

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

UPDATE ON G03 RESEARCH PROGRAMME

Issue

Members are asked to note the commissioning of four research projects and three new research requirements within the Food Standards Agency's G03 research programme (The safety assessment of novel and GM foods).

Background

1. The Committee considered potential research requirements for the safety assessment of GM and novel foods at its July 2004 meeting (ACNFP/67/2). Many of these ideas were incorporated into the Agency's rationale for financial authority for the research programme, which was presented to the committee for information in March 2005 (ACNFP/71/6).

2. The aim of the G03 programme is to build on and continue to support the mandatory safety assessment of novel foods, applying existing information. A number of research areas are proposed. For example, metabolic profiling, proteomic analysis, analysis of junction sequences, and new approaches to allergenicity testing.

3. Two new projects have been commissioned and are currently underway. Two more are currently being commissioned and will commence in the next few months.

G03012: Development of unified data models and data pre-processing strategies and the generation of meaningful, standardised statistical analyses of metabolome variability in crop plants.

4. A two-year study at University of Wales, Aberystwyth started in November 2005 and directly addresses the need to have baseline metabolomic data for crops to use as a reference in assessing new crop varieties (GM or non-GM). It also addresses how the quality of the raw data used for assessment purposes may affect the safety assessment. The applicants will use previous data from the Agency's G01 and G02 programmes to establish baselines with particular reference to GM potato cultivars. The project will also include the further development of an internet accessible metabolomics database (ArMet) to include the metabolomic information from the Agency's previous G02 projects.

G03016: An investigation into the use of MudPIT as a tool for the separation and quantification of proteins for GM crop safety assessments.

5. A three-year study at Royal Holloway, University of London started in January 2006. This work investigates the use of Multidimensional Protein Identification Technology as a quantitative procedure to compare protein profiles in GM and non-GM plants. This will enable the identification of any unintended effects of the genetic modification process. Previous work in the G02 programme identified MuDPIT as a method worthy of further investigation because it is less labour intensive and more sensitive than traditional gel based protein separation techniques and can be linked directly to a mass spectrometer in order to provide a more accurate quantitative protein profile. Isotopic labelled standards and isobaric tags¹ will be used to label peptides in order that quantification can be undertaken by complementary mass spectrometry techniques. This project particularly aims to focus on extraction and preparation procedures to enable the detection of proteins in low abundance or those that are difficult to extract. Tomato will be used to develop the method. Once the method has been tested in a variety of tomato varieties it will be trialled in at least one other crop.

Other projects

6. The Agency has also agreed to co-fund work by LGC Ltd carried out as a part of an EU programme, "Co-Extra". This European integrated research project will study and validate biological containment methods, model supply chain organisation, and provide practical tools and methods for implementing co-existence of GM and non-GM based supply chains. This specific work package will develop the appropriate control plans for the use of selected GM detection methods. The project will use an approach based on the separate validation of different modules of analytical methods using specific GM food examples.

7. The Agency is also commissioning Taylor Nelson Sofres (a market research company) to carry out post market monitoring of phytosterol products. A two-stage approach will be used. The first stage will use TNS family food panel data to gain an understanding of types of consumers and how often people consume products with added phytosterols. A second stage will involve the use of a questionnaire to examine how an individual's consumption changes over a long period of time and their awareness and understanding of the labelling on such products.

8. Three new research requirements were issued in December 2005 and proposals are requested by 1 March 2006. These are for the development of a standard validated method(s) for the analysis of junction sequences in GM crop plants, the development of new or improved methods for the identification of allergenic epitopes in novel (including GM) foods and DNA detection methods for GM foods that can be used as simple screening methods for enforcement work. It is not possible to predict the duration of these projects at present. The requirements are detailed at Annex 1.

¹ Non polymeric, isobaric reagents yield amine-derivatised peptides from a protein digest. These are chromatographically identical and indistinguishable in MS but produce strong low-mass MS/MS signature ions that permit quantitation.

Committee Action Required

9. Members are asked to note the commissioning of these research projects and the call for new research.

**Secretariat
January 2006**

Annex attached:

Annex 1: G03 Research Requirements December 2005.

ACNFP/75/10 Annex 1

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

G03 Research Requirements December 2005.

**Secretariat
January 2006**

G03 – The safety assessment of novel and GM food

Introduction

Research funded by the Novel Foods, Additives and Supplements Division of the FSA supports the Agency's role in the rigorous safety assessment of all novel and genetically modified (GM) foods. This research ensures that sound science is applied to consumer safety issues concerning novel and GM foods.

This new research programme will build upon the results obtained in two previous programmes on the safety (G01) and safety assessment (G02) of novel foods and continue to support the mandatory safety assessment of GM and non-GM novel foods.

The G01 and G02 programmes aimed to underpin the safety evaluation of novel foods and refine the current safety assessment procedures for GM foods to cover the next generation of GM plants. G01 focused on projects to ensure that the introduction of novel foods is achieved safely by providing a framework of generic methods and information against which the safety evaluation of a specific novel food can be assessed. Under G01, analytical procedures were developed with a view to ensuring that existing and proposed labelling regulations can be enforced. The programme also funded projects which addressed the potential for horizontal gene transfer from the GM organism to gut bacteria, the potential for GM and novel foods to be allergenic, addressed transgene stability and looked for unintended effects arising from transgene insertion. Under G02, emerging techniques were developed, which explored the applicability and practicality of using a variety of technologies in genomics, proteomics and metabolic profiling in the safety assessment process.

The new G03 programme will build on and continue to support the mandatory safety assessment of GM and novel foods in order that the most up to date scientific knowledge may be used, and to support the enforcement of GM labelling regulations.

Research/Survey Requirements

Develop a standard validated method(s) for the analysis of junction sequences in GM crop plants and investigate the process of transgene insertion in GM crop plants

Until recently the characterisation of the transgene insertion point for crop plants has been difficult and time consuming. However, work carried out under the G02 programme and other recently published work has resulted in a method(s) for the rapid analysis of junction sequences, which will assist in the risk assessment of GM crops.

Junction sequences are the DNA sequences that delimit the insertion of a transgene into the host genome. The ability to analyse junction sequences is crucial to the molecular characterisation of transgenic crops as the information can be used to establish the position of the transgene in the plant genome.

The European Food Safety Authority (EFSA) guidelines for the risk assessment of GM plants lists the characterisation of the insertion point of the introduced transgenic trait as one of the requirements for establishing the safety of GM crop plants. This is because once the site of insertion has been determined this will provide information as to whether any functional genes are disrupted, which may lead to undesirable unintended effects, and whether any new open reading frames (ORFs) are created resulting in the synthesis of novel proteins. If so, further work can be carried out to determine whether these ORFs may code for potential allergens or toxins.

The discovery of a rapid polymerase chain reaction (PCR) based method for the identification of junction sequences paves the way for the refinement and validation of this method and its use to investigate factors affecting transgene insertion. This may lead to a better understanding of the mechanism of transgene insertion into the plant genome.

Proposals are therefore invited to:

Requirement Reference: G03R0009

Develop a standard validated method(s) for the analysis of junction sequences in GM crop plants and investigate the process of transgene insertion in GM crop plants.

Investigate the use of state of the art scientific techniques (in bioinformatics and proteomics) to develop new or improved methods for the identification of allergenic epitopes in novel (including GM) foods

There are no inherent grounds for assuming that GM or other novel foods are more or less allergenic than traditional foods. However, the safety assessment of novel (including GM) foods includes a consideration of the potential of the modification to illicit an allergic response, and considers the allergenic potential of novel foods. This requires assessment of the allergenicity of any new protein(s) by predictive methods or experimental testing.

The EFSA guidelines for the risk assessment of GM plants include the characterisation of the potential allergenicity of any new proteins introduced into a GM plant. Or those created by the production of new open reading frames at the site of the DNA insertion into the plant genome that may result in the synthesis of novel peptides or proteins.

Current methods for the assessment of the allergenicity of novel (including GM) foods involve comparison of linear sequence data from novel proteins with databases of known allergens (bioinformatics) together with tests, for example, serum cross reactivity tests involving potential new allergens. Other tests include the susceptibility of a protein to digestion in simulated gastric fluid. This test is used to determine the ability of a potential allergen to survive passage through the gut. If a protein is susceptible to digestion then its potential as an allergen is much reduced as it will not survive long enough to provoke an allergic reaction. While these methods are currently considered adequate in the context of the safety assessment, recent advances in bioinformatics such as 3-dimensional modelling of proteins and proteomics could be used to further refine the process. Specifically relating to bioinformatics improvements to, and harmonisation of, the algorithms that are used to compare sequence data and development of databases (which include information on the 3-dimensional structure and function of known allergens and allergenic protein families) would be welcome. However, these suggestions are not exhaustive and other approaches will be considered.

Proposals are therefore invited to:

Requirement Reference: **G03R0010**

Investigate the use of state of the art scientific techniques (in bioinformatics and proteomics) to develop new or improved methods for the identification of allergenic epitopes in novel (including GM) foods.

Develop new DNA detection methods (or refine existing ones) for GM foods that can be used as simple screening methods for enforcement work

The Agency is the Competent Authority for the enforcement of the GM Food and Feed Regulation (EC 1829/2003). This lays down labelling requirements for GM food and feed ingredients. A threshold is in place for the accidental presence of GM material, below which labelling is not required (0.9% threshold for authorised genetically modified organisms (GMOs) and 0.5% for non-authorised GMOs where there has been a favourable safety assessment from an EC scientific committee). There have been calls by some stakeholders for the threshold limit to be reduced to 0.1%.

To enable checks into whether these labelling regulations are working in practice it is necessary for GM DNA detection methods in foods to be available using high through put, low cost methodologies. Polymerase chain reaction (PCR) methods require expensive equipment, which is inaccessible to the majority of Public Analyst laboratories. Further techniques therefore need to be developed for a range of GM ingredients, with particular focus on a screening method for raw materials for routine enforcement work.

Although Regulation EC 1829/2003 does not specify how the percentage of GM content is calculated, there has been recent debate on the fact that the DNA ratio of a certain GM crop may not necessarily be proportional to the weight ratio of that cultivar. The Commission has therefore recommended that rather than use a weight per weight ratio the results for quantitative analysis should be expressed as the percentage GM-DNA copy numbers in relation to target taxon specific DNA copy numbers calculated in terms of haploid genomes. Applications should demonstrate consideration of this issue.

Work carried out under the Agency's G01 programme aimed to use mass spectrometric techniques for the detection of GM protein and DNA. These and other techniques, need to be developed further so that they become low cost and accessible for use on simple instrumentation.

Proposals are therefore invited to:

Requirement Reference: **G03R0011**

Develop new DNA detection methods (or refine existing ones) for GM foods that can be used as simple screening methods for enforcement work.