalls in the United States. In general, the complexity of the food is associated with more allergen recalls. "Prepared dishes and snacks" and "Cereals and bakery products" are the food categories that are reported most frequently. This is an indication that food business operators in those areas should devote particular attention to food allergen management. A food category analysis (for example, the salience of milk for cereal products, or of peanuts for spices) suggests a need for more focused risk analyses based on food industry type. Data further show that incidents (Mahaleb in cumin e.g.,) are rapidly detected by food allergen databases. Overall analysis of recall data provides useful information for improving food allergen management.

Acknowledgements

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/focus on

Threshold doses: necessary for industry, hard work for regulators

How the VITAL scientific expert panel developed their reference doses; understanding and managing the reference doses and reference quantities

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Introduction

Food allergy is a major public health concern globally, which potentially affects up to 5% of adults and 8-10% of children (Gupta et al. 2011, Osborne et al. 2011, Nwaru 2014). In the absence of a treatment for food allergy the only adequate measure is the avoidance of the food(s) to which the patient is sensitive. Accurate labeling of the presence of allergenic foods is therefore critical (Sheth et al. 2010). Mandatory labeling of the major allergenic foods of concern, when intentionally added to food products, is the most common risk management strategy adopted by food regulatory authorities worldwide, although the implementation varies from jurisdiction to jurisdiction (Yeung & Robert 2018). The priority allergens (and their definitions) included for mandatory declaration as well as specific exemptions and labeling style requirements vary. However, with very few exceptions, requirements are only mandated for deliberate inclusion of allergenic constituents, not their unintended presence. Despite the application of Good Manufacturing Practices, allergens may also be present in foods as a result of cross-contact between foods either during harvest, storage, transport or processing in a food manufacturing facility. Voluntary precautionary labeling is used in varying formats by food manufacturers around the world to inform consumers of the potential unintentional presence of allergens in a food product. Overuse of precautionary labeling, in the absence of an appropriate risk assessment process, presents the scenario that allergic consumers will be denied access to a variety of safe foods or may drive them towards ignoring label advice entirely.

The VITAL® Program

The Allergen Bureau is the peak industry body representing food industry allergen management in Australia and New Zealand[1]. Established in 2005, it operates on a membership basis, without government support, with the objective of sharing information and experience within the food industry on the management of food allergens to ensure consumers receive relevant, consistent and easy to understand information on food allergens.

The Allergen Bureau's VITAL® (Voluntary Incidental Trace Allergen Labeling) Program is an allergen risk assessment and management process for food industry that was developed to provide a single simple standardised precautionary statement, based on scientific evidence, that could be used by food producers in presenting consistent allergen advice for allergic consumers and their carers.

The VITAL Program has three key parts:

1. assisting food producers in assessing likely sources of allergen cross-contact from raw materials and the processing environment,
2. evaluating the amount of allergen present and assessing the potential risk it poses for allergic consumers, in each of their products, and
3. providing a standard precautionary allergen statement to be used above the defined level of risk associated with the cross-contact allergen.

VITAL also provides for ongoing monitoring and verification of the allergen risk assessment process to ensure any changes to the level of risk are acted upon without delay.

As indicated in the name, VITAL is a voluntary process. There is no regulatory requirement in Australia or New Zealand for unintentionally present allergens in food products to be declared on food labels. However, unlabeled allergens may result in the food being recalled from the market and between 2016 and 2019, approximately 50% of recalled foods involved incorrectly labelled food allergens[2]. Food manufactures may also face prosecution for selling food that is "unsafe" or "unsuitable" if it contains undeclared allergens at levels of public health concern.

Reference Doses and Reference Quantities

Under VITAL, labeling is recommended when the amount of an allergen present in a Reference Quantity of a food is likely to exceed an amount considered to be of public health significance, the Reference Dose.

1 - allergenbureau.net
2 - http://www.foodstandards.gov.au/industry/foodrecalls/recalls/Pages/default.aspx

The Reference Dose is a property of the allergen and its determination, from the available clinical data, incorporates a judgement of the acceptable level of risk to allergic consumers.
In 2011, the VITAL Scientific Expert Panel (VSEP) was formed to make recommendations for the Reference Doses implemented in the VITAL Program (Allen et al. 2014; Taylor et al. 2014). The VSEP is a collaboration between the Allergen Bureau (Australia & New Zealand), the Food Allergy Research & Resource Program (FARRP) of the University of Nebraska (USA) & the Netherlands Organisation for Applied Scientific Research TNO (The Netherlands). The VSEP makes its recommendations using allergen dose distribution modelling of data from challenge studies[3]. The models allow Eliciting Doses (EDs) to be determined for each allergen, defined as the specific percentage of the allergic population predicted to respond: the ED_{01} and ED_{05} represent the doses at which only 1% and 5% or allergic individuals are likely to respond, respectively. For its latest recommendations, forming the basis of the revision termed VITAL 3.0, which is scheduled to be implemented during 2019, the VSEP has implemented a Stacked Model Averaging program (Remington et al., in press) that incorporates 5 different statistical models[4] and produces a single "averaged" distribution.
The Reference Doses recommended by the VSEP in 2014 and adopted into the previous version (VITAL 2.0) were a combination of the ED_{01} or the 95th percentile lower confidence limit of the ED_{05} depending on the number of datapoints and the fit of the models, as determined by expert judgement (Allen et al. 2014; Taylor et al. 2014). Other bodies considering similar approaches to VITAL, but based on essentially the same data, have chosen to use different thresholds. The Dutch Bureau for Risk Assessment and Research Programming (BuRO) of The Netherlands Food and Consumer Product Safety Authority (NVWA), for example, proposed a more precautionary approach in recommending (provisional) Reference Doses that were 10 times lower than the VITAL 2.0 Reference Doses, whereas the Scientific Committee of the Federal Agency for the Safety of the Food Chain in Belgium recommended using the lower 95% confidence interval of the ED_{05}. The latter resulted in a more than 10-fold higher Reference Dose for some allergenic foods in comparison to those of VITAL 2.0. Recently, the VSEP identified ED_{01} and ED_{05} values from the new Stacked Model Averaging program (Remington et al. in press) and has recommended adoption of the ED_{01} for all allergenic foods for VITAL 3.0 on the basis that they better meet the requirements of the Allergen Bureau, including: minimising the percentage of the allergic population at risk from cross-contact allergens in unlabeled products; increasing transparency/reduced complexity through selection of a single level of (acceptable) risk; increasing the likelihood of global acceptance of VITAL; and a level of risk no greater than VITAL 2.0.
Ultimately, for Reference Doses to be meaningful and for the allergen management strategy adopting them to be likely to be accepted and used, they must balance a number of competing interests, including that the levels must fall within a range that can be managed and verified within the context of an HACCP-based food safety management program, that labeling applied as a result must provide choices for allergic consumers and that if reactions to unlabeled allergens do occur, they will be mild and transient, requiring no emergency medical intervention. If labeling thresholds are set too high, there is a risk that allergic consumers may be exposed to unlabeled allergens at levels potentially causing more frequent or more severe reactions. If the thresholds are too precautionary, they will be difficult for food manufacturers to manage and control which may exacerbate the uses of default or "just in case" labeling of food products that do not present an appreciable risk and also unnecessarily limit access to foods for a majority of allergic consumers. The units used to define the Reference Dose may also affect its uptake, for which reason VITAL Reference Doses are based on total protein from the allergenic source rather than specific proteins, which may be more difficult to detect and quantify.
The Reference Quantity is the amount of a food containing the protein from an allergenic source that is likely to be consumed on a typical eating occasion. It takes into account the way different foods are eaten. Thus, for example, a condiment such as mustard may be eaten in very small quantities (~5g) whereas other foods, such as rice or bread, may be eaten as a substantial part of a meal. The Reference Quantity may be determined on a case-by-case basis, as in VITAL, by each manufacturer using their experience and knowledge of their own food product/brand, or it can be established generically for foods, for example, by reference to national or regional food consumption survey data (Blom et al. 2019). In any case, it should be emphasised that often food intake data are reported as average intakes per day or over even longer time periods. In the application of Reference Quantities, it is however crucial to only use food consumption figures representing the amount of a food that is likely to be consumed on a typical single eating occasion (one meal!) because the allergic response will occur soon (from minutes up to four hours) after consumption. As a general guide, the reference quantity will not be less than a serving of the food but may be set at a higher level of consumption, for example, to take into account "grazing foods" that may be consumed over an extended period of time (i.e., a long single eating occasion) or the consumption patterns of bigger eaters. Blom et al. (2019) established that the 75th percentile of consumption during single eating occasions is the optimal Reference Quantity point estimate for use in deterministic food allergy risk assessment and the application of reference doses. The larger the Reference Quantity, the lower the concentration of an allergen that will trigger a labeling requirement. For example, using the VITAL 2.0 Reference Dose for peanuts (0.2 mg total peanut protein), for foods with a Reference Quantity of 400 g, precautionary labeling will apply when total peanut protein is likely to exceed 0.50 ppm, whereas a food with a Reference Quantity of 10 g may contain up to 20 ppm peanut protein before label declaration is recommended.

3 - All the data from adults were derived from Double Blind Placebo Controlled Food Challenges (DBPCFCs), whereas, blinding was not considered absolutely necessary in the case of data from infants and very young children on the basis of clinical opinion.
4 - Weibull, Log Logistic, Log Normal, Log Double Exponential, General Pareto

	VITAL 2 (Taylor 2014)	Vital 3.0	VITAL 3	Belgium FAVV/Scicomm 2017	Germany (Waiblinger 2018)
Peanut	0,2	0,1	0,015	1,1	0,2
Milk	0,1	0,2	0,016	1,2	0,1
Egg	0,03	0,2	0,0043	0,3	0,03
Hazelnut	0,1	0,1	0,011	0,5 (other nuts)	0,1
Soy Flour	1	0,5	0,078	2,9	1
Wheat	1	0,7	0,14	1,3	1
Cashew nut	2	0,05	1,4	0,6	2
Mustard	0,05	0,01	0,022	0,1	0,05
Lupin	4	2,6	0,83	4,5	4
Sesame	0,2	0,1	0,1	0,4	0,2
Shrimp	10	25	3,7	12,1	10

Reference doses (mg total protein of the allergenic food) established by some expert groups (VITAL) or governmental bodies (Dutch NUWA, Belgium FAVV, german Official Control Laboratories) that represent action levels to manage the precautionary labels on food products. ***(Table added by the editor)***

Outcomes

Since its inception, over three thousand Australia and New Zealand food industry personnel have been trained in the use of the VITAL Program. The Allergen Bureau's 2017 Allergen Collaboration survey indicated that over 70% of industry respondents were aware of and over 50% were actively using the VITAL Guide and/or VITAL Best Practice Labeling Guide to place allergen labeling declarations on their products[5].
During the period 2016-18, half of all VITAL Online Users (50%) and about two thirds of all VITAL Online Sessions (68%) were from within Australasia[6]. This suggests that, currently, Australasian Users are more actively using VITAL Online than international Users – most likely because ANZ Users have a longer history of using, and are more familiar with, the VITAL Program than Users outside of ANZ. However, interest in VITAL Online from overseas Users appears to be increasing.
VITAL provides a consistent approach and a common language to food allergen management. Industry benefits from this common standard, as shown by the increasing proportion adopting it not only in Australasia but, anecdotally, more widely across the world. The transparency of this approach also facilitates risk communication with consumers and increases their trust in product safety with regard to allergens.

5 - http://allergenbureau.net/wp-content/uploads/2018/09/Allergen-Bureau_AIFST2018-allergen-management-session_Sept2018.pdf (Slides 39 and 40).
6 - http://allergenbureau.net/wp-content/uploads/2019/04/July-Dec-2018_Activities_Final.pdf

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/focus on

EU Food allergen regulation and its impact on the industry

Product labeling is uneven in different countries and, even at the European level, legislation has gaps both for food producers and for consumers. Some countries, such as the UK, are moving to implement new national legislation

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Introduction

According to the final RASFF (Rapid Alert System for Food and Feed) report for 2018 (European Commission 2018), alert notifications related to food allergens in the European Union are on the rise. Last year 149 notifications were registered on the system (up by 31% compared to 2017). Overall, they account for just 4% of the total notifications of food safety related risks uploaded on the system (3699 for 2018). Despite the fact that such figures might seem meager compared to the US or Canada, the spike in the statistics cannot be ignored. Official controls and the attention of the public are plainly increasing.

Milk, gluten and nuts are the most commonly reported allergens. Prepared dishes and snacks are the most affected categories, possibly due to the heavy processing and the increased risk of cross contamination.

Typically, most food allergen-related incidents are prompted by labeling mistakes leading to undeclared allergens. It could be that several notifications about products with undeclared allergens can be traced back to the same labeling defect but this fact of course does not diminish the high level of risk in such cases.

PAL-Precautionary allergen labeling

It is important to remember that not all allergen-related issues are harmonised in EU legislation and covered by Regulation (EU) 1169/2011 (European Parliament and Council of Europe 2011) on the provision of food information to consumers.

Quite often, on the RASFF system, traces of allergens are notified, occurring in foods due to cross-contamination. Such allergen occurrence is not regulated at the EU level, threshold levels have not been set to define the concept of "traces", and reference doses have not been established.

This situation leads to:

- uncertainty and inconsistency across the supply chain in the risk assessment process put in place by the food industry to determine the use of PAL ("Precautionary allergen labeling") warnings;
- confusion for consumers, due to different wordings used for PAL warnings (e.g., "May contain", "May contain traces", "Produced in a facility …") and a generic overuse of such statements without proper risk assessments, especially in the SME (small medium enterprises) sector;
- an inconsistent approach by the competent authorities, especially where local guidance about thresholds for the use of PALs where reference doses have been established.

Despite European Food Safety Authority (EFSA) efforts in defining the problem (see Scientific Opinion on the evaluation of allergenic foods and food ingredients for labeling purposes, 2014), such institutions have refrained from establishing specific reference doses because: "the purpose of the risk assessment (e.g., exemptions from labeling, labeling of allergens unintentionally present in food) and the level of risk that may be acceptable (e.g., the fraction of the allergic population that is intended to be protected and to what extent) are risk management decisions, which are outside EFSA's remit." Indeed the task is competence of the EU Commission, as risk manager.

Mandatory allergen labeling

According to art. 21 of the Reg. (EU) 1169/2011, the 14 categories of ingredients that might cause allergies or intolerances – provided by Annex II - shall be indicated in the list of ingredients of pre-packed foods:

(a) with a clear reference to the name of the substance or product as listed in Annex II;

(b) emphasised through a typeset that clearly distinguishes it from the rest of the list of ingredients, for example by means of the font, style (e.g., bold) or background colour.

In the absence of a list of ingredients, the indication of the allergens must be comprised of the word 'contains' followed by the name of the substance.

Where several ingredients or processing aids of a food originate from a single substance or product listed in Annex II, the labeling shall make it clear for each ingredient or processing aid concerned.

If needed, the EU Commission shall systematically re-examine and, where necessary, update the list in Annex II. At the mo-

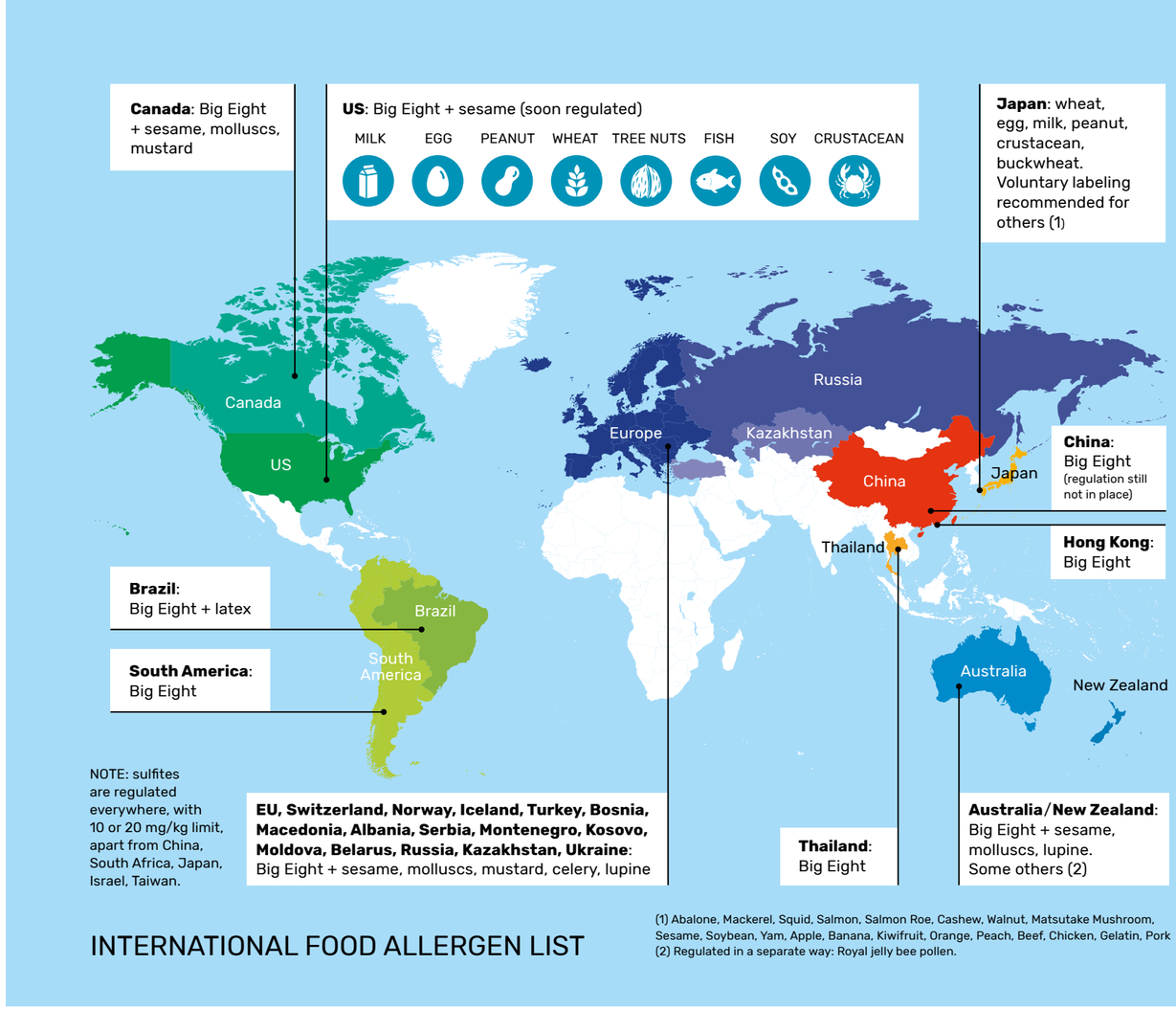
ment the list contains: cereals containing gluten (above 20 mg/kg - ppm), crustaceans, eggs, fish, peanuts, soybeans, milk (including lactose), nuts[1], celery, mustard, sesame seeds, sulphur dioxide and sulphites at concentrations of more than 10 mg/kg or 10 mg/litre in terms of the total SO2, lupin and molluscs.
If rules on pre-packed food are consistent and clear across the EU, they might not be necessarily valid for non-EU countries (e.g., in the US, allergens would not be emphasized in bold). Moreover, the Annex II list does not match the ones applied in different countries, like the US where we have just 8 allergens ("Big Eight") or Japan (7 mandatory + 20 recommended). The following tables might be useful to understand how great the differences are and how they could impact company operating costs (e.g., different allergen management for products destined for different jurisdictions, barriers to the creation of multi-country labels etc.):

Tree Nuts	EU	USA	Canada
Almonds *(Amygdalus communis L.)*	●	●	●
Hazelnuts *(Corylus avellana)*	●	●	●
walnuts *(Juglans regia)*	●	●	●
Cashews *(Anacardium occidentale)*	●	●	●
Pecan nuts (*Carya illinoinensis* (Wangenh.) K. Koch)	●	●	●
Brazil nuts *(Bertholletia excelsa)*	●	●	●
Pistachio nuts *(Pistacia vera)*	●	●	●
Macadamia or **Queensland nuts** *(Macadamia ternifolia)*	●	●	●
Pine nut *(Pinus spp)*	–	●	●
Beech nut *(Fagus spp)*	–	●	–
Heartnut, Butternut *(Juglans spp, Juglans cinereal)*	–	●	–
Chestnut *(Castanea spp)*	–	●	–
Chinquapin *(Castanea pumila)*	–	●	–
Coconut *(Cocos nucifera L.)*	–	●	–
Gingko nut *(Gingko biloba L.)*	–	●	–
Hickory nut *(Carya spp)*	–	●	–
Lichee nut *(Litchi chinensis)*	–	●	–
Pili nut (*Canarium ovatum)*	–	●	–
Shea nut *(Vitellaria paradoxa)*	–	●	–

1 - namely: almonds (*Amygdalus communis L.*), hazelnuts (*Corylus avellana*), walnuts (*Juglans regia*), cashews (*Anacardium occidentale*), pecan nuts (*Carya illinoinensis*), Brazil nuts (*Bertholletia excelsa*), pistachio nuts (*Pistacia vera*), macadamia or Queensland nuts (*Macadamia ternifolia*)

Non-prepacked food allergen labeling and emerging issues

While the labeling rules for pre-packaged food are overall clear and harmonized – at least at EU level - the same cannot be said for food sold loose or consumed in restaurants, through catering companies, or at cafeterias.
According to Reg. (EU) 1169/2011, Member States of the EU retain the right, depending on local practical conditions and circumstances, to enact regulations respecting the provision of information concerning non-pre-packaged foods.
Non pre-packaged foods, according to art. 2.2 lett. e) of the Regulation, include "foods packed on the sales premises at the consumer's request or prepacked for direct sale".
Although consumer demand for additional information is limited in such cases, information about potential allergens is considered very important. According to EU Commission preliminary findings on the topic, evidence suggests that most food allergy incidents can be traced back to non-pre-packaged food, possibly linked to the fact that cross-contact contaminations – especially in small kitchens with limited working space – might not be easy to manage.
Art. 44 of the Reg. (EU) 1169/2011 establishes that:
"1. Where foods are offered for sale to the final consumer or to mass caterers without prepackaging, or where foods are packed on the sales premises at the consumer's request or prepacked for direct sale:
(a) the provision of the particulars specified in point (c) [ALLERGENS] of Article 9(1) is mandatory;
(b) the provision of other particulars referred to in Articles 9 and 10 is not mandatory unless Member States adopt national measures requiring the provision of some or all of those particulars or elements of those particulars.
2. Member States may adopt national measures concerning the means through which the particulars or elements of those particulars specified in paragraph 1 are to be made available and, where appropriate, their form of expression and presentation."
Therefore, basically the only obligation - harmonized at EU level - on such foods is to give allergen information to consumers. How this and other mandatory information has to be made available has been left to Member States' implementing rules.
An obvious consequence of such an approach is that we might find relevant differences across the different EU markets. For instance, the matter has been addressed in Italy by art. 19 of the Legislative Decree n. 231/2017 (Decreto Legislativo. 15 dicembre 2017). It provides that for non-pre-packaged food the allergens shall be provided – together with the full ingredients list – on a menu, signpost, billboard, register (also informatic) promptly available to consumers and competent authorities, following the presentation rules provided by art. 21 of the Reg. (EU) 1169/2011 that state that they shall be emphasized with a different typeset or colour, as with pre-packaged foods. In my experience this is a step forward compared to the most common approaches adopted by other Member States.
Food-allergen related incidents recently prompted a deep rethinking of such national measures. For instance, the recent introduction in the UK of the so called "Natasha's law" (UK Government 2019), prompted by the death of a girl bearing the name Natasha.
In our opinion, an emerging area of risk is posed by food delivery services and the "dark kitchens" needed to sustain the demand of such food-to-go.
If it is clear that such players are to be considered food business operators and registered as such under Reg. (EC) 852/2004 - since they prepare, detain or transport food - until now an inconsistent approach has been adopted regarding allergen information at the moment of purchase.
If it is true that managing such information on a food delivery online portal - with hundreds of restaurants acting as suppliers - might be highly complex, there is no legal reason to deny allergen information to consumers. Similar operations might be legally defined as online sellers of non-pre-packaged food and as such they should be required to follow related provisions under art. 14.2 and 44 of the Reg. (EU) 1169/2011.



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Towards the development of food allergen reference materials

Standardization of methods could soon be easier

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Introduction

Effective food allergen risk assessment and food allergen management are important to protect allergic consumers and to comply with allergen labeling regulations. Such approaches require reliable analytical tools for the detection of allergens in food. Due to the nature of the analytes and their susceptibility to various processing effects, reliability and comparability of results have posed a great challenge. Both reference methods and reference materials are urgently needed to assure the quality, reliability and comparability of analytical results obtained with different methods. Being an important component of this analytical quality assurance, reference materials contribute to reliable and accurate results. Ensuring the correctness of analytical results is crucial to laboratories because incorrect results may trigger decisions that can cause economic damage (over-estimation, producer's risk) or pose a risk to public health (under-estimation, buyer's risk).

The use of reference materials

Validated reference materials/ quality control materials and certified reference materials are indispensable for:

– Method development
– Method calibration
– Calibration of instruments
– Validation of methods
– Method verification
– Proficiency testing
– Process control and quality assurance in laboratory routine
– Required use by ISO/IEC 17025

The quality of reference materials is critical for accuracy and comparability of analysis results. Reference materials must be sufficiently homogenous, stable and traceable. Usually extensive material characterisation and testing for homogeneity and stability of the material precede the availability of reference materials. Ideally a certified reference material (CRM) shall be used, which has been validated by accredited institutions and

Both reference methods and reference materials are urgently needed to assure the quality, reliability and comparability of analytical results obtained with different methods.

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is subject to strict quality testing. Certified reference materials usually come with a certificate with information on the methods used for validation/assigning a value, the measurement uncertainty and traceability of the numerical value of the analyte's concentration in the material or the analyte's purity. According to ISO/IEC 17025, accredited laboratories are required to use certified reference material. At this point the currently available knowledge base and methodological abilities do not allow the certification of food allergen reference materials according to international standards requirements. However, for the currently available internationally validated materials, the international task force led by MoniQA Association is discussing appropriate procedures for the certification of the offered food allergen reference materials according to ISO Standards.

Towards reference materials for allergens

The availability of reference materials for allergens in food would offer the possibility of the harmonization, standardization and and calibration of corresponding methods to achieve international traceability, i.e. world-wide comparability, of such measurement results. Furthermore, food allergen reference materials could offer the basis for further development and production of antibodies and detection systems. What makes a food allergen reference material in the end is its use and a general agreement as an internationally accepted reference. At the moment there is no such material that has earned the merits of an internationally accepted reference. Nonetheless, several food matrix reference materials containing food allergens are available from producers of reference materials (e.g., National Institute of Standards and Technology (NIST), USA, and the Institute for Reference Materials and Measurements (IRMM), European Commission), such as milk powder, egg powder, wheat flour, soy isolates and peanut butter. Despite the fact that these materials were certified for components other than allergens, they have been widely used to support method development and to calibrate methods, and in some cases have been accepted as reference materials by AOAC. Similarly, the Cyprus-based Food Allergens Laboratory (FAL) offers certified food allergen reference materials. Gluten, crustaceans, peanuts, soybeans, lactose, nuts, eggs, fish, celery, mustard, sesame, sulfites, lupine, and mollusks contained in various food matrices at concentrations of 5, 10, 50, 100 mg/kg are offered. It is worth noting that the term "certified" in connection with food allergen reference materials may not be used, if validation and metrological traceability requirements have not been met. Another kind of reference materials is offered by FAPAS, which sources materials from proficiency testing schemes and offers food products containing food allergens at assigned value concentrations. Examples of these materials are low levels of histamine in canned fish, almonds in chocolate, or egg, gluten & milk in cake. Within the frame of various research projects, validated food allergen reference materials were developed in the past (e.g., by FARRP – the Food Allergen Research and Resource Program at the University of Nebraska, USA, or by the EU funded EuroPrevall and iFAAM projects, or the MoniQA Network of Excellence). However, the available quantities were often only allowed for limited applications and thus were not readily available for global use and contributed only very little to harmonization and comparison of analytical results internationally. New initiatives at the IRMM, MoniQA Association, and LGC (Laboratory of the Government Chemist) are bringing food allergen reference materials to a new level of validation and documented quality. The IRMM has recently validated incurred milk materials for use by the EU national reference laboratories. The UK-FSA (Food Standards Agency) is funding a project to produce and validate various matrix reference materials containing skimmed milk powder, egg white powder, almond flour, hazelnut flour and walnut flour individually and in combination. These materials should be made available by LGC in the coming years.

The first validated Food Allergen Reference Material

The first validated reference materials for food allergen analysis became available in 2017 and are provided by the MoniQA Association, www.moniqa.org. This first set of materials includes testing materials for milk allergen analysis comprising a Positive Control (SMP-MQA 092014, characterized dried skim milk powder, validated protein content), Negative Control (BLANK-MQA 082015, based on a gluten free cookie), and 2 Incurred Materials: LOW-MQA 102016 (SMP incurred in gluten free cookies, milled, concentration approx. 3.5 ppm milk protein, validated) and HIGH-MQA 082016 (SMP incurred in gluten free cookies, milled, concentration approx. 35 ppm milk protein, validated). The materials were produced by Trilogy Laboratories USA and have been commercially available starting 01 January 2017. All materials come with a data sheet and a reference certificate to the analytical results, a measurement uncertainty and validation information. Distribution and shipment of the materials is subcontracted to authorized distributors among the MoniQA Member Institutions. Further reference materials are in preparation (gluten, egg, soy) and will become available shortly.

MATERIAL		KNOWN ALLERGENS
SRM 1549a	Whole **milk** powder	
SRM 1845a	Whole **egg** powder	
RM 8445	Spray-dried whole **egg** for allergen detection	
SRM 1567b	**Wheat** flour	
SRM 3233	Fortified breakfast cereal	
SRM 3235	**Soy** milk	
SRM 3236	**Soy** protein isolate	
SRM 3237	**Soy** protein concentrate	
SRM 3234	**Soy** flour	
SRM 3238	**Soy**-containing solid oral dosage form	
SRM 2338	**Peanut** butter	
SRM 3290	Dry cat food	
SRM 2384	Baking chocolate	
SRM 1548b	Typical diet	
SRM 1849a	Infant/adult nutritional formula I	
SRM 1869	Infant/adult nutritional formula II	
SRM 3252	Protein drink mix	

LEGEND

- Milk
- Egg
- Wheat
- Soy
- Peanut
- Fish
- Tree nuts

A list of available NIST RMs and SRMs to support food allergen measurements.

The initiative – who is behind the project

The design and production of these materials was in response to the urgent need for reference materials expressed by the food industry and food analytical laboratories, as well as providers of food allergen test kits and other methodologies, and national authorities. An international initiative (since 2013) led by the MoniQA Association discussed and agreed upon the requirements for food allergen reference materials. For this purpose MoniQA has liaised with the EU funded project iFAAM, the Prolamin Working Group, Health Canada, FARRP, Australia's Allergen Bureau (Vital), and others. The initial group of 15 experts from the global analytical community grew over time to a group of some 50 institutions contributing to the design of the materials and giving scientific and technological input during the testing and production phase of the materials.

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Diagnostic tests for detection of allergens in foods

ELISA kits can hardly be considered quantitative and LFDs play a key role in the food industry but performance is rarely documented

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Regulatory environment

EU Regulation No 1169/2011 specifies fourteen substances or products causing allergens or intolerances for which food labeling is mandatory when they are known ingredients. If there is a risk of a food product being affected by allergen cross-contamination, there should be precautionary 'may contain' labeling. However, precautionary allergen labeling should only be used if the risk of allergen cross-contamination is real and cannot be removed. From a food control perspective, it is interesting to note that in the 12-month period prior to September 2019 the Rapid Alert System for Food & Feed (RASFF) shows 204 notifications of products containing undeclared allergens including gluten. This compares with 289 alerts for pesticide residues and 595 alerts for mycotoxins in the same period but nevertheless represents a significant and growing number of rapid alerts for allergens. Additionally, at the national level, there are a large number of product recalls initiated by manufacturers mostly due to incorrect labeling or mislabeling rather than apparently occurring through cross-contact with allergens (cross-contamination). A recent publication has analysed trends in allergen product recalls (Bucchini et al. 2016) and survey work has been reported identifying undeclared allergens in foods on the market, as well as identifying foods where allergens have been labelled as present but were not found (Sefat et al. 2016). Media coverage of recent allergen sufferer fatalities due to failures in providing information about the presence of allergens in takeaway foods and sandwiches have also significantly raised public awareness of this important area, and has been a driver for further regulation.

Options for food testing

In terms of testing for allergens, there is an abundance of commercially available diagnostic test kits available to detect the presence of allergens in foods, probably more so than in any other area of food safety. A recent count showed that ELISA, Lateral Flow Devices (LFDs) and polymer chain reaction (PCR) diagnostic kits are commercially available from at least 16 different suppliers and these cover more than 24 specific food allergens (Senyuva et al. 2019). Indeed, for allergens such as milk and eggs there are even multiple ELISA kits targeted at different specified proteins in both of these two commodities. Whilst on the one hand having such a wide choice of diagnostic kits should be welcomed, unfortunately, method performance data is frequently lacking and comparability of results from different kits for the same matrix sample is not good. Routine allergen testing by the food industry relies upon employing commercial test kits, but frequently the suppliers provide disappointingly little specification detail on the grounds that this is proprietary information. The lack of comparability is understandable when one reflects that ELISA and LFD kits are based on antibodies, which in many cases have been raised against different proteins. In contrast, PCR is based on detection not of an allergenic protein but detection of DNA indicative of the presence of the component which is potentially allergenic but not of the protein itself. PCR is an ultra-sensitive technique, which in areas such as forensic science is a tremendous advantage, but for allergen detection may unnecessarily give rise to concern when there are no specified thresholds for labeling.

Pros and cons of diagnostic test kits

In 2014, the European Food Safety Authority (EFSA) noted that commercial ELISA kits for quantitative analysis of allergens employ different extraction buffers and different calibration procedures, they differ in the quality of the antibodies used, and consequently the results vary among commercial brands and batches (EFSA 2014). Other major limitations noted included matrix effects, insufficient extraction of the protein, insufficient specificity due to cross-reactions, and insufficient reproducibility of results. LFDs have the attraction of simplicity because they can be deployed without the specialist skills required for ELISA and PCR kits. LFDs are often visual and can have end-points that are not always so easy to discern although they do contain positive controls to demonstrate the LFD is functioning correctly. Meeting the simplicity objective is often at the expense of suppliers providing even less performance and validation data than

LFDs have the attraction of simplicity because they can be deployed without the specialist skills required for ELISA and PCR kits.

is available for ELISA kits. Those employing LFDs, therefore, need to conduct adequate testing and validation to demonstrate adequate performance for their own specific set of circumstances. The most objective evidence of method performance can be found from the results of proficiency testing (Senyuva et al. 2019). For example, for milk and soya allergen proficiency testing carried out over a six-year period, it was very evident that different ELISA kits report different results for the same test material. The most extreme example in the data is for a test material with assigned values of 2040 mg/kg and 12.6 mg/kg using ß-lactoglobulin kits supplied by two different companies. Neither assigned value corresponds well with the target preparation level (40 mg/kg ß-lactoglobulin), although the former is likely to be converting to whole milk equivalent. The homogeneity mean (37.2 mg/kg), however, does compare well to the target level but used an ELISA kit which was not well-represented in the proficiency test data. The best that can be said of the outcome of this proficiency test is that it was qualitative with limited quantitative value.

Future requirements

It is well-recognised that commercial ELISA tests for allergen analysis differ significantly in terms of their antibodies (for example, their production, avidity, specificity), target protein, calibrators used and extraction protocols. As a consequence of all these factors, different results for the same allergen are reported depending on the ELISA kit used, as evidenced by proficiency test results. Furthermore, the food matrix and level of processing has a significant impact on the reported results. Heat-treatment has the greatest effect on the accuracy. Unfortunately, not many extraction protocols employed for commercially available ELISAs are for processed foods, making it even more difficult to accurately determine proteins after processing. EFSA concluded that the main problem for the quantification of allergens by immunological or DNA-based methods is the lack of suitable certified reference materials (EFSA 2014).

Some uncertified reference materials developed by different producers are commercially available for the most important food allergens but the results obtained may not be comparable. Only when these shortcomings have been addressed can minimum required performance characteristics be drafted for these diagnostic kits to meet different testing requirements. If reference doses for certain food allergens and clinical relevant concentrations are established this should be a basis for reference material development. However, if such reference values are given as concentrations of specific proteins, it will be necessary to convert measurements from test kits where different units are employed. This would be a further step in the direction of harmonising food allergen measurements but without these clinically defined allergen levels there is no meaningful framework for harmonising testing methods.

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/country focus

Food allergen safety: a US perspective

FDA is increasing its efforts to enforce FSMA. “Cross-contact” must be controlled in items exported to the US. Rapid methods play a key role in the Allergen Control Plans of manufacturers. New regulations for private third-party food laboratory accreditation are expected soon

The authors of the recently published “Prevalence and Severity of Food Allergies among U.S. Adults,”[1] estimate 10.8% of US adults have at least one current food allergy. That’s more than 26 million people age 18 or older. The majority of food allergies are caused by one or more allergenic proteins, which elicit an allergic response mediated by IgE. Food intolerance such as Celiac disease and lactose intolerance are distinct from food allergies as they are mediated through IgA and IgG, negating the risk of anaphylactic shock. It has been reported by CDC that approximately 175 people die from anaphylactic shock in the US per year, and in most cases, it’s linked to a food allergy.[2] Non-Celiac gluten intolerance (gluten sensitivity) affects a higher percentage of US population, prompting an upsurge in gluten-free diets, and consequently a greater demand for gluten control programs. This, in turn, has helped spawn a growing market for “Free From” Foods. Undeclared allergens, and their derived ingredients can enter the food supply inadvertently by errors made by processing mistakes, incorrect labeling, improper storage, formulation misunderstandings between suppliers, co-packer and food manufacturers. Sometimes a change of suppliers for the same ingredients, additives or processing aids can introduce an unexpected allergen. Errors may occur after improper utilization of re-work product, improper or inadequate cleaning after a production run with a known allergen and by cross-contact with common utensils and equipment. An emerging concern is that food allergens may also enter the food supply chain through food fraud. Undeclared allergens continues to be responsible for the highest percentage of reported food recalls. In the 4th quarter of 2018, 46% of the food recalls under FDA’s jurisdiction were due to undeclared food allergens and the trend is continuing through September of 2019[3].

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Harmonization challenges for imported and exported foods abound as regulatory agencies around the world target different allergens for labeling compliance.

The US food industry has invested heavily to prevent mislabeling of foods that contain allergens.

US regulations

The US food industry (including the dietary supplement sector) must comply with the Food Allergen Labeling and Consumer Protection Act (FALCPA), which took effect on January 1, 2006. It requires food manufacturers to use common names to identify eight major allergens (Big 8) as "Peanut, Tree Nut, Milk, Egg, Soy, Fish, Shellfish and/or Wheat". The Federal Food, Drug, and Cosmetic Act gives the FDA the authority to issue regulations requiring the disclosure of food ingredients, spices, flavorings, colorings and incidental additives that contain allergens other than the eight major food allergens. Highly refined oils are exempt from allergen labeling requirements if the manufacturer can demonstrate that processing removes all traces of the allergen protein. Harmonization challenges for imported and exported foods abound as regulatory agencies around the world[4] target different allergens for labeling compliance. FDA announced in late 2018 that it was investigating the prevalence and severity of sesame allergies in the US to inform possible regulatory action that would require sesame to be labeled as an allergen on packaged foods.

FDA uses a level of "detectable" as its threshold of acceptability for the presence of an allergen in a food, while using "regulatory discretion" on how strongly they enforce the allergen requirements when very low levels are detected. Only gluten has an established threshold of 20 ppm which is harmonized with Codex, EU and Canada. For labeling purposes, the FDA defined a 'gluten-containing grain' as wheat, rye, barley, and crossbred hybrids of wheat, rye, or barley (e.g., triticale). FDA's standard for voluntary gluten-free labeling claims requires that food products do not contain an ingredient that is a gluten-containing grain; an ingredient that is derived from a gluten-containing grain that has not been processed to remove gluten; or an ingredient that is derived from a gluten-containing grain that has been processed to remove gluten, if the use of that ingredient results in the presence of 20 ppm or more gluten in the food; or 20 ppm or more gluten in the food. Although there is industry pressure in the US to establish threshold limits or action limits for other food allergens, it remains a formidable barrier to find agreement among all the stakeholders, especially consumer advocacy groups. US manufacturers of allergen free foods must rely on ingredient sourcing and the limits of detection of selected allergen test methods.

Under FDA's Food Safety Modernization Act (FSMA), domestic food facilities and those that export to the US, are required to conduct a hazard analysis and implement risk based preventative controls for identified hazards. FSMA embraces Hazard Analysis and Risk based Preventative Controls (HARPC). FSMA identifies allergens as a hazard requiring "preventive control" hazard, so an allergen control program (ACP) is required where allergens must be "monitored" and a follow-up corrective action procedure when an allergen mistake is identified during processing, packaging or labeling. FSMA demands supplier onsite audits for food manufacturers located outside the US, conducted by a "Qualified Auditor", sampling and testing for allergens as some frequency and review of food safety records to provide assurance that allergen hazards requiring a control have been prevented.

The US food industry has invested heavily to prevent mislabeling of foods that contain allergens. One of the food industry challenges related to allergen labeling is the use of "may contain" or similar statements such as "produce on the same line as (insert allergen name)". FDA discourages the use of these allergen labeling statements as it represents a lack of allergen processing controls; however, they have not taken any action against companies that use these "may contain" type of allergen labeling.

Cross contamination is a common term associated in the past with allergens, but under FSMA's Preventive Control regulation, the correct term in is "cross-contact". Any food food manufacturer or food ingredient supplier shipping into the US market must identify and implement controls for potential allergen cross-contact within the ACP as part of its overall Preventive Control-based food safety program (sometimes known as "HARPC"). Revisions to GMPs under the FDA FSMA Preventive Control rule significantly strengthen FDA's requirements for allergen control, especially related to the receipt, storage, handling, processing and labeling of foods and food ingredients

4 - https://farrp.unl.edu/documents/Regulatory/International%20Allergens%20Phillippines%209-11-18.pdf

and the related sanitation practices to remove allergen residues from common processing equipment and utensils.
FDA also requires recordkeeping of the allergen monitoring, testing, verification and corrective action activities. FSMA has given FDA greater enforcement authority related access to manufacturing and processing records, demanding mandatory recalls and product detentions for reluctant food processors. Examples of expanded records access include all types of processing records (hard copy and electronic) such as traceability, mock recall, internal audit, third party and internal laboratory testing results for environmental, in-process and finished products. FDA also has the authority to assess inspection fees for follow-up inspections, mandating financial penalties for repeat food safety violators and suspension of the processing facilities FDA FSMA registration.
Under another FSMA regulations, the "Foreign Supplier Verification Program (FSVP)" requires US importers to *verify* that the *food* they import meets U.S. safety standards and that the *food* is not adulterated or misbranded with respect to *allergen* labeling. In addition, FSVP "Importers" are required to have their own written food safety plan that evaluates the food safety risk of the imported food. The risk evaluation should include a hazard analysis of the imported food, food safety documents from the foreign food manufacturer, periodic laboratory analysis of the imported food for known or "reasonably likely" hazards including allergens, copies of recent third party audits, and any other information that will allow the FSVP importer to accurately identify the potential for a food safety problem related to the imported food. FDA will hold the FSVP Importer accountable and apply enforcement against the FSVP importer if a food safety problem develops with the imported food(s).

The critical role of allergen testing

In the US, the main diagnostic providers of allergen test kits, for example, are those produced by Neogen, R-biopharm, 3M, Romer Labs, Hygienia, BioFront Technologies, Elisa Systems, Elisa Technologies and Morinaga. Several rapid diagnostic platforms exist for allergen detection in foodstuffs and food contact surfaces. These include lateral flow, ELISA and PCR, and LC-MS/MS. Lateral Flow analysis of allergens is primarily conducted by food manufacturers on surfaces and rinse waters and is typically a presence /absence test. ELISA is primarily conducted by third party contract laboratories for quantitative measurement of allergens on push-through product, re-work product, and end-product. PCR methods hone-in on DNA molecules of allergens, and have a distinct advantage over immune-based methods because DNA typically remains intact after being exposed to thermal processing. However, the presence of DNA does not confirm that an allergenic protein exists and PCR methods cannot distinguish milk or beef DNA, or chicken or egg DNA. FDA recently developed the *xMAP* Food *Allergen* Detection Assay that can detect the major food *allergens* in a single assay run[5]. This multiplex approach allows FDA to better investigate individual food allergy reaction incidents and verify "free from" label claims.
Allergen testing plays a critical role in any food manufacturer's "Allergen Control Plan (ACP) as it can be used to monitor and verify ingredient claims, validate allergen changeover/ sanitation efficiency, and verify label claims of finished product. Allergen changeover occurs after a production line is being used to produce more than one end product, and the switch between products poses a risk of allergen cross contact even after a thorough cleaning has being performed. Dedicated lines and scheduling processing allergen products after allergen-free products have been produced is the preferred approach for ACP to achieve the highest level of confidence that there is no allergen cross-contact. Repeat analysis of the first products manufactured after changeover gives additional assurance that ACP clean-up practices are in control. When testing a representative portion of a food product, it is important to understand that the food may contain an uneven distribution of allergen.
Finished product testing has a limited role as FSMA emphasizes "*prevention of hazards in foods is much more effective than trying to differentiate safe from unsafe food*." Some food companies test to validate the ACP for new products and thereafter testing is performed less frequently to monitor and verify the "validated ACP" is working. If multiple allergens are in play, it is an industry "best practice" to test for all allergens individually in the validation process. Testing can include a records review, surrogate tests, but more importantly allergen tests on surfaces, "rinsates" and the first product off the production line. Ideally, testing should be performed on multiple occasions. Some manufacturers employ "push-through" to clear pipelines containing food product with salt and insert materials in certain situations to remove any allergen-containing ingredients. The development of an effective ACP testing program should reflect a balance between employing the available resources efficiently and monitoring at sufficient intervals so as to ensure that a risk-based assessment of the levels and nature of allergen contamination can be minimized.
Positive surface allergen test results require a corrective re-cleaning. If a "positive" testing result is obtained, the affected product needs to be held for further evaluation, destroyed or re-worked into a new formulation that declares the potential allergenic ingredients. A single test, or even a few tests, do not provide sufficient information about the absence of allergens on product contact surfaces, in rinse waters, or the foodstuff. Smart strategic routine testing, downstream and upstream, should be encouraged. Testing frequency, sample size, sample intervals along with other tools, should be a carefully evaluated and established as part of a holistic allergen management approach to ACP oversight. For instance, if 60 potential sampling sites are identified, 10 to 15 can be randomly selected each week, making sure that each site is sampled at least once per month. The ACP must be re-validated when there is a system failure, a product recall for allergens, when a significant change occurs in the manufacturing process, or new scientific data becomes available. Surrogate tests like ATP are inappropriate to monitor and verify whether the cleaning program and allergen control measures are effective at removing allergens as they do not detect the presence of an allergen protein. The role of surrogate tests should be limited to verification of the effectiveness of a processing equipment cleaning and sanitizing program, which is one of the Preventive Controls under FSMA.

Laboratory accreditation

This summer, FDA noted that FSMA mandated that a regulatory oversight regulation be developed for the evaluation and certification of private third-part food laboratories. Frank Yiannas, U.S. FDA Deputy Commissioner for Food Policy and Response, stated recently that the proposed rule for food testing laboratories was "in the pipeline" with the intent to ensuring that private laboratories conducting food safety and allergen testing of food industry samples must meet defined model laboratory standards for accreditation purposes. This long-awaited rule has private third-party food testing laboratories gearing up in anticipation of more government intervention and oversight in their "world". Most of the enforcement of this new laboratory accreditation program will be conducted by private third-party

This summer, FDA noted that FSMA mandated that a regulatory oversight regulation be developed for the evaluation and certification of private third party food laboratories.

certification bodies that have been evaluated and accepted by FDA. FSMA currently requires that any laboratory testing identified in a food processor's written food safety program must originate from a laboratory compliant with ISO/IEC's 17025 standard, but until FDA finalizes its food laboratory regulation, there has been only limited enforcement. It is clear that most private third-party laboratories used by the US food industry are privately accredited and meet both the ISO 9001:2005 and ISO/IEC 17025 standards, which provides significant confidence that these laboratories will have an easier time to meet FDA's laboratory regulation, including the proper use of allergen testing procedures and rapid detection kits.
More allergen test methods have achieved AOAC Performance tested validation and are available for food processors as well as private third-party laboratories. Several methods for Gluten/ Gliadin have achieved AOAC Official Method status. Approximately twenty test methods have achieved AOAC Performance Tested status for allergens, gluten/gliadin, sulfites and histamine, which leaves significant gaps in selection for validated methods. Homogeneity of sample, matrix interference, incurred versus spiked for validation, extraction and recovery efficacy, and ease of sample collection will impact selectivity and sensitivity for the test method. Many allergen test kit manufacturers will provide their own internal validation reports to their end-users but it's important to note that no matter the validation source, it may not include the product matrix that is being produced by the food manufacturer, so every effort should be made to bridge any gaps by utilizing spiked samples, QC materials, reference materials, and when seeking laboratory accreditation, incorporate the use of food allergen proficiency test materials (PTMs). Food allergen PTMs provide confidence in a testing laboratory's technical abilities. In addition to documenting that a laboratory is certified, the FDA will require accredited third-party certification bodies to maintain laboratory testing records and results. Laboratory analyses performed in or used by a food facility must be accounted for in a regulatory audit. Understanding that once the FDA publishes the final rule on food laboratory accreditation and certification, the food industry needs to prepare by having a serious dialogue with their private third-party laboratory(s) to ensure the food processor does not become non-compliant because of using an uncertified laboratory whose allergen testing results will not be accepted by FDA, nor their customers.

Summary

To summarize, expect continued increase in the US FDA's continuing allergen enforcement efforts in order to meet its FSMA responsibilities. Examples include the anticipated addition of sesame seed as a regulated allergen in the US, the release of the final rule on third-party laboratory accreditation and certification of private laboratories. FDA will become more aggressive in enforcing the allergen FSMA requirements the food manufacturing industry to identify allergens as a hazard and in the case of the FSVP importer, the risk assessment of the allergen hazard extends to the foreign supplier or its ingredient supplier. FSMA's Preventive Controls regulation requires that cross-contact and other food allergen risks must now be addressed in each facility's food safety plan. It is also likely that more food laboratories will become certified to test for food allergens to meet the anticipated increased demand by the food processing industry and more PTMs will be available for food allergens.

5 - Pedersen RO, et al. 2018. Cross-reactivity by botanicals used in dietary supplements and spices using the multiplex xMAP food allergen detection assay (xMAP FADA). Analytical and Bioanalytical Chemistry. 410(23):5791-806

/interviews

Perspectives in the food industry

Comparing food producers and caterers: what differences exist for managing allergens?

The majority of food allergens so far studied show common features: they are low molecular weight proteins (10-70 kd) and they are stable in the presence of heat, proteases, and acid. Allergic reactions are relatively dose-independent and there is great variability in the subjective response. For some subjects, for example, even a very small protein dose is enough to provoke the immune response and cause allergy symptoms. The Commission for the Codex Alimentarius, the European Commission, and other international organizations have defined the scientific criteria for the selection of allergenic foods to be indicated on food labels. All over the world, the food industry is subject to the legal obligation to produce safe food, based on the regulations in the countries in which they operate. The food industry differs from the restaurant and catering industry in that there are a limited number of products and ingredients in the food industry, making the control phase simpler, while the restaurant and catering industry have menus that change seasonally and rely on raw materials rarely used in the food industry. However, the management of allergens for both the food industry and for restaurants is difficult. In the food industry there are standardized procedures and a high degree of surveillance while, in the restaurant industry, everything depends on the menu and customer choices. Depending on its size, a restaurant may find it difficult to dedicate a separate kitchen to preparing food for allergy sufferers.
To understand more about these challenges, we interviewed three key managers: Dr. Stefano Del Frate, Dr. Marina Sternieri and Dr. Simone Gozzi.

Dr Stefano Del Frate

Global Scientific, Regulatory Affairs, Nutrition, and Food Risk Manager, GBfoods, Milano (Italy)

What are the critical points for you in managing allergen risks?

Raw materials are the point of greatest attention. Often these raw materials are not simple and homogeneous raw materials but mixtures or semi-finished products. These materials are extensively controlled both by suppliers and by our company as well. We manage possible cross-contamination in our factories and we manage possible trace allergens accidentally present in the goods we receive from suppliers. As a result, the list on the label gets longer because it reflects this approach.

Do you carry out analyses in the factory or do you commission them from external laboratories?

In the past, we performed most of the tests in the plant. Now, however, analyses for allergens are referred to external independent laboratories with better abilities to detect correctly the presence of allergens. Furthermore, they provide validated and certified results.

Do you think, like most food companies and diagnostic kit makers, that thresholds should be set? Why do you think European legislators do not set them?

For years, the scientific community has been challenged by the concept of thresholds, both at a European and at a global level. The fact that it is not possible to identify with full certainty a minimum amount of allergen under which there is adequate consumer protection affects the effort to set limits. The European Food Safety Agency (EFSA) itself, in its document dated 2014, did not provide any allergen thresholds other than for gluten and sulphites. The lack of robust, scientific data that relate dose-effect and the subjectivity of the response itself are the points that most hinder the establishment of thresholds. Thus, several arbitrary schemes like VITAL have been proposed on a voluntary basis but, even if these are beginning to be recognized outside of Europe, it does not resolve the issue. And when we talk about consumer protection and public health we need a harmonized approach.

Do you think the current list of allergens (the 14 listed in the EU standard) is adequate?

The list has already been expanded once and probably will be expanded again in the future, depending on progressively available scientific evidence, epidemiological studies, and event records.

The lack of robust, scientific data that relate dose-effect and the subjectivity of the response itself are the points that most hinder the establishment of thresholds.

And where do you see challenges from an analytical point of view?

We say that from our point of view the proliferation of high-sensitivity methods, which is a result of competitiveness among diagnostic kit manufacturers, is linked to more complexity and requires highly specialised professionals in the laboratory. Addressing the issue of allergens, it is necessary to specify that the analytical approach must not be the same as that used for residues and contaminants. In the case of allergens, we are speaking about food nutrients, often proteins, that undergo important changes depending on how they are treated. Analytically, this is an important variable because the effectiveness of a method is affected by the food production process. A further critical issue is the lack of adequate multiplex screening methods. We have been looking for them for years, but it seems clear to us that they are not yet ready.

Do you have any other comments to make?

The food industry follows good manufacturing practices and limits the number of allergens present in the food. The consumer, therefore, has precise information. The industries are doing a great job and the risk for the consumers is almost nil when they consume an industrial product.

Dr. Marina Sternieri

Industrial Process Quality Assurance Specialist, Quality & Innovation Direction, Granarolo Group, Bologna (Italy)

Are there difficulties in managing food production when traces of allergens can be detected but do not represent a risk even for allergy sufferers?

The Granarolo plants have conducted a risk assessment to assess whether and which allergens are present in the production cycle or that could be introduced accidentally. The Granarolo Group plants apply the Granarolo Group Allergen Policy comprised of these characteristic elements:

- disclosure of food allergies;
- epidemiology and clinical manifestations;
- preventive measures implemented in the production sites

(for example, it is prohibited to introduce peanut-containing foods to the factory, even in the company lunchroom);

- specific training of technicians and departmental staff; and
- compliance with predefined operating sequences.

Any traces of an allergen detected by our analytical method, even at the lowest LOQ, both on finished products and on ingredients, are considered a potential risk.

What difficulties emerge in the choice of an analytical method in the absence of a predetermined threshold value?

Granarolo chooses the method with the lowest LOQ among those proposed by the accredited laboratories for the specific matrix/test. Usually a PCR screening is performed for allergens linked to a certain plant species while in other cases we use an ELISA kit with the lowest LOQ available (e.g., for milk proteins). Unfortunately, the method with the lowest LOQ is not always accredited for a specific matrix. Over the years, Granarolo has worked with the main analysis laboratories present in the area, soliciting them for the development of increasingly sensitive methods applicable to different matrices. Some Granarolo plants where food is produced for the most sensitive categories (production for early childhood or gluten-free) instead carry out on-site analyses, both on the process and on the finished product. Any positive results are validated by an accredited external laboratory.

Which approach have you taken to reduce the number of allergens included on the label as a precaution (Precautionary Allergen Labeling, PAL)?

Granarolo adopts an approach based on risk analysis. Where allergen cross-contamination is possible, strict preventive measures are put in place to minimize as much as possible this risk: production line are cleaned properly and the absence of allergens is validated, packaging procedures are respected, production line drainage times are adhered to, and tools dedicated exclusively to handling allergen-containing ingredients are cleaned carefully. Furthermore, Granarolo is committed to requesting documentary evidence from suppliers and carrying out supplier audits aimed at gathering a clear picture of the possible risk of allergens coming from the raw materials used in its production processes whether this derives from the composition of the raw material itself, from the production technology, or from possible cross-contamination in some stages of the supply chain. We also carry out analytical activities on raw materials of interest. From a risk management perspective, the company is, therefore, active in verifying that any presence of allergens deriving from cross-contamination is included on labeling, pursuant to Article 36 par 3 a) of EU Reg 1169/2011. We voluntarily include the words “may contain…” only in the event that the preventive measures mentioned above are not sufficient to guarantee the reduction of risk to acceptable levels (segregation of lines or absence of traces in the validation of cleaning processes). Validation of cleaning processes is one of the most critical points given the absence of legal limits and the difficulty of detecting traces of these contaminants (e.g., active and inactive forms of the allergenic protein). Where it is not possible to minimize the risk to acceptable levels, the company prefers to inform the consumer exhaustively about the possible presence of the cross-contaminated allergen on the label.

Validation of cleaning processes is one of the most critical points given the absence of legal limits and the difficulty of detecting traces of these contaminants.

Do your products have a very small list of allergens that are not ingredients? Your company use PAL only in a few cases, right?

Yes, in most cases we do not use PAL because most of our products are free from trace of allergens.

Do you think is it difficult to use different labels for export to different countries, where the list of allergens and/or any temporary thresholds are different?

Granarolo diversifies all the labels according to the country of destination, taking into account the legislative peculiarities through the Consumer Care, Food Legislation, and Nutrition headquarters with the help of headquarters AQs that evaluate any different thresholds. For example, for export to Chile, the gluten limit is <3 mg/kg and the analysis on our finished product was performed with an ELISA-type method with a LOQ 3 mg/kg level at a Granarolo-qualified laboratory.

Do you see the need for multi-allergen testing methods for use in the company?

Thanks to careful risk analysis, we are able to restrict the numbers of possible allergens and cross-contaminations. The need, rather than for multi-allergen methods, is for the lowest possible LOQ methods for single allergens. In other words, we need methods that can detect, for example, traces in CIP (Cleaning In Place) rinse waters or highly repeatable methods on single allergens even on complex matrices such as multi-flavor yoghurt, vegetable drinks, or gastronomic preparations that do not have too high a rate of false positives (obviously, only methods with 0% false negatives are acceptable).

Do you use rapid test systems such as lateral-flow or strips to detect allergens?

Currently, the lateral flow kit that we have in use is for finding gluten in food and on surfaces and it is used in factories that have products with "gluten free" claims and that, therefore, also need more restrictive process controls; for this kit, having a legal limit with which to compare, you can more easily manage the critical acceptability thresholds (they usually have detection limits much lower than the legal limit). Positive results obtained from the lateral flow method are still confirmed by the ELISA method which, although used as a screening tool, is semi-quantitative and allows us to assess contamination levels.

For milk allergens such as casein in beverages and vegetable yoghurts, ELISA kits with a more basic LOQ are used. In the latter case we prefer the ELISA because the number of samples is greater and the ELISA in this situation is cheaper.

Do you have accredited internal tests?

No, but we have validated the kits to our matrices, using control or reference materials where available and we always send a certain number of analyses to external laboratories. The same external laboratories have been validated by us. We also participate in a Proficiency Test.

Have you ever had the need to recall a product because of allergens?

It has never happened. However, we have blocked products before they were packaged and distributed, for example, due to the presence of casein.

Dr. Simone Gozzi

Expert in Food Quality, Safety, and Sustainability from the Field to the Table, CAMST Group, Bologna (Italy)

How do you assess the current legislation on allergens, both for the food production industry and for the catering industry?

Behind the legislation on allergens there is the will to protect a sensitive population that until a decade ago was not even recognized. This can partly be deduced from the reading of the community legislation, where it is reiterated that the interest is to protect minorities. The legislation is divided into two areas: distribution and catering. Applying it to the production and distribution front is certainly simpler than applying it to catering. While the production plants are, on average, structured for a limited number of products and ingredients, making the control phase simpler and more automated, the same cannot be said for a restaurant with a menu that changes on a seasonal basis and with a selection of raw materials very different from those found in the food production industry. We must also think that in the kitchens of restaurants there is a greater number of ingredients, often at the same time, while in the industrial world there is greater programming that allows the identification of food traces.

What strategies should be adopted by the food production industry and the catering industry?

In the industrial field, the problem of allergens can be overcome by making precise choices upstream, intervening in the production process. Operator training is important both in food production and in catering, but in catering, because the contact between food and operator is frequent, it is even more important. The human contribution in industrial production is less important, so it is clear that different strategies are needed.

Industries often recall products, but there have never been any deaths from anaphylactic shock linked to food products of industrial origin. On the other hand there is more fragmented management in the catering industry and some fatal cases - albeit rare - have occurred. Why is this so?

My experience is a bit different; in my opinion, the consumer who knows he is particularly allergic and that he can experience anaphylactic shock is unlikely to turn to the world of restaurants. The problem can be linked to a lack of consumer awareness about certain ingredients. It should also be added that European legislation provides a list of allergenic ingredients, which has been developed over time based on the most frequent allergic reactions of the European population over time, but it is anything but exhaustive. The legislation calls for labeling food products on the basis of this list, but we cannot exclude the idea that there is a minority consumer population with allergic responses to other molecules present in food but not present in European legislation.

Companies face the problem of having to apply the voluntary wording "traces may be present..." when they are unable to ensure an absolute lack of trace allergens. How do you deal with this problem in the preparation of collective meals? What is the relevance of the issue?

It has enormous importance. If it is a public setting where different types of dishes are produced with many ingredients, it is obviously declared that all types of allergens could be present. A different matter concerns hospital or school catering, in which a specific diet is requested for a patient or a child based on a medical certificate, which makes the creation of an ad hoc meal much easier. For the general public, which is offered a wide variety of foods, it is impossible to guarantee the absolute absence of allergens. If there is a client who regularly attends a restaurant, you could agree on a specific dish, which should be prepared in different moments and spaces than the food for clients without food allergies.

Operator training is important both in food production and in catering, but in catering, because the contact between food and operator is frequent, it is even more important.

What limits do you find in current legislation?

The current legislation is vague; it speaks of having to draw up a list of allergenic elements but it does not mention the traces. One of the limitations is that we talk about allergens, but the minimum acceptable dose is never clarified. In any case, there are no rapid detection methods suitable for catering.

Would the introduction of thresholds change anything?

In my opinion, it would be useful to introduce both thresholds and rapid detection methods.

Thinking of companies like CAMST that deal with collective catering, is it easier to provide effective supervision?

In the field of collective catering we deal with the social-welfare, hospital, and school sectors; when the client is identified and there are very precise indications, everything is much simpler. In school catering, there are about 10% special meals but it is clear that these are previously agreed and planned diets; the raw material is kept under control from the beginning, there are precise agreements with suppliers, and there are both spaces and procedures to produce a certain number of controlled meals. In collective catering, unlike the restaurant, separate spaces (sometimes entirely separate kitchens) are explicitly provided for the management of special diets.

In addition to training and procedures, does it make sense for you to have analytical checks on some raw materials?

Analyses are carried out both on finished products and on raw materials and also to validate HACCP management procedures. We currently use external laboratories.

/interviews

ELISA kits... quantitative or not?

The point of view of the test kit manufacturers

Service laboratories and industries, as well as governmental bodies, rely on ELISA kits for the detection of food allergens. Recently, a number of guidelines for the validation of ELISA methods for detecting allergens have been issued by the analytical chemistry community (AOAC) and by technical bodies that promote standardization (ISO, CEN). Today, however, there are neither fully validated confirmatory methods nor complete Certified Reference Materials (though some Reference Materials are available; see R. Poms, page 24 in this volume). Without any internationally accepted thresholds, there is an expectation that tests kits are designed to detect the lowest possible concentrations of the target molecules (Granarolo, page 38). The scientific literature, however, as well as the results of proficiency tests, reveal doubts about recovery and detectability in processed food. To gain further insight, we interviewed three large test kit producers (R-Biopharm, Romerlabs, Neogen) and two smaller companies that also manufacture test kits, one producing LFDs (Zeulab) and the other producing RT-PCR kits (Generon).

Kit sensitivity

The Limit of Detection (LOD) of assays is an important element for kit purchasers. In Australia and New Zealand, following the VITAL approach, the target concentration depends on the potency of an allergen to exert an allergic reaction, but also on the amount of allergen in the food portion. However, most of the rest of the world does not agree with this threshold approach and industries generally look for the method with the lowest LOD. For some customers, requests for the lowest possible LOD are related to the absence of actual accepted limits, as a representative of R-Biopharm explains. “If the VITAL limits were accepted nobody would ask for lower LODs. This is what happened in case of gluten, for instance. Very few customers ask for a gluten sensitivity lower than 20ppm.” A representative of Neogen states, “Some industries are establishing the cut-offs for each product after considering proposed thresholds and portion sizes while others simply look for the kit with the lowest LOD. At present, it is not clear if the threshold approach will be accepted throughout the industry.”

Testing must guarantee enough protection for the consumer but at the same time testing should not create unnecessary burdens for the food industry.

“To look for the lowest LOD has one risk,” said R-Biopharm’s representative. “In some cases, it could be very critical to manage this information into the real production site. If industries start finding very low but detectable concentrations then, considering there is no threshold, what should they do? So there should be a balance: testing must guarantee enough protection for the consumer but at the same time testing should not create unnecessary burdens for the food industry.”
According to a representative of Generon, clients usually request the most sensitive kit, but there is little knowledge about the concept of LOD in matrices, thus creating concern about the need for matrix validations for ELISA kits. Because these kits are often considered “universal,” the necessity of adding further matrix validations can disappoint clients.

How have kit LODs been established?

Considering the absence of legal thresholds and the lack of suitable Certified Reference Materials (CRM) for many allergens, calculating the LOD of any kit is a challenge. “Our kits are validated following the most up-to-date validation guidelines,” declares a representative of Zeu. “In the case of ELISA kits, we

“Customers in the industry have to validate their own matrices, a service we offer them to ensure the accuracy of the methods.”

follow the AOAC guidelines which are very useful since they give specific indications about the matrices to be tested for each allergen. Thus, LODs are calculated by spiking such matrices with the specific allergen. In addition, we include a panel of at least 3 products with several levels of allergens which have been manufactured at an industrial pilot plant.”

R-Biopharm has a different approach. “Generally, we test 5 to 10 different matrices with different levels of contamination and we extract them 10 times before then making a double determination. In this way, we determine both LOD and LOQ. It is well-described in the AOAC validation reports of our products.”

“There are multiple ways to determine LOD values,” states Romerlabs’ representative. “A very common one is to test the extraction or dilution buffer the method uses. In this way, one can determine which will be the minimum possible LOD of the method, allowing for better comparisons between methods. Nevertheless, since LOD values are matrix-dependent, other approaches can include testing a number of matrices to find individual LOD values for each one. We go for an approach that ensures that our kits are suitable for most commonly tested matrices in terms not only of LOD but, more importantly, of LOQ. Nevertheless, we encourage our customers to perform matrix validations of their individual matrices before integrating our products into their routines.”

More about validation

In other analytical areas (veterinary drug residues, for example), the test kit (used for screening purposes) should guarantee, in the EU, a false compliant rate lower than five percent and there is an obligation to test at least 20 or sometimes 40 different samples of the same matrix, starting with the blanks (The Commission of the European Communities 2012). However, this is not the case for allergens so far.

When there is no maximum allowable concentration threshold, the problem is to define what constitutes a negative result. R-Biopharm also pointed this out. “There are no blank CRMs. If we take 20 different industrial chocolates and some

have low but detectable concentrations, how do we know if that is background or not? In the case of mycotoxin analysis, for instance, the job is easier because the target has a much simpler chemical structure. In the case of the allergens, which are proteins, the entire process is more complicated. So we are in a situation in which the differences in the matrix effect in different products are combined with the modification of the target in a way that affects detectability. We do not think that these problems can be solved until there are established thresholds.” With the virtually infinite variety of matrices in the food industry, one method will not cover every type of matrix.

“The customers understand that and invest in the validation of their own matrices,” confirms the management of Romerlabs. “Customers in the industry have to validate their own matrices, a service we offer them to ensure the accuracy of the methods.”

In the AOAC literature (Abbot et al. 2010), we found, as an example, the suggestion to test 6 matrices in order to validate an egg test kit. The “working group for Chicken Egg” clearly stated that “recovery data using incurred samples must be provided for all claimed matrices” (Godefroy et al. 2018).

The representative of Neogen provides two examples. “If we take the dairy industry as an example, we can understand the problem. We use non-fat dry milk powder for calibration, but the dairy ingredients used in food manufacturing can be diverse. Using skimmed milk powder for the standard curve, it is possible to use a protein conversion. However, this, too, is challenging because different dairy sources have different protein profiles. Another example comes from soy sauce. With soy sauce, there is a delicate fermentation process, usually requiring a couple of years until the proteins are hydrolyzed. This can be difficult to test with any methodology. To understand the source of an allergen used by producers is important and can make a difference. Risk assessment experts are discussing the communication of allergen analysis results in protein rather than the whole food but for now it is a debate that is still open.”

In any case, the AOAC Guidelines (Abbot et al. 2010) say “The developer should also identify any matrices the method is known to have difficulties with and identify clearly which state of the food allergen (raw, cooked or both) the method is capable of detecting.” More work should be done by the majority of Test Kit Manufactures (TKMs) on this issue.

Risk assessment experts are discussing the communication of allergen analysis results in protein rather than the whole food but for now it is a debate that is still open.

Accuracy

Proficiency Test (PT) results show that all providers are clustering data based on the kit used. The *z-score* measures agreement with other users of the same kits rather than how close the result is to a previously-determined value. This method is unfamiliar to those outside the “allergen community.”

Neogen thinks there is some work to be done: “The analytical community understands what proficiency test means, but there is no consensus about the large number of results that are generated. We think that sometimes the proficiency tests are difficult to interpret for the food industry. The analytical community understands quite well but the two groups would benefit from collaborating more on this issue.”

“Customers are very concerned, indeed,” Romerlabs’ representative stated. “This is clearly something that those in laboratories take into account more than those in the industry. The laboratories among our customers are constantly checking on the latest PT results and actively participate in PTs themselves.”

Ten years ago, this was a controversial topic but now the situation is different. “Now, both end users and the method developers are unsatisfied and we hope this situation can change,” explains the management of R-Biopharm. “A couple of years ago, we started discussing a standardization process with the other TKMs. It would be useful to use the same RMs (Reference Materials) for calibration but, until now, we haven’t done so. We developed some RMs but the issue remains unsolved. We could be more transparent and easier to understand for customers. We are still missing many RMs and even when we have an RM but the results weren’t the ones hoped for, the test might not be selected by the manufacturer. So we do think there should be some official standardization.” However, this is a long process and the analytical community has just begun addressing it.

On the other hand, Zeu finds this issue less relevant. “In general, users are not aware. Big companies with access to international studies are, but it is not a common practice.”

“Traceability should be mandatory, but there are only a few RMs available and they are not manufactured according to ISO17034.”

Shouldn’t traceability to existing RMs be mandatory in order to reduce inter-kit differences in results?

“Yes,” states R-Biopharm, “but we see that the JRC, the Joint Research Center of the European Community, that should be responsible for producing ERMs (European Reference Materials) is not very active in this area. It is an unsolved problem.”
For Neogen, a solution requires time and coordination with all stakeholders.
While more RMs have become available recently, not all of them are suitable because they correspond exclusively to a standardized allergen material such as milk powder or egg powder but RMs for processed incurred products do not exist. This could be a problem, explains the management of Zeu. “With the objective of obtaining the most precise conversion factors, qualified CRMs are indispensable. The use of CRMs is currently the only way to compare LODs between methods even though they might not give an accurate indication of their global performance. Nevertheless, inter-kit (or even inter-method) differences are from the result of many factors such as the target to be detected, the standard material used, the use (or not) of conversion factors to a reference material, the units in which the results are expressed, recovery in processed products, etc.”
“As of today,” Romerlabs stated, “the number and availability of CRMs is very limited, although new ones seem to be on the horizon. Once more of them are available, they will be a very useful tool for method development and validation. This should help solve the problem of differences between kits, since there will be a common point of reference. The problem is more complicated, though, since what we are still lacking is an appropriate reference method to determine with accuracy the allergen content of these CRMs in the first place. Because of this, although these reference points will help us better compare different kits, they will not necessarily help us find out which one is the most accurate.”
“Yes, traceability should be mandatory,” confirmed Generon management, “but there are only a few RMs available and they are not manufactured according to ISO17034. Considering the limitations of the PTs, we are helping customers in the validation process through laboratory reference materials we are producing internally.”

How is your company managing the risk of poor recoveries with processed foods?

“Our approach when we design an antibody is to take into account the possible transformation of the target because of the production process. Sometimes, in the assay, in order to increase sensitivity, we use a cocktail of antibodies against the target after heating it,” explains R-Biopharm’s representative. Indeed, food allergens are subjected to many kinds of manufacturing processes that might disrupt the epitopes.
According to Romerlabs, “In such a case, maybe an alternative kit using a different antibody can be offered, although this is not always possible. What we can do is evaluate and validate particular matrices to eliminate or minimize interferences and to optimize the extraction if possible. This is something we routinely do with our customers.”
Zeu also expressed their point of view on this important topic. “Our tests are evaluated against a wide range of food products to detect any matrix effect coming from composition or production processes. They are then corrected, if necessary, by adding specific reagents or improving the extraction conditions. During the development steps we use both spiked matrices and incurred processed products to deal with these issues.”
Generon’s approach is different. “We try to make the customer understand that it is important to grasp the details and carry out protocol optimizations, using, for example, temperatures or further treatments of the matrix to increase recovery. Unfortunately, this level of attention doesn’t exist throughout the market. Perhaps these treatments are done only for chocolate.”

What is your opinion about thresholds? Do you think it is advisable to establish such limits? Would it make the job of TKMs easier or more difficult?

For the allergen community, thresholds could be a positive innovation, “for example, in the reduction of food recalls and a reduction in unsubstantiated precautionary allergen labeling (PALs), which should result in a wider choice of food products available for consumers with food allergies,” explains the representative of Neogen. “For those who produce kits instead, these thresholds could be used to optimize the outputs for food producers. However, it may be difficult to communicate to consumers with food allergies trying to make informed food purchasing decisions which products have been processed in facilities with allergen management procedures utilizing an allergen threshold-based approach.”
“If authorities would confirm that threshold values are what industries should consider, well, it would be much better than now. Today, it is very complicated. Some countries in the EU have actually established their own limits. For example, now the threshold for peanuts in Belgium is 100 times higher than in the Netherlands,” states R-Biopharm.
The position of Zeu is that establishing food allergen thresholds can help all stakeholders calculate a more real risk of allergen presence and the efficiency of their countermeasures. “However, to achieve this situation, the threshold allergen doses should be detectable by current analytical methods.

In addition, we should harmonize the threshold as much as possible among countries. It could also be very helpful to encourage the food industry to strengthen efforts in food allergen risk management. Of course, to have defined thresholds for allergens would benefit kit manufacturers and method developers but also food industry quality managers and public health authorities.”
Romerlabs’ representative reflects on clinicians’ opinions on thresholds. “Despite their extensive discussions about the matter, it is doubtful that clinicians would agree on a maximum allergen dose. Furthermore, if a given concentration is set as a maximum, the total amount of the consumed allergenic protein will still depend on the serving size: a product with low allergic concentration could still elicit severe adverse reactions if consumed in large amounts.”
Finally, Generon also confirms the importance of thresholds. “We think the thresholds should be established. I understand that false security can be created but industry needs some guidance. For now, food companies must tend towards absence, but we know that the absence from the chemical point of view corresponds to the undetectable. It would then be ideal to set low thresholds rather than not have them. The body that establishes the limit must be aware of the specific technological characteristics, otherwise it could be a counterproductive choice.”

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/interviews

Perspectives in the service laboratories

Laboratories primarily use ELISA kits and while sensitivity is considered satisfactory, recoveries in some matrices are not – opinions diverge about thresholds and the need for multiplex methods

The allergen testing laboratory point of view is interesting because laboratories operate between test kit manufacturers and food businesses.
Allergen testing is a growing business with a significant segment in a market (food safety testing services) that has a value (2018) of at least 7 billion US dollars worldwide (including gluten testing). Various market studies report the allergen testing segment as already worth at least 500 million US dollars worldwide. While it is unclear whether or not the prevalence of food allergies is actually increasing, it is a matter of fact that industries and retailers are demanding more and more analytical services and analytical products for allergen testing, particularly in Europe and North America. Below are interviews with managers from 3 labs specialized in allergen testing.

While the market appears to be growing, it also faces challenges. Let's first have a look at what is happening in Russia. Alexandr Galkin of Stylab says: "The situation here in Russia is controversial: there is formal regulation, but it is not fully applied. The Russian labeling regulation is similar to the European one; in fact, it is necessary to indicate 14 allergens on the label, as in Europe. There is also special attention paid to gluten-free foods and to foods intended for those who have special dietary needs. At the same time, there is no public awareness and we have no consumer organizations for people with allergies, just some organizations for people with celiac disease. We are the only accredited Russian laboratory for all types of allergens and the requests for testing and kits mainly come from foreign companies (like international companies operating in Russia)."
The European allergen-testing market, on the other hand, faces different circumstances. "It is not only the market as such that evolves, but also the customer base," commented Roberto Lattanzio of Eurofins Hamburg. "Mainly, we are observing an increase in demand from our ever more diversified customer base. As the allergen issue is somewhat unique and hard to handle, some global food players have been slow and cautious to implement their own allergen management systems. Ultimately, however, many companies have comprehensively im-

THE LABS

Stylab, located in Moscow, is the only accredited Russian laboratory for testing all food allergens. It is also the Russian dealer of FAPAS, the leading proficiency test provider from the UK.
Food Allergens Labs consist of 4 independent laboratories, located in central and southern Greece, Cyprus, and Poland. FAL has extensive experience testing food allergens and they also produce several Reference Materials for validation and quality assurance of allergen testing.
Eurofins a world-leading food and feed testing laboratory group, deploying a comprehensive range of state-of-the-art analytical techniques. Eurofins Analytic Gmbh is located in Germany where they have a highly specialized allergen test unit at their Hamburg campus.

plemented such systems, which include careful risk assessment and extensive monitoring of their whole food supply chain. Most recently, some companies have prompted all the stakeholders in their supply chain to take action. Today, there are not only the major global players who are active in the field, but even relatively small companies are spending considerable resources on their allergen management systems. The food products that we typically analyze have changed from just chocolates and biscuits to an increasing number of different raw materials and finished products. This growth also applies to the number of environmental swab samples from surface checks and CIP (Cleaning In Place) final rinse water in accordance with the increasing number of quality controls on decontamination procedures in production sites. Last but not least, another reason for this growth arises from the rapidly evolving interest in "free-from" products (vegan, gluten-free, lactose-free, etc.) in the food market that target special consumer groups with specific health or ethical issues."

"In recent years, in addition to gluten, we have observed peaks of interest in the detection of soy, a rather common contamination in wheat and also mustard," says George Siragakis of Food Allergens Lab in Greece. "Sometimes we also look for sesame which can be present in the same flours." While gluten remains the primary request coming to laboratories, testing for other allergens is significant and can require specialized equipment and testing kits. "It is known that there are some limits, as well," says Lattanzio. "In particular, regarding processed and fermented foods, there are few kits that are able to provide adequate results, as sometimes the allergen present is underestimated or not detected at all due to low extraction yields or limited detection of the modified target protein. Some further points of improvement would be the development of an ELISA kit for celery as well as the development of a specific mustard kit." Siragakis added, "It must be said that to get good results with an ELISA test you need a good kit but also trained operators and adequate skills."

"One of the most controversial topics currently dividing the market is the establishment of allergen thresholds. In light of the threshold values established by the Allergen Bureau in Australia, referred to as VITAL, based on our experience," says Lattanzio, "we can say that most of the kits - if these were the legal values - would be suitable for checks, even by means of VITAL3, which expresses drastically lowered values regarding some allergens. Only a few kits developed many years ago now show inadequate sensitivity. Perhaps a somewhat critical situation may appear if the recovery of the allergen is low in the specific matrix. Maybe some of the nut thresholds might be challenging. Due to their high allergenic potential, the thresholds are very low (e.g., peanut). The more important the quantification of the detected allergen becomes, the more important the expected comparability of the available ELISA method becomes, which until now has been a weakness of the ELISA allergen detection methods."

But there are also divergent opinions, which see the institution of thresholds as a useless choice that is not scientifically founded. "We are not convinced that it is a good idea to introduce thresholds," says Siragakis. "What should they be, considering that there is no agreement in the scientific community itself on what doses may actually provoke a serious reaction?" This view is in

accordance with Galkin, who said, "I think that the thresholds do not have scientific bases. This stems from the fact that every allergist has a different idea about any limits to be set; therefore, there is no scientific basis for promoting universal thresholds."

Moreover, according to Siragakis, "Today, without thresholds, the accuracy of the dosage is not important; it is much more important to verify the actual sensitivity and specificity. But having to validate the method from the quantitative point of view, without a full range of reference materials, in the absence of a confirmation method, with the known differences between the various kit brands, the difficulties would grow."

Other significant differences of opinion emerged on the need to develop multiplex kits.

Galkin considers them a useful technology for the future of the market. "Yes, this is the future, because it's also an immunological method. I can imagine that a product like this could also be modular, able to meet the needs of laboratories."

Lattanzio, on the other hand, is not so convinced. "The utility of multi-target systems is limited. In fact, it rarely happens that a customer asks us to verify different allergens in the same product. They usually ask for 1-2 allergens to be checked at most and, in rare cases, 3-5 targets are requested. An obvious practical application would be a milk kit that detects milk protein and whey protein separately. Perhaps another case in which a multiplex kit would actually be requested is a test for different kinds of nuts."

Siragakis proposes another method. "We believe the best performance to detect many targets simultaneously, if not all, is the LCMSMS. This is an analysis that in some cases might be useful to industries, but not for routine checks. Then there are some specific cases in which a kit has been developed, combining simplicity and multiplex detection, but they are really rare cases (see the lateral-flow for 6 NEOGEN tree-nuts)."

An increasingly important issue is the validation of the kits. "We check the possible false negatives and false positives and determine recovery rates with a certain number of expected matrices. Sometimes the products that we receive contain ingredients that have never been validated or verified, in which case we may observe unsatisfactory kit performance," says Lattanzio. "Thus, it is necessary to conduct appropriate tests to avoid such an event. Against an unexpected positive sample, a fairly rare event, we ask the customer to provide us with the list of ingredients. In some cases, a certain cross-reactivity to an ingredient may already be known and, in others, tests will be carried out to confirm or exclude that the positive result was a result of the presence of an ingredient. If there is cross-reactivity of this type in a certain product, we are sometimes forced to change the testing method or to refuse the analysis on the finished product. Then, each ingredient is checked to determine if there is an unexpected matrix effect or a real cross-contamination. Using finished products supplied by companies to validate the kits is risky because it is possible to have different problems with cross-reactivity."

"With finished products, no one guarantees a representative procedure for adequate testing for allergens. The first sampling should be in the industry," explains Galkin.

Communicating results to customers (test certificate) is very important. How is a "negative" result communicated? What do laboratories report when the result is in between LOD and LOQ? Eurofins and Stylab report negative results as "< LOQ", while Food Allergens Laboratory reports it as "<LOD". "In case of a qualitative analysis, anyway," says Galkin, "we report the result as 'not detected'." Communicating results this way "avoids any interpretation," as Galkin states.

With a result between LOD and LOQ, Eurofins reports the sample as "positive <LOQ", explaining in a comment that they have detected traces that cannot be quantified. Food Allergens Laboratory reports this as "LOD<value<LOQ". Stylab reports "< LOQ", again avoiding interpretation.

Units, such as mg of commodity or mg protein/kg food sample, are also an important consideration.

"We normally use the reporting unit used by the kit manufacturer," says Lattanzio. "Only in rare cases, when we are convinced that changing the original reporting unit is a real improvement, do we convert the reporting unit. All our results are expressed as mg/kg or mg/l."

Siragakis points out that Food Allergens Laboratory must defer to the national accreditation bodies: "In our labs in Greece we give mg/kg of the total allergen but in our lab in Poland we use mg/kg of allergenic protein as the Polish accreditation body (PCA) directs. If a customer requests it, we can provide both options using the conversion factors provided by the kit manufacturer."

"Usually the reporting unit is mg of a commodity" says Galkin "If our customer requests us to recalculate the result into mg of protein, we do this."

How will the situation evolve in the future? Accreditation bodies are becoming more demanding and, as a result, the validation work to guarantee the performance of the methods is going to be more complicated and expensive. Certified test kits would make the accreditation job much easier. For the moment very few ELISA kits have third-party certification. "The number of certified kits is increasing and we believe that in the next few years more kits will have some kind of certification," added Sirigakis.

/technology & company news

Biosens

Every year, companies involved in **agriculture businesses experience significant financial losses because of mycotoxins** – invisible and dangerous for human health foodborne toxins, which contaminates 25% of the global food supply. Farmers, grain elevator owners, and food processing companies suffer the most from this issue and crave for the solution that will allow them easily, swiftly and accurately detect mycotoxins on-site. Timely detection of mycotoxins will prevent them from unsuccessful trade or border rejections and will lead to the revenue increase.
BIOsens provides a cutting-edge solution that successfully tackles the problem of agriculture companies by creating an **easy-to-use portable device** for mycotoxin analysis.
BIOsens developed a portable and rapid precise mycotoxins detection device. This unique solution is the first to provide an automated way to prepare samples of plant material, analyze them on the content of mycotoxins only within 25 minutes, and deliver results on a built-in screen or save them in the cloud. BIOsens device covers all steps of the food analysis process and enables to perform the test outside of the laboratory: it can be easily used by farmers, grain elevator or processing company employees when they are on the field, at the crop reception stage or on borders and need to swiftly carry out toxin analysis.

Andrii Karpiuk, BIOsens Inc. / info@sens.bio

Inspecto hooks food contamination with real-time results

In all major industries lab-based testing has been taken out to the user's environment to provide real time results for immediate, informed action (Examples are the breathalyzer and home pregnancy test). However, the food industry, despite its size, still lacks an "out of the lab" solution for contaminant detection that meets the industry needs. The main reasons for this are complexity of food matrices and accuracy requirement.

Inspecto is filling this void by offering a portable, accurate and immediate food contaminant scanner, offering a one stop-shop for contaminant detection. It includes a fully automated, smart process for both sample preparation and quantified analysis.
The company's first product, for detection of Acrylamide, will be launched in late 2020, with additional detection focus already in the works.
Inspecto's model resembles the coffee machine and capsules model. The user inserts a food sample: raw or processed, solid or liquid. The capsule is then inserted into the device and with a press of a button scanning begins.
Inspecto has partnered with leading investors and food producers, sharing the vision for a cleaner, transparent food industry.
Come be part of Inspecto's future.

Yair Moneta, VP business development / yair@inspecto.io

www.inspecto.io

Herb identification using a smartphone and Artificial Intelligence

Britescan is a US start-up founded with the of goal developing a system that -according to them- can "authenticate materials instantly, accurately and affordably from anywhere in the world". **The BriteScan Verification System is the first of its kind to use Artificial Intelligence (AI) to analyze photos of materials** taken with smartphone camera and the portable BriteScan Box. The device is a simple light box that eliminates all external light and ensures consistency between photos.
The starting point was the identification of the botanical species in processed herbs and spices. Now, there is a public database that allows for the reliable identification of more than 100 dried culinary and medicinal herbs and spices. BriteScan also offers customers the ability to create their own custom private image databases for testing a wide range of materials and applications. It has been successfully used for verification of the source origin of coffee and vanilla beans, identification of fish and meat species, detection of adulteration in herbs and spices, as well as olive oil and beverages. While the limit of detection varies depending on the nature of the material, studies have demonstrated the ability to detect powdered adulterants even down to the 1% level in some cases.
We think that at the border controls as well at raw materials acceptance by the industry, there is a clear need to objectively evaluate the appropriateness of food labeling by a real fast system, able to determine the origin of some food stuff in less than a minute. In many cases, if the specificity is insufficent, integration with a traditional, more specific analytical method (like LFDs or DNA) could produce a very reliable analytical screening check point.

Danica Harbaugh Reynaud, Chief Science Officer and Co-Founder, Britescan, LLC.

www.britescan.com

Allergen detect startups

Some startups are producing and/or developing devices for consumer allergen detection. Here, we present three companies, one of which (Nima in the US) has already been selling its system for a couple of years and two (Alleguard in Israel and Allergy Amulet in the US) who are still in the R&D phase.

Nima, established in 2013, is the first company to introduce a rapid portable device able to detect allergens designed for consumers. The system is comprised of a disposable cartridge ("capsule") and a reader. The cartridge is used to probe the food and then it makes a simple extraction before being moved to the sensor. The principle of the method is an immunoassay, a lateral flow whose result is presented to the user as either

"positive" or "negative" on the basis of a pre-established cut-off signal value. The reader can send the result to a smartphone and the smartphone can share the result with Nima's user community. The gluten assay has been available since early 2017 while the peanut test has been on the market for about a year. Nima performed extensive validation trials for gluten. There is no real third-party certification but a highly specialized external laboratory confirmed that at 20 ppm the test is reliable (Taylor SL 2018). In the case of peanuts, the claimed sensitivity is 10 ppm. Nima is expecting to release the test for detecting dairy ingredients in 2021.

www.nimasensor.com

Allergy Amulet was established in early 2016. Like Nima, the system is comprised of a disposable unit and a reader. The principle of the method is not immunoassay but it is still based on molecular recognition; instead of antibodies, the target

molecule is captured by Molecular Imprinted Polymers (MIP). Apart from the molecular detector used, the Amulet appears to work in a similar way to Nima's sensor. The reader is much smaller than Nima's and its appearance is more elegant. The product is in development so there are no data about its performance. According to its web site, the Amulet is expected to detect the whole range of US-regulated allergens. This startup has already raised about 1.5 million US dollars from investors.

www.allergyamulet.com

Founded in 2016, **Allerguard** is developing a handheld device that scans and analyzes the vapors emitted by prepared food to determine the presence of allergens, such as peanuts. It identifies an allergen right down to the parts per billion, which is recognized as the safest allowable amount. The startup says it can carry out this process in under a minute. To use the device, it is held just above the meal and nanotechnology absorbs

vapor for detection. Once absorbed, electrochemical sensors then identify any possible allergen molecules. According to the startup's website, artificial intelligence analyzes the binding events to identify any allergen presence down to the maximum allowable presence of an allergen deemed safe to eat. Allerguard has raised 2.2 million US dollars (1.5 million US dollars in October 2019 alone). As with AllergyAmulet, no performance data have been made available either by the company or by a third party. What looks very interesting is that the Allerguard detection system apparently overcomes the risk due to sampling. Because meals are often quite complex, and considering that we may look just for a cross-contamination, probing just one or a few parts of the food increases the risk of false negative results. Whether all allergens contain volatile compounds is another question.

allerguardsystems.com

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/conference & exhibition news

WMF Meets Asia

January 13-15, Bangkok, Thailand

The World Mycotoxin Forum is working on the first Asian edition of the event, which will be held from the 13th to the 15th of January in Bangkok (Thailand). With the growing livestock and aquaculture sectors in Asia, the need for effective mycotoxin strategies is becoming a key topic and the WMF Meets Asia aims to spread the latest knowledge on the prevention of and solutions to this growing problem.

GFSI Conference 2020

March 22-28, Seattle, USA

The Global Food Safety Conference 2020 will take place from the 22nd to the 28th of March in Seattle (USA). It will bring together over 1000 food safety experts, both from the private and public sectors, to advance global food safety.

EuroResidue IX

May 18-20, Egmond aan Zee, The Netherlands

EuroResidue IX is going to take place from the 18th to the 20th of May in Egmond aan Zee (The Netherlands) and it will cover everything related to veterinary drug analysis residues.

NAFS20

June 2-3, Chicago, USA

The North America Food Safety and Quality 2020 event is going to be held on the 2nd and 3rd of June in Chicago (USA) and it will be the premier event in North America covering all issues related to food safety and quality from farm to fork.

IAFP 2020

August 2-3, Cleveland, USA

The International Association of Food Protection's 2020 annual meeting will be held from the 2nd to the 5th of August in Cleveland (USA). It is a renowned event offering information, innovative solutions, and networking opportunities for thousands of food safety professionals.

AOAC International

September 11-17, Orlando, USA

The Association of Official Analytical Chemists will hold its 134th annual meeting & exposition from the 11th to the 17th of September in Orlando (USA). This event will bring together government, industry, and academic experts dedicated to developing and validating standards, methods, and technologies and ensuring the safety and integrity of foods and other products that impact global public health.

RME 2020

November 2-4, Amsterdam, The Netherlands

The 13th Rapid Methods Europe Conference will be held from the 2nd to the 4th of November in Amsterdam (The Netherlands). RME 2020 will be dedicated to innovations and breakthroughs in rapid food contaminant analysis. It will also aim to further strengthen academia-industry relations.

/food law news

USA - Sesame labelled allergen in Illinois: what now?

30th July 2019 _ A study published last August by researchers from Northwestern University found that 0.49% of Americans, or 1.5 million children and adults, reported having an allergy to sesame, based on responses to a national survey of over 50,000 households.

The results of the study indicate that there may be more Americans with a sesame allergy than there are people allergic to tree nuts, like pine and macadamia nuts. This is why Illinois has decided to follow the example of Canada, the European Union, Australia, and Israel and has included sesame in its list of major allergens. The US state has obligated food producers to indicate the presence of sesame on the product label, just like the eight allergens already recognized by the FDA. Always considered the great absentee in the list of US allergens, the new law could also affect the situation in other countries because large American producers sell on an international scale.

https://will.illinois.edu/news/story/illinois-requires-food-manufacturers-to-label-sesame-allergen

UK - Food allergen labeling changes become law

5th September 2019 _ New law introduced to extend labeling requirements for people with food allergies and intolerances.

Millions of allergy sufferers across the country will be protected by a new law laid in Parliament which will require more foods to be labelled with allergen information. The law, which comes into effect from October 2021, will require businesses to provide full ingredient and allergen labeling on foods which are pre-packed for direct sale. This is the result of a UK-wide consultation which followed the tragic death of teenager Natasha Ednan-Laperouse, because of an allergic reaction to a baguette she had eaten which did not display allergen information on the packaging.

https://www.food.gov.uk/news-alerts/news/food-allergen-labelling-changes-become-law

USA - The CCA Coconut Allergen Project

10th September 2019 _ The Coconut Coalition of the Americas is going to spearhead the submission of a citizen petition (CP) requesting that FDA revise the FALCPA Guidance Document to remove coconut from the list of "tree nuts" identified as a major food allergen.

The 2004 Food Allergen Labeling and Consumer Protection Act (FALCPA) requires foods to declare "major food allergens" (defined as: Milk, egg, fish (e.g., bass, flounder, or cod), Crustacean shellfish (e.g., crab, lobster, or shrimp), tree nuts (e.g., almonds, pecans, or walnuts), wheat, peanuts, and soybeans. A 2006 FDA guidance document on FALCPA includes a list of ingredients it identifies as "tree nuts" that includes coconut (Cocos nucifera). The Coconut Coalition of the Americas is then going to spearhead the submission of a citizen petition (CP) requesting that FDA revise the FALCPA Guidance Document to remove coconut from the list of "tree nuts" identified as a major food allergen.

https://coconutcoalition.org/allergen-project/

UK - FSA Board announces plans to protect people with food allergies and intolerances

18th September 2019 _ The FSA Board confirmed a series of measures to protect those with food allergies and intolerances. This comes a week after the conclusion of the inquest into the tragic death of Owen Carey, who died after having an allergic reaction to milk at a London restaurant.

The measures were discussed as part of the quarterly Board meeting on Wednesday 18th September in Belfast.
The actions include:
- issuing a clear and easy to follow aide-memoire for enforcement officers (Environmental Health Officers and Trading Standards Officers) which is focused specifically on the action they should be taking within business in relation to food allergies;
- publishing an urgent update of the highly-regarded 'Safer Food Better Business' guide, including a review of on the allergens information included;
- at the end of the year, launching of an awareness campaign to remind businesses and consumers about how to keep people with food allergies safe;
- implementating a pilot project to develop better reporting of allergic reactions;
- focusing on the concerns raised by Owen's case at the next Industry Leadership Forum on food hypersensitivity in November;
- meeting with Byron and their local authority to discuss the detail of Owen's case and lessons learned;
- once all information is available, commission a full root cause analysis of this specific incident to ensure that lessons are shared.

https://www.food.gov.uk/news-alerts/news/fsa-board-announces-plans-to-protect-people-with-food-allergies-and-intolerances

UE - RASFF Annual Report

18th September 2019 _ RASFF The Rapid Alert System for Food and Feed 2018 Annual Report

The European Commission has published its annual report on the Rapid Alert System for Food and Feed (RASFF): in 2018, a total of 3699 original notifications were transmitted through RASFF, of which 1118 were classified as alert, 493 as information for follow-up, 675 as information for attention, 1401 as border rejection notification and 12 as news notification.

UE - Ruling on plant protection product

1st October 2019 _ JUDGMENT OF THE COURT (Grand Chamber) 1 October 2019 (Reference for a preliminary ruling - Environment - Placing of plant protection products on the market - Regulation (EC) No 1107/2009 - Validity - Precautionary principle - Definition of the concept of 'active substance' - Combination of active substances - Reliability of the assessment procedure - Public access to the dossier - Tests of long-term toxicity - Pesticides - Glyphosate)

This request for a preliminary ruling concerns the validity of Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market. The Court stated that:
- an applicant is bound to identify, when submitting his application for authorisation of a plant protection product, any substance forming part of the composition of that product that corresponds to the criteria set out in Article 2(2) of Regulation No 1107/2009, so that an applicant does not have the option of choosing at his discretion which constituent of that product is to be considered to be an active substance for the purposes of the examination of that application;
- it does not appear that Regulation No 1107/2009 is vitiated by a manifest error of assessment in that it provides that the tests, studies and analyses necessary in the procedures for approval of an active substance and for authorisation of a plant protection product are to be submitted by the applicant, but does not systematically require that an independent counter-analysis be carried out;
- the procedures leading to the authorisation of a plant protection product must necessarily include an assessment not only of the specific effects of the active substances contained in that product, but also of the cumulative effects of those substances and their effects combined with other constituents of that product;
- it is the task of the competent authorities, when examining an application for the authorisation of a plant protection product, to verify that the material submitted by the applicant, and primarily the tests, analyses and studies of the product, is sufficient to exclude, in the light of current scientific and technical knowledge, the risk that that product exhibits such carcinogenicity or toxicity.

/product news

Romer Labs launches AgraStrip Coconut Test Kit

Romer Labs is once again expanding its AgraStrip® Allergen testing portfolio, the largest commercially available line of rapid test kits for allergens. **The AgraStrip® Coconut kit** detects coconut in foods, beverages and rinse waters and on surfaces at an LOD of 10 ppm. All AgraStrip® allergen test kits share the same extraction procedure, ensuring a convenient and streamlined workflow.

These sensitive, immunochromatographic LFDs are designed for the detection of coconut residues in foods and beverages and for the validation and monitoring of cleaning procedures by testing rinse waters and environmental swab samples.

Other benefits of the AgraStrip® Coconut test kit:

– Same extraction procedure as with all other AgraStrip® Allergen kits
– Simple procedure with ready-to-use components
– Designed for on-site testing
– LOD of 10 ppm coconut
– 11-minute test time including extraction
– 12-month shelf life at room temperature.

Ensuring safe food for people with egg allergy

Because of their technological characteristics, eggs are a popular additive in the food industry and are used in a variety of processed foods. However, they also are one of the most common allergy triggers worldwide. Therefore, eggs must be labelled in the list of ingredients. To ensure correct labeling, a reliable analysis is essential for the food industry. Given the varied use of eggs, it is particularly important that test systems are able to reliably detect native as well as processed egg. The new **Ridascreen® Egg** (Art. No. R6411) allows this analysis.

Test for detection of milk

Proteon Duo Milk Express is a double test for detection of milk by combining the presence of ß-lactoglobulin (ß-LG), as indicator of whey proteins, and casein showing presence of caseinates. It is an immunochromatographic test in strip format, based on specific antibodies obtained against ß-LG and casein which are bound to red particles, will react with these proteins when they are present in the sample, producing one or two red test lines. In addition, a blue line (control line) indicates that the test has worked properly. Food or working surfaces containing milk residues above the limit of detection will show two red lines. In case of samples containing either of whey or caseinates, a control blue line and a ß-LG or casein red line will appear, respectively.

Kits for allergen harder to detect

3M™ Allergen Protein Rapid Kits and Protein ELISA Kits can be used on environmental swabs, clean-in-place (CIP) final rinse water, and food product.

Complex processing can alter the nature of allergenic proteins in food, making them harder to detect. 3M™ Allergen Testing Products overcome this challenge by detecting both processed and unprocessed proteins for more predictable, accurate results in your lab.

Our Lateral Flow Device features our signature hook line, which can alert you of a possible false negative due to high amounts of target protein in a sample. This feature can increase confidence in your allergen testing results.

Generon Tree Nuts Kit

Generon develops and distributes reagents for the detection of food contaminants. Generon can provide a complete portfolio of products (using ELISA, lateral flows and PCR technologies) for allergens detection. The latest tool developed by the R&D team is the SPECIALfinder Tree Nuts Kit, detecting traces down to 0.5 ppm of all the nuts (including peanuts) considered allergens according to the Reg. EU1169/2011 Annex II, in just two Real-Time PCR reactions using a single DNA extract in 80 minutes. A market unique and convenient product to protect your customers and your brand reputation. For more info get in touch at www.generon.it

Announcing: a change in the name of our Plant Derived Alternative Drink Detection Kits

The increasing demand for soy-based and nut-based alternatives to dairy products has raised widespread international concern regarding appropriate labeling for plant derived foods. There is a growing consensus that application of dairy-associated terms such as “milk” to plant-based substitutes may result in confusion among consumers, particularly in regard to nutritional content. In some jurisdictions, this has led to regulations specifying that the term ‘milk’ cannot be used to designate a purely plant-based product, unless specifically exempted.

The range of ELISA Systems Assay Kits designed for the detection of soy and nut “milks” are now re-labelled to reflect the current international environment regarding labeling of such plant derived foods. Consequently, the term “milk” is now to be replaced with the term “drink” for the following ELISA Systems kits:

New Name	Almond Drink Residue Detection Kit	Hazelnut Drink Residue Detection Kit	Soy Drink Residue Detection Kit
Code	**ESALMK-48**	**ESHZMK-48**	**ESSMLK-48**
Previous Name	Almond Milk Residue Detection Kit	Hazelnut Milk Residue Detection Kit	Soy Milk Residue Detection Kit
Kit Range (ppm)	**0.4 - 4.0** Almond Drink Protein	**1.0 - 10** Hazelnut Drink Protein	**1.0 - 10** Soy Drink Protein

food test compass

Around the world, a growing number of analyses are required at every step in the food and feed supply chains. Numerous scandals have occurred over the past 20 years, creating an increased awareness of food hazards, caused both by naturally-occurring and manmade spoilages and contaminations. Facing an enormous demand for testing, both the Analytical Service Market and the Test Kit Market (TKM) have been growing at an average rate of 5-10% annually even when and where the economic crisis was quite serious. Market analysts forecast further similar growth over the next 5 years due both to consumer demand for safe food and to the implementation of new regulations (the allergen testing market is a good example of this growth). Some industries prefer to outsource testing but in some cases it is mandatory or advisable to conduct rapid on-site controls, particularly to verify the quality of incoming raw materials.

When a Food Business Operator (FBO) has to choose between outsourcing or purchasing a test kit, or when an external laboratory or kit supplier must be selected, there is no resource to support rational management purchasing decisions. Where can a FBO find a list of laboratories able to test for the presence of soy in a food product? Where can a laboratory find a test kit for acrylamide, if any are even available? Do any laboratory have the ISO17025 accreditation for the test kit I want to buy? Accreditation bodies have data bases of laboratories, but they do not provide information about the Turn Around Time (TAT) or the LOD of the accredited method. Detailed test kit information is often available on manufacturers' web sites but each company presents this information in a different way and, in any case, we don't know how many web sites we might need to visit to make an informed choice.

Food Test Compass is a unique tool designed to help you choose the analytical solution you need. It will no longer be necessary to Google the analytical target and spend hours trying to understand which supplier is right for you. With just a few clicks, Food Test Compass will provide you with the whole spectra of analytical possibilities, help you compare products, show you reviews from other users, and allow you to share your own experiences in order to improve the entire food safety community.

We're asking for the cooperation of both method providers and end-users in order to improve this innovative service. Please do not hesitate to send us any requests or suggestions.

In the following pages we present an example of what we do. For the first time you can easily see in one place all of the known LFD test kits for detecting soy protein on surfaces after cleaning, in raw materials, and even in finished products.

BIOMEDAL

BIOMEDAL
AlerTox Sticks Soy

PRODUCT CODE	KT-6125	#OF TESTS	10
LIMIT OF DETECTION	1 ppm	ASSAY TIME	10'
SAMPLE PREPARATION	SOLID	GR, EX, SH, SE	
	LIQUID	(DI or FI), EX, SH	
	SURFACE	SW, EX, SH	

MATRICES
SOLID: Corn flour, Rice flour, Milk powder, Spices, Bread, Cookies, Cakes, Snacks, Meat, Fish, Sausage, Black pudding, Patè, Canned meat, Canned fish
LIQUID: Milk, Juice, Condensed milk, Yogurt, Soup, Gravy, Sauce, Cream
SURFACE: Yes

STORAGE	18-35° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	no
CERTIFICATION	no	READER	NR

LEGEND

SW = Swabbing
GR = Grinding
EX = Extraction
SH = Shaking
HE = Heating
CH = Chilling
SE = Sedimentation
PH = Checking pH
FI = Filtration
DA = Dampening
DI = Dilution
BU = Buffering
CE = Centrifugation
() = If Needed
NA = Not Available
NR = Not Required
/ = not declared

BioSystems REAGENTS & INSTRUMENTS

BYOSISTEMS ES
SOY Rapid Test

PRODUCT CODE	14215	#OF TESTS	10
LIMIT OF DETECTION	1 ppm	ASSAY TIME	10'
SAMPLE PREPARATION	SOLID	GR, EX, SH, SE, (FI)	
	LIQUID	EX, SH, SE, (FI)	
	SURFACE	/	

MATRICES
SOLID: Food samples
LIQUID: Liquid Food Samples
SURFACE: /

STORAGE	18-35° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	no	VALIDATION REPORT	no
CERTIFICATION	no	READER	NR

COSMO BIO

COSMOBIO
FastkitT Slim Soybeans

PRODUCT CODE	NPH-NFS006	#OF TESTS	10
LIMIT OF DETECTION	25 ppm	ASSAY TIME	15'
SAMPLE PREPARATION	SOLID	GR, EX, SH, CE (4° C), FI, DI (PH)	
	LIQUID	EX, SH, CE (4° C), FI, DI (PH)	
	SURFACE	SW, EX, SH, SE	

MATRICES
SOLID: Food samples
LIQUID: Liquid food samples
SURFACE: Yes

STORAGE	2-8° C	SHELF LIFE	12 months
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	no
CERTIFICATION	no	READER	NR

eurofins | Tecna

EUROFINS TECHNOLOGIES
SensiStrip Soy

PRODUCT CODE	HU0030096	#OF TESTS	20
LIMIT OF DETECTION	1 ppm	ASSAY TIME	15'
SAMPLE PREPARATION	SOLID	GR, EX, SH, SE; Untreated soy: DA and HE 100° C, CH RT, EX, SH, SE	
	LIQUID	EX, SH	
	SURFACE	SW, EX, SH, SE	

MATRICES
SOLID: Food samples (Raw soy)
LIQUID: Liquid food samples, Beverages
SURFACE: Yes

STORAGE	2-30° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	yes
CERTIFICATION	no	READER	NR

MORINAGA

MORINAGA
Rapid Test Easy for Soy

PRODUCT CODE	M2246	#OF TESTS	10
LIMIT OF DETECTION	0.5 ppm	ASSAY TIME	10'
SAMPLE PREPARATION	SOLID	/	
	LIQUID	As it is	
	SURFACE	SW, EX, SH	

MATRICES
SOLID: /
LIQUID: Rinse water
SURFACE: Yes

STORAGE	2-8° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	no	VALIDATION REPORT	no
CERTIFICATION	no	READER	NR

Data are from manufacturers web sites / documentation. We invite once again all the companies to provide us with updated correct informations, we will introduce any change needed in the on-line version.

MORINAGA

MORINAGA
Rapid Test Pro II for food allergens

PRODUCT CODE	M2266	#OF TESTS	10
LIMIT OF DETECTION	5 ppm; 1 ug/swab	ASSAY TIME	15'

SAMPLE PREPARATION

SOLID: GR, EX, SH, HE 90° C, CH RT, SH, SE, (FI or SE), DI; GR, EX, SH, SE, (FI or SE), DI

LIQUID: EX, SH, HE 90° C, CH RT, SH, SE, (FI or SE), DI; EX, SH, SE, (FI or SE), DI

SURFACE: SW, EX, SH, HE 90° C, CH RT, SH, SE, (FI or SE), DI; SW, EX, SH, SE, (FI or SE), DI

MATRICES

SOLID: Food samples

LIQUID: Rinse water

SURFACE: Yes

STORAGE	2-8° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	no
CERTIFICATION	no	READER	NR

NEOGEN

NEOGEN
Reveal 3-D Soy Allergen

PRODUCT CODE	902093K	#OF TESTS	10
LIMIT OF DETECTION	5 ppm; 2 ug/10 cm2	ASSAY TIME	5'

SAMPLE PREPARATION	SOLID	GR, EX, SH, SE
	LIQUID	EX, SH, SE
	SURFACE	SW, EX, SH, SE

MATRICES

SOLID: On a case by case basis following a successful technical services evaluation (raw soy)

LIQUID: Rinse water, Liquid samples

SURFACE: Stainless steel surface, Non-stick surface, Plastic surface

STORAGE	2-8° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	yes
CERTIFICATION	no	READER	NR

r-biopharm

R-BIOPHARM
Rida Quick Soya

PRODUCT CODE	R7103	#OF TESTS	25
LIMIT OF DETECTION	0.5 ppm; 0.5 ug/dm2	ASSAY TIME	10'

SAMPLE PREPARATION	SOLID	GR, EX, SH, HE 100° C, CH RT, FI
	LIQUID	/
	SURFACE	SW, EX, HE 100° C, CH RT

MATRICES

SOLID: Soy flour in wheat flour, Processed food samples, Bread mix, Rye bread, Minced meat

LIQUID: /

SURFACE: Yes

STORAGE	2-8° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	yes
CERTIFICATION	no	READER	NR

Regabio

REGABIO
Agitest Food Allergen Rapid Test Raw Soybean

PRODUCT CODE	RT10278020	#OF TESTS	20
LIMIT OF DETECTION	1 ppm	ASSAY TIME	15'

SAMPLE PREPARATION	SOLID	GR, EX, SH, SE
	LIQUID	EX, SH
	SURFACE	SW, EX, SH, SE

MATRICES

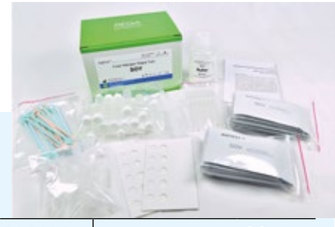
SOLID: Solid food samples (raw soy)

LIQUID: Liquid food samples, Beverages

SURFACE: Yes

STORAGE	2-30° C	SHELF LIFE	24 months
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	yes
CERTIFICATION	no	READER	NR

Regabio



REGABIO
Agitest Food Allergen Rapid Test Test - Soy

PRODUCT CODE	RT10206020	#OF TESTS	20
LIMIT OF DETECTION	10 ppm	ASSAY TIME	15'

SAMPLE PREPARATION	SOLID	GR, EX, SH, SE
	LIQUID	EX, SH
	SURFACE	SW, EX, SH, SE

MATRICES

SOLID: Solid food samples

LIQUID: Liquid food samples, Beverages

SURFACE: Yes

STORAGE	2-30° C	SHELF LIFE	24 months
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	yes
CERTIFICATION	no	READER	NR

ROMER Romer Labs

ROMER
Agrastrip soy

PRODUCT CODE	COKAL0410AS	#OF TESTS	10
LIMIT OF DETECTION	2 ppm; 2 ug/25cm2	ASSAY TIME	5'

SAMPLE PREPARATION	SOLID	GR, EX,SH, BU, SH, SE
	LIQUID	EX, SH, BU, SH, SE
	SURFACE	SW, EX, SH, BU, SH, SE

MATRICES

SOLID: Soy Flour, Soybean, Soy Hulls, Soy Protein Isolate, Tofu, Textured Soy Protein, Soybean (roasted), Dairy free margarine, Sausage, Biscuit crumb, Dark chocolate, Rice flour, Digestive Biscuit, Dairy Free Soya, Spread Casein, Nut Free Chocolate, Balti Curry Cooking Sauce, Pork Sausage (Wheat listed as an ingredient), Rice Flour, Internal Quality Control Soy Extract (STI 15% of total protein)

LIQUID: Soy Milk, Yoghurt, Curry sauce, Plain Yoghurt

SURFACE: Plastic Chopping Board, Stainless Steel Surface

STORAGE	15-25° C (RT)	SHELF LIFE	/
DISPOSABLE AVAILABLE	yes	VALIDATION REPORT	yes
CERTIFICATION	no	READER	NR

3M

3M
Soy Protein Rapid Kit

PRODUCT CODE	L25SOY	#OF TESTS	25
LIMIT OF DETECTION	2 ppm; 2 ug/mL	ASSAY TIME	11'

SAMPLE PREPARATION	SOLID	GR, EX, SH, CE
	LIQUID	EX, SH, PH (5-10); diverse DI for diverse matrices; Chocolate: EX I, SH, EX II, SH, CE
	SURFACE	SW, EX, SH

MATRICES

SOLID: Food ingredients, Processed food samples

LIQUID: Liquid Food Samples, Liquid Chocolate, Rinse water.

SURFACE: Yes

STORAGE	2-8° C	SHELF LIFE	/
DISPOSABLE AVAILABLE	no	VALIDATION REPORT	no
CERTIFICATION	no	READER	NR

ZEULAB

ZEULAB
Proteon Express

PRODUCT CODE	ZE/PR/S10 y ZE/PR/S10SW	#OF TESTS	10
LIMIT OF DETECTION	1,2 ppm of soy proteins 0,8 mg of soy proteins / 100 cm2	ASSAY TIME	10+5', surfaces 5+30+10'

SAMPLE PREPARATION	SOLID	EX
	LIQUID	/
	SURFACE	SW, EX

MATRICES

SOLID: yogurt, ice cream, pasta, biscuits, bread, sausage, pate

LIQUID: juice, chocolate shake, red wine, UHT milk, soup, infant formula

SURFACE: Yes

STORAGE	/	SHELF LIFE	/
DISPOSABLE AVAILABLE	no	VALIDATION REPORT	no
CERTIFICATION	no	READER	/

/point of view

Paper, a key factor in food diagnostics

At the beginning of my career in the in-vitro diagnostic industry, I was attending a seminar in Milan on biosensors for the agri-food industry. It was 1988 or so. Many speakers told us that biosensor technology was going to allow the food industry to rapidly detect any kind of contaminant. I was impressed. As a young biotechnologist busy with ELISA kit development, I thought, "Maybe the ELISA will soon be replaced by faster and more efficient small instruments." A few weeks later, some researchers from the clinical diagnostic industry told me that "ELISA plates will soon disappear." Honestly, as a scientist, I had some doubts. And in the following 30 years, I saw a carousel of biosensors, bearing any kind of physical interface linked to the detector (bio) molecules, passing through a variety of B2B meeting and scientific conferences, some of them even presented as results of EU RD projects. The era of "end-point" immunoassays, in any case, is far from over, I think. Many startups and even a number of giant players broke their bones trying to introduce all kinds of new biosensors into the food testing market. Whether, small, portable, or, more frequently, bench top, such instruments did not satisfy the needs of end users. Does anyone remember the Biacore?

At the same time, yes, the "poor" microplate had a hard time, but certainly not because of biosensors. While tons of paper and rivers of ink have been used to claim the wonderful sensitivity of the new technologies, an "old" immuno-method, not even a real-time one, still holds center stage: the "Lateral Flow Device" (LFD). I am pretty sure the EU Commission has spent tens of millions of euros in the past 30 years to develop prototypes of sensors that are less sensitive than LFDs already on the market, but with longer assay times and, often, with more complicated sample preparations. Still, many applicants or startups write that they have a much more rapid method than existing immunoassay kits that require half an hour or more to get the result.

What can we learn from this story? Small is fine? Simple is better? Well I do believe that forecasting the length of a technology lifecycle is very difficult. However, while we know that tech fashions are good for grant applications, they have little to do with the market success of a product. I am no longer impressed by the decision of large companies that sometimes follow this trend; small, experienced, specialized companies have little to be afraid of. The large companies come, they spend a few million, and with the same speed they disappear.

Long life to end-point immunoassay. Paper-based LFDs are more and more efficient and reliable. Even the poor microtiter is going to have a new life with 2D simple array technology (while 3D arrays don't look to me like the right system for screening purposes).

Maurizio Paleologo

affidia

your food safety partner

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