

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

AN UPDATE ON NOVEL FOODS RESEARCH

ISSUE

This paper provides members with information on the Agency's research programme for novel foods.

BACKGROUND

1. In July 2004, the Committee was asked to consider priorities for commissioning future research by the Novel Foods, Additives and Supplements Division, to underpin the safety of GM and novel foods (paper ACNFP/70/4).
2. The Committee's response was incorporated into an application for funding document, which is currently being considered by the Agency's Resources Sub-committee. An update of progress will be given at the ACNFP meeting. A copy of the funding document (RCU-B1) is at Annex 1.
3. Key areas where funding is sought include:
 - Further developing the profiling technologies for GM plants, established under the G02 programme, for use in the safety assessment of both novel and GM foods, particularly focussing on metabolomics and their potential in toxicological assessment. Also, investigating the use of MudPIT (Multidimensional protein identification technology) as a quantitative method for protein analysis in GM and non-GM safety assessments.
 - Building upon the success of the G02 programme by collating the data it generated, into easily utilisable internet accessible databases. This will ensure that the knowledge gained in G02 is maintained and can be specifically applied to research being carried out in the international arena (e.g. setting baselines for metabolite variation in GM crop plants in order to inform safety assessment under the GM Food and Feed Regulation). Such information can easily be used by others in the Agency e.g. for nutritional profiling and authenticity work.
 - Building upon the outcome of project G01021 (which looked at the use of commercial databases and their potential for post-market monitoring) to investigate methods for examining how newly introduced foods are consumed by subsets of the population. Using these methods to carry out post market monitoring activities on specific food products such as the

expanding range of products containing phytosterol and phytostanol ingredients. This will directly address concerns raised by the Committee regarding the consumption of these products by non-target groups.

- In collaboration with the Agency's programme on Data Quality and Improved Methods of Analysis, funding work to improve sampling approaches and validation of detection methods for use in the enforcement of the GM Food and Feed regulation.
- Investigating further the potential for horizontal gene transfer from GM food to bacteria and cells in the gastrointestinal tract by considering recommendations made by the GM Science Review Panel.
- Improving our understanding of how properties of the food matrix can have an effect in determining allergenic potential of foods, with a particular focus on GM and novel foods.
- Assessing emerging, novel techniques for food production in relation to their effects on food safety and assessment procedures that may be necessary.
- Addressing more specific, contentious, areas of the safety assessment of GM foods such as
 - a) implications of transgene insertion (in regions flanking the new gene)
 - b) whether proteins expressed in GM plants are truly equivalent to their microbial counterparts and
 - c) whether allergenicity assessments that are currently carried out using existing bioinformatic techniques can be improved.

NFASD have also sought funding to co-support some projects in the European Framework 6 Programme:

- The Agency can collaborate within a Framework 6 project (CoExtra) which is aiming to improve the detectability of GM DNA / protein in foods and produce best practice guidelines for data analysis and methods validation. An input of approximately £100,000 will gain the Agency access to a UK partner's research worth at least double this amount (and potentially millions more within the EU).
- There is also potential for collaboration with another EU Framework 6 project (EuroPrevall), assessing aspects of allergy that are particularly relevant to novel foods (a UK birth cohort study to determine the prevalence of allergenicity – funded by Consumer Choice and Allergy Division). The Agency would gain access to approximately £12M of research on all aspects of allergy research. Of particular relevance for novel and GM foods is the need to investigate the role of the food matrix in determining the allergic potential of food.

**Secretariat
March 2005**

Annexes attached:

Annex 1: Financial Authority for a new Research Programme.
G03: The Safety Assessment of Novel Foods.

ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES

Financial Authority for a new Research Programme.
G03: the safety assessment of novel foods

**Secretariat
March 2005**

RCU-B1

Financial Authority for a new Research Programme

SECTION 1 - GENERAL

(see Guidance Notes, Section 1)

- | | | | | |
|----|---------------------------------------|--|-----------------|--|
| 1. | Proposer's full name and title | DR TRUDY NETHERWOOD | Tel. No. | X8592 |
| | Position held | HEAD OF GM LABELLING AND FOOD SUPPLEMENTS BRANCH | E-mail | trudy.netherwood@foodstandards.gsi.gov.uk |
| 2. | Policy division | NOVEL FOODS, ADDITIVES AND SUPPLEMENTS DIVISION (NFAS) | | |
| 3. | Programme title | G03: THE SAFETY ASSESSMENT OF NOVEL AND GM FOODS | | |

4. **Aim of the research:**

The aim of this new programme is to build on, and continue to support the mandatory safety assessment of novel foods, applying existing information. The programme will build upon the results that have been obtained in two previous programmes on the safety, and safety assessment, of novel foods (G01 and G02), as well as recommendations from relevant experts and the Agency's Advisory Committee on Novel Foods and Processes (ACNFP). It will also deliver or underpin delivery of the Agency's Strategic Plan targets and / or other Agency business needs.

5. **Abstract of research.**

A novel food is defined as a food or food ingredient not hitherto consumed significantly within the EC prior to the implementation of the EC Novel Food Regulation in May 1997. GM foods were also assessed under this Regulation until 18 April 2004 when the GM Food and Feed Regulation came into force.

The safety assessment of novel foods involves one Member State taking the lead, with all other MS commenting on the initial opinion of the lead MS before a decision is made by qualified majority vote. The UK is advised by the Advisory Committee on Novel Foods and Processes, with respect to the risk assessment. Since 18 April 2004, the risk assessment process for GM foods has been centralised within EFSA, but with decisions still being taken by MS.

Examples of applications looked at to date include: the use of isomaltulose as a novel food ingredient; juices and nectars with added phytosterols, aimed at lowering blood cholesterol levels; lycopene from a fungal source and tomatoes, used as an antioxidant and; Omega 3 rich oil from a fungal source.

The G01 (Safety of novel foods) and G02 (Safety assessment of novel foods) 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. This programme also aimed to provide Government with information necessary to facilitate the development of scientifically valid, internationally acceptable procedures for the safety evaluation of novel foods including those from Genetically Modified Organisms (GMOs) to ensure consumer safety. 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 to gut bacteria, 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 G02 programme was funded by the treasury as a special award to the FSA.

In 2002, the Government began a national dialogue on GM issues to assess and discuss the concerns and queries of the many, varied stakeholders involved. This included addressing public concerns regarding the science around GM. The GM Science Review Panel identified certain areas as requiring further study, including horizontal gene transfer from all GM foods.

Novel food authorisations recently have included those for phytosterol ingredients that have specific health benefits for target groups, e.g. cholesterol lowering properties. However, particular groups, e.g. young children and women who are pregnant or breast feeding, should avoid such products because of concerns regarding vitamin consumption. Risk management measures have been put in place that are intended to discourage consumption by non-intended groups and to ensure that the products are not over-consumed by the target group. ACNFP are concerned, however, that these measures should be demonstrated to be effective, through a programme of post market monitoring (PMM), and have recommended strongly that phytosterol-containing products (which are to be avoided by young children) should be the focus of a PMM programme. In the case of GM foods, the GM Food and Feed Regulation contains a provision that all approved GM foods may be subject to PMM if deemed appropriate.

The proposed 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. This programme fulfils the Division's policy objective to ensure food safety through the rigorous assessment of GM and novel foods. It also forms part of the Agency's strategic plan to ensure the safety of food, effectively enforced food safety legislation and strengthening of the evidence base by taking account of the best available science. Specifically the programme aims to:

- Develop further, the profiling technologies for GM plants, established under the G02 programme, for use in the safety assessment of both novel and GM foods particularly focussing on metabolomics and their potential in toxicological assessment. Also, to investigate the use of MudPIT (Multidimensional protein identification technology) as a quantitative method for protein analysis in GM and non-GM safety assessments.
- Build upon the success of the G02 programme by collating the data it generated, into easily utilisable internet accessible databases. This will ensure that the knowledge gained in G02 is maintained and can be specifically applied to research being carried out in the international arena (e.g. setting baselines for metabolite variation in GM crop plants in order to inform safety assessment under the GM Food and Feed Regulation). Such information can easily

be used by others in the Agency e.g. for nutritional profiling and authenticity work.

- Build upon the outcome of project G01021 (which looked at the use of commercial databases and their potential for post-market monitoring) to investigate methods for examining how newly introduced foods are consumed by subsets of the population. Use these methods to carry out post market monitoring activities on specific food products such as the expanding range of products containing phytosterol and phytostanol ingredients. This will directly address concerns raised by the ACNFP regarding the consumption of these products by non-target groups.
- In collaboration with the E01 Data Quality and Improved Methods of Analysis programme, fund work to improve sampling approaches and validation of detection methods for use in the enforcement of the GM Food and Feed regulation.
- Investigate further the potential for horizontal gene transfer from GM food to bacteria and cells in the gastrointestinal tract by considering recommendations made by the GM Science Review Panel¹.
- Improve our understanding of how properties of the food matrix can have an effect in determining allergenic potential of foods, with a particular focus on GM and novel foods.
- Assess emerging, novel techniques for food production in relation to their effects on food safety and assessment procedures that may be necessary
- Address more specific, contentious, areas of the safety assessment of GM foods such as
 - a) implications of transgene insertion (in regions flanking the new gene)
 - b) whether proteins expressed in GM plants are truly equivalent to their microbial counterparts and
 - c) whether allergenicity assessments that are currently carried out using existing bioinformatic techniques can be improved.

Cost estimates are based on the costs of currently funded projects.

6a. **Total budget requested (ex VAT)**

6b. **Programme duration in years**

6c. **Proposed start date** 6d. **Proposed end date**

¹ GM Science Review Panel (2003). GM Science Review. First Report. An open review of the science relevant to GM crops and food based on the interests and concerns of the public.
www.gmsciencedebate.org.uk/report/default.htm#first

7. **What policy objective(s) does the proposed research address?**

- The safety assessment of novel and GM foods must continue to be based on up to date scientific knowledge in order for the Division to take forward its role in relation to the safety of foods approved under both the Novel Foods Regulation and GM Food and Feed regulation.
- More sensitive methods for GM detection will be needed to ensure that GM material can be identified in food and feed ingredients at levels below 0.5%. These techniques will help to assess how the new GM labelling regulations, implemented in April 2004, work in practice for consumers.
- New technologies for food production and processing are likely to raise new challenges for safety assessment, which the G03 programme will address.

8. **How does the research inform or influence current and future FSA strategy?**

Current: The programme will ensure that the most up to date science is used to improve the safety assessment of novel and GM foods, thereby providing greater protection for consumers.

Future: The Agency will build upon its reputation for developing “cutting-edge” science following the success of the G02 programme which was funded as a special award from the Treasury to the FSA. The FSA has already led the way in Europe by funding research in this area.

SECTION TWO - RATIONALE

(see Guidance Notes, Section 2)

9. **Summarise why the research programme is needed, why other approaches are not appropriate and the potential for adding value by collaboration with other organisations.**

What is the political and societal context driving the research?

- **Stakeholder concerns** – especially with regard to consumer’s concerns for potential horizontal gene transfer from GM foods, and post-market monitoring of novel foods in relation to identifying which sub-sets of the population consume these foods. Of particular interest to the ACNFP are the extended range of products containing phytosterols. They are concerned as to whether these products are being consumed by relevant groups.
- **Recommendations for future research** – these have been identified by a panel of scientific experts which met in July 2004 to discuss work carried out to date and the future direction of research in this area and by the Advisory Committee on Novel Foods and Processes (ACNFP) which includes consumer representatives. The Government’s GM Science Review panel has also identified certain areas as requiring further study, including those listed under “stakeholder concerns” (above).
- **Requirements to support existing legislation**
 - a) As scientific knowledge and techniques advance, information is required to continue to support the safety assessment process under two sets of EU legislation (the Novel Foods Regulation and GM Food and Feed Regulation) to ensure that the most up to date knowledge is applied. The Agency is the competent authority within the UK for both. Improving molecular and bioinformatic methods could potentially reduce the need for animal experimentation (e.g. in assessing toxicity).
 - b) Further development of methods are needed for the detection of GM material in food and feed ingredients.

Gap analysis – what are the key knowledge gaps to be addressed and how were they identified?

- The Government’s GM Science Review Panel report outlined a number of areas where further information would be valuable in the safety assessment of GM food and feed:
 - i) better methods for assessing nutritional and toxicological differences between GM and non-GM crops
 - ii) better methods for predicting allergenic effects of GM crops
 - iii) further information on the fate of transgenic DNA in the gastrointestinal tract
 - iv) the effect of GM derived feed in the human food chain
- The Division has considered the recommendations from the GM Science Review and sought further advice by holding a meeting with independent external scientific experts and other bodies that fund work in similar areas (such as the BBSRC and Defra). The ACNFP (including consumer experts) was also consulted on the recommendations made by the panel at this meeting. The Division is aware of the many views of its various stakeholders, through the regular correspondence it receives. Other sources of information in identifying research needs have been research contractors, the views of other bodies and the expertise of Agency staff and the G01/G02 programme advisor.

- The areas that have been identified fall under the broad remit of safety assessment of novel foods and safety assessment of GM foods as outlined below.

Safety assessment of novel foods:

A novel food is defined as a food or food ingredient which has not hitherto been used for human consumption to a significant degree within the European Community prior to the implementation of the EC Novel Food Regulation in May 1997.

- a) Further research is needed into viable methods for post-market monitoring of novel foods (including GM foods). Predictive modelling has been identified as a potential approach and the efficacy of this strategy can be tested on examples of previously introduced foods. Previous work in this area has been commissioned by the Agency in the form of a project, which investigated the feasibility of using commercially available databases on household food consumption, and sales through major supermarkets, to carry out national surveillance. The study only examined the feasibility of carrying out long-term surveillance and did not explore health databases. This work was carried out, for the most part, in relation to GM ingredients, however it was concluded that the study could be used for the monitoring of novel foods after sale. Health Canada is also considering taking forward exploratory work on post-market monitoring, shortly, through the use of computer modelling systems which is more likely to focus on novel products rather than GM ingredients or novel foods. The Agency intends to monitor progress of this Canadian study. The Agency is not currently aware of any other initiatives on the post-market monitoring of novel and GM ingredients. The Chief Medical Officer, the Science Review Panel, the British Medical Association and the ACNFP have identified this as a research need. It would also ensure that the Agency's commitment to food safety was being met, with respect to GM and novel foods.
- b) A number of recent EU novel food applications have looked at the use, as ingredients, of a number of extracts isolated from plants, algae or fungi. Whilst there are reports relating to the benefits of the consumption of such components, often the effect of long-term raised level consumption in the general population as a whole, and in particular any identified at-risk groups is poorly understood. Information on consumption is therefore needed in order to assess the effectiveness of risk management measures that accompany novel food authorisations and confirm assumptions made during the pre-market evaluation. The ACNFP has identified this as an important research need. It would also contribute towards meeting the Agency's commitment to food safety.
- c) The safety assessment of novel foods could continue to be improved using molecular profiling techniques (such as metabolomics / proteomics) to detect unintended effects. This would build upon successful work in several of the G02 programme projects, which studied the use of mass spectrometry, proton-nuclear magnetic resonance spectroscopy and 2D gels to look at metabolite differences in GM and non-GM plants. It would be appropriate to commission work to define these techniques for novel foods as metabolomic techniques have potential in this area and have been used successfully in other areas (e.g. human/animal studies). A particular area of interest is the development of metabolomics for toxicological analysis of novel foods *per se* (e.g. cytochrome P450² screening). The ACNFP, the Division's Research Review and the independent programme advisor for the G01 and G02 programmes have identified this research need.

² Cytochrome P450 is a series of enzymes produced as a part of the body's strategy to dispose of potentially harmful substances

d) The Agency has carried out a review of novel food processing techniques to enable it to evaluate the potential hazards and the risks posed by them. Seventy-five novel food processes were considered and fifteen of these were reviewed in detail, involving a qualitative risk assessment that produced a ranking of the hazards identified. The final report recommended that the Agency commission research on a further eighteen key novel processes, taking into account any chemical, physical and microbiological hazards that may be of relevance to the safety assessment. This work is being taken forward elsewhere in the Agency (CCFSSP Division) however it is not likely to extend beyond the initial prioritisation studies. It would be appropriate to commission research to look in detail at issues identified by the initial studies in order to contribute fully towards meeting the Agency's commitment to food safety.

Safety assessment of GM foods:

Considerable progress in this area has been made under the G02 programme, which studied the application of 'omics technologies examining DNA, RNA, protein and metabolite differences, to the assessment of unintended effects in GM foods. Methods, which have the potential for use in the safety assessment of the next generation of GM crops, have been identified and now need refining further.

- a) The GM Science Review identified the potential for horizontal transfer of DNA from GM plants to humans or to bacteria in the human gastrointestinal tract as an area for further investigation. Previous research in the G01 programme looked at the potential for horizontal gene transfer within the human gastrointestinal tract. In general it was concluded from this programme that there was a low risk of gene transfer but one study left some unanswered questions over whether there was gene transfer from GM soya to intestinal microflora of the small bowel. A follow up study is now being carried out through a BBSRC research grant which will further investigate this area by looking at both the extent and mechanism of gene transfer from GM plants to human epithelial cells and human small bowel flora. However, there has been limited research on the potential for horizontal transfer of GM DNA in other materials (e.g. silage, manure or probiotics). The ACNFP and the panel of experts, consulted in 2004, have identified this research need.
- b) Baselines of metabolite variation in crop plants are needed if these techniques are to be used in the safety assessment of the next generation of GM crops. Previous projects carried out as part of the G02 programme, looked at the use of mass spectrometry and proton-nuclear magnetic resonance spectroscopy to identify differences in metabolites between GM and non-GM tomato, potato, wheat and barley, and are a major source of information for such metabolomic data. It is envisaged that this information would be posted on an on-line database. The ACNFP and the panel of experts, consulted in 2004, have identified this research need.
- c) It is necessary to collate data from profiling work carried out in G01 and G02 in order to inform future research in this area into both novel and GM foods (such techniques could be applied to work in other areas of the Agency such as nutritional profiling). The ACNFP and the panel of experts, consulted in 2004, have identified this research need.
- d) The use of MudPIT (Multidimensional protein identification technology)³ has been briefly

³ MudPIT (Multidimensional Protein Identification Technology) is a technique for the separation and identification of complex protein peptide mixtures. Rather than use traditional 2D gel electrophoresis, MudPIT separates peptides in 2D liquid chromatography. In this way, the separation can be interfaced directly with the ion source of a mass spectrometer.

explored in the G02 programme (G02004 – Development and comparison of molecular profiling methods for improved safety evaluation using GM brassicas). MudPIT has been shown to be very successful for protein quantification as an alternative to standard 2D gels (where there is often a loss of resolution). This technology only became available towards the end of the G02 programme and it would be prudent to investigate it further as a tool for the safety assessment of GM crops. The Division, its existing research contractors and programme advisor, identified this research need.

- e) Three areas have been identified by the ACNFP as a significant concern during recent safety assessments:
- Techniques to investigate junction sequences at transgene insertion sites are needed as there may be potential for the production of unintended novel proteins. Previous work has been carried out on junction sequences in project G02002 (Methods for the analysis of GM wheat and barley for unexpected consequences of the transgenic insertion).
 - An investigation is required to establish whether utilising a bioinformatic database will identify potential allergens / cross-reactivity with high specificity and sensitivity. This would need to include establishing the optimum length of sequences to be tested for homology and testing these techniques against known allergens (i.e. how many consecutive amino acids should be compared in database homology searches). There is also a need to investigate the role of both allergen structure and interactions with the food matrix, which would be of value to both novel and GM food safety assessments. Co-funding of the EU “EuroPrevall” programme would gain access to such research on a wider scale.
 - An investigation is needed to assess whether the proteins produced in GM plants are fully equivalent to those produced in microbes (e.g. do the post-translational modifications that occur in eukaryotes, including plants, but not prokaryotes (microbes) alter the properties, including toxicity and allergenicity, of a protein). There has been no previous research in this area.
- f) It is necessary to improve efficiency of GM protein/DNA detection in foods by producing best practice guidelines for data analysis and method validation. PCR methods have failed to provide an adequate combination of reliability and sensitivity and only a limited number of validated techniques are currently available for GM testing. Further techniques need to be developed for a range of products, in particular processed foods. Some work has previously been carried out to develop techniques under the G01 programme and within European Networks. Three projects (G01023, G01024 and G01025) are currently being carried out to assess mass spectrometric methods for the detection of GM protein and DNA with a view to the eventual application of these techniques by public analyst laboratories. However, further refinement would be needed before the techniques studied could be used for this purpose. There is also a major EU funded Framework 6 programme dealing with this issue, which is looking to develop specific protocols for detection of certain GM material, and the Agency could be involved in this through funding a small project at LGC. The ACNFP, existing FSA research contractors and the Division itself have identified this research need. It will also allow the Agency to address its target to assess how the new GM labelling regulations, implemented in April 2004, work in practice for consumers.

Are there alternative approaches to research that could address the concerns of this research programme?

No.

What is the potential for adding value by collaboration with other organisations?

- The Agency can collaborate within an EU Framework 6 project (CoExtra) which is aiming to improve the detectability of GM DNA / protein in foods and produce best practice guidelines for data analysis and methods validation. An input of approximately £100,000 will gain the Agency access to a UK partner's research worth at least double this amount (and potentially millions more within the EU).
- There is also potential for collaboration with another EU Framework 6 project (EuroPrevall) in assessing aspects of allergy that are particularly relevant to novel foods (a UK birth cohort study to determine the prevalence of allergenicity – funded by Consumer Choice and Allergy Division). The Agency would gain access to approximately £12M of research on all aspects of allergy research.⁵ Of particular relevance for novel and GM foods is the need to investigate the role of the food matrix in determining the allergic potential of food. NFAS division would need to contribute approximately £50,000 over 4 years.
- There is the possibility of collaboration with the BBSRC (via the government partnership award scheme) as they are already conducting follow up research on gene transfer. There may also be potential to collaborate on metabolomics work as they have an interest in this area through their funding of the establishment of the Met-RO centre of excellence. This has now moved into a second phase of funding, supporting work which identifies effective uses for the resources held within Met-RO.

What would be the consequences of not conducting the research for (1) the FSA and (2) in general?

For the FSA

- The research proposed is very applied and specific to the needs of the Agency in its role of assessing the safety of novel foods and acting as UK competent authority for the approval of GM foods. As such, it either delivers (or underpins delivery) of Strategic Plan targets and / or other Agency business needs.
- Under the G02 programme, the FSA has taken a prominent lead (within the UK and the EU) in supporting the exploration of molecular profiling techniques for analysing GM crops. This has implications for many fields as 'omic technologies have a wider application (e.g. nutritional profiling and authenticity) and can be applied across the work of the FSA.

In general

- The research proposed addresses the Agency's needs in its role of assessing the safety of novel and GM foods. Outputs will allow the best possible safety assessments to be made providing direct benefits to consumers.

Is there a need to counter inaccurate or misleading information from other parties in any of the research areas covered by this programme/theme?

The safety of GM foods continues to remain a contentious, high profile area. Safety issues can be misreported in the press and it is important that the FSA is able to counterbalance this with robust scientific data.

Are there legal requirements and other formal commitments associated with the research?

- Yes, because the Agency is the competent authority for two regulations that require thorough safety assessment and because it has a responsibility to the public to ensure that up to date scientific knowledge is applied.
- The GM Food and Feed Regulation requires that adventitious contamination of GM in non-GM food should be less than 0.9% for authorised GM material (less than 0.5% for unauthorised) and validated (sensitive, robust and reproducible) methods to detect this are needed in a wide variety of food matrices.

⁴ Although allergy was identified in an important issue in the Division's overview of research it is not the intention for this to be the main focus of the G03 programme. The areas identified are not specific to novel or GM foods and fall within the policy remit of another division in the Agency (and other organisations).

10. **Summarise any cross cutting issues such as how the programme supports, or is relevant to, wider Agency research programmes or other activities.**

Does the research underpin other areas of the Agency's work?

Yes, the further development of metabolomic techniques is likely to have implications across many areas of food safety, particularly toxicology, authenticity and nutritional assessment.

Does the research contribute to the maintenance of essential infrastructure, capabilities or skills (such as that required in emergencies)?

It will contribute towards the development of the sensitive methodologies and generate data required to deliver effective safety assessments of novel foods and the next generation of GM food and feed.

What are the political risks associated with the research?

As previously, there are likely to be questions as to why GM foods continue to be approved (e.g. is the science sufficient to support the safety evaluation?). However, the approach used continues to demonstrate a commitment to the assessment of food safety on a case by case basis.

How does the research address economic and social science aspects of the issue(s) to be addressed?

Economic: As outlined in box 11 it is not possible to attribute actual costs in this area to the UK as very little is known about the economic impact of GM and novel foods (e.g. GM crops are not being grown in the EU but tend to be imported from third countries).

Social: It is recognised that consumers have concerns over, amongst other things, the marketing of GM and novel foods. Risk assessment management needs to be effectively applied and communication is an important issue for consumers to ensure that they can make informed choices.

- 11 **Summarise the overall economic (not research) costs to the UK associated with the issues to be tackled by the programme area, e.g. are there associated human health costs to the economy?**

Are there human health costs to the economy (in terms of mortality and morbidity) associated with this research area?

No. The mandatory pre-market safety assessment is in place to protect consumers in relation to the consumption of GM and Novel Foods. However, consideration needs to be given to sub-sets of the population that may be more vulnerable by consuming certain types of foods.

Are there direct or indirect costs to consumers related to the research area?

To the extent that this research has the potential to prove / show the safety of GM crops (should they indeed be safe) then they represent a potentially cheaper food production technique which has the possibility of benefiting consumers in the form of lower food costs /prices. Conversely, novel foods (such as products containing plant sterols) often command a premium price.

Are there other broader economic costs associated with the research area e.g. to farmers, other producers, enforcement agencies, animal health etc?

Enforcement agencies may be better equipped to carry out their role under the GM Food and Feed Regulation if more sensitive techniques to identify GM material can be developed for use in public analyst laboratories.

12. **List the overall objectives of the research programme and assess the extent to which the success of one objective depends on the successful completion of another objective.**

Objective Number	Description	Performance Indicator	Related Objective(s)
01	Investigation of the potential for transgene survival and transfer to humans via the food chain including GM derived feed. Potential areas for study might include survival of transgenes in silage, manure and probiotics but further expert advice will be taken before projects are commissioned.	<ul style="list-style-type: none"> • Up to 3 research projects commissioned in this area by July 07 • Initial indications of transgene survival by July 08 • Potential for transfer to humans investigated and project complete by July 09 	
02	Development of pre and post market monitoring strategies to identify vulnerable consumers of novel foods – to include predictive modelling techniques and evaluation of actual consumption of certain products by at risk groups – and carry out such post market monitoring.	<ul style="list-style-type: none"> • At least 2 research projects on predictive modelling of consumption rates following introduction of novel foods (probably using previously introduced foods) commissioned by July 05, concentrating on relevant population subgroups • Identification of strategies by July 07 • Validation of strategies and projects complete by July 08 	
03	Expansion of metabolomic and other 'omic technologies to safety assessment of (non-GM) novel foods. One area for particular focus is the screening of cytochrome P450s for toxicological analysis.	<ul style="list-style-type: none"> • Commission research project(s) by July 06 • Techniques using existing foods established by January 08 • Techniques evaluated on a wider range of foods, trialed out for new foods and projects complete by July 09. 	
04	Progress research into key Novel Food processes (each process assessed to determine the extent to which it had been evaluated in relation to food safety) by studying in more detail, the issues identified by initial studies.	<ul style="list-style-type: none"> • Commission research by July 06 • A range of examples assessed by July 07 • Project completed and recommendations given by July 08 	
05	Consolidation of existing	<ul style="list-style-type: none"> • Commission research 	06 – Linked but

	metabolomic data on natural variation to establish baselines in crop plants and inform safety assessment procedures	<p>project by July 05.</p> <ul style="list-style-type: none"> Final databases in place and project complete by July 07 	not dependent
06	Collation of existing molecular profiling data on GM crop plants in databases (data obtained from earlier G01/G02 programmes)	<ul style="list-style-type: none"> Commission research project by July 05 Final database in place and project complete by July 07 	05 – Linked but not dependent
07	Investigation of site of integration of transgenes	<ul style="list-style-type: none"> Commission research project by July 06 Methods developed to study junction sequences in a variety of plant genomes by January 08 Methods applied to several food crop species and project complete by July 09 	
08	Assessment of current bioinformatic techniques to predict allergic responses and investigation of the role of different epitopes of non-linear allergens	<ul style="list-style-type: none"> Commission research project by July 08 Project complete by July 09 	
09	Investigation of the equivalence of GM plant produced proteins with those produced by microbes, with particular reference to the effects of post-translational modification	<ul style="list-style-type: none"> Commission research project by July 07 Identify suitable examples for assessment by Jan 08 A range of examples assessed, recommendations given and project complete by July 09 	
10	Investigate the potential for the use of MudPIT as an additional tool for separation of proteins and quantitative analysis during GM crop safety assessments	<ul style="list-style-type: none"> Commission research project by July 05 Project completed and recommendations given by July 06 	
11	Further refinement of Mass Spectrometry detection methods developed under G01 for application to existing authorised GM crops.	<ul style="list-style-type: none"> Contract in place by July 05 Completed project(s) by July 07. 	12 – Linked but not dependent
12	Co-funding of framework 6 “Co-Extra” project to validate detection methods for GM protein and DNA in foods using a modular approach which builds upon different steps to reach a final standard.	<ul style="list-style-type: none"> Contract in place by July 05 Guidelines for implementation of a modular approach produced by Jan 07 	11 – Linked but not dependent

		<ul style="list-style-type: none"> • Statistical models for combinations of modular methods developed, 3-5 validated methods submitted for standardisation and project complete by July 09 	
13	Co-funding of framework 6 “EuroPrevall” project to identify the effects of allergen structure and the food matrix for Novel and GM foods	<ul style="list-style-type: none"> • Contract in place by July 05 • Yearly updates • Work complete by July 09 	

What skills will be required to meet these objectives?

- Molecular biology and molecular profiling expertise
- Statistical expertise
- Information technology expertise/production of databases
- Marketing research expertise (for PMM studies)
- Specialist mass spectrometry expertise
- Protein biochemistry expertise (for allergenicity)
- Toxicological / pharmacological understanding of the effect of novel ingredients from plants

To what extent does the success of one objective depend on the successful completion of another objective?

In general the objectives represent separate areas of safety assessment where gaps have been identified. These complement each other rather than depending on each other.

13. **Give details of any internal or external factors that might prevent the objectives being achieved and summarise the measures you will take to minimise the effect of these factors.**

Risk assessment

1) Gene transfer:

- a) The Division may discover this is a high risk in some commodities (unlikely)
- b) This is likely to be high profile research

2) Post market monitoring:

- a) It may be difficult to obtain information on purchasing patterns required for effective research
- b) There may be ethical concerns in accessing information regarding consumption of certain food products by subsets of the population.

3) 'Omics techniques and bioinformatics:

It may be difficult to attract experienced workers in this area

4) Research procurement

High quality proposals will be required to ensure that the programme is successful.

Risk management

1) Gene transfer:

- a) The Division will monitor the situation and take action if appropriate based on the best available evidence
- b) The Division will keep Communications Division informed

2) Post market monitoring:

- a) The Division will work with contractors and product manufacturers and retailers to identify the best sources for information and tailor the project as appropriate And build on previous lessons learnt in project G01021 on the applicability of commercial databases for PMM.
- b) The Division will ensure that contractors give the full picture on what ethical consents may be required and apply for these as early as possible.

3) 'Omics techniques and bioinformatics:

The Division will allow as much time as possible for staff recruitment. The Division already has excellent contacts via the G02 programme. Agency staff and the expert programme advisor will closely monitor projects to ensure difficulties are overcome or a project proceeds in the suitable alternative direction if this is not possible.

4) Research procurement:

The Division will ensure that calls for proposals attract interest from a wide range of applicants.

SECTION THREE – OUTPUTS AND POTENTIAL VALUE FOR MONEY OF THE RESEARCH

(see *Guidance Notes, Section 3*)

14. **What are the expected practical outputs of this programme and how and by whom are they likely to be used?**

- **Gene transfer:** The principle output will be further knowledge regarding gene transfer risk in areas identified by the GM Science Review (e.g. in the GI tract). This will be useful for those involved in safety assessment, contributing to better-informed assessments and improved consumer confidence. Data may also be a useful resource for industry and could potentially prompt further research.
- **Post market monitoring:** The results of these projects will directly address the concerns held by the ACNFP regarding the effectiveness of risk management measures aimed at discouraging consumption by particular groups of the population. The work will initially focus on cholesterol lowering products (which should be avoided by young children) but approaches adopted could be used for other products in the future.
- **Development of 'omics techniques:** These projects are expected to further develop methods and refine the existing methods developed in the G02 programme so that they can be used for safety assessment. The need for extensive animal experimentation will be reduced. The results will be of use to both those who are involved in the safety assessment and manufacture of novel / GM foods, and techniques are widely applicable across the Agency in relation to nutrition, toxicity, allergenicity and food authenticity.
- **Development of validated detection methods:** Public analyst laboratories will be able to use these new techniques. There is a continued need to improve detection methodology and robustness of methods to allow wider applicability of these methods, reduced costs for enforcement and higher throughput.

15. **Estimate the potential value for money of the research, i.e. compare the costs of conducting the research with the potential benefits of the outputs (box 14) it is expected to produce.**

What are the overall potential costs of meeting each of the objectives listed in box 14?

- 01 Potentially 3 projects over 2 years at approx £200K each = £600K (£400K-£800K)
- 02 Potentially 2 or more projects over 2 years at approx £300K each = £600K (£400-£800K)
- 03 1 or more projects over 3 years, total value likely to be approx £600K (£400-£800K)
- 04 1 project over 2 years, total value likely to be approx £100K (£75-£125K)
- 05 1 project over 2 years, total value likely to be approx £250K (£200K-£300K)
- 06 1 project over 2 years, total value likely to be approx £400K (£300K-£500K)
- 07 1 project over 3 years, total value likely to be approx £500K (£400K-600K)
- 08 1 project over 1 year, total value likely to be approx £150K (£100K-£200K)
- 09 1 project over 2 years, total value likely to be approx £250K (£200K-£300K)
- 10 1 project over 2 years, total value likely to be approx £400K
- 11 1 or 2 projects over 2 years, total value likely to be approx £400K (£300K-£500K)
- 12 Co-funding for 1 project over 4 yrs likely to be approx £100K (£75K-125K)
- 13 Co-funding for 1 project over 4 yrs likely to be approx £50K

What factors are likely to affect the use of the outputs of the research results if it is completed successfully?

As metabolomics and other molecular profiling techniques require specific expertise in order to ensure reproducibility, there may be difficulties in adopting these as part of a routine safety assessment.

What economic benefits will the research produce or contribute to producing?

This research is not being carried out with the view of bringing about economic benefits however some of the techniques may be helpful in the enforcement of the Novel Foods and GM Food and Feed legislation.

Has the research enabled buy-in to larger programmes through which we have access to a wider range of information and expertise, or other added value?

- There is the opportunity to buy-in to 50% funding of a EU Framework 6 project validating techniques to detect GM food at below the 0.9% threshold level. This may lead to access to other EU funded work, including that such as new techniques to meet the challenges raised by stacked genes in as yet unapproved or unexamined GMOs.
- There will be an opportunity to buy-in to and access the results of the EuroPrevall (EU Framework 6) project (looking at a wide range of allergenicity issues) as Consumer Choice and Allergy Division are funding a UK birth cohort study. NFAS intends to contribute to work on the effect of the food matrix in determining allergenic potential.
- There may be the opportunity to buy-in to research carried out by the BBSRC in the areas of gene transfer and metabolomics if co-funding opportunities can be utilised. The BBSRC has a metabolomic programme and a centre of excellence and wishes now to fund opportunities to use these facilities.

SECTION FOUR - RESEARCH PLAN

(see Guidance Notes, Section 4)

16. **Outline the approaches and research plan to be used in realising the objectives (box 12) and set out the work plan for the life of the programme stating clearly how you intend to proceed. Number the approaches in the same manner as the objectives.**

01 Review research into Novel and GM Foods to identify areas of research and appoint a programme manager for new programme.

02 Commission and complete research on phase 1 (Phase 1a: projects on gene transfer, metabolite baselines, molecular profiling databases and detectability of GM material. Phase 1b: novel food processes, MudPIT).

03 Commission and complete research for phase 2 (projects on post-market monitoring, vulnerable consumers, metabolomics and novel foods, junction sequences,).

04 Commission and complete research for phase 3 (projects on bioinformatics and equivalence of plant produced proteins).

05 Forward look, final review and evaluation.

17. **Based on your research plan, give milestones (i.e. points at which progress can be assessed).**

Milestone Number	Milestone Date	Description of milestone
01/01	31.07.04	Hold research review meeting and consult ACNFP and other stakeholders
01/02	31.12.04	Appoint programme manager
02/01	28.02.05	Call for initial research on phase 1 (metabolite baselines, molecular profiling databases and detectability of GM material, MUDPIT, post market monitoring)
02/02	30.05.05	Appraisals held, phase 1 awards confirmed and project negotiations completed
02/03	31.07.05	Phase 1a projects start – initial visits held by end of month
02/04	Every 6-9 months	Phase 1a project visits to monitor progress, contractors steering group/workshop
02/05	31.07.06	Phase 1b projects start – initial visits held by end of month
02/06	31.07.06	1 year interim reports for phase 1a, assessment and review progress
03/01	31.04.06	Call for interim research on phase 2 (novel food processes, junction sequences, metabolomics and novel foods, allergic response)
03/02	30.04.07	Appraisals held, phase 2 awards confirmed and project negotiations completed
02/07	31.07.07	Final reports of phase 1a
02/08	31.07.07	Interim report of phase 1b projects
03/03	31.07.07	Phase 2 projects start – initial visits held by end of month
03/04	Every 6-9 months	Phase 2 project visits to monitor progress, contractors steering groups/workshop

04/01	31.10.07	Call for final research on phase 3 (bioinformatics and equivalence of plant produced proteins, gene transfer)
02/09	31.01.08	MID TERM REVIEW e.g. review progress, refocus the programme, develop new ideas, and begin preparing a follow on programme in necessary.
04/02	30.04.08	Appraisals held for phase 3 projects, awards confirmed and negotiations complete
	31.07.08	Final report of phase 1b projects
04/03	31.07.08	Phase 3 projects start – initial visits held by end of month
04/04	Every 6-9 months	Phase 3 project visits to monitor progress, contractors steering groups/workshop
03/05	31.07.08	1 year interim reports for phase 2, assessment and review progress
03/06	31.07.09	2 year interim report for phase 2 metabolomics and novel foods, junction sequences projects, assessment and review progress
02/10	31.07.09	Final report of phase 1a project on GM detection
03/07	31.07.09	Final reports of phase 2 projects on post market monitoring, vulnerable consumers
04/05	31.07.09	1 year interim report for phase 3 on equivalence of plant produced proteins and final report on bioinformatics project, project assessment and review progress
05/01	31.12.09	Forward look to future research priorities to include an overview of all previous research.
03/08	31.07.10	Final reports of phase 2 projects on metabolomics and novel foods, junction sequences
04/06	31.07.10	Final report on phase 3 on equivalence of plant produced proteins
05/02	As necessary throughout programme	Peer review of final reports using relevant experts.
05/03	31.12.10	EVALUATION OF COMPLETED PROGRAMME

SECTION FIVE – PROGRAMME EVALUATION

(see Guidance Notes, Section 5)

18. **Describe how you will evaluate programme outputs and their uptake (box 14). What criteria will you use to determine the success of the programme?**

Final Evaluation will include:

- A programme workshop to rate the success of projects/programme
- Evaluation by the ACNFP
- Peer review of individual projects

Criteria for success:

The following questions will be addressed.

- Has the programme answered the required questions to build upon and continue to support the safety assessment of novel and GM foods?
- Can recommendations be put forward to revise existing safety assessment guidelines if necessary?
- Is the research of a good quality compared with previous research?
- Will the results inform the direction of future research in these areas?

SECTION SIX – RESULTS DISSEMINATION

(see Guidance Notes, Section 6)

19. **Explain how results from the programme will be disseminated to relevant stakeholders (minimum requirement is through yearly programme workshops, Food Standards Agency News and, wherever possible, publication of data in peer reviewed journals)**

The following dissemination methods will be utilised.

- Programme workshops
- FSA news
- FSA website
- Publications
- Conferences
- Annual research open meeting
- Press releases (if appropriate)

20. **Is it likely that the research programme or issues arising from it will cause media interest and, if so, how will you manage this?**

This is possible, especially with gene transfer projects. The Division will maintain an awareness of this possibility and liaise with COMS prior to the publication of each project, and on an ongoing basis, with projects that are particularly contentious.

SECTION SEVEN – DETAILS OF ESTIMATED PROGRAMME COSTS

(see Guidance Notes, Section 7)

21. Estimated yearly programme costs⁴.

Project Year	Project Year 1 2005-2006	Project Year 2 2006-2007	Project Year 3 2007-2008	Project Year 4 2008-2009	Project Year 5 2009-2010	Total (£)
Projects^{1,2}						
Planned research projects	495,750	1091,500	1361,500	804,500	648,750	4,402,000
Planned surveys	N/A	N/A	N/A	N/A	N/A	N/A
Total – planned projects (a)	495,750	1091,500	1361,500	804,500	648,750	4,402,000
Other programme activities^{1,2}						
Programme advisor (20 days per year)	15,000	15,000	15,000	15,000	15,000	75,000
Monitoring work (2 visits a year allowed for)	4000	5000	4500	3500	1500	18,500
Workshops Forward look	500	500	500	500	500 20000	2500 20000
Mid term and Final Review			15,000		25000	40,000
Other relevant exp e.g. publications (peer reviewers)			1,200	200	1000	2400
Total other expenditure (b)	19,500	20,500	36,200	19,200	63,000	158,400
TOTAL ESTIMATED COST (£) (a+b)	515,250	1,112,000	1,397,700	823,700	711,750	4,560,400
Estimated costs recovered ³ (c)	N/A	N/A	N/A	N/A	N/A	N/A
TOTAL NET COST (a+b) - c	515,250	1,112,000	1,397,700	823,700	711,750	4,560,400

NOTES

- Costs included in each category under this heading should include VAT where this is not recoverable. Otherwise, provide costs ex VAT. Guidance on VAT issues can be obtained from the Research Guidelines, under Research Procurement, the Finance Manual, Chapter 19 or FPIT/RCU.
- Re research, surveys or other activities, e.g. monitoring programmes, covered by an SLA which contribute towards the aims and objectives of the ROAME programme - estimated costs for these should be included under the relevant category above and appropriate details included in FaRMs, to allow reporting against programme allocations.
- The costs of some projects are recovered from industry or other sources. Please include an estimate.
- Where work is jointed funded with other organisations, only the Agency's contribution should be provided in this table.

SECTION EIGHT – HOD DECLARATION

22. I am content with the rationale of this programme of work. I confirm that the programme will support Agency aims and objectives and that the estimated programme costs (box 21) should be sufficient for the objectives of the programme (box 12) to be achieved.

Signature

Date

SECTION NINE – DIRECTOR DECLARATION

23. I consider this work contributes to Group objectives and that the amount of the proposed spend is justified.

Signature

Date

SECTION TEN – DCE AUTHORISATION

24. I agree the proposed spend is justified and give financial authority for the project to proceed subject to the spend being met from existing delegated budgets.

Signature

Date