Impact Objectives

- Build an interdisciplinary European network of scientists to discuss more predictive models and approaches to improve the current allergenicity risk assessment strategy of novel or modified proteins
- Facilitate international collaboration in the development of more predictive tools to assess allergenicity

Assessing the allergy risk of novel proteins

*Dr Kitty Verhoeckx, the chair of the **Improving Allergy Risk Assessment Strategy for novel food proteins (ImpARAS)** project, explains its importance and details the broad collaborative approach adopted*

Can you describe the different types of expertise the research partners contribute to ImpARAS?

Partners from different sectors are essential to the success of ImpARAS. Industry is a key user of the current risk assessment. They inform us about their experiences, the obstacles they encounter, and the gaps in predicting allergenicity. They also provide information on their needs and the practical application of the allergenicity prediction methods. Clinicians have information on the needs of the at-risk population and knowledge on clinical aspects of food allergy that must be taken in to account in the allergenicity assessment strategy (e.g. severity, prevalence of allergic disorders, threshold levels). The regulators contribute insight into the current risk assessment strategy and guidelines, and knowledge on how the guidelines are applied in dossiers and the conditions needed for developing new guidelines. Finally, the scientists provide the fundamental knowledge on biological mechanisms involved in food allergy and proteins. This includes the applicability of in vivo and in vitro methods and the development of risk assessment methodology and parameters in consultation with the stakeholders. The collaboration between the different sectors strengthens the knowledge of each and keeps us focused on end-use applications.

What do you see as being the main challenges or obstacles presented by this project, and how are you overcoming them?

ImpARAS provides the framework and resources to bring together a sizeable number of scientists and experts and thereby facilitate networking. To get all stakeholders involved is challenging, but we have been quite successful thus far. ImpARAS is one of the few projects including significant involvement of industry. Most sectors were involved in defining our common interest and in writing the European Cooperation in Science and Technology (COST) Action proposal. Furthermore, we invite experts from different sectors to be keynote speakers at our meetings and get them involved in our network to share their expertise with us.

One of your goals is to ensure this topic is covered in the Horizon 2020 research agenda. How have you gone about achieving this?

During an ImpARAS working group meeting held in Barcelona in March 2016, we invited the National Contact Point (NCP) for Spain to give us insight into the Horizon 2020 process. We discussed with all participants the possibility of a call text on allergenicity prediction for the Horizon 2020 2018–2019 research agenda. The comments discussed at the meeting were adapted for the text and the final proposal from the ImpARAS network was made available to NCPs, the European Commission, and stakeholder groups such as the Joint Programming Initiative (JPI), Directorate-General for Health and Food Safety, JPI on Agriculture, Food Security and Climate Change (FACCE-JPI) and the Directorate-General Research and Innovation.

Do you have any planned workshops or outreach events coming up that will be of interest to readers?

ImpARAS holds meetings, conferences and workshops at regular intervals (approximately biannually). A number of activities are planned for the near future, including a working group meeting in Vienna from 30 November to 1 December 2016, and a meeting in Brussels in February 2017. More information on these events can be found at www.imparas.eu.

Engaging all stakeholders as partners

Dr Antonio Fernandez Dumont of the European Food Safety Authority, Dr René Crevel of Unilever and Dr André Knulst from the University Medical Center Utrecht explain how regulators and industry are key to the success of ImpARAS

Who are the important stakeholders for ImpARAS?

RC: Stakeholders as represented by individual partners are critical to the success of the project – researchers to develop methodologies, industry to be prepared to implement them, and food safety agencies and regulators to evaluate them and support their ultimate use. However, beyond those stakeholders, all those who will be using products containing novel proteins will need to know that the proteins are safe and that they have been developed and evaluated in a manner which meets prevailing ethical imperatives.

Can you discuss the current allergenicity risk assessment strategy and the challenges it presents?

AFD: For allergenicity assessment, the EFSA follows a weight-of-evidence approach, as do several international risk assessment bodies. The strength of this is that the assessment takes into account all the information available on the novel proteins as no single piece of information or experimental method yields sufficient evidence to predict allergenicity. However, inherently, such an approach is affected by a degree of uncertainty which can only be reduced by taking into account new developments in the area.

RC: The current risk assessment uses a number of methods, the outputs of which are generally associated with allergenicity rather than proof of it, that is, they are proxy measures. They have proved reasonably successful insofar as no novel protein with a significant allergenicity burden has been introduced. However, this may have been achieved largely because exposure to novel proteins has been extremely limited compared to the exposure that would occur if such proteins were nutrient sources. This approach has perceptibly reduced the use of novel protein sources as the development process is similar to that of pharmaceutical drugs, that is, it is necessary to screen a very large number of candidates to obtain a single usable one. This imposes considerable costs which are difficult to amortise through food applications.

What is the significance of the impact this project could potentially have on the food and healthcare sectors?

AFD: The EFSA relies on its guidance documents which are grounded on internationally agreed principles set by Codex Alimentarius. These principles are based on high-quality science which is a key value of the EFSA. The main objective of ImpARAS is to develop new strategies for allergenicity prediction, which implies improved methods for allergenicity risk assessment. The need for robust, high-quality science-based guidelines is crucial for appropriate risk assessment. ImpARAS can contribute to identify scientific advances that could be implemented in the risk assessment strategy. It will also highlight and define elements of that strategy that should be prioritised.

AK: Patients and clinicians will strongly benefit from knowledge on improved risk assessment strategies for novel proteins. There is a strong need for novel, sustainable proteins, but they should be safe for allergic consumers. The current situation is that on average every food allergic patient suffers from one unexpected reaction per year. This results in anxiety, social isolation, mistrust of food producers, inadequate elimination diets and an impaired food choice. Any progress in this area will directly impact the quality of life of food allergic consumers. An important aspect is also the communication with patients and patient organisations and healthcare providers as well as adequate labelling, when it turns out that the novel proteins are safe.

RC: In the short term, ImpARAS will develop a coherent framework for allergenicity risk characterisation and assessment which can form the basis for individual research projects to address the necessary methodological questions. It will also catalyse the formation of project teams with the required diversity of expertise. In the longer term, ImpARAS' ultimate success will ensure that novel proteins can be introduced safely into the food supply, whilst minimising the potential public health burden caused by allergy.

Food for thought

*The **ImpARAS** project aims to develop new ways to assess the allergenicity of novel proteins in response to an increasing demand for sustainable and safe food from a growing global population*

> *In the longer term, ImpARAS' ultimate success will ensure that novel proteins can be introduced safely into the food supply, minimising the potential public health burden caused by allergy*

Proteins are essential for life and are vital to the well-being of all. They are essential to our bodies' functions (e.g. as enzymes, components of muscles, etc.). As the population of the world grows, the demand for new sustainable proteins and protein sources will only increase. However, proteins also represent the dietary component associated with allergies.

Consequently, any new protein or protein source requires allergenicity testing before it can be deemed suitable for public consumption. With around 17 million food allergy sufferers in Europe alone, the scale of the issue cannot be underestimated. Unfortunately, there are currently no validated methods that reliably and consistently predict the allergenicity of a protein. This is where Dr Kitty Verhoeckx and the ImpARAS project come into play.

Verhoeckx, a researcher from TNO, a research institute in the Netherlands, has teamed up with key representatives from different sectors to create ImpARAS. The four-year project aims to construct an interdisciplinary network of scientists and other stakeholders across Europe to better understand the mechanisms of allergy and create ideas and strategies to improve allergenicity testing. Currently, ImpARAS encompasses 29 European countries, multiple industrial partners, academia, risk assessors, clinicians and the European Food Safety Authority (EFSA) as observer. Verhoeckx succinctly explains the scope of the network: 'We are working on state-of-the-art papers: gaps in current risk assessment, strategy for scaling allergenicity, mechanistic understanding of food allergy and food tolerance, available analytical methods, and a comparison of the available methods for allergenicity assessment.'

CONTEMPORARY TESTING

As it stands, there are four stages to the safety assessment of a protein with regard to its potential to provoke allergic reactions. First, the source of the protein is assessed and then its amino acid sequence checked for homology with known allergens. Thirdly, the target is tested for binding to immunoglobulin E (IgE) antibodies from allergic individuals. This stage is only requested on a case by case basis – only if issues are identified in the bioinformatics analysis or from the information on the source of the protein. IgE antibodies are responsible for initiating an immune response to allergens which should otherwise be harmless. Finally, the stability of the protein to heat, pH and resistance to breakdown by pepsin is evaluated. Pepsin is one of the key digestive enzymes found in the stomach and a common determinant of the chance of a protein surviving ingestion. The main issue with these methods is the inherent uncertainty linked to them. The results are merely indicative and could easily miss, over- or underestimate the potential allergenicity of a given protein. These methods are effective in assessing cross-reactivity with already known allergens but are particularly less effective when attempting to predict sensitisation (production of IgE to a new protein) – the initial priming of the immune system to an allergen that is a prerequisite to future allergic reactions.

ImpARAS aims to overhaul the old testing system with one that will be quantitative and serve the needs of all those involved in the process of developing and using novel proteins and protein sources. Industry experts such as Dr René Crevel at Unilever are directly involved in the project to ensure that developed methods help them to comply with regulations and are able to screen potential candidates accurately – cheaply – and early on in the process. From his viewpoint, Crevel would like to see ImpARAS develop 'individual, well-characterised methods providing specific pieces of information relevant to allergenicity assessment as determined by an overall conceptual framework for the development of food allergy'. To this end, it has been vital that the project includes regulators such as the EFSA to ensure that the tests developed fully meet public health safety criteria. Naturally, clinicians and academic researchers are also essential to the process as they are on the front line of allergy effects and are well positioned to identify the value of a given method in protecting current (and potential) allergy sufferers. Equally, they should be in an excellent situation to provide real-world data on the prevalence, effects and context of allergic reactions.

Project Insights

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PARTICIPANTS

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ACTION CHAIR BIO

Dr Kitty Verhoeckx has a keen interest in food allergy research and analytical chemistry. As well as being Chair of the COST Action ImpARAS, she is responsible for the Shared Research Program Line 2 – Allergenicity Assessment of (New and Modified) Food Proteins at TNO, in which private and public resources are combined to address major research challenges in food allergy. Verhoeckx is also a member of the EFSA's focus group on food allergy and a visiting researcher at the University Medical Center Utrecht (UMCU).