FOOD STANDARDS AGENCY

REPORT OF THE FOOD ALLERGY AND INTOLERENCE RESEARCH PROGRAMME REVIEW

19 – 21 NOVEMBER 2012

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1. Foreword

Food allergy and food intolerance are important complaints, and for those affected the health consequences can be very significant.

It is the responsibility of the Food Standards Agency to seek ways to reduce the burden of these diseases, and to provide sound guidance to those who have food allergy or intolerance, and those who care for them, about to how to manage their diets and make sensible and informed choices about the foods they eat.

One way in which the Agency addresses these issues is to ensure that policies and guidance are based on the best possible scientific evidence obtained through commissioning targeted research. These research projects are managed under the auspices of the Agency Food Allergy and Intolerance Research Programme. This Programme was launched initially in 1994 (at that time within the Ministry of Agriculture, Fisheries and Food) and since then has delivered a wide variety of important research projects that have had a significant impact on our understanding of food allergy and intolerance, and have informed the Agency's evolving policy and guidelines in this area.

To ensure that the Food Allergy and Intolerance Research Programme continues to deliver high quality and cost-effective research that is focused on the important challenges posed by food allergy and intolerance, the policy has been to conduct regular reviews. The programme was last reviewed in 2008 and a detailed report of that was published later that year.

The most recent review was conducted in November 2012 when an independent Panel of distinguished experts considered in detail the strategic objectives of the programme, the quality and productivity of the individual research projects that have been commissioned during the last 5 years, and the impact those projects have had on the development of evidence-based guidance.

The results of that review are made available here, together with the conclusions drawn by the Panel and the specific recommendations they recorded.

This review process has again provided invaluable guidance in planning how commissioned research can most effectively support the Agency in tackling the problems of food allergy and intolerance, and delivering benefit to consumers.

2. Executive Summary

Every 5 years the Food Standards Agency reviews individual Programmes of research that it has commissioned with the aim of evaluating their success and productivity. The Food Allergy and Intolerance Research Programme was reviewed in November 2012. The purpose of that review was to assess the quality, relevance and delivery of research commissioned during the preceding 5 years and to consider future aims and objectives.

The Review meeting was held from the 19th – 21st November 2012. The first 2 days of the meeting were an open meeting consisting of presentations and discussions on Food Allergy and Intolerance projects. The third day of the meeting was a closed session for the expert Review Panel, Agency officials and the Food Allergy and Intolerance Research Programme Advisor, in which individual projects within the Programme and the Programme as a whole were reviewed and recommendations were made.

It was considered by the Review Panel that the Research Programme had been successful in addressing the majority of its aims. Collectively the projects funded within the Programme over the last 5 years have contributed significantly to understanding of sensitisation and allergy to foods in a number of important areas. It was considered by the Panel that not only had the research generally been conducted very well, but it had also delivered a large number of important outputs. The Panel also concluded that those outputs had been of direct relevance to the Agency's policy, and had translated into sound consumer advice. Of particular importance in that context were advances in understanding of the prevalence of food allergy, the impact of skin exposure on allergic sensitisation to food proteins, and consumer perceptions of current food allergen labelling and their value and limitations.

When considering the future direction of the Programme, the Panel suggested a number of areas of particular priority, including further investigation of the impact of the timing and route of exposure to food allergens, the prevalence of food allergy in adulthood and the mechanisms through which allergy develops later in life (sometimes after the food had been consumed for many years previously) and a better understanding of the prevalence and impact of food intolerances other than coeliac disease and lactose intolerance. The Agency will take account of the valuable comments and recommendations that were made by the Review Panel about the performance, productivity and scientific quality of the Programme when determining its direction over the next 5 years.

3. Introduction

i. Aim of the Agency's work on food allergy and intolerance (including background to the scientific problem)

Adverse reactions to food may take a number of different forms. Food intolerance is an adverse reaction to a food that is reproducible and takes place every time contact is made with a particular food or food ingredient. The reaction may involve the immune system, in which case it is known as a food allergy. It may also be mediated by non-immunological mechanisms such as a fault in the way the body breaks down food, which can be due to the lack of a particular enzyme, and this would be classed as a food intolerance. The exception to this definition is coeliac disease, an intolerance to dietary gluten, which does involve the immune system, although in a different way to food allergies. Generally, food intolerance is not so severe or immediately life-threatening as food allergies. However, food intolerances can still make someone feel ill and significantly affect longer term health and wellbeing.

The Agency's work on food allergy and food intolerance aims to protect food allergic and food intolerant consumers and to help them to make informed choices about food[1]. We do this via four key strands of activities: 1) negotiating and implementing legislation to improve statutory controls on the labelling of food allergens, 2) provision of best practice guidance for industry and enforcement bodies to encourage greater awareness and control of food allergens through the food supply chain, 3) provision of advice about food allergy and intolerance to consumers and other stakeholders, and 4) commissioning scientific and consumer research on food allergy and intolerance to ensure that policies are based on robust scientific evidence.

ii. Rationale for the programme and aims and objectives

The Food Allergy & Intolerance Research Programme

The programme was established in 1994 by the Ministry of Agriculture Fisheries and Food (MAFF) with the primary aim of investigating the causes and mechanisms of severe food allergy in order to reduce its incidence and severity. In 2000, when the Food Standards Agency was created, the research programme on food allergy and intolerance was transferred from MAFF to the FSA. In the last 10 years, the focus of the programme has largely been on commissioning projects in five specific areas identified as being key to informing the development of policy and advice by the Agency. These areas, or Aims of the programme, were described in an underpinning

[1] http://www.food.gov.uk/multimedia/pdfs/strategicplan2010e.pdf

document (previously known within the Agency as the ROAME A document). The high level aims from that ROAME A that are relevant to this review are reproduced here for reference:

1. To identify the risk factors (e.g. genetic, environmental, dietary and other) associated with the development of sensitisation to food proteins and the development of clinical food allergy, particularly in early life. Knowledge of these factors and how they influence the development of sensitisation and allergy will enable us to develop appropriate advice for consumers to reduce the risk of development of food allergy.

2. To investigate the immunological mechanisms of food allergy to understand, at the immunological level, what factors are important in determining/regulating the allergic versus tolerant status.

3. To determine the prevalence of food allergy (both total food allergy and the prevalence of allergy to specific foods) in the UK in infants, children and adults, and whether prevalence is changing over time.

4. To develop suitable methods for the detection of allergens in food.

5. To determine the factors that influence the severity of allergic reactions to food

The ROAME system within the Agency has ceased to be used as the document for setting out the rationale and aims of its research programmes, with research needs now being identified on a rolling and more frequent basis to enable the Agency to be more flexible in ensuring that its available research spend is used most effectively to address policy needs. However, the above research Aims are still relevant to the Food Allergy and Intolerance Research Programme today. In addition, the overall aims of the Agency's evidence gathering work in relation to food allergy and intolerance, have been captured in the Agency's Science and Evidence Strategy 2010-2015[2] which sets out a specific objective to "improve our understanding of the nature, patterns, trends and importance for health of risks from chemical and biological hazards and from allergens in food and feed". Within this objective, a priority 'evidence need' has been identified as being to understand "the incidence, development of and thresholds for allergic reactions to underpin effective, targeted controls and advice".

External Programme Advisors can be appointed to research programmes in the Agency, to provide independent expert scientific advice and to assist the Agency in procuring and delivering a high quality research programme that meets the Agency's needs and delivers value for money. Professor Ian Kimber, who is Professor of Toxicology at the University of Manchester, is the current programme advisor for the Food Allergy and Intolerance Research Programme.

[2] http://www.food.gov.uk/science/researchpolicy/scistrat

4. The Food Allergy and Intolerance Research Programme Review

4.1 Background to the Programme review

The Agency has a commitment to reviewing its research programmes regularly to gain an independent view of how relevant, productive and informative the commissioned research has been in addressing the Agency's needs, and to inform future research needs. The Food Allergy and Intolerance Programme was last reviewed in 2008[3] where projects active from 2003-2008 where reviewed by a Panel of independent scientific experts. The expert Review Panel and the Programme advisor (Professor Ian Kimber) suggested areas for future research. These recommendations were taken into consideration in planning research calls issued since 2008.

Since that time, a number of projects have completed while others have been commissioned. It was therefore considered both timely and appropriate to review the Programme formally again. The purpose of the review was to evaluate the projects that have collectively made up the Programme since 2008 (19 projects in total), and to assess their productivity and success in terms of scientific quality, impact on policy and overall value for money of the research programme under which the majority of the projects were commissioned. In addition, the Review considered the future direction of the Programme and sought to identify, in conjunction with stakeholders, possible priority areas for Agency Allergy and Intolerance Research Programme funding for the next 5 years.

4.2 Programme review meeting

The review meeting was held at the Devere hotel; Wokefield Park, near Reading from the 19th- 21st November 2012. The first 2 days of the meeting were an open meeting consisting of presentations and discussions on projects, grouped according to subject area themes. In excess of 65 participants attended the open meeting, including representatives from academia, industry, research funding organisations, research contractors and Government officials (see **Annex 1** and **2** for a list of attendees from both the open and closed meetings). Some of these participants were specifically invited because of their expertise or interests in food allergy and intolerance research or policy. The third day of the meeting was a closed session for the expert Review Panel, Agency officials and the Programme Advisor, in which projects within the Food Allergy and Intolerance Research Programme and the Programme as a whole were reviewed and recommendations made.

3 http://www.food.gov.uk/science/research/foodcomponentsresearch/allergyresearch/t07review2008/

Projects were presented and reviewed in thematic groups to indicate the policy context of the research and to show, (where relevant), how projects were linked. There were 7 different themes, with a total of 19 projects being presented over the course of the first and second day of the Review. There were opportunities for questions and discussion after each presentation as well as at the end of each theme and in addition there was also a separate Forward Look session at the end of Day 2, which allowed for all those in attendance to put forward and discuss possible future areas of research for the Programme to address. The Programme for the Review meeting can be found at **Annex 3**.

4.3 The Review Panel and Process

The expert independent Review Panel was appointed by the Agency and consisted of 6 scientific experts (including the Panel Chair) with, collectively, expertise in the fields of clinical allergy, paediatrics, immunology, Biochemistry and social science. The biographies of the Panel members can be found at **Annex 4**. Panel Members were assigned specific projects relevant to their area(s) of expertise and asked to assess these in detail prior to the Review meeting with respect to scientific quality and delivery. For each of these projects, the reviewers were provided with the relevant research call under which the work was originally commissioned, the original research proposal, scope of work (including any amendments) and pricing schedule(s). In addition and where relevant, interim and final reports were provided, as well as any other information on the progress and delivery of the projects. The reviewers' provisional assessments were submitted to the Agency in advance of the meeting. As individual projects to be reviewed were at very different stages of their life cycle, with some not yet yielding any results and others completed, it was inappropriate to assess all projects using exactly the same criteria. Therefore, reviewers were provided with 2 forms with which to complete their assessments, one for completed projects, and the other for ongoing projects.

Following presentations during the first 2 days of the meeting, reviewers has the opportunity to ask questions of clarification and to revise their comments and project evaluations accordingly.

In addition, to the reviewers' comments, the Agency assessed each project against its relevance to the Agency policy. These assessments, together with those of the reviewers, were considered and discussed during the closed meeting on the third day chaired by the Review Panel Chains, Professor Tony Frew, Professor of Allergy and Respiratory Medicine at Brighton & Sussex University Hospitals NHS Trust. During these sessions individual projects were discussed and evaluated by the Panel as a whole. All provisional project scores were finalised. It should be noted that although Agency officials were present, this was primarily to observe proceedings and to provide clarification or context to the projects where invited to do so by the Panel.

The project evaluations were followed by a Panel discussion on the scientific quality and productivity of the Programme as a whole, taking into consideration on the scores and comments of all the projects involved and how the Programme has

performed against the aims and objectives that were set in 2003 and 2007 and against Agency policy needs. There was also a separate Forward Look session at the end of day 3, where the Review Panel was invited to consider whether further research was needed in any themed areas covered by the current or past projects. This enabled the Panel to suggest possible future areas of research for the Programme in other areas of relevance to the Agency's interests in food allergy and intolerance.

A summary of the discussions and conclusions of the Panel can be found in Section 5.

4.4 Projects reviewed as part of the Allergy and Intolerance Research Programme Review

A total of 19 projects, in seven themed subject areas were reviewed. These projects are summarised in Annex **5** with more detailed summaries available in **Annex 6**. A list of publications arising from each project as of November 2012 can be found in **Annex 7**.

5. Findings of the Review

The purpose of this Section is to summarise the main findings and consensus views of the Review Panel with respect to the quality, productivity and relevance of the Food Allergy and Intolerance Research Programme on Food Allergy and Intolerance.

- The views of the Panel were considered under the following headings: Scientific Quality and Productivity of the Programme
- Delivery against the Aims and Objectives of the Food Allergy and Intolerance Research Programme
- Overall Conclusions Drawn by the Review Panel
- Impact of the Food Allergy and Intolerance Research Programme on Agency Policy

It is not the purpose of this Section to detail and consider the Panel's discussions and views on individual research projects; where relevant, this information has been shared with contractors. The purpose here is rather to summarise the views of the Panel on the Food Allergy and Intolerance Research Programme as a whole.

5.1 Scientific Quality and Productivity of the Programme

The Review Panel considered that the scientific quality of the Food Allergy and Intolerance Research Programme since the last review (February 2008) had been generally high, and in some instances of very high quality indeed. The Review Panel were of the view also that most elements of the Research Programme had been productive, and that the Programme as a whole had been very productive and delivered relevant science in a number of important areas.

The Panel also acknowledged that that the Food Allergy and Intolerance Programme comprised a number of truly groundbreaking projects with international reputations that are likely to have a very significant impact on understanding on the relationship between diet and susceptibility to food allergy. These studies, the like of which are not being conducted elsewhere in the world, were viewed by the Panel as being of considerable importance and the Agency was applauded for its foresight and for making the necessary investments.

There were, however, two important issues raised by the Panel that are summarised here.

One concern voiced by the Panel regarded the quality of the mechanistic immunology in some of the projects. As characterisation of the immunological

basis for the acquisition of sensitisation to dietary proteins and the development of food allergy is one of the aims of the Food Allergy and Intolerance Research Programme this issue will be addressed in greater detail in the next section.

The second concern raised by the Panel related to some of the social science research projects that have been commissioned by the Agency as part of the Food Allergy and Intolerance Programme. Although it was acknowledged by the Panel that in all cases these projects had delivered valuable information required by the Agency, there was, in some instances, room for improvement, specifically with respect to methodologies employed for qualitative research, and the need for consideration of research findings in the context of data available elsewhere in the published literature. The delivery of social science research projects within the Food Allergy and Intolerance Research Programme will be considered in the next section.

5.2 Delivery against the Aims and Objectives of the Food Allergy and Intolerance Research Programme

The Panel expressed satisfaction that the content, productivity and delivery of the Food Allergy and Intolerance Research Programme during the period since the last review had been generally consistent with stated aims and objectives, and that some of the outputs from the Programme have already, or are likely to be, truly influential in improving understanding and management of food allergy. In this context mention was made particularly of the LEAP and EAT studies that are both now well advanced and which were regarded by the Panel as having the potential to transform our understanding of how weaning practices and infant diet impact on the development of food allergy.

It is appropriate to summarise the views of the Panel in relation to each of the aims of the Food Allergy and Intolerance Research Programme.

To identify risk factors associated with the development of sensitisation to food proteins and the development of clinical food allergy, particularly in early life.

The Panel was of the view that the Food Allergy and Intolerance Research Programme has already made an outstanding contribution to this area through its support for the LEAP and EAT studies. As indicated above, the anticipation is that these studies are likely to provide information of considerable importance in informing our understanding of the factors that govern susceptibility to sensitisation and food allergy. The Panel voiced the opinion that in both instances the studies had been designed and conducted with considerable care and attention, and praised the industry and expertise of the contractors.

The Panel also acknowledged that a number of other projects within the compass of the Food Allergy and Intolerance Research Programme had already contributed to an improved understanding of factors that influence susceptibility to sensitisation and food allergy, or are likely to do so in the future. In this context the Panel noted the objective to improve understanding of the role of the skin, and of skin barrier function in particular, in the development

of food allergy. The latter project serves to build on the important observation from studies supported previously by the Food Allergy and Intolerance Research Programme that the skin represents a potentially important route of exposure for the acquisition of allergic sensitisation to food proteins.

Associated with this research theme was a systematic literature review supported by the Food Allergy and Intolerance Research Programme to examine the influence of early life exposure to, and avoidance of, food allergens on the subsequent development of sensitisation and allergy. This project was commissioned by the Agency to inform a review of Department of Health advice on avoidance of peanuts during pregnancy and lactation that was undertaken by the UK Committee on Toxicity (COT). The Panel viewed this as being a very well conducted study that added value to the deliberations of the COT.

To investigate the immunological mechanisms of food allergy, to understand at an immunological level what factors are important in determining/regulating the allergic versus tolerant status.

This was an area where the Panel believed that there was some room for improvement. Although the Panel were of the opinion that some immunological aspects of the projects reviewed were of a high standard, quality was not uniform, and in some instances there was evidence of lack of experience. One concern was that in some projects the immunology research elements were essentially descriptive rather than mechanistic. Moreover, in one case progress had been impaired due to an apparent lack of expertise in the relevant immunological research methodology.

It is relevant in this context to draw attention to the fact that the need for incorporation of more immunological expertise in relevant research projects had been identified by the Panel that last reviewed the Food Allergy and Intolerance Research Programme in 2008. In the light of that recommendation the Agency has developed a close alignment with the Medical Research Council (MRC) with an agreement to co-fund suitable research projects that seek to explore basic immunological mechanisms that result in sensitisation to dietary proteins and the development of food allergy. This cooperation between the Agency and MRC was launched in 2009 with a joint Workshop convened in London. Since that time several applications have been reviewed by the Agency and FSA, but thus far none has been of the standard necessary to warrant an award. The Agency continues to seek opportunities to co-fund research on immunological mechanisms in food allergy with the MRC.

It is relevant also to note here that since the recommendation made in 2008 no new research projects that contain a significant element of immunological research have been commissioned by the Agency as part of the Food Allergy and Intolerance Research Programme.

The Review Panel recognised the difficulties inherent in combining in a single project the experience and expertise necessary to deliver first rate clinical studies, including demanding intervention studies, with high level mechanistic

immunology. Nevertheless, the Panel encouraged the Agency to explore new ways in which to align clinical research with high quality immunology; one recommendation being that in future calls where there is a need for immunological expertise that there should be an explicit requirement for collaboration between clinical groups and independent immunologists in the same or different institutions.

Notwithstanding the above considerations, the Panel were of the view that the inclusion of immunological readouts in the LEAP and EAT intervention studies would provide insights into immunological processes that might be affected should changes in the incidence of clinical allergy.

To determine the prevalence of food allergy (both total food allergy and the prevalence of allergy to specific foods) in the UK - in infants, children and adults, and whether prevalence is changing over time.

The Review Panel commended the investment made by the Food Allergy and Intolerance Research Programme in supporting another UK prevalence study that provided confirmatory data about food allergy in the UK. In addition, the Panel applauded the fact that this project formed part of a wider EU FP7 programme (EuroPrevall) that sought to characterise patterns of food allergy across Europe. The Panel recognised that the alignment with EuroPrevall provided the FSA with considerable leverage and access to detailed information about the prevalence and patterns of food allergy in other European countries.

Associated with the above prevalence study was a complementary exercise designed to explore the nutritional adequacy in children of a milk exclusion diet. Although the analyses were based on data from only a small number of children the view was that the information obtained was useful insofar as the Agency were provided with reassurance that infants placed on milk exclusion diets were not at risk of nutritional insufficiency.

With a similar objective in mind a literature review was commissioned by the Food Allergy and Intolerance Research Programme to examine the nutritional adequacy for patients with coeliac disease of a gluten-free diet. The quality of research was commended, but it was recognised that the strength of the analysis was affected by the relative paucity of high quality data. Nevertheless, the conclusion drawn was that there is no evidence for any nutritional insufficiency associated with gluten-free diets and the Panel acknowledged that this allowed the Agency that to conclude that no action is required currently.

To develop suitable methods for the detection of allergens in food

Since the last review in 2008 no new research has been commissioned in this area by the Food Allergy and Intolerance Research Programme. Nevertheless, the issue remains an important one and the Panel recognised that the utility of defining management thresholds for allergens in foodstuffs was dependent upon the availability of accurate analytical methods that are both sensitive and reliable. (See Section 6. Suggestions for Future Research).

To determine the factors that influence the severity of allergic reactions to food

This remains a high priority within the Food Allergy and Intolerance Research Programme. A large study is in the process of being commissioned that is designed to examine the influence of two independent extrinsic factors (exercise and sleep deprivation) on thresholds for, and the severity of, allergic reactions to peanuts. The Review Panel recognised the importance of this research, but drew attention to the complexity of the project and of the need for rigour in experimental design.

Other research:

To work towards the definition of management thresholds

The Panel viewed very favourably a study that had been commissioned by the Food Allergy and Intolerance Research Programme with the aim of using data collected as part of the EuroPrevall project (see above) to model challenge dose distribution curves and to derive from these threshold doses for the elicitation of food allergic reactions. The Panel also found valuable the other information supplied by this project regarding the current inadequacy and unreliability of analytical methods for the measurement of allergenic proteins within foodstuffs.

To understand the value and limitations for consumers of current food allergen labelling

The Panel commended a suite of small qualitative research projects that had collectively sought to explore consumer understanding of, and reactions to, food allergen labelling. It was acknowledged that these cost-effective projects had supplied the Agency with valuable data for guiding the development of improved food labelling, and for providing advice for consumers and industry.

However, two points were raised by the Panel with regard to social science research commissioned through the Food Allergy and Intolerance Research Programme. The first was the need to ensure that such projects employ robust methodology. The second was a recommendation that contractors conducting social science research should be encouraged to consider their findings in the broader context of data available in the published literature.

Notwithstanding those comments, the Review Panel acknowledged the importance to the Agency of a clear understanding of consumer reactions to food labelling, and recognised the value of the information that had been collected through the Food Allergy and Intolerance Research Programme.

To evaluate the effectiveness of FSA guidance

The Panel commended as being of very high quality two small projects commissioned through the Food Allergy and Intolerance Research Programme to evaluate the effectiveness of guidance given by the FSA on allergen management and consumer information, and on allergen information of pre-

packed foods. It was recognised by the Panel that these projects had delivered valuable information to the Agency that will guide future policy.

5.3 Overall Conclusions Drawn by the Review Panel

The Panel was of the view that during the period since the previous review the Food Allergy and Intolerance Research Programme had delivered high quality research.

The Panel also concluded that the Programme had provided excellent value for money and had succeeded in addressing important policy issues identified by the Agency.

Finally, the Panel complimented the Agency on managing so effectively such a broad palette of diverse research projects.

The two issues raised by the Panel, and discussed earlier in Section 5 (the need to have access to stronger mechanistic immunology, and the recommendation that social science research should employ robust methodology and consider data generated in the context of information available elsewhere in the published literature), will receive the full attention of the Food Allergy and Intolerance Research Programme.

5.4 Impact of the Food Allergy and Intolerance Research Programme on Agency Policy

As part of the review process Agency staff had independently assessed each of the research projects commissioned during the period since the review in 2008. Although there was some variation between individual projects with regard to the extent to which they had met the needs identified by the Agency, overall, there was found to be a high level of delivery against policy requirements.

In summary the Agency was of the view that important policy needs in the following areas have been addressed, or will be addressed when projects have been completed:

- *Factors influencing susceptibility to sensitisation and food allergy,*
- *the prevalence of food allergy in the UK,*
- *the impact of nutrition on the development of food allergy,*
- *the nutritional adequacy of exclusion diets,*
- *the impact of skin exposure on allergic sensitisation,*
- *the influence of extrinsic factors on the severity of, and thresholds for, allergic reactions to peanuts,*
- *progress towards the identification of management thresholds,*
- *the value and limitations - and customer perceptions of – current allergen food labelling*

6. Suggestions for Future Research for the Food Allergy and Intolerance Programme

The Programme Review meeting allowed all those in attendance to make recommendations to the Agency regarding the future funding for the Food Allergy and Intolerance Research Programme.

To inform discussions, all meeting participants were invited to consider the following question prior to the meeting: -

What one thing would make a real difference to those with food allergy and/or food intolerance?

During the closed session on the third day, the Review Panel also discussed this topic. Suggestions made during the Horizon Scanning session on the 2nd day of the meeting were taken into consideration and a number of recommendations for future research were made.

The Review Panel were unanimous in identifying the importance of continued support for the Food Allergy and Intolerance Research Programme.

The Review Panel believed that the Programme had delivered important and highly relevant information in several areas during the last five years and that this information had informed Agency policy and contributed significantly to an understanding of food allergy and intolerance.

Given the current portfolio of research projects, it was the Panel considered that the Programme will continue to have an important impact during the coming 5 years.

The majority of recommendations made for future research can be categorised into seven themed areas (as outlined below). The Panel commented on the importance and relevance of the themes, and they also highlighted a small number of other areas of research that might be considered. Finally several general recommendations were made regarding the commissioning, management and dissemination of research.

It should be noted that some of the areas that were suggested for future research, and which are detailed below, may fall outside the remit of the Programme. However, they have been included in this report for completeness and since they may inform research planning and prioritisation processes by other funders with an interest in food allergy and intolerance.

Risk Assessment and Use of Precautionary Allergen Labelling

The Panel recognised the significant amount of work being undertaken by the Agency to assist the international community in deriving allergen management thresholds. In advance of threshold levels being adopted by industry, it was considered that the Agency should undertake research in partnership with a range of relevant stakeholders to establish the descriptors that should be used by industry (particularly on food labels) to communicate these issues effectively to the consumer. The Panel highlighted that consumer understanding of the possible new descriptors is of great importance in allowing them to manage their condition effectively. The Panel was also of the opinion that research should also be conducted to understand how to communicate the changes that will be introduced to consumers. It was emphasised that there was a need for the Agency and/or other relevant Government Departments to involve healthcare professionals in the development of this policy, as well as ensuring they are provided with appropriate training regarding the meaning of new labels, so this can be communicated effectively to the allergic consumer by health care professionals.

It was recognised by the Panel that consideration needs to be given to portion size when agreeing allergen management threshold levels. An information gap currently exists on the size of the food portions eaten by the allergic consumer at a single eating occasion. This information is required to convert threshold doses to maximum concentration levels in particular types of food. It was therefore considered that research could be conducted to establish food consumption patterns and intake among the allergic population. However, it was recognised that compared with other areas of research, this would not be a priority for the Agency at this time, and that other organisations may be better placed to fund such studies. If the Agency did consider it was appropriate to fund research in this area, the Panel recommended that a collaborative approach to funding be considered.

Provision of Information and Advice to Consumers and Industry, Particularly With Regard to the Food Information for Consumers Regulation

The Panel considered this was a key area of research for the Agency over the next few years.

It was recommended that the Agency undertake an education campaign to inform consumers, industry (particularly the catering sector) and healthcare professionals about the changes that will be introduced when the Food Information for Consumers Regulation (FIR) comes into effect. The Panel agreed that research could be undertaken to establish how best to communicate these changes to the range of stakeholders.

The Panel recommended that the Agency consider conducting research to evaluate the understanding and impact of the new requirements amongst consumers. Particular focus should be given to the provision of food allergy information in catering establishments and understanding consumer choices when eating out.

The Panel also considered that the changes that would be introduced on food labels over the next few years could be used as a platform to test interventions in the labelling industry. These findings could be used more widely to determine how best to communicate food label changes to consumers. It was agreed that this research would not necessarily be for the Agency Food Allergy and Intolerance Research Programme to fund.

It was also considered by the Panel that there may be some benefit in undertaking a general piece of research to consolidate existing knowledge about provision of information for food allergic consumers that could be used to inform generic guidelines and emerging issues.

As a separate issue, the Panel also recognised the need to promote greater awareness/knowledge and consistency in approach in the management of food allergy in schools. However, it was agreed that this does not fall within the remit of the Agency.

The Basis for Differences in Susceptibility and Severity of Reaction

The Panel considered that further research was required to provide greater understanding of the mechanisms that determine the severity of allergic reactions. Of particular importance is identification of the factors that prevent individuals with demonstrable sensitisation to food proteins (i.e. high allergen specific IgE) from manifesting an allergic reaction.

The Panel also suggested that there would be benefit from identifying biomarkers that could be used for predicting the severity of allergic reactions to foods. It is important to be able to identify those individuals that are at greatest risk of mounting severe allergic reactions to food. Further research in this area would enable the development of appropriate strategies, including more targeted advice to help those most at risk.

Importance of Route and Timing of Exposure to Food Allergens

The Panel acknowledge the very significant contribution that the Programme is making to identification of the risk factors associated with the development of sensitisation and food allergy. The Panel agreed that this should be a continued focus for the Programme over the next 5 years.

The Panel stressed the importance of having a complete evidence base before changing UK infant feeding advice for the prevention of allergic disease. They recommended that both the EAT and LEAP study cohorts are followed up to establish the longevity and breadth of any protective effect observed. Of particular importance is establishing whether long term tolerance has been achieved, and whether such tolerance is allergen or disease specific.

The Panel also emphasised the importance of studying children who are sensitised at an early age (such as those children in the EAT and LEAP studies who are sensitised at 3/4 months of age). Exposure patterns in the first few months of life could be studied as well the success of interventions aimed at preventing the development of allergic disease. This research may allow the Agency to characterise how and why this 'at risk' group of children have become sensitised, which in turn, would be important for establishing the safety of the early introduction of allergenic foods, before any policy changes are considered.

Improved clinical Provision for Food Allergy

Improved clinical provision for food allergy was not discussed to any extent by the Review Panel because it was considered to be outside the remit of the Agency. However it was recognised that patients would benefit from improved food allergy diagnosis and advice to manage the condition. Healthcare professionals would also benefit from improved training and education with regard to food allergy. It was suggested that given the broad spectrum of conditions that health professionals are expected to cover, and the limited time that can be dedicated to food allergy, that educational material needs to be compact and succinct. The Panel advised that the Agency make these recommendations to the relevant Government Departments.

Adult Food Allergy

The Panel commented that the Food Allergy and Intolerance Research Programme to date had focussed heavily on food allergy/intolerance in children which is when the condition tends to manifest in the majority of cases and is most prevalent. It was considered that there would be merit in conducting a review of adult food allergy. The Panel recommended that a clinic or a population based study could be undertaken to establish the prevalence and characteristic of food allergy in adults. It was recommended that before commissioning research in this area, the Agency should review the information collected about food allergy in adults as part of Europrevall.

The Panel strongly recommended that research should also be undertaken to understand why people develop food allergies later in life, what routes of exposure are relevant, and why it is that individuals acquire allergy to foods that they have previously eaten for long periods without ill effect. This would inform Agency advice to consumers regarding adult food allergy.

Analytical Methods

The Panel were unanimous that the Agency had an important role to play in undertaking research to the fill some of the knowledge gaps in this area. As the Agency has only a limited budget there would be a need to consider which areas of work to take forward to ensure maximum impact on policy. The Panel also recognised that some of the suggested areas were outside the remit of the Agency, or should be funded in collaboration with other organisations.

It was agreed by the Panel that there was a need to focus on improving and addressing the current limitations of analytical methodologies for detecting and quantifying allergens in food. This would aid enforcement and protection of consumers, particularly when food allergen management thresholds levels are adopted. The following areas of research were identified for consideration by the Agency: -

- Improvement of currently available methods for allergen testing with a focus on sensitivity and accuracy.
- The development of reliable reference materials for the major allergenic foods, to calibrate methods.
- Characterisation of the effect of food matrix on both allergenicity and on performance of methods.
- The development of new methods utilising other technologies.

Other Areas of Work and Recommendations

The Panel also considered other areas of potential importance to the Food Allergy and Intolerance Research Programme that are outside the current themes of work, and made several general recommendations regarding commissioning research in the future.

Relevant Expertise

The Panel reiterated a recommendation made at the 2008 Programme Review meeting. The Agency should always ensure research teams have the right balance and breadth of scientific expertise, or have access to it via collaboration. This should be in place at the outset of new projects in order to maintain high scientific quality and success, particularly where projects cover several different scientific areas. Although this has improved significantly since the last Programme Review, and the current portfolio has the relevant expertise included, the Agency should remain vigilant and ensure the appropriate balance of expertise is available during all stages of a projects life.

Collaboration

The Agency should continue to seek out opportunities to collaborate with other relevant funding bodies when commissioning research on food allergy and intolerance.

Social research

The Panel suggested that, before social research is commissioned by the Food Allergy and Intolerance Research Programme, a review of the evidence base in the area of interest is undertaken. This would help to identify evidence gaps and minimise the risk of duplication. The Panel also recommended that the Agency undertake research to inform communications with consumers on scientifically complicated areas.

The Panel made a general point about ensuring appropriate and extensive dissemination of the outcomes of Food Allergy and Intolerance funded social research. It was considered that a number of the social science projects funded by the Programme had important results which would be of interest to both scientific and non-scientific audiences. In future researchers should disseminate their findings through relevant publications to ensure maximum impact.

Food Intolerance

The Panel considered that much of the Programme's research had previously focused on food allergy and there would be merit in undertaking more research to increase the understanding of food intolerance. This could include studies to characterise the disorders and establish prevalence. The Panel also recommended that work could be undertaken to ascertain whether elimination diets (such as low fermentable oligo, di- and mono-saccharides and polyols diets) are effective in the managing such conditions. The Panel recognised that the ability to undertake such research is hampered by limitations in reliable diagnostics for many forms of food intolerance.

Food Matrix

The Panel considered that further research could be undertaken to understand more fully the effect of food processing and food matrix on protein structure/conformation and on protein allergenicity. It was considered that this could be important in improving food allergen risk assessment and risk management practices.

Quality of life

The Panel made a general point that research could be undertaken to measure the impacts of food allergy and intolerance policy and advice in terms of quality of life and health economic impacts.

Register of Food Allergic Reactions

As had been highlighted in the previous Programme Review, the Panel suggested that it would be helpful for the UK to develop a severe reactions register to record food allergic reactions. However, it was recognised that this

would not be within the remit of the Agency to set up and manage this register. It was suggested that the Agency made this recommendation to the relevant Government Department.

7. Conclusions and Way Forward

The Agency's work on food allergy and intolerance aims to protect food allergic and food intolerant consumers and to help them to make informed choices about food, as well as advising families with children at risk of developing food allergy. The outputs of research funded by the Food Allergy and Intolerance Research Programme over the last 5 years have collectively served to improve the advice given by the Agency to consumers with food allergies, in several different areas, as outlined above. The Programme has also made very significant contributions to increasing scientific knowledge in several key areas, including the prevalence of food allergy in the UK, the impact of nutrition on the development of food allergy, the nutritional adequacy of exclusion diets, the impact of skin exposure on allergic sensitisation to food proteins, the value and limitations - and customer perceptions of – current allergen food labelling, and progress towards the identification of management thresholds. In addition, a recently commissioned project will inform understanding on the influence of extrinsic factors on the severity of, and thresholds for, allergic reactions to peanuts,

Looking forward to the next 5 years of the Programme's life, the Agency will reflect on the valuable comments and recommendations that have been made by the Review Panel about the performance, productivity and scientific quality of the Programme, with the hope of improving the Programme even further in the future.

With regard to the suggested areas for future research, these have been considered carefully by the Agency alongside other criteria and requirements in formulating a forward plan. As part of this process, all ideas put forward during both Horizon Scanning sessions at the Review meeting have been considered by the Agency against the remit of the Programme and of the wider Agency, the strength of the policy need, feasibility and the available budget. Our knowledge of research that is already being undertaken by other organisations or funding bodies on food allergy and intolerance has also been taken into account.

The result of these considerations is that a number of different areas were considered to be of particular importance, as listed below. It must be noted that this is not an exhaustive or exclusive list of the activities/funding areas that the Programme will embrace during the next 5 years and beyond, but rather a list of those areas that have been identified as being of particular importance for us to address in the short to medium term. Further developments in our scientific knowledge and/or changing or new policy needs may well emerge which will influence the Agency's decisions about specific areas in which to call for research and at what time in the future.

Areas of focus of the Food allergy and Intolerance programme for the next 5 years: -

- Timing and route of exposure to food allergens. If the EAT and/or LEAP intervention studies show significant effects, it will be a high priority to follow this up in order to:
    - determine whether changes in prevalence are transient or long-lived,
    - determine whether changes in susceptibility to food allergy are specific or non-specific, and
    - monitor longitudinal changes in relevant immunological metrics.

- Adult allergy. It is important to understand better the prevalence of food allergy in adulthood and to determine why food sensitisation and allergy can develop later in life, after the food had been tolerated for many years. The Agency intends to hold an initial workshop to discuss these issues and better focus the questions for subsequent specific research calls.

- Food Intolerance. This research programme has mainly concentrated on IgE-mediated food allergy in recent years, with some work on coeliac disease. The prevalence and impact of food intolerances other than to gluten and lactose are poorly understood at the present time. The Agency intends to hold a workshop to explore this area and to identify key issues that could realistically be investigated further via subsequent specific research calls.

- Social science research. There is a continuing need to investigate consumer understanding of food allergen labelling and information provisions, particularly in relation to the changes being introduced by the Food Information for Consumers Regulation in relation to the food service sector. The impact of these changes will also need to be evaluated.

In the longer term, other areas identified for investigation were:

- Work collaboratively to address the current limitations of analytical methodologies for detecting and quantifying allergens in food. This would aid enforcement and protection of consumers, particularly when food allergen management thresholds levels are adopted. This could include work to improve the sensitivity and accuracy of currently available methods for allergen testing; development of reliable reference materials for the major allergenic foods, to calibrate methods; characterisation of the effect of the food matrix on both allergenicity and on performance of methods and the development of new methods utilising other technologies.

- The basis for inter-individual differences in susceptibility to food allergy, and in the severity of food allergic reactions, focussing on life-style or environmental factors rather than genetic predisposition. The identification of biomarkers that predict/reflect the likely severity of food allergic reactions.

- Investigation of the basis for the absence of a close correlation between the level of specific IgE antibodies and the manifestation of clinical food allergy, particularly the mechanisms that prevent the elicitation of food allergic reactions in subjects that are sensitised.

ANNEX 1

Attendees for Day 1 and Day 2 of the Review Meeting

Dr Alan Mackie		Institute of Food Research (IFR)
Dr Alick Stephens		King's College London
Prof Allan Mowat	Review Panel Member	University of Glasgow
Dr Andy Clark		University of Cambridge
Ann Whalley		People Partnership
Prof Anthony Frew	Review Panel Chairman	Royal Sussex County Hospital
Prof Aziz Sheikh		Royal College of GPs
Barbara Hirst		Reading Scientific Services Ltd. (RSSL)
Dr Carina Venter	Review Panel Member	University of Portsmouth
Prof Christine Edwards		University of Glasgow
Dr Chun-Han Chan		Food Standards Agency
Prof Clare Mills		University of Manchester
Clifton Gay		Food Standards Agency
Dr David Gott		Food Standards Agency
Erin Oliver		University of Southampton
Gemma Jones		Reading Scientific Services Ltd. (RSSL)
Prof Gideon Lack		King's College London
Gimara Duncan		Food Standards Agency
Prof Graham Roberts		University of Southampton
Mrs Hazel Gowland		Allergy Action
Prof Ian Kimber	Programme Advisor	University of Manchester
Ms Isabel Skypala		Royal Brompton & Harefield NHS Trust
Dr Jacqui Oakley		Medical Research Council (MRC)
James Flack		Jigsaw Research
Dr Jane Ince		Food Standards Agency
Dr Jane Lucas		University of Southampton
Jessica Sage		Reading Scientific Services Ltd. (RSSL)
Joanna Topping		Laboratory of Government Chemists (LGC)
Joceline Jones		Define Research & Insight Ltd
Dr Joelle Buck		Food Standards Agency
Prof Jonathan Hourihane		University College Cork
Dr Julie Barnett		Brunel University
Karen Brunas		Patient Representative

Prof Kirsten Beyer	Review Panel Member	Charité Universitätsmedizin Berlin
Dr Kirsty Logan		King's College London
Lindsey McManus		Allergy UK
Prof Lynn Frewer	Review Panel Member	Newcastle University
Lynne Regent		Anaphylaxis Campaign
Dr Maeve Kelleher		University College Cork
Dr Marty Blom	Review Panel Member	TNO
Mervyn Briggs		Food Standards Agency
Dr Michael Perkin		King's College London
Michael Walker		Laboratory of Government Chemists (LGC)
Moira Austin		Anaphylaxis Campaign
Nathalie Shapiro		Food Standards Agency
Norma McGough		Coeliac UK
Prof Pam Ewan		University of Cambridge
Dr Paul Turner		University College London
Peter Millard		Premier Foods
Rachel Elsom		Department of Health
Rachel White		Department of Health
Dr René Crevel		Unilever
Dr Robert Boyle		Imperial College London
Prof Robert Smith		COT Lay member
Ros Payne		Creative Research
Russell Napier		Food Standards Agency
Dr Sabita Islam		University of Cambridge
Sarah Hardy		Food Standards Agency
Selina Paine		Food and Drink Federation (FDF)
Shuhana Begum		Food Standards Agency
Simon Flanagan		Reading Scientific Services Ltd. (RSSL)
Stephen Hendry		Food Standards Agency
Stephen Pugh		Department of Environment, Food and Rural Affairs (DEFRA)
Sue Hattersley		Food Standards Agency
Terry Donohoe		Food Standards Agency
Dr Victor Turcanu		King's College London
Victoria Page		Define Research & Insight Ltd

ANNEX 2

Closed Session Attendees (Day 3)

The review panel compromised of 6 independent experts with relevant experience in allergy and immunology.

Chairman

Professor A Frew	Royal Sussex County Hospital

External reviewers

Professor K Beyer	Charité Universitätsmedizin Berlin
Dr C Venter	University of Portsmouth
Professor A Mowat	University of Glasgow
Dr M Blom	TNO
Professor LJ Frewer	Newcastle University

Programme Advisor

Professor Ian Kimber	University of Manchester

FSA Officials

Mrs Sue Hattersley	Food Allergy Branch
Dr. Joelle Buck	Food Allergy Branch
Dr Chun-Han Chan	Food Allergy Branch
Ms Sarah Hardy	Food Allergy Branch
Ms Shuhana Begum	Food Allergy Branch
Ms Nathalie Shapiro	Food Allergy Branch
Dr. Jane Ince	Chief Scientist Team
Mr. Clifton Gay	Statistics Unit
Ms Helen Atkinson	Social Science Unit

ANNEX 3

Programme for FSA Food Allergy & Intolerance Research Programme Review Meeting

Please note that the current affiliation of the presenter for each project has been given in the programme of events. In some cases this is different from where the work was conducted.

Monday 19th November

Day One: Registration and Introduction

12.00 – 1.00	Lunch and Registration	
1.00 – 1.10	Welcome and Introduction to FSA strategic aims and policy needs on food allergy & intolerance	Mrs Sue Hattersley *(Food Standards Agency)*
1.10 – 1.20	Establishment and Evolution of the Food Allergy and Intolerance Research Programme	Professor Ian Kimber *(Programme Advisor)*

Day one: Presentations on themes of research

Session One	**Research Theme: Prevalence**	
1.20 – 1.25	Introduction to research need	Professor Ian Kimber *(Programme Advisor)*
1.25 – 1.50	T07046: The Prevalence of food allergy and weaning practices in a birth cohort of UK infants	Professor Graham Roberts *(University of Southampton)*
1.50 – 2.05	Questions	
Session Two	**Research Theme: Nutrition and food allergy**	
2.05 – 2.10	Introduction to research need	Professor Ian Kimber *(Programme Advisor)*
2.10 – 2.20	T07046 addendum: Additional analysis of infant dietary data to investigate the nutritional adequacy of a milk exclusion diet	Erin Oliver *(University of Southampton)*
2.20 – 2.25	Questions	
2.25 – 2.40	T07053: A systematic literature review on the nutritional adequacy of a typical gluten-free diet, with particular reference	Norma McGough *(Coeliac UK)*

	to , iron, calcium, folate and B vitamins	
2.40 – 2.50	Questions	
2.50 – 3.05	Tea & Coffee Break	
Session Three	**Research Theme: Development of management thresholds for allergenic foods to inform risk assessment and risk management practices'**	
3.05 – 3.10	Introduction to research need	Professor Ian Kimber *(Programme Advisor)*
3.10 – 3.35	T07062: Management of food allergens: from threshold doses to analysis in foods	Professor Clare Mills *(University of Manchester)*
3.35 – 3.50	Questions	
3.50 – 4.10	T07067: Survey of allergen labelling and allergen content of UK retail pre-packed processed foods.	Barbara Hirst *(Reading Scientific Services (RSSL))*
4.10 – 4.20	Questions	
4.20 – 4.45	T07068: The effect of extrinsic factors on food allergy: Ex-Factor	Dr Andy Clark *(University of Cambridge)*
4.45 – 5.00	Questions	
7.30 – 9.00	Dinner for all participants	

Tuesday 20th November

Day Two: Presentations on Themes of Research

Session Four	**Research Theme: Route and Timing of exposure to food allergens in early life including maternal factors**	
08.30 – 08.35	Introduction to research need	Professor Ian Kimber *(Programme Advisor)*
08.35 – 08.55	T07052: Systematic review of literature on early life patterns of exposure to and avoidance of food allergens and later development of sensitisation and clinical allergy, with particular reference to peanut allergy	Dr Joelle Buck *(Food Standards Agency)*
08.55 – 09.05	Questions	
09. 05 – 09.35	T07051: Randomised controlled trial of early introduction of allergenic foods to induce tolerance in infants (EAT Study)	Dr Michael Perkin *(King's College London)*

09.35 – 09.50	Questions	
09.50 – 10.15	T07060: Investigation of the association of skin barrier structure and function and the development of food allergy. A prospective birth cohort study.	Dr Maeve Kelleher *(University College Cork)*
10.15 – 10.25	Questions	
10.25 – 10.40	Tea & Coffee Break	
Session five	**Research Theme: Immunological aspects of food allergy**	
10.40 – 10.45	Introduction to research need	Professor Ian Kimber *(Programme Advisor)*
10.45 – 11.10	T07049 : Characterisation of the immune mechanisms involved in the induction of oral tolerance to peanuts in children	Dr Victor Turcanu *(King's College London)*
11.10 – 11.25	Questions	
11.25 –11.45	T07041: The role of peanut-specific T cell responses in children with peanut allergy and in children who are tolerant to peanuts	Dr Victor Turcanu *(King's College London)*
11.45 – 11.55	Questions	
11.55 – 12.10	T07042: Study of T cells in allergy and resolution	Dr Sabita Islam *(University of Cambridge)*
12.10 – 12.20	Questions	
12.20 – 1.20	Lunch	
Session six	**Research Theme: Food allergen labelling and consumer choice research**	
1.20 – 1.25	Introduction to research need	Professor Ian Kimber *(Programme Advisor)*
1.25 – 1.45	T07058: Understanding the food choice reasoning of nut allergic consumers	Dr Julie Barnett *(Brunel University)*
1.45 – 1.55	Questions	
1.55 – 2.15	T07059: Consumer understanding of new labelling terms for foods marketed for people with gluten intolerance	Joceline Jones *(Define Research & Insight Ltd)*
	T07065: Consumer understanding of	Victoria Page

	additional labelling terms for foods without cereals containing gluten as ingredients	*(Define Research & Insight Ltd)*
2.15 – 2.25	Questions	
2.25 – 2.40	T07061: Consumer understanding of revised government advice concerning peanut consumption in early life	Ann Whalley *(People Partnership)*
2.40 – 2.50	Questions	
2.40 – 2.55	T07064: Understanding of food labelling terms used to indicate the absence or reduction of lactose, milk or dairy	Ros Payne *(Creative Research)*
2.55 – 3.05	Questions	
3.05 – 3.20	Tea and Coffee break	
Session seven	**Research Theme: FSA best-practice industry guidance**	
3.20 – 3.25	Introduction to research need	Professor Ian Kimber *(Programme Advisor)*
3.25 – 3.45	T07057: Evaluation of the effectiveness of the best practice guidance on allergen management and consumer information	James Flack *(Jigsaw Research)*
	T07063: Guidance on the provision of allergen information for non pre-packed foods evaluation	James Flack *(Jigsaw Research)*
3.45 – 3.55	Questions	
Session eight	**Forward look discussion**	
Chair –Professor Ian Kimber		
3.55 – 4.05	Introduction to Forward Look session	Dr Joelle Buck *(Food Standards Agency)*
4.05 – 4.50	Forward Look discussion for contractors and other review participants	
4.50 – 5.00	**Close of meeting for contractors and delegates**	

Wednesday 21st November 2012

Day Three: Closed meeting for Review Panel and FSA staff only

ANNEX 4

Biographies of the 2012 Food Allergy and Intolerance Research Programme Review Panel

Chair of the Review Panel

Professor Anthony Frew

Anthony Frew is professor of allergy and respiratory medicine at Brighton & Sussex University Hospitals NHS Trust. He qualified in Medicine in 1980 and completed his MD thesis on mechanisms of allergic inflammation in 1989. Since 2005 he has been in Brighton where he has a busy clinical practice in allergy, respiratory and general medicine.

His main research interests have been clinical trials of allergen immunotherapy and the health effects of air pollution. He served for seven years on the editorial board of JACI (3 years as associate editor) and was until recently an associate editor of Allergy. He is currently president of the British Society for Allergy & Clinical Immunology.

Review Panel Members

Professor Kirsten Beyer

Kirsten Beyer qualified as a MD at the Free University in Berlin, Germany, in 1991. She carried out her pediatric training and fellowship at the Humboldt University in Berlin. From 1996-1997 she became a visiting scientist at the Division of Allergy & Clinical Immunology at Johns Hopkins, University in Baltimore, USA. From 1997-2003 Dr. Beyer worked at the Division of Pediatric Allergy & Immunology at Mount Sinai School of Medicine, New York, where she was appointed as an Assistant Professor of Pediatrics in 2001. In 2003 she returned to Berlin where she is appointed Professor at the University Hospital Charité.

Prof. Beyer is a member of numerous national and international organizations. Her research experience spans the spectrum of paediatric allergy with a particular focus on food allergy. Her interests include food allergy prevention, as well as its diagnosis and treatment. She is principle investigator on several national and international studies. Currently, her group is studying the induction of oral tolerance through oral immunotherapy in food allergic children. Another project is investigating the early food allergen avoidance strategies, using a randomized placebo-controlled study design. Moreover, Prof. Beyer started within the EU-funded project EuroPrevall the first European birth cohort of over 12,000 babies with the main focus on food allergy.

Dr Carina Venter

Dr Venter is a registered dietitian in the UK and USA and gained her PhD in 2007: *Food Hypersensitivity amongst children on the Isle of Wight - An in depth dietary investigation* from the University of Southampton United Kingdom. This was a study funded by the Food Standards Agency.

Dr Venter is currently employed as a NIHR Post Doctorate Research Fellow at the University of Portsmouth and provides weekly dietetic cover to two allergy clinics (one adult and one paediatric) on the Isle of Wight. Her current role also includes Food Allergy Module Leader on the MSc in Allergy at the University of Southampton. She is chair of the British Dietetic Association's Food Allergy and Intolerance Specialist Group and a member of the British Society of Allergy and Clinical Immunology Council. Dr Venter is also an Allied Health Interest Group Board member of the European Academy of Allergy and Clinical Immunology and a member of the American Academy of Allergy, Asthma and Immunology.

Dr Venter has authored many book chapters and papers in food allergy and is co-author of the book: Food Hypersensitivity: Diagnosing and Managing Food Allergies and Intolerances.

Professor Allan Mowat

Allan Mowat is Professor of Mucosal Immunology at the University of Glasgow and Consultant Clinical Immunologist at Gartnavel General Hospital. He trained in Medicine in Glasgow, followed by a PhD in Immunology at the University of Edinburgh and then an MRCPath in Immunology.

He has been involved in experimental research into the cellular basis of immune responses in the intestine for more than 30 years and current interests focus on the roles of dendritic cells and macrophages in intestinal health and disease. He also has a large teaching load and has an NHS contract in Diagnostic Clinical Immunology.

Professor Lynn Frewer

Professor Lynn J. Frewer has a background in psychology. Lynn is currently Professor of Food and Society at Newcastle University. Previously she was professor of Food Safety and Consumer Behaviour at the University Of Wageningen (where she still has an emeritus chair) and Head of the Consumer Science Group at the Institute of Food Research in the UK.

Lynn has research interests focused on understanding societal and individual responses to both risk and benefit, in particular linked to the agrifood sector. Current research activities focus on understanding how people make decisions about the risks and benefits associated different dietary choices, and how to develop effective communication about these issues, understanding citizen attitudes to emerging technologies such as nanotechnology, and developing best practice in stakeholder and citizen consultation linked to risk governance. Other research activities include research directed towards understanding the impact of legislative changes on the food chain actors as well as the broad socio-economic impact of some important public health issues (for example, food allergy or domestic food hygiene preparation practices).

A particular focus of Lynn's research relates to developing interdisciplinary activities between the social and natural sciences. Lynn has published over 160 refereed journal articles and edited 5 books in these areas. In the area of food allergy, Lynn has conducted research in the area of societal acceptance of novel foods and processes designed to alleviate food allergies, risk perception and communication (including labelling), socio-economic impact of food allergy, and policy development and regulation associated with consumer protection.

Dr Marty Blom

Dr Marty Blom achieved her PhD in Cellular Toxicology in 2000 at Leiden University, The Netherlands investigating various cellular mechanisms leading to cell death during liver toxicity and obtained the registration as Toxicologist. From 1998-1999 she worked as risk assessor for the National Institute for Public Health and the Environment, The Netherlands. In 1999 she joined a multinational food company and until 2007 she delivered expert knowledge on immune responses of a variety of compounds for the introduction of new food products to the market and coordinated the laboratory studies at the cellular level and in humans. In 2007 she started as risk assessor of food allergens at TNO, The Netherlands, and she is currently portfolio manager within the Food Safety program of TNO coordinating Food Allergy projects.

The focus is on developing accepted statistical methods and the scientific evidence to assess the potential risk of allergens/proteins for the allergic consumer, in close collaboration with (inter-) national clinical scientists, governments and food companies. A large part of the work is focused on working towards an accepted quantitative guidance for may contain warning on products containing accidental traces of allergens and development and maintenance of a threshold database.

More recently her interest is on developing probabilistic methods to predict the allergenicity of new proteins or protein sources and thereby supporting the safe introduction of these in our daily food. She participated in the National Working Group on May Contain Labeling in The Netherlands, and is an active member of the Utrecht Center for Food Allergy since 2009 in which scientists from

university, research institutes and hospital closely work together to identify biomarkers of food allergy.

Food Allergy and Intolerance Research Programme Advisor

Professor Ian Kimber

Ian Kimber has been the Programme Advisor to the Food Allergy and Intolerance Research Programme since the Agency's inception in 2000.

Ian Kimber is currently Professor of Toxicology and Associate Dean for Business Development in the Faculty of Life Sciences at the University of Manchester.

Previous to that he was Head of Research and Principal Fellow at the Syngenta Central Toxicology Laboratory.

He has broad research interests based around immunotoxicology, including: (a) the characteristics of allergy caused by chemical, drugs and proteins, (b) cutaneous immune responses and the roles played by Langerhans cells (c) functional subpopulations of T lymphocytes and (d) the development and evaluation of novel approaches to safety assessment.

Professor Kimber holds, and has held, a variety of positions on national and international expert and scientific advisory committees. Currently these include the following: Member UK Medicines and Healthcare products Regulatory Agency

(MHRA) Committee for Safety of Devices, Programme Advisor Food Standards Agency Food Allergy and Intolerance Research Programme and Member of the Executive Committee of the MRC Centre for Drug Safety Sciences. Professor Kimber is also President of the British Society for Toxicology, and is Chairman of the Board of the UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs).

He has published over 570 research papers, review articles and book chapters and serves currently on the editorial boards of toxicology, immunology, dermatology and pathology journals.

Professor Kimber has received a number of awards and prizes. These include: the SmithKline Beecham Laboratory Animal Welfare Prize (2000) (jointly with David Basketter and Frank Gerberick), the 9th Robert A Scala Award in Toxicology (2001), the Doerenkamp-Zbinden Foundation Prize for Realistic Animal Protection in Biomedical Research (2001), Society of Toxicology Enhancement of Animal Welfare Award (2003) (jointly with Frank Gerberick), and Society of Toxicology Immunotoxicology Career Achievement Award (2005).

In 2010 Professor Kimber received the Bo Holmstedt Memorial Fellowship Award and Lecture at the International Congress of Toxicology.

In 2011 Professor Kimber was awarded an OBE in the Queen's Birthday Honours list for services to science.

ANNEX 5

Projects and Themes reviewed at the 2012 programme review

THEME – PREVALENCE					
Project Code	**Project Title**	**Organisation**	**Lead Contractor**	**FSA Project Officer**	**Project Duration**
T07046	The prevalence of food allergy and weaning practices in a birth cohort of UK infants	University of Southampton	Professor Graham Roberts	Dr Joelle Buck/Sarah Hardy	August 2005 to October 2009

THEME – NUTRITION AND FOOD ALLERGY					
Project Code	**Project Title**	**Organisation**	**Lead Contractor**	**Project Officer**	**Project Duration**
T07046 addendum	Additional analysis of infant dietary data to investigate the nutritional adequacy of a milk exclusion diet	University of Southampton	Professor Graham Roberts/Dr Kate Grimshaw	Dr Joelle Buck/Sarah Hardy	August 2005 to January 2011
T07053	A systematic literature review on the nutritional adequacy of a typical gluten-free diet, with particular reference to , iron, calcium, folate and B vitamins	Coeliac UK	Norma McGough	Sarah Hardy	March 2008-September 2008

THEME - DEVELOPMENT OF MANAGEMENT THRESHOLDS FOR ALLERGENIC FOODS TO INFORM RISK ASSESSMENT AND RISK MANAGEMENT PRACTICES					
Project Code	**Project Title**	**Organisation**	**Lead Contractor**	**Project Officer**	**Project Duration**
T07062	Management of food allergens: from threshold doses to analysis in foods	Institute of Food Research (IFR) /University of Manchester	Professor Clare Mills	Dr Chun-Han Chan	December 2009- February 2012
T07067	Survey of allergen labelling and allergen content of UK retail pre-packed processed foods	Reading Scientific Services	Barbara Hirst	Nathalie Shapiro	May 2012- May 2013
T07068	The effect of extrinsic factors on food allergy: Ex-Factor	University of Cambridge	Dr Andy Clark	Nathalie Shapiro	April 2012 - August 2016

THEME- ROUTE AND TIMING OF EXPOSURE TO FOOD ALLERGENS IN EARLY LIFE INCLUDING MATERNAL FACTORS					
Project Code	**Project Title**	**Organisation**	**Lead Contractor**	**Project Officer**	**Project Duration**
T07052	Systematic review of literature on early life patterns of exposure to and avoidance of food allergens and later development of sensitisation and clinical allergy, with particular reference to peanut allergy	British Nutrition Foundation	Professor Judy Buttriss	Dr Joelle Buck	October 2007- May 2008
T07051	Randomised controlled trial of early introduction of allergenic foods to induce tolerance in infants (EAT Study)	King's College London	Professor Gideon Lack	Shuhana Begum	15th January 2008- 31st May 2015
T07060	Investigation of the association of skin barrier structure and function and the development of food allergy. A prospective birth cohort study	University College Cork	Professor Jonathan Hourihane	Shuhana Begum	July 2009- October 2013

THEME – IMMUNOLOGICAL ASPECTS OF FOOD ALLERGY					
Project Code	**Project Title**	**Organisation**	**Lead Contractor**	**Project Officer**	**Project Duration**
T07041	The role of peanut-specific T cell responses in children with peanut allergy and in children who are tolerant to peanuts	King's College London	Professor Gideon Lack	Sarah Hardy	April 2004 to March 2008
T07042	Study of T cells in allergy and resolution	University of Cambridge	Professor Pamela Ewan	Dr Joelle Buck	July 2004 to May 2010
T07049	Characterisation of the immune mechanisms involved in the induction of oral tolerance to peanuts in children	King's College London	Professor Gideon Lack	Nathalie Shapiro	July 2007-January 2013 (although due to be extended to September 2014)

THEME - FSA GUIDANCE					
Project Code	**Project Title**	**Organisation**	**Lead Contractor**	**Project Officer**	**Project Duration**
T07057	Evaluation of the effectiveness of the best practice guidance on allergen management and consumer information	Jigsaw Research	James Flack	Sue Hattersley	September-November 2008
T07063	Guidance on the provision of allergen information for non pre-packed foods evaluation	Jigsaw Research	James Flack	Sue Hattersley	January-March 2010

THEME – FOOD ALLERGEN LABELLING AND CONSUMER CHOICE RESEARCH					
Project Code	**Project Title**	**Organisation**	**Lead Contractor**	**Project Officer**	**Project Duration**
T07058	Understanding the food choice reasoning of nut allergic consumers	University of Surrey	Dr Julie Barnett	Dr Joelle Buck	February 2009 to April 2010
T07059	Consumer understanding of new labelling terms for foods marketed for people with gluten intolerance	Define Research & Insight Ltd	Joceline Jones	Sarah Hardy	March-May 2009
T07065	Consumer understanding of additional labelling terms for foods without cereals containing gluten as ingredients	Define Research & Insight Ltd	Joceline Jones	Sarah Hardy	May-July 2010
T07061	Consumer understanding of revised government advice concerning peanut consumption in early life	People Partnership	Ann Whalley	Dr Joelle Buck	April 2009 to May 2009
T07064	Understanding of food labelling terms used to indicate the absence or reduction of lactose, milk or dairy	Creative Research	Ros Payne	Sarah Hardy	Jan 2010-April 2010

ANNEX 6

Project Summaries

Summaries of the 19 research projects that were included in the programme review are given below.

Research Project T07046:

The Prevalence of food allergy and weaning practices in a birth cohort of UK infants

Contractor: University of Southampton

Principal Investigator(s): Professor Graham Roberts

Start and End date: August 2005 to October 2009

Scientific/policy question being addressed:

This project was part of a large-scale European Union funded project called EuroPrevall, which was set up to study the aetiology of food allergy in infancy across Europe, with the overall aim of improving the quality of life of those with food allergy. Part of EuroPrevall was concerned with gathering accurate information from across Europe on the patterns and prevalence of food allergies in infants, children and adults. Project T07046 formed the UK part of the EuroPrevall birth cohort work package, and aimed to recruit a UK birth cohort and through prospective follow-up evaluate the current prevalence and pattern of food allergies in UK infants, using gold standard clinical methodologies agreed at European level. The study also aimed to improve understanding of current weaning practices of mothers in the UK, and to understand what influence the timing and introduction of allergenic foods (e.g. peanuts, eggs, milk, and wheat) may have on the developing immune system and the later development of food sensitisation and food allergy.

How the study was carried out:

Pregnant women were recruited onto the study from Southampton, and Winchester and Eastleigh NHS Trust areas, and followed from birth to 2 years. At recruitment, parents completed a detailed standardised and validated questionnaire (consistent across all the EU birth cohorts) from which data on their allergic and dietary history as well as on a variety of other relevant environmental and experiential factors were gathered. A further questionnaire was completed at one and two years of age to collect information on the child's health, environmental and dietary exposures.

Infants developing signs of a food allergy during the study were assessed in clinic using validated and standardised protocols (consistent across all the EU birth cohorts) to establish if they had a food allergy or not. Prevalence rates of parent perceived, physician perceived, physician confirmed and double blind challenge confirmed cumulative prevalence of food allergy, were determined at 1 and 2 years of age for the entire cohort.

In addition, and unique to the UK birth cohort, detailed dietary intake information was collected prospectively from birth to 12 months of age, via weekly diary records. This enabled dietary pattern analysis on the weaning data

obtained to be conducted and used to explore the relationships between such parameters as timing of solids introduction and length of breastfeeding on development of food allergy by two years of age. It also provided unique (prospective) data on breastfeeding and weaning practices of UK mothers from a general population cohort.

Key findings:

- Of 1203 infants delivered to mothers enrolled onto the study, 1172 were entered into the cohort. Cumulative incidence of parental perceived food allergy at 2 years of was 28.4% (95%CI 25.4-31.6%). Cumulative incidence of physician perceived food allergy at 2 years of age was 16.4% (95%CI 13.9-19.1) with cumulative incidence of physician diagnosed food allergy at 2 years of age being 9.0% (95%CI 7.1-11.2%).Cumulative incidence of double blind challenge confirmed food allergy at 2 years of age was 5% (95% CI 3.6-6.7%)

- The commonest foods giving rise to reactions were cow's milk, egg, peanut, soy, wheat and fish.

- *Quantitative* food diary data analysed from birth until symptoms developed for the 31 food allergic infants with sufficient diary data showed no significant differences in dietary intake for any of the pre-specified nutrients when compared to similar data collected from 62 age matched control infants.

- Food diary data showed 91% of infants with the median duration of breast feeding being 17 weeks (inter-quartile range 4.0 to 28.0 weeks).

- Pattern analysis conducted on the data collected from prospective weekly food diaries (from birth to 12 months of age) of 41 infants who developed a food allergy along with 82 age-matched infants who did not have a food allergy showed that food allergic infants were introduced to solids earlier (before 17 weeks), were less likely to be receiving breast milk when first being exposed to cow's milk protein and followed a weaning diet which did not follow the infant feeding guidelines.

Impact on Agency policies/policy development/advice:

The project has delivered a wealth of novel, robust and prospectively collected data and information about the prevalence and epidemiology of food allergies in UK children at the current time, as well as on current breastfeeding and weaning behaviours (albeit the cohort in this respect is dominated by well educated mothers and is therefore not necessarily generalisable). The findings have and will continue to be cited by the Agency as evidence highlighting food allergy as a significant problem in UK children which warrants research focus and funding to address, and will help us to assess trends in prevalence over the long term when combined with previous (and future) research studies the Agency has funded on prevalence. The prospective detailed data on breastfeeding and weaning behaviour in relation to later allergy development is

novel and has been shared with other Government Departments. The particular suggestion from the results that infants receiving breastmilk at the time of introduction of solids might have a reduced risk of food allergy development, whilst preliminary and unconfirmed, is particularly interesting and will contribute, along with the findings from other ongoing studies in this area, to the developing picture regarding how and when might be best to introduce allergenic foods into the infant diet from the point of view of minimising food allergy risks. Several publications have already emerged from this project and more are being prepared for submission to scientific journals.

Research Project T07046 addendum:

Additional analysis of infant dietary data to investigate the nutritional adequacy of a milk exclusion diet

Contractor: University of Southampton

Principal Investigator(s): Professor Graham Roberts/Dr Kate Grimshaw

Start and End date: August 2005 to January 2011

Scientific/policy question being addressed:

This project was funded as an add-on to the parent project T07046, and aimed to conduct additional analysis of the infant dietary data collected as part of project T07046. The purpose of this additional analysis was to investigate whether there are any obvious nutritional differences in major macro and micro nutrient intakes between infants fed on a milk exclusion diet (because of cows' milk allergy symptoms) and infants fed on a 'normal' diet including cows' milk.

It was anticipated that the results would inform our understanding of whether infants on a milk exclusion diet were at risk of nutritional deficiency and if so to give appropriate dietary advice to address this.

How the study was carried out:

This study looked at the nutrient intake of two groups of infants; one group followed a milk exclusion diet due to suspected milk allergy the other group ate a normal diet for their age.

A quantitative record of the infants' dietary intake was recorded once a month and this was analysed to give the mean daily intake for energy, protein, carbohydrate, fat, calcium, iron, selenium, zinc, and vitamins A, C and E. These mean intakes were compared using repeated measures ANOVA to see if there were any significant differences in nutrient intake between the groups. 13 symptomatic infants (infants following a milk exclusion diet because of milk allergy symptoms), had at least three weeks milk-free quantitative data (covering 12 weeks in time) available for analysis. Each of these symptomatic infants had 2 control infants who had the same amount of quantitative data available to analyse, which gave 26 control infants. 297 weekly dairies were analysed in total.

Key findings:

There was a difference in nutrient intake between the two groups at differing time points for the intake of protein, fat, calcium, iron, selenium and vitamin E. However intakes for all infants were above the recommended nutrient intake values for all nutrients in all cases except for selenium intake for infants following a normal diet between 24 and 26 weeks of age ($p=0.03$),

Iron containing (follow-on) formula made a marked contribution to iron intake in all infants involved in the study (whether following a milk-free or normal diet), mainly because their diets did not contain many other iron-rich foods. Whilst these milks can provide a safety net for iron intake whilst infants progress onto consuming a wider diet, parents and carers need to be encouraged not to rely on them to ensure their infant receives adequate iron but to include iron-rich foods in their infants/toddlers diet along with the introduction of other nutrient-rich foods.

The work shows nutrient intake for infants following a milk free diet was at least as good as infants following a normal diet but it need to be highlighted that these infants all received milk avoidance advice from a specialist allergy dietitian which is often not the case for infants following a milk free diet in the general population. Additionally, these infants were born to well-educated mothers who may be more motivated and more able to manage an infant's milk-free diet adequately than mothers from the general population.

Impact on Agency policies/policy development/advice:

The results are reassuring for the Agency in that they have indicated no need for specific advice to parents of infants with a diagnosed milk allergy about improving the nutritional adequacy of the diet (although the Agency should continue to encourage this group to seek expert advice regarding how to follow a milk exclusion diet). The results have indicated that further research on this topic does not need to be a priority for the Agency at the current time.

Research Project T07053:

A systematic literature review on the nutritional adequacy of a typical gluten-free diet, with particular reference to, iron, calcium, folate and B vitamins

Contractor: Coeliac UK

Principal Investigator(s): Norma McGough

Start and End date: March 2008- September 2008

Scientific/policy question being addressed:

The purpose of the research was to inform the Agency's understanding of whether the diet of UK consumers with diagnosed coeliac disease, who are following a gluten-free diet, is nutritionally adequate. Given that this group of consumers are, in theory, at increased risk of certain nutritional inadequacies because of the dietary restrictions imposed by their condition, it is important to find out whether or not, in practice, following a gluten-free diet is likely to lead to any nutritional inadequacies. This would help the FSA and wider Government bodies to advise these consumers and in developing food policy.

How the study was carried out:

The researchers carried out a systematic literature review searching electronic bibliographic databases Medline, Embase, the Cochrane Library and CINAHL, followed by hand searching of reference lists to identify relevant evidence. In addition, the researchers contacted the leading authors plus other key individuals and organisations in order to identify any relevant unpublished data.

A list of inclusion and exclusion criteria was agreed and only papers including subjects with medically diagnosed coeliac disease following a gluten-free diet for six months or more were evaluated. Scottish Intercollegiate Guidelines Network (SIGN) assessment checklists, were used to analyse the cohort studies and case control studies. Criteria used to assess the quality of studies differed for each study type. A data extraction tool was developed by the research team specific to the protocol for the systematic review taking into account the inclusion and exclusion criteria. A quality assessment was carried out by two independent reviewers in order to grade the evidence. Each paper was assessed for the risk of bias by using checklists and a grading system as recommended by Scottish Intercollegiate Guidelines Network (SIGN).

Key findings:

- There is a limited evidence base available on the nutritional adequacy of the gluten-free diet (only eleven papers met the specified criteria to be included in the review. These consisted of ten case-control studies and one cohort

study). The methodologies applied in the individual studies included in the review differed significantly from one study to another, eliminating the possibility of pooling of data and meta-analysis. This made statistically significant comparisons and conclusions impossible.

- Most papers concluded that individuals with coeliac disease following a gluten free diet had the same nutritional intake as the general population. Where the results were found to differ between these groups, there was often no values of statistical significance given so it was difficult to comment on those results. All papers were found to have moderate or high risk of bias, meaning that that the sources of bias identified either raised some doubts about the results, or seriously weakened confidence in the results.
- It was concluded that there was no existing robust evidence to show that individuals with coeliac disease adhering to a gluten-free diet experience any nutritional deficiency. However, these conclusions may reflect the small amount of data, rather than a genuine absence of nutritional deficiencies between conventional and gluten-free diets.

Impact on Agency policies/policy development/advice:

The results of this research provided the Agency with reassurance that the current dietary advice given to coeliacs on a 'gluten-free' diet is sufficient and that it was not necessary for the Agency to develop specific dietary advice for coeliacs to ensure they have a nutritionally adequate diet. However, it was acknowledged that this may reflect the paucity of data, rather than a genuine absence of nutritional deficiencies. Given the findings, this area of research is not considered by the Agency to be a priority for future research by the Agency at the current time against other areas.

Research Project T07062:

Management of food allergens: from threshold doses to analysis in foods

Contractor: Institute of Food Research; Institute of Inflammation and Repair, Manchester Institute of Biotechnology, The University of Manchester

Principal Investigator(s): Professor Clare Mills

Start and End date: December 2009- February 2012 (Final Technical Report currently undergoing finalisation)

Scientific/policy question being addressed:

The study aimed to use unique clinical food challenge data collected as part of the major European Commission funded Europrevall project, to derive robust clinical population threshold doses for allergenic foods (the highest level of an allergen that does not cause a reaction in the food allergic population) and to model dose distributions, for use in risk assessment methodologies by the Agency and other stakeholders. These data are a vital part of being able to derive robust management thresholds or 'action levels' for allergenic foods to inform risk management and risk communication strategies. The project also aimed to obtain data to demonstrate that available methods of analysis can reliably detect and quantify allergens in foods at or around the clinical threshold levels derived by the project and to determine if they are robust and fit for purpose.

How the study was carried out:

Using pre-existing data and materials developed in the EU-funded EuroPrevall project studying the prevalence of food allergy in Europe, this project developed a customised database containing data on double blind placebo controlled food challenges from individuals across Europe using seven foods (cows' milk, hen's egg, hazelnut, peanut, celeriac, shrimp and fish). The database was used for development of dose distributions for seven major allergenic foods, including cows' milk, egg, peanut, hazelnut, celery, fish and shrimp.

A scoring system was developed for reaction severity and these were used to support the development of clinical threshold doses suitable for use in risk assessments. Dose distribution curves were produced for seven allergenic foods using Europrevall clinical challenge data. Clinically validated reference materials were developed for hens' egg and cows' milk, building on work conducted as part of the Europrevall project, and this reference material (chocolate dessert matrix) was used to undertake a collaborative trial of UK commercially available test kits for these allergenic foods. This enabled clinically derived threshold doses to be explicitly linked to performance of analytical methods for determination of allergens in foods.

The data generated and tools developed from this project will support allergenic risk assessment and risk management processes, as well as the development of analytical methods with appropriate sensitivity for determination of allergens in foods.

Key findings:

- Dose distribution curves generated objective symptom ED_{10} values for peanut, hazelnut, celery and fish ranging from 1.6-9.6 mg protein with shrimp having a higher ED_{10} value of 3.1-3.4 g protein. It may be practicable to develop a single "action-level" for these allergenic foods.

- ED_{10} values for cows' milk and egg in the (majority) paediatric population were significantly lower, (0.5-1mg of protein for egg and 0.1-0.2mg protein for milk). Only relatively small numbers of adult patients had positive challenges to these foods but the dose distributions indicated higher ED_{10} values (20.4-27.1 mg for egg and 5.3-7.6mg for cows' milk).

- A prototype symptom score and ranking was used to develop a visualisation tool which allowed representation of symptoms developed across the course of a challenge. This showed objective symptoms appeared later on in the challenge and that oral allergy syndrome was a poor predictor of the severity of later symptoms. PCA showed that ten principal components are needed to explain 90% of the variation in symptom score.

- Ring trial assessment of the Europrevall dessert challenge matrix as an analytical quality control material (using incurred egg and cows' milk as exemplar food allergens) to prove its utility with regards stability and usability with little difference in performance observed between laboratories. Comparison of allergen test kits for egg and cows' milk produced variable results including poor quantification across the full range of levels of allergen inclusion.

- Overall, the data suggest that current methodology can determine the presence, but largely not quantify accurately, the levels of allergens in foods. However, this is not so for cows' milk because of the low ED_{10} values in the paediatric population which may require different management strategies and further data to assess the extent to which threshold doses for these allergens change with age.

Impact on Agency policies/policy development/advice:

The findings have provided the Agency with an indication of what action levels would be for seven allergenic foods and whether the current state of the art would be able to measure against any agreed action level. Going forwards, the EuroPrevall data will be combined with other clinical food study data by the ILSI-Expert group to see whether the proposed action levels they have derived have changed.

The ring trial also demonstrated that the chocolate dessert matrix used in the EuroPrevall food challenges would be suitable for use in the laboratory as a quality control material to ensure that methods used for allergen analyses are calibrated appropriately to be accurate, robust and fit for purpose.

Research Project T07067:

Survey of allergen advisory labelling and allergen content of UK retail pre-packed processed foods

Contractor: Reading Scientific Services Ltd (RSSL)

Principal Investigator(s): Barbara Hirst

Start and End date: May 2012 – May 2013

Scientific/policy question being addressed:

This survey aims to gain a better understanding of the type of allergen advisory labelling (such as 'May Contain X') present on pre-packed processed foods sold in the UK. It also aims to quantify the level of allergens that may be present in the food as a result of cross-contamination and establish whether the type of advisory labelling used relates to the level of allergen present.

How the study is being carried out:

Five hundred pre-packed processed foods that do not contain as ingredients, milk, gluten, peanut or hazelnut will be purchased in duplicate (two samples with identical batch/production codes giving a total of 1,000 products) from a range of retail outlets across the UK, including major and smaller national supermarkets as well as independent retailers. A broad range of pre-packed processed foods from 12 product categories will be sampled and analytically tested. Products with allergen advisory statements and an equal number of comparable products without such statements will be purchased.

Samples will be tested for the unintentional presence and quantity of one or more of the following four major food allergens: milk, gluten, peanut and hazelnut. These allergens have been chosen due to the large number of incidents the FSA has received over the past four years and because of their public health importance. Analyses will be carried out using appropriate ELISA based commercial testing kits which will undergo in-house validation where necessary to ensure that they are fit for purpose.

The survey will examine the different types of advisory statements used on pre-packed foods and compare the use of these phrases to the levels of allergens found to be present. It is anticipated this may help to establish whether or not the use of certain advisory statements are linked to the level of allergen present and indicate whether or not different types of statements convey different levels of risk to the consumer. In addition, the survey will examine whether the suggested advisory labelling statements set out in the FSA's Best Practice Guidance are being used by industry.

Progress/findings to date:

The survey has only recently started and is in the sample collection/analysis phase. Results will be reported at the end of the project.

Research Project T07068:

The effect of extrinsic factors on food allergy: Ex-factor

Contractor: University of Cambridge

Principal Investigator(s): Dr Andrew Clark

Start and End date: April 2012 – August 2016

Scientific/policy question being addressed:

This is a randomised cross-over clinical trial that will investigate whether common extrinsic factors, such as exercise and sleep deprivation, can modulate responses to allergenic foods. The effect of these extrinsic factors on clinical severity will be quantified in a representative group of adults from the peanut allergic population by measuring changes in threshold doses (i.e. individual no-observed-adverse-effect-levels (NOAELs), lowest-observed-adverse-effect-levels (LOAELs) and the distribution of minimum eliciting doses (MEDs), as well as the severity of allergic reactions elicited during each food challenge. It is anticipated that this information will inform work that the Agency is undertaking to develop management threshold levels (or 'action levels') for the unintentional presence of allergens in food to inform labelling and risk management/communication decisions. It will do this by providing us with information that will reduce the level of uncertainty surrounding population risk estimates that are derived from risk assessment models when applied to allergenic foods. It is also expected that the evidence gathered will enable the Agency to improve the advice given to peanut allergic consumers to help them better manage their condition.

How the study is being carried out:

This is a randomised cross-over clinical trial being conducted by a UK consortium comprising of 4 organisations, including 3 clinical sites. Cambridge University Hospital Trust is the coordinating centre for the study. Peanut allergic individuals will be recruited from clinical centres located in Cambridge (Addenbrookes Hospital) and London (Royal Brompton and St Mary's Hospital).

In the Trial, 100 adults with diagnosed peanut allergy will be recruited to undergo a total of 4 food (peanut) challenges at 12 week intervals - a baseline peanut double blind placebo controlled food challenge (DBPCFC), followed by three further challenges in random order, these comprising of one repeat baseline challenge, and two further challenges each in the presence of one of two extrinsic factors thought to have a possible influence on the thresholds and/or severity of reaction (these being either exercise or sleep deprivation). Each challenge consists of 2 days each, one with peanut, and another with placebo doses. The order is randomized for each participant. On the peanut day, doses are increased slowly from a level below the likely threshold.

After drop-outs, it is anticipated that complete data for all four challenges will be available for 72 subjects which will ensure that the study has sufficient statistical powering for the primary data analyses. Each clinical centre will perform both baseline and interventional challenges, and both extrinsic factors will be investigated at each centre, to ensure diversity of sampling. Pilot work will determine the feasibility of studying extrinsic factors using healthy volunteers to study (exercise and sleep restriction). The primary measurement for each participant will be the amount of peanut which causes a reaction during each challenge. This is known as the participants challenge threshold (mg peanut protein) and will be recorded for all four challenges. The data will be used primarily to model the variability of challenge thresholds over time within individuals, as a result of repeat challenges, and to examine how the extrinsic factors shift the dose response curve.

The University of Manchester will manufacture and distribute standardised peanut challenge meals to each clinical centre. The University of Manchester will develop an EX-FACTOR application of Allerg-e-lab to allow data input from the EX-FACTOR clinical study and facilitate retrospective analysis with relevant EuroPrevall data sets, in particular the further development and application of a numeric severity score.

The University of Cambridge (Centre for Applied Medical Statistics) will undertake the main and final analysis.

Progress/findings to date:

The project has only recently started and is currently awaiting ethical approval.

Research Project T07052:

Systematic review of literature on early life patterns of exposure to and avoidance of food allergens and later development of sensitisation and clinical allergy, with particular reference to peanut allergy

Contractor: British Nutrition Foundation

Principal Investigators: Professor Judy Buttriss

Start and End date: October 2007 – May 2008

Scientific/policy question being addressed:

This study was commissioned in support of a review by the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) of the COT precautionary advice issued in 1998 that had recommended avoidance of peanut consumption during pregnancy and breastfeeding amongst mothers of infants with a family history of allergic disease, and delayed introduction of peanut into the diet of those infants until 3 years of age.

Since 1998, this advice had come under scrutiny, as further scientific evidence on the development of peanut allergy and other food allergies in children had emerged and it was therefore timely to revisit the evidence base. A systematic review was therefore commissioned of all the published scientific literature since 1998 relevant to the early life patterns of exposure to, and avoidance of, food allergens and later development of sensitisation and clinical food allergy, with particular reference to peanut allergy, with the intention of updating and/or amending the existing advice to consumers.

How the study was carried out:

The review was conducted using, where relevant, established methodologies and protocols for conducting systematic literature reviews, and comprised seven smaller reviews of the literature incorporating both studies in humans and from experimental studies in animals, which addressed the following specific areas:

- The effect of maternal diet (in relation to food allergen consumption) in pregnancy and lactation, on the development of later sensitisation and food allergy in the offspring
- The diet of infants (in terms of food allergen consumption) and later development of sensitisation and allergy to foods
- The effect of fetal exposure to food proteins (*in utero*) and later development of food allergy
- The possible influence of non-dietary exposure to peanuts in infancy (for example via skin or respiratory tract) and the development of sensitisation or allergy to peanuts

- The impact of the 1998 Government advice on dietary consumption of peanuts and peanut products on the prevalence of sensitisation and allergy to peanuts in UK children

Key findings:

The main findings of the systematic review were:

- That the overall quality of available published studies for review was not high and did not provide sufficient evidence upon which to draw firm conclusions. In particular in relation to allergy risks in relation to non-dietary exposure to peanuts in infancy and in relation to the timing of introduction of solids/specific foods. The available evidence was very heterogeneous.

- Available evidence from human studies did not suggest that maternal exposure to, or avoidance of, food allergens during pregnancy or lactation led to the subsequent development of food sensitisation or food allergy in the child. Evidence from animal model studies indicated that exposure via maternal oral intake may be protective. *In vitro* studies of cord blood cell responses are not necessarily indicative of fetal exposure to, or sensitisation by, maternally consumed allergens.

- Available evidence from human studies did not suggest that dietary exposure to or avoidance/delaying introduction of allergenic foods in childhood provided protection from subsequent development of sensitisation or allergy to foods

- There was little information in humans available on the effects of non-dietary exposure to peanuts on the development of sensitisation and allergy. However, one study did show an increased risk of peanut allergy in children who were exposed to skin creams containing peanut oil. There is some supportive evidence from experimental animal studies examining responses to peanut or ovalbumin. Further studies in humans are required in this area.

- There appeared to be confusion among the general public about the 1998 COT advice and it has not been interpreted as intended. More than 60% of women reported having reduced (few totally avoided) consumption of peanuts during pregnancy and lactation, including those not targeted by the COT advice. There appeared to have been a rise in the prevalence of peanut sensitisation and allergy between 1989 and 1996 but there was no evidence of any significant changes in the prevalence of peanut allergy in the UK since that time.

Impact on Agency policies/policy development/advice:

The project was commissioned for a very specific policy related purpose which was to inform a review by the Committee on Toxicity of their 1998 recommendations on peanut avoidance, to see if the evidence base had changed which might necessitate a change to the advice. The project delivered very well against that purpose in that the overall quality and scientific rigour of

the literature review was commended by the COT and, whilst the overall evidence base was found to be limited, the findings of the project were very informative to the review that COT conducted, and to the COT Statement that was subsequently published. That Statement and the findings of project T07052 directly informed the formulation of updated advice to consumers and health professionals which was subsequently issued in 2009 jointly by the Agency and the Department of Health. The project (and the COT Statement that it informed) also helped to highlight to the Agency where the specific gaps in the evidence base are currently where further research funded by the Agency might be required in order to be able to provide more definitive advice to consumers in the longer term. The findings of project T07052 have also been published in the scientific press.

Research Project T07051:

Randomised trial of early introduction of allergenic foods to induce tolerance in infants (EAT Study)

Contractor: King's College London

Principal Investigators: Professor Gideon Lack, Dr Michael Perkin

Start and End date: January 2008- May 2015

Scientific/policy question being addressed:

The EAT Study is testing the hypothesis that the early introduction of allergenic foods (from 3 months of age) into the infant diet, alongside continued breastfeeding, will induce regulatory mechanisms that result in a reduction in the prevalence of food allergies by three years of age. This will help us understand the influence of timing of the introduction of allergenic foods into the infant diet, on the subsequent risk of development of allergies and possibly other atopic conditions.

How the study is being carried out:

The project is a randomised controlled trial in which 1300 infants who have been exclusively breastfed to 3 months of age are being recruited to participate in the study. At 3 months of age (i.e. at recruitment), infants are randomly assigned to one of two groups. One half (the early introduction group) are introducing sequentially, a number of allergenic foods (egg, milk, wheat, sesame, fish and peanut) into the diet under close dietetic direction, alongside continued breastfeeding. Infants in this group are given baby rice mixed with breast milk or water first between 3 – 4 months of age, followed by a cows' milk based yoghurt and then from around 4 months of age egg, fish (cod), peanut and sesame are introduced in random order with wheat being introduced last and not before 4 months. Infants in the other group (the standard introduction group) are encouraged to follow the current Government infant feeding advice of exclusive breastfeeding until around 6 months of age, and no introduction of allergenic foods before this age.

Participants undergo further study visits with comprehensive clinical assessments at one and three years of age by which point the impact of the intervention on food allergy and other secondary allergy endpoints (eczema prevalence, inhalant allergen sensitisation, atopic wheeze, phenotype and combined allergy prevalence) will be assessed. Validated questionnaires, administered at recruitment, are being used to collect information on all aspects of maternal as well as household and family exposure to allergens. Dietary assessment of the infants is being monitored by a combination of validated food frequency questionnaires completed monthly until one year of age and three monthly thereafter, and 5 day food diaries completed at 6 months, 12 months and 3 years of age.

Progress to date:

- The study has recently completed recruitment (1305 infants).
- The results of the study intervention will not be available until completion of the three year assessments
- However, a key finding to date has emerged from the skin barrier work (British Journal of Dermatology 2010;163:1333-6): By the age of 3 months, Filaggrin (FLG) mutations are associated with an eczema phenotype, dry skin and Transepidermal water loss (TEWL). The observation that TEWL is elevated in unaffected FLG mutation carriers suggests that skin barrier impairment precedes clinical eczema.

Research Project T07060:

Investigation of the association of skin barrier structure and function and the development of food allergy. A prospective birth cohort study

Contractor: University College Cork

Principal Investigator(s): Professor Jonathan Hourihane

Start and End date: July 2009- October 2013

Scientific/policy question being addressed:

The study aims to test two specific hypotheses: The primary hypothesis is that abnormal skin barrier function (with or without eczema) predates and predicts food allergen sensitisation, independent of other post-natal dietary and environmental factors. The secondary hypothesis is that any relationship between skin barrier function and food allergen sensitisation is driven by loss-of-function mutations in the filaggrin (FLG) protein. It is anticipated that addressing these two hypotheses will improve the Agency's (and wider scientific) understanding of what specific risk factors are involved in the development of sensitisation and clinical allergy to foods in early life, and of exactly how, and under what circumstances, allergic sensitisation to foods is acquired. This will help inform possible preventative or immunomodulatory strategies as well as the Agency's advice to consumers about how to minimise the risk of developing a food allergy.

How the study is being carried out:

The project is building upon data being obtained from two on-going linked Irish studies: SCOPE and BASELINE. In SCOPE, 3000 first-time mothers are being recruited in early pregnancy with the aim of establishing biomarkers to help predict pregnancy outcomes. The BASELINE Study aims to provide a detailed follow-up of the babies born from SCOPE, including collection and storage of umbilical cord blood, assessment of growth and health, collection of data on breast-feeding and weaning practices, and assessment of eczema status.

Project T07060 is using established clinical protocols to determine the status of 2000 SCOPE/BASELINE babies with regards to FLG mutation, skin barrier function, and food allergen sensitisation and food allergy in the first 2 years of life.

FLG mutation status is being determined by rapid mutation screening analysis of umbilical cord blood collected in the BASELINE Study. Skin barrier function will be determined at 2 days, 2 months and 6 months of age by measuring the amount of water lost from the skin using a procedure known as Transepidermal Water Loss (TEWL).

Food allergen sensitisation status will be determined by Skin Prick Tests (SPTs) and blood tests for Specific Immunoglobulin E (SpIgE) antibodies at 2 years of age.

Children whose parents report adverse reactions to foods during the study will undergo Double-Blind Placebo-Controlled Food Challenges (DBPCFCs) in order to determine their food allergic status.

Progress/findings to date:

The study is currently on-going. Subject recruitment is now complete (1903 infants born onto the study), and the study is now in the follow-up phase.

Research Project T07049: Characterisation of the immune-mechanisms involved in the induction or oral tolerance to peanuts in children

Contractor: King's College London

Principal Investigators: Professor Gideon Lack

Start and End date: July 2007- January 2013

Scientific/policy question being addressed:

The study is utilising stored blood samples collected from children taking part in a randomised controlled trial of early introduction of peanut into the infant diet amongst a cohort of infants at high risk of peanut allergy, to determine the immunological mechanisms underlying the acquisition of oral tolerance to peanut as well as of those underlying sensitisation and clinical allergy to peanuts.

How the study is being carried out:

T07049 is utilising blood samples taken at specific time points throughout the study, specifically at recruitment (when infants are between 4 and 10 months of age), at 1 year of age, at 2.5 years of age and at 5 years of age (the end of the clinical trial intervention period). At these time-points samples are being analysed for specific immunological markers that may be associated with allergy or tolerance, using a suite of existing established and novel immunological methodologies. The clinical Trial has recruited 640 subjects and this project is monitoring longitudinally peanut-specific T cell responses (frequency of circulating peanut-specific T helper cells and cytokine production and cytokine producing phenotype of cells), and B cell responses (IgE), as well as regulatory T cell activity (including CD25+ regulatory T cell activity) and antibody isotypes, in blood samples from a sub-set of children from the intervention and control arm of the study. These analyses will be used to explore and identify differences over time and amongst different patient phenotype groups (sensitised, tolerant, allergic).

Progress/findings to date:

- The clinical trial is blinded and therefore analyses of immunological responses between the intervention and control arm have not yet been initiated, except for a preliminary analysis conducted on the first 60 children recruited into each arm of the trial. That analysis indicated the following key results to date:
- In the pilot analysis of the immunological responses to peanut of the clinical trial participants the viability of the frozen PBMC was high; negative controls (unstimulated PBMC) did not show the emergence of a significant CFSElow population and peanut-stimulated PBMC cultures showed the

emergence of a CFSElow T cell population at both the baseline (V-1) visit and at the 12-months-of-age (V12) visit;

- Peanut-specific cytokine production show positive intracellular cytokine staining distinctly above background levels, as defined by isotype control antibodies both at V-1 and V12 visits and peanut-specific cytokine production could be detected in more LEAP study participants from the consumption group at the 12-months-of-age (V12) visit than at the baseline (V-1) visit;
- Peanut-specific IgG4 levels were similar in the two groups at baseline but higher in the peanut-consumption group at the12-months-of-age (V12) visit.

- Clearly these results are too preliminary to draw conclusions but they have provided early indications of trends emerging across the two groups (intervention and control arms) in relation to peanut-specific T cell responses.

Research Project T07041:

The role of peanut specific T cell responses in children with peanut allergy and in children who are tolerant to peanuts

Contractor: King's College London

Principal Investigator(s): Professor Gideon Lack

Start and End date: April 2004 to March 2008

Scientific/policy question being addressed:

The study aimed to improve our understanding of the immunological mechanisms involved in the induction, development and persistence of peanut allergy. Specifically, the study aimed to investigate the roles played by T cells and functional sub-populations of T cells, in the pathogenesis of food allergy and in particular to try to find out why T helper cell responses to peanut antigens differ in peanut allergic individuals compared with peanut sensitised and peanut tolerant individuals. Four specific hypotheses that might explain these differences were investigated. Answering this question could inform the development of immunomodulatory strategies that could allow T cell responses to be normalised in future therapies and is otherwise critical to our understanding of what constitutes immunological tolerance to peanut antigens.

How the study was carried out:

In this study, a novel flow cytometry method that had been developed during a previous FSA funded research study, was used to investigate (*in vitro*) functional differences between the responses of T cells and sub populations of T cells to peanut antigen, utilising blood samples taken from known peanut allergic, peanut tolerant and peanut sensitised but non-allergic donors.

Flow cytometry was used to identify the peanut-specific cells amongst the peanut -stimulated PBMC by using CFSE labelling, and to measure the degree of allergenic polarization (Th2 skewing of the cytokine production phenotype) of peanut-specific T cells using intracellular cytokine staining.

In a further stage of the study, the same methodologies were used to investigate the site (via the skin or gut) where sensitization to peanut was likely to have occurred in peanut allergic individuals, by isolating specific subsets of memory T cells that proliferate in response to peanut antigen (i.e. those cells expressing the CLA antigen indicating initial antigen exposure via the skin, and those expressing the alpha 4 beta 7 marker indicating exposure via the gut).

Key findings:

- That the differences in T cell proliferative responses between peanut allergic and non-allergic children can be explained by on-going peanut-specific IgE production (in peanut allergic children) through the positive

feedback mechanism driven by IgE-mediated FAP (facilitated antigen presentation). This could underlie the persistence of peanut allergy despite stringent peanut avoidance.

- That in both peanut allergic and non-allergic donors peanut-specific T cell responses are driven by memory T helper cells not naive T cells.

- That observed differences in T cell proliferative responses between peanut allergic and non-allergic children are unlikely to be the result of suppressor cytokine activity

- That in peanut allergic donors the peanut-specific T cell response is predominantly generated by skin-homing CLA positive memory T cells that have initially seen peanut antigens in the skin, whilst in non-allergic individuals the responses are generated by a mixed (CLA positive and alpha 4 beta 7) population of memory T cells, supporting the notion that allergic sensitisation may occur through the skin and oral tolerance results from gut exposure.

Impact on Agency policies/policy development/advice:

The findings in relation to peanut allergic individuals tending to have higher peanut specific IgE levels and linked with this higher levels of peanut specific proliferating T cells, have added significantly to our understanding of what immunological factors might be key in the maintenance of the peanut allergy phenotype, and about the possible mechanisms for this, which will be important in the future in the design of effective interventions and/or therapies. The findings from the skin-homing and gut-homing memory T helper cell experiments, whilst from small numbers and unconfirmed, support the growing hypothesis that exposure through the skin might be the route leading to sensitisation whilst exposure via the gut is important in developing tolerance. These results have informed and led to the Agency commissioning further research to find out how important the skin is in the development of food allergy (e.g. project T07060), and will add to the findings of all the studies which the Agency is currently funding on routes and timing of exposure to food allergens. It is hoped that the totality of evidence that emerges from all of these studies will significantly inform the development of new dietary/environmental interventions/consumer advice aimed at minimising risk and promoting the acquisition of tolerance to food allergens in early life. The findings of project T07041 have been published in the scientific press.

Research Project T07042:

Study of T cells in allergy and resolution

Contractor: University of Cambridge

Principal Investigator(s): Professor Pamela Ewan

Start and End date: July 2004 to May 2010

Scientific/policy question being addressed:

This study aimed to determine what immunological mechanisms/features underlie the resolution of food allergy, specifically of egg allergy, in order to improve our understanding of the pathogenesis of food allergy and its resolution and to inform clinical decision making and advice to those with egg allergy.

How the study was carried out:

This longitudinal study followed 60 children (aged 2 – 15) with food challenge confirmed egg allergy for three years in order to capture resolution and persistence. Also included in the study were two control groups (sensitised but non-allergic and non sensitised non-egg allergic) made up of 20 children each.

Egg-allergic patients underwent repeated annual open oral egg challenges with well cooked egg and if negative, uncooked (pasteurized) egg over time to confirm resolution or persistence of allergy. Blood samples were taken and used to measure specific IgE as well as total and specific IgG. T cell proliferation and TH1/2 cytokine production were measured annually using stored (frozen) PBMC samples and employing flow cytometry and intracellular staining methods, to demonstrate changes in T cell proliferation and cytokine production (IL-4/10 and IFN-grella esohw nerdlihc ni (γy resolves or persists. Subjects from both control groups were tested at enrolment and again in the final year of the project.

Key findings:

- Results of the immunological assays have provided evidence indicating that the resolution of egg allergy is associated with a change in the cytokine producing phenotype of OVA-specific T cells from T-helper 2 (Th2) to T-helper 1 (Th1), which is accompanied by an increase in the production of OVA-specific IgG4 and reduction in the production of egg-specific IgE.
- Results of the clinical assessments indicate that resolution of egg allergy takes place over many years, with children outgrowing allergy to well-cooked egg approximately twice as quickly as they outgrow allergy to uncooked egg.
- The Data support initiation of home reintroduction of well-cooked egg from 2-3yr of age in children with previous mild reactions and no asthma.

Resolution continued to occur in older children, so that despite an earlier positive challenge, attempts at reintroduction should be continued.

Impact on Agency policies/policy development/advice:

The findings have given us insight, for the first time, into the immunologically relevant changes that occur in the course of resolution of egg allergy. The findings have been published and have informed scientific understanding, adding to the wider body of evidence that is emerging on this topic, which may in the long term lead to targets for immunotherapy being identified. In addition, the findings of the longitudinal clinical assessments have directly informed recently published UK guidelines on the clinical management of egg allergy (published by BSACI[4]), which will help inform and improve clinical practice leading to fewer egg allergic reactions if reintroduction is done safely, and have also informed the advice and information given by the Agency to consumers who contact us regarding egg allergy.

4 http://www.bsaci.org/index.php?option=com_content&task=view&id=117&Itemid=1

Research Project T07058:

Understanding the food choice reasoning of nut allergic consumers

Contractor: University of Surrey

Principal Investigator(s): Dr Julie Barnett

Start and End date: February 2009 to April 2010

Scientific/policy question being addressed:

This study investigated how people with peanut and tree nut allergies use food labels and other pack information when making choices about what food to eat and buy, and what types of strategies they adopt when selecting foods (shopping and eating out) to minimise the risk of triggering an allergic reaction. Information in these areas was needed to inform the development of policy and practice in this area, and specifically to inform FSA work to improve the current (allergen) labelling on products and to improve the quality of dietary advice given to those with nut allergies.

How the study was carried out:

Thirty-two adult volunteers with a doctor diagnosed peanut and/or tree nut allergy were recruited to the study from 5 sources across the UK (recruited participants had no other food allergies (except for Oral Allergy Syndrome to fruit or vegetables)). Each participant took part in three tasks which were designed to gather qualitative information on how food allergic consumers make their food choices and food purchasing decisions. These tasks were:

1. An accompanied shop in their usual supermarket where participants were asked to talk aloud about what they were thinking when they chose each food product (methodology for this 'think aloud' task was trialled and refined prior to use)
2. An in-depth semi-structured interview which followed on (on the same day) from the accompanied shop and was conducted in each participants own home
3. A Product Choice Reasoning Task (PCRT) designed specifically for this study with input from the FSA and food allergy experts. Each participant was given 13 packaged food products (these were real and mainstream foods sold through major retailers) chosen on the basis that allergy experts believed that they would pose particular dilemmas for nut allergic consumers. Participants were asked to 'think aloud' and say if they would be happy to buy the product and how they reached their decision

The results from each of the above methods were recorded, transcribed and analysed considering key themes to identify patterns of behaviour and key factors involved in food purchasing decisions.

Key findings:

Participants used a range of strategies (rules of thumb) to make choices about what foods to eat and buy when food shopping and eating out. These included 1) personal experiences, preferences and sensory judgements (participant based characteristics), 2) product based characteristics, and 3) characteristics of the food producer, including trust accorded to brands and supermarkets.

Strategies used when food shopping:

- Food labels were used as well as previous experience of eating a product. e.g. particular brand names they trusted more in terms of quality of products and labelling.
- Most relied on the allergy advice box over and above the ingredients list. However they did not understand the voluntary nature of allergen advice boxes. Expressed and revealed preferences for ingredients lists or allergy advice boxes did not seem to relate in any systematic way to allergy severity, and absence of an allergy advice box was wrongfully interpreted by many as an indication of absence of allergens.
- Participants had a complex and detailed range of views about 'may contain' labelling. Although many participants chose to respond in consistent ways to may contain labelling, most participants considered that the underlying message of 'may contain' labelling was not credible or desirable, and many discounted the 'may contain' label in their decision making.

Strategies used when eating out:

- Nut allergic individuals tended to adopt an avoidance and communication strategy to manage the risk of triggering an allergic reaction when eating outside the home. Particular problems when eating abroad were identified and translation cards were reported as useful.
- Participants generally asked restaurant staff whether a dish contained nuts or not or asked them to inform the chef they had a nut allergy. The most helpful scenario for eating out in restaurants was when staff were responsive and when the allergic consumer was recognised and known by restaurant staff – many participants reported embarrassment at drawing attention to their allergy in a restaurant setting.

Impact on Agency policies/policy development/advice:

The project findings have been published in the scientific press and have provided the Agency with a wealth of new information regarding how nut allergic consumers use the food label and other information to inform their decision making and about what the issues are for them when eating out. The methodology developed in the shopping basket task is novel and is likely to inform future research on consumer decision making in relation to prepacked

food (the Agency has shared details of this methodology with other relevant Government Departments). In addition, the findings have informed the following:

1. Work to develop management thresholds/action levels for cross-contamination of prepacked foods with allergenic foods – the research has informed the Agency's thinking further regarding the likely need to try and move away from the phrase 'may contain' if and when such thresholds are rolled out because of the preconceptions regarding interpretation of the phrase in addition to many disregarding it entirely.
2. EU negotiations on the new Food Information Regulation (FIR) – The findings of the research were shared with DEFRA who are leading on the UK negotiations on the FIR, highlighting the need to ensure consumers are pointed towards the ingredients list as the primary source of allergen information because other information (e.g. the allergy advice box) is not always present. The FIR (now published) has included a requirement for allergens to be in highlighted text in the ingredients list so this should help to address this issue. The results of the 'eating out' part of the research will also inform the Agency's guidance to UK industry regarding provision of allergen information for foods solds non-prepacked which is a new requirement of the FIR.
3. The finding that many nut allergic consumers refer to the allergy advice box as the first point of allergen information has informed the Agency's correspondence with industry where we now specifically emphasise the importance of manufacturers ensuring that the allergy advice box matches the ingredients list as regards allergens present.

Research Project T07059:

Consumer understanding of new labelling terms for foods marketed for people with gluten intolerance

Contractor: Define Research & Insight Ltd

Principal Investigator(s): Joceline Jones

Start and End date: March-May 2009

Scientific/policy question being addressed:

This research was commissioned in advance of new EU rules coming into force on the labelling of foodstuffs suitable for those with coeliac disease (intolerance to gluten), in order to explore how best to communicate the labelling changes to consumers, when they come into force. In particular, the research aimed to explore how consumers would interpret the new terms 'Gluten-Free' for foods which contain less than 20 parts per million gluten, and 'Very Low Gluten' for foods containing cereal ingredients that have been treated to reduce their gluten content and which will contain less than 100 parts per million gluten. In addition the research explored how best to communicate the meaning of these terms under the new legislation to consumers, how best to inform consumers about the changes, and to inform the technical guidance for industry that was being drawn up to accompany the legislation.

How the study was carried out:

A series of discussion groups, paired depth interviews and face to face interviews were conducted with adults who had either been clinically diagnosed with coeliac disease (majority of sample) or non-clinically diagnosed, that is those who considered themselves gluten intolerant and were buying gluten-free products or had been advised that they may be gluten intolerant by their GP. The sample also included parents who had children with coeliac disease and who bought food for them. Participants were recruited from all four regions of the UK as well as a spread of periods of time for which the sufferer (whether the respondent or a child) had been diagnosed as gluten intolerant, and a mix of levels of tolerance to gluten. All respondents were asked to complete a food diary exercise prior to attending research. In addition the sample also included a small number of health professionals and two telephone interviews with Coeliac UK telephone advisors.

Key findings:

- A wide range of information sources were being used and accessed to understand which foods are suitable for consumption, with Coeliac UK being predominant. Dietitians were also considered an effective resource especially at the point of diagnosis. Beyond this, the Internet also served to provide access to additional information, for example, manufacturers and

supermarkets websites. Word of mouth and relevant literature was also being used by respondents, but there was little or no evidence of the Food Standards Agency (FSA) being used as a source of information by those in the sample.

- Respondents reported that upon initial diagnosis purchasing appropriate foods was confusing, time-consuming and potentially risky. For some this was an on-going concern particularly where products were not specifically labelled/marketed as gluten-free.

- Reaction to the new label ‘gluten-free’ as a standalone was generally accepted, with the assumption that this would mean (as these consumers has assumed previously) that this product would not include any gluten. Further explanation of its gluten content (less than 20ppm), although small, did raise concerns within the sample because of their position of understanding that it currently contained no gluten at all, although they were generally reassured once they heard that it would be suitable for most.

- 'Very Low Gluten' as a label was less straightforward for nearly all, as it was seen as requiring a judgement as to whether a product displaying this claim was suitable or not for them and their child. This caused anxiety amongst most of the sample who felt that rather than take the risk, they would avoid these products.

Impact on Agency policies/policy development/advice:

The results of this research have had a significant impact on Agency policy and advice, including: -

- The results informed the UK Government interpretation of Regulation 41/2009 and particularly the best practice guidance provided within the guidance to compliance. As a result of this research it was recommended that suitability statements (e.g. ‘suitable for coeliacs’), should be placed alongside the labelling terms ‘gluten-free’ and ‘very low gluten’.
- The results of this research prompted and informed an initiative that was undertaken by the Agency to raise the awareness of the new Regulation among consumers. This was done through a number of targeted avenues including magazine articles (such as Coeliac UK (CUK) crossed grain and food matters), web stories (such as food.gov, CUK website, NHS choices) and by attending and presenting at consumer stakeholder meetings.
- The results of the research were also disseminated through CUK, who used the findings to ensure their consumer education campaign was targeted effectively.
- The findings of the research were also used to inform the production of a leaflet aimed at consumers to explain the key requirements of the new regulation. This leaflet was produced in collaboration with a number of stakeholders including CUK.

Research Project T07065:

Consumer understanding of additional labelling terms for foods without cereals containing gluten as ingredients

Contractor: Define Research and Insight Ltd

Principal Investigator(s): Joceline Jones

Start and End date: Jan 2010 to April 2010

Scientific/policy question being addressed:

This project was a follow-on from related project T07059. Following that project, and after a public consultation on the UK laws that would implement the new EU legislation on labelling of foods as suitable for coeliacs, it became clear that many food businesses (but particularly caterers) would not be able to meet the new criteria of the legislation supporting 'gluten-free' or 'very low gluten' type statements. This may have led to a reduced choice for UK coeliacs with the possible risk that coeliacs might make riskier decisions because of an absence of information. Therefore the Agency worked to develop a solution and formulated a specific factual statement for use by these food businesses on food labels where there are no gluten containing ingredients and the food producer has taken all reasonable steps to control cross-contamination. This follow-up research was commissioned in order to explore consumer and health professionals' reactions to the proposed factual phrase '*no gluten containing ingredients*' for use on menus, food labels and product lists of foodstuffs falling in to this category

How the study was carried out:

Respondents were re-contacted from the related study T07059, on gluten labelling, (plus some new respondents to top up the sample). They were initially asked for a spontaneous response to the statement 'Non Gluten Containing Ingredients' at re-contact stage. They were then given a written description of the background and context relating to the proposed issuing of the new statement, and asked to consider the statement in the light of this information prior to an in-depth 30 minute telephone interview during which their reactions and interpretations of the new phrase were explored in more depth The sample consisted of 6 health professionals (1 GP, 3 dieticians, 2 practice nurses), 29 sufferers and 4 parents of sufferers.

Key findings:

- The statement *'No Gluten Containing Ingredients'* was generally welcomed by the audience, and was considered the most effective and appropriate compared with some alternatives tested. It was perceived as a useful and positive statement for making decisions when eating out.

- The meaning of *'No Gluten Containing Ingredients'* and implications were not always clear to many of the coeliac patients and some of the health professionals, particularly in that it did not convey the potential risk of cross-contamination with cereals containing gluten.
- As a stand-alone statement, 'No gluten-containing' ingredients is initially thought by many to be equivalent to 'gluten-free' unless accompanied by further supporting information to convey this risk of cross contamination and differentiate from the term 'gluten-free'
- The context in which the phrase will be used is likely to have an impact on the levels of understanding and further supporting information is likely to be required to increase understanding and fully inform decision making by coeliac consumers.
- The research Contractors, made a number of detailed recommendations regarding further information and supporting materials that might be helpful to coeliac consumers in these settings to help inform their choices.

Impact on Agency policies/policy development/advice:

The results of this research have had a significant impact on Agency policy and advice, including the following:

- The results informed the UK Government interpretation of Regulation 41/2009 and particularly the development of best practice guidance provided within the guidance to compliance that accompanied this Regulation. As a result of the research findings the Agency recommended that food business operators use the factual statement 'no gluten containing ingredients'. However the Agency stated it could only be used where cross contamination was controlled and the statements could not be used in a way which misleads the consumer in to thinking it has an equivalent meaning to the claim 'gluten-free'. The guidance also recommended that the business should also explain the meaning of this factual statement to the consumer when it is used.
- It was also recommended that this phrase should be used mainly on foods sold in catering establishments as it would be difficult to explain the meaning of the factual statement when used on a label.
- It was recommended that where possible a 'gluten-free' claim should be made on packaged foods, as opposed to the 'no gluten-containing ingredients statement.
- There was a concern that both consumers and health professionals did not understand the risk of gluten cross contamination that was associated with foods carrying the factual statement. Therefore an education campaign was undertaken with Coeliac UK (CUK) to make the groups aware of the conditions of use that were associated with the statement. This was undertaken through a number of targeted avenues including magazine articles (such as CUK, Crossed Grain and Food Matters), web stories (such as on food.gov.uk, CUK website, NHS choices) and by attending and presenting at consumer, health professional and CUK stakeholder meetings.

- The findings of the research were also used to inform the production of 2 leaflets. The first aimed at caterers to explain the key requirements of the new regulation and help them to understand which claim they could make and the requirements they would need to fulfill. The second was aimed at consumers and not only explained the requirements of the new Regulation but also when, why and how the factual statement would be used. This leaflet was produced and disseminated in collaboration with a number of stakeholders including Coeliac UK.

Research Project T07061:

Testing of draft revised Government advice on peanut consumption in early life

Contractor: The People Partnership

Principal Investigator(s): Ann Whalley

Start and End date: April 2009 to May 2009

Scientific/policy question being addressed:

The overall aim of this research was to explore consumers' and health professionals' understanding and opinions of draft revised Government advice on peanut consumption in early life, before the advice was issued and disseminated. This would enable the Agency and DH to ensure, as far as is possible, that the final advice that was issued was clear, understandable, and would be taken up as intended.

The proposed change in advice followed a major review (in 2008-2009) by the Committee on Toxicity (COT) of the scientific evidence on early life exposure (via maternal diet during pregnancy and whilst breastfeeding as well as in the infant diet), to peanut and peanut products in relation to the later development of peanut sensitisation and peanut allergy. That review concluded that there was no clear evidence that eating or not eating peanuts (or foods containing peanuts) during pregnancy, breastfeeding or early childhood has any effect on the chances of a child developing a peanut allergy. Therefore, the Government's previous advice (issued in 1998) that women may wish to avoid peanuts during pregnancy and breastfeeding and not introduce peanuts into their child's diet before three years of age, if their child has a family history of allergy, was considered no longer appropriate. Revised advice reflecting the current scientific uncertainty was drafted for issue to consumers and health professionals, and this draft advice was the subject of this research project.

How the study was carried out:

The method involved qualitative research amongst consumers, health professionals and their representative bodies, from across the UK.

The consumer research comprised:

- Group discussions with mothers and mothers-to-be with no family history of allergy;
- Group discussions with mothers and mothers-to-be with allergy in the family;
- Depth interviews with mothers with a food allergy and mothers of a child under 3 with an allergy (high risk consumers).

The health professional and health professional representative bodies research comprised 14 x 45 minute depth-Interviews and included two GPs, two health visitors, two midwives, two paediatricians, two dieticians, two staff from the Anaphylaxis Campaign and advisers from two Royal Colleges (the Royal College of Paediatrics and Child Health and the Royal College of General Practitioners).

Key findings:

- The most informed (in terms of allergy)**/**literate consumers and health professionals**/**health professional bodies tended to be very positive about the draft revised advice that was exposed in the research.

- However, other health professionals and consumers who were less well informed about allergy and**/**or who had literacy issues were much less positive about the revised advice in terms of its structure and presentation, as well as in relation to specific content issues, which the research highlighted and discussed.

- Use of proposed routes to disseminate the advice were endorsed, although were not felt to be sufficient on their own. Many consumers felt much more should be done to provide the relevant advice proactively. At an overall level, many healthcare professionals were often criticised as lacking the time and sufficiently up to date knowledge to be able to provide adequate support in this area. Suggestions for a 'first point of call' and for other ways of highlighting the advice were given.

- The revised advice was consistently endorsed as extremely clear and easy to understand by health professionals. However, not all felt that their patients or the general public would understand or engage with it. Health professionals' views on whether or not they would disseminate the revised advice to consumers were extremely mixed.

Impact on Agency policies/policy development/advice:

As expected, the findings directly informed the development of the final updated advice to consumers that was issued by the Government. In particular the advice was re-worked to structure it by life stage rather than by risk group, and was put in a greater level of context in relation to the previous advice and the ongoing uncertainty in the evidence base. In addition (also in response to the findings of the research), the dissemination of the advice was phased so that health professionals received the advice before consumers, and consumers were directed to their health professional for further advice.

Research Project T07064:

Understanding of Food Labelling Terms used to indicate the absence or reduction of lactose, milk or dairy

Contractor: Creative Research

Principal Investigator(s): Ros Payne

Start and End date: Jan 2010 to April 2010

Scientific/policy question being addressed:

The aim of the research was to explore understanding of the terms 'lactose free', 'milk free' and 'dairy free' among consumers with sensitivity to milk or milk components, health professionals who advise such consumers and food businesses who provide products for these consumers. This information was needed in advance of possible EU level discussions on legislating for claims about levels of lactose in foods, including the possible setting of management thresholds for the absence or reduction of lactose in foods. It was anticipated that the results of this research would inform UK negotiations and input into such discussions, and would inform the guidance that would need to be drawn up to accompany the new legislation.

How the study was carried out:

The research was conducted using a mix of telephone and face to face interviews with participants. Sixty-three interviews were conducted in total, approximately half of these (32) with consumers who had a milk sensitivity (milk allergy, milk intolerance, lactose intolerance or galactosaemia), and the other half split between health professionals (15) and businesses (16) drawn from across the UK. Interviews were supported by discussion guides which had been developed for each participant group in order to explore, amongst other relevant aspects, understanding of the labelling terms 'dairy free', 'milk free' and 'lactose free'.

Key findings:

- The key food labelling information that is scrutinised by consumers is still the ingredients list and specialised allergen information/advice statements. The claims on food labels indicating the absence or reduction of milk/lactose/dairy have not yet established themselves as a device that consumers and health professionals feel they can rely on. Health professionals focus on educating consumers to exclude specific ingredients rather than seeking out products making these types of claims. 'Lactose free' was generally assumed to be suitable for people with lactose intolerance; there was uncertainty about whether or not products labelled as 'lactose free' were suitable for people with a milk allergy or intolerance, particularly amongst health professionals. People with lactose intolerance

were uncertain about the suitability of products described as ‘dairy free’ or ‘milk free’ for them.

- ‘Dairy free’ was the most widely used and most widely understood term, as this was understood to refer to the absence of both milk and products derived from milk, such as butter, yoghurt and cheese, although some mistakenly thought that such products were also free from eggs. There was significant confusion about the term ‘milk free’, as this was thought by some to mean the absence of alternative ‘milks’ made from plants such as soya or rice, as well as of animal milks, but others thought that it only referred to cows’ milk. There was also confusion about whether ‘milk free’ products could contain butter, yoghurt and cheese or were just free from milk itself.

- Greater guidance was felt to be needed to help consumers understand what the terms mean if they are to make appropriate use of them

Impact on Agency policies/policy development/advice:

The results of this research fed into European Commission discussions on whether it was appropriate to develop labelling legislation for foods labelled as ‘lactose free’ and ‘low lactose’. Partly as a result of these findings, the European Commission decided that it was not appropriate to develop legislation in this area at that time. This was a positive outcome for UK consumers as the legislation developed may have resulted in claims such as ‘dairy free’ (which are widely understood by the UK consumer) no longer being permitted for foods suitable for people with a lactose intolerance.

This research also highlighted the confusion and lack of understanding that exists with labelling terms used to indicate the absence or reduction of lactose, milk or dairy. Therefore the findings of this research will be useful for the Agency should future guidance be developed in this area.

Research Project T07057:

Evaluation of the effectiveness of Food Standards Agency best practice guidance on allergen management and consumer information

Contractor: Jigsaw Research

Principal Investigator(s): James Flack

Start and End date: September- November 2008

Scientific/policy question being addressed:

In 2006, the Food Standards Agency published voluntary Guidance on Allergen Management and Consumer Information, which comprised of a main guidance document aimed at larger food businesses and enforcement officers and a leaflet for smaller businesses. This document is 'best practice' guidance aimed at UK food businesses, on how effectively to control food allergens in the factory setting, with particular reference to avoiding cross-contamination and using appropriate advisory labelling on food products for retail sale (e.g. 'may contain' warning). This research aimed to assess the uptake (by UK food businesses) and effectiveness of the 2006 guidance, in order to enable the Agency to decide whether any improvements and/or further dissemination activities were required and to inform future policy development.

How the study was carried out:

The project comprised both qualitative and quantitative research. For the quantitative stage, a total of 382 semi-structured telephone interviews were conducted with 255 'free-found' (randomly selected) Food Manufacturers (who were aware of the guidance), 27 Food Manufacturers who had ordered a hard copy of the guidance from FSA and 100 Enforcement officers. For the qualitative stage, a total of 35 in-depth interviews were conducted with 18 food manufacturers, 6 large retailers, 3 training bodies, 8 enforcers (EHOs/TSOs) from across the UK.

Key findings:

- Just over half of the food manufacturers interviewed (53%) were aware of either the full guidance or the leaflet. 48% of these were aware of the full guidance document, while 22% were aware of the leaflet (with some aware of both). Most manufacturers reported that they became aware of the guidance either through internet searches leading to the FSA website or, particularly in the case of smaller organisations, through their environmental health officer or Trading Standards Officer.
- Awareness amongst retailers was mixed. Most training bodies and 78% of enforcement officers were aware of the guidance and 90% of these were actively using it.

- Opinion of the guidance amongst manufacturers who were aware of the guidance was very positive with 100% of manufacturers rating the full guidance as useful, while 74% did the same for the leaflet. In addition, those manufacturers who were unaware of the guidance thought it would be useful to them. 83% thought it would very or fairly useful. Manufacturers considered that both the leaflet and particularly the full guidance had had a large impact on their business.
- Negative comments about the guidance were centred around frustration among some that the guidance was not updated more regularly which can undermine its usefulness as some thought it was out of date. A few manufacturers and Enforcement Officers thought there needed to be something that was longer than the leaflet but shorter than the full guidance.

Impact on Agency policies/policy development/advice:

The positive impact of the guidance and the importance of EHOs/TSOs as a route of dissemination to smaller businesses led the Agency to increase the resources directed towards raising awareness of the guidance with enforcement officers through a variety of training forums. The Agency also made a decision to focus additional resources towards informational initiatives such as to develop allergen management thresholds, which could be used as a quantitative element to the existing Guidance that was currently predominantly qualitative.

Research Project T07063:

Guidance on the provision of allergen information for non pre-packed foods - Evaluation Research

Contractor: Jigsaw Research

Principal Investigator(s): James Flack

Start and End date: January – March 2010

Scientific/policy question being addressed:

In 2008 the Food Standards Agency (FSA) produced voluntary best practice Guidance on the Provision of Allergen Information for Non Pre-packed Foods aimed at caterers and retailers, which gave advice on controlling food allergens in food businesses where the food has not been pre-packed e.g. take-aways, restaurants, bakeries, deli counters, sandwich bars and schools etc.

This research was commissioned to assess the awareness and uptake of the guidance amongst these businesses and with food law enforcement officers, and to gauge its impact on businesses. The guidance was accompanied by a leaflet and a poster, and research also examined the impact of these supporting materials amongst the target audience. This information would enable the Agency to decide whether the guidance was effective and if any changes to it were necessary and would also help to assess whether the existing guidance would be sufficient for businesses if a statutory requirement to provide allergen information was introduced.

How the study was carried out:

The project consisted of both qualitative and quantitative research. For the qualitative stage, a total of 16 in-depth interviews were conducted with various caterers and retailers, some training bodies and Environmental Health and Trading Standards Officers (EHOs and TSOs) from across the UK. For the quantitative stage, a total of 374 semi-structured telephone interviews were conducted with caterers and EHO's and TSO's from across the UK.

Key findings:

- Only a quarter of businesses were aware of the guidance. Small and micro-businesses were less aware than the larger businesses. Awareness was much higher amongst enforcement officers (89%), where most had accessed and read the guidance.
- The vast majority of businesses and enforcers thought the guidance was useful and opinion on all elements was generally very positive. Different elements tended to be utilised to a greater/lesser extent by the different parties/types of business, as expected.

- There was some evidence that those aware of the guidance had more controls in place and are more proactive with regard to allergen issues, i.e. the guidance is driving change in some businesses.
- FSA and local authorities were considered appropriate routes for businesses to gain access to the guidance. Suggestions were made for improving dissemination and awareness amongst the target group.
- The researchers recommended that, given the above, no major changes were needed to the full guidance, leaflet or poster. The key issue for the FSA was to boost awareness and usage of the guidance among both enforcers and businesses, by:

- Stressing the importance of allergen controls and customer notification in non pre-packed foods,
- ensuring as many businesses as possible are aware of the guidance,
- in the longer term, by increasing consumer awareness in the expectation of this leading to higher levels of business engagement

Impact on Agency policies/policy development/advice:

The findings of this work were used when developing UK negotiating lines on the requirements for non-prepacked foods as the EU Food Information for Consumers Regulation (FIR) was being negotiated. A decision was taken not to increase dissemination efforts for this best practice guidance after this review as the FIR negotiations had already commenced.

ANNEX 7

Publications arising from Food Allergy and Intolerance Research Programme projects included in the review (as of November 2012)

Project Code	Publications
T07046	• Keil, T., et al., The multinational birth cohort of EuroPrevall: background, aims and methods 2010 Allergy. Apr;65(4):482-90. • Grimshaw, K., et al., Infant feeding and allergy prevention: a review of current knowledge and recommendations. A EuroPrevall state of the art paper. 2009. Allergy.Oct;64(10):1407-16. • Mills. E. N., et al., The prevalence, cost and basis of food allergy across Europe. 2007. Allergy. Jul;62(7):717-22.
T07046 addendum	• Not applicable
T07053	• Not applicable
T07062	• Not applicable
T07067	• Not applicable
T07068	• Not applicable
T07052	• Thompson, R., et al., Peanut sensitisation and allergy: influence of early life exposure to peanuts. 2010. British Journal of Nutrition, Br J Nutr. 2010 May;103(9):1278-86.
T07051	• Not applicable
T07060	• Not applicable

T07049	• Not applicable
T07041	• Chan, S., et al., Cutaneous lymphocyte antigen and a4b7 T-lymphocyte responses are associated with peanut allergy and tolerance in children. Allergy. 2012 Mar;67(3):336-42 • Turcanu, V., et al., Peanut-specific B and T cell responses are correlated in peanut-allergic but not in non-allergic individuals. Clin. Exp. Allergy, 38: 1132-1139 • Turcanu, V., et al., IgE-mediated facilitated antigen presentation underlies higher immune responses in peanut allergy. Allergy. 2010 Oct;65(10):1274-81.
T07042	• Clark A, et al., A longitudinal study of resolution of allergy to well-cooked and uncooked egg. Clin Exp Allergy. 2011 May;41(5):706-12. doi: 10.1111/j.1365-2222.2011.03697.x. • Tay, S., et al., Patterns of immunoglobulin G responses to egg and peanut allergens are distinct: ovalbumin-specific immunoglobulin responses are ubiquitous, but peanut-specific immunoglobulin responses are up-regulated in peanut allergy. Clin Exp Allergy 2007, 37: 1512-1518 • Tay, S., et al., T cell proliferation and cytokine responses to ovalbumin and ovomucoid detected in children with and without egg allergy. Clin Exp Allergy 2007, 37: 1519-1527
T07058	• Leftwich, J., et al., The challenges for nut-allergic consumers of eating out. 2010. Clin. Exp. Allergy, 41: 243-249 • Barnett, J., et al., The strategies that peanut and nut-allergic consumers employ to remain safe when travelling abroad. 2012. Clin Transl Allergy. Jul 9;2(1):12. [Epub ahead of print] • Barnett, J., et al., How do peanut and nut-allergic consumers use information on the packaging to avoid allergens? 2011. Allergy. Jul;66(7):969-78. • Barnett, J., et al., Using 'may contain' labelling to inform food choice: a qualitative study of nut allergic consumers. 2011. BMC Public Health. Sep 26;11:734.

T07059	• Not applicable
T07065	• Not applicable
T07061	• Not applicable
T07064	• Not applicable
T07057	• Not applicable
T07063	• Not applicable