Development of reference materials: Introduction

Food hypersensitivity is an increasing problem for many stakeholders with much effort focused on assessment and management of the risks including risk assessment toolkits (for example, the Allergen Bureau Voluntary Incidental Trace Allergen Labelling VITAL®, the iFAAM consortium and the ILSI-Europe Allergen Quantitative Risk Assessment guidance). These toolkits describe the use of action levels and reference doses to assess the risks. A combination of the estimated eliciting dose of allergenic food, (in milligrams as protein) and the amount of food consumed in a single eating occasion can give a threshold or action level as milligrams (as protein) per kilogram (kg) of food) (mg kg-1 as protein) that would provoke an reaction in a given proportion of the allergic population. The eliciting dose is extrapolated from oral food clinical dose-distribution relationships. The results of analysis can be compared to the thresholds or action levels in risk assessment and risk management. Precautionary allergen labelling, well recognized as sub-optimal, could also be improved via an action level approach. Implementation and regulation depend on the ability to measure allergens properly; yet all current analytical approaches exhibit deficiencies, many of which can be addressed by the proper use of appropriate allergen reference materials (RMs). This report describes a pilot project to:

1) Systematically review allergen analytical targets used in ELISA, PCR and MS to allow the creation of a repository of reliable markers and open access verified allergen sequence sets for the studied allergens;
2) Facilitate a guided stakeholder workshop to achieve consensus on priority allergens, physical format of RMs, incurred concentrations and impact of processing;
3) Prepare a RM kit containing (a) a food matrix shown to be devoid of the target allergens, (b) the food matrix incurred with 5 allergens and (c) the raw materials (the allergenic foods);
4) Disseminate to encourage RM use to achieve tangible improvements in allergen analysis, establish a template of best practice for the future and make recommendations for follow up work to complete a set of RMs for the legislated and priority allergens.

The RM matrix is based on that used for clinical dose-distribution studies and the raw allergen materials have been characterised by proteomics. The matrix and incurred allergens are industrially relevant to processed foods and the allergen concentrations are clinically relevant in the light of eliciting dose studies. The RM kit has been prepared following a well-established process that includes prescribed homogeneity and stability studies and a formal sign-off procedure of the statements of measurement, in accordance with ISO 17034:2016 ‘General requirements for the competence of reference material producers’ (an updated standard originally ISO GUIDE 34:2009). In October 2020 following detailed external assessment the RM kit was confirmed within the NML scope of ISO 17034 accreditation. ISO 17034:2016 covers the production of all reference materials, including certified reference materials. It is intended as part of the general quality assurance procedures of the reference material producer.

LGC formed a consortium which was awarded this project by the FSA following an open competitive tender. The consortium consisted of LGC, the University of Manchester and Romer Laboratories Ltd. The consortium is world leading in (a) the preparation, curation and distribution

of RMs in an accredited environment and (b) the characterisation of allergen proteins. Synergy with other concurrent work (for example, by iFAAM, EFSA, ILSI, MoniQA, JRC, and AOAC) has ensured value for money.

This report has been compiled from a review of a broad range of data sources including:

- the scientific literature
- the tender documents
- progress reports and minutes of project meetings
- LGC internal documents and in particular the Material Report[1]
- UoM reports
- Romer Lab reports.