The Advisory Committee on Novel Foods and Processes (ACNFP)

2013 Report

Contents

and EPA – rich oils.

Foreward

I am pleased to present the 2013 Annual Report of the Advisory Committee on Novel Foods and Processes (ACNFP).

The primary role of the ACNFP remains the safety assessment of novel foods and processes in line with the EU procedures set out in Regulation (EC) No 258/97. However, as is reflected by the contents of this report, the Committee continues to have a role in advising the Food Standards Agency on matters related to genetically modified (GM) foods.

In order to fulfil its role, the ACNFP has an impressive membership with highly qualified expertise in a wide range of scientific disciplines as well as two consumer representatives and an ethicist. I would like to take this opportunity to thank my fellow Committee members for their expert advice, hard work and support throughout the year. I would also like to acknowledge the enthusiasm and invaluable contributions of Dr Andrew Chesson who ended his term of appointment at the end of 2013.

The contents of this report once again reflect the number and variety of applications that have been considered by the Committee and the hard work of the secretariat whose assistance and support is invaluable to the effective operation of the Committee.

Professor Peter Gregory
February 2014

INTRODUCTION

The primary role of the ACNFP is the safety assessment of any novel food or process submitted for approval or notification under the Novel Foods Regulations (EC) No. 258/97.

Under the Novel Foods Regulations (EC) No. 258/97 a novel food is defined as a food that does not have a significant history of consumption within the European union before 15 May 1997. Such foods are subject to a pre-market safety assessment before a decision is made on EU wide authorisations.

A company planning to market a novel food submits an application to a single EU Member State. Once the application has been accepted the Member State produces an initial opinion. This opinion is then circulated to Member States who are given a further 60 days to comment or make a reasoned objection. If there are no objections the novel food will be authorised. If there are objections a decision on the authorisation will be taken by a vote among Member States at the Standing Committee on the Food Chain and Animal Health. Prior to a vote taking place the European Food Safety Authority may be asked its opinion on any outstanding safety questions.

The Novel Food Regulation provides a simplified route for manufacturers to bring certain novel foods and food ingredients to the market by making a notification in accordance with article 5 of the regulations. The product must be shown to be substantially equivalent to an existing food or food ingredient as regards its composition, nutritional value, metabolism, intended use and level of undesirable substances. Each notification requires a suitable opinion from a single EU Member State.

The following tables provide details of novel food applications submitted to the Food Standards Agency as the UK Competent Authority, applications from other EU Member States and notifications under the simplified procedure.

The following tables provide details of:

- novel food applications submitted to the Food Standards Agency as the UK Competent Authority,
- applications from other EU Member States,
- notifications under the simplified procedure, and
- other issues discussed by the Committee during the year.

1. NOVEL FOOD APPLICATIONS SUBMITTED TO THE UK

(a) Full applications

In 2013 the ACNFP considered seven new applications under Article 4 of regulation (EC) 258/97. These are detailed in Table 1, below. Details of the issues that were raised by the Committee can be found in the Minutes of the relevant meetings (Annex 2). The Committee concluded its assessment of four of these applications during this calendar year and also completed its assessment of three applications which were carried over from previous years.

Table 1: Novel food applications made via the UK that were considered by the Committee during 2013

Novel food (Applicant)	*Meeting discussed*	*Initial opinion*	*Comment*
Clostridium butyricum probiotic Miyarisan Pharmaceutical Co.Ltd	Feb	Completed Annex 3a	A positive initial opinion was issued on 14 May 2013
DHA and EPA- rich oils DSM Nutritional Products	Feb	Completed Annex 3b	A positive initial opinion was issued on 29 April 2013
* DHA rich microalgal oil DSM Nutritional Products	Feb	Completed Annex 3c	A positive initial opinion was issued on 29 April 2013
Chia Oil Functional Products Trading	Feb/April	Completed Annex 3d	A positive initial opinion was issued on 8 July 2013
* Sporopollenin shells Sporomex Ltd	Feb/Nov	-	Evaluation continued in 2014
D-Ribose Bioenergy Inc	April/Nov	-	Evaluation continued in 2014
* 1-Methylnicotinamide Chloride Pharmena SE	June/Nov	-	Evaluation continued in 2014
* Phytosterols – extension of use Unilever	June/Sept/Nov	-	Evaluation continued in 2014
* Calanus Oil Calanus AS	June	-	Evaluation continued in 2014
* Buglossoides Oil Technology Crops International	June/Sept/Nov	Completed Annex 3e	A positive initial opinion was issued on 6 January 2014
* Ketone Ester TdeltaS Limited International	Sept/Nov	-	Evaluation continued in 2014
* DHA rich algal oil from Schizochtrium DSM Nutritional Products	Sept/Nov	-	Evaluation continued in 2014

* New applications received during 2013. Other evaluations were continued from the previous year

(b) Opinions on substantial equivalence

In 2013 the ACNFP considered four requests for an opinion on equivalence in accordance with Article 3(4) of regulation (EC) 258/97. This is detailed in Table 2, below. Details of the issues that were raised by the Committee can be found in the Minutes of the relevant meeting (Annex 2). The ACNFP concluded its assessment of three requests during this calendar year.

Table 2: Applications for an opinion on substantial equivalence that were considered by the Committee during 2013

Novel food (Applicant)	*Meeting discussed*	*ACNFP Opinion*	*Comment*
Bugloissoides Oil (Technology Crops International)	Feb	Completed	The Committee agreed equivalence had not been demonstrated between and this oil and an existing product.
Chia Seed (Inversora Agropecuaria)	April/Sept	-	Evaluation continued in 2014
Chia Seed (Infood Ltd)	April	Completed Annex 3f	The Committee agreed equivalence had been demonstrated between and this oil and an existing product.
Chia Seed (Supernutrients)	Nov	Completed Annex 3g	The Committee agreed equivalence had been demonstrated between and this oil and an existing product.

2. NOVEL FOOD APPLICATIONS SUBMITTED TO OTHER MEMBER STATES

In 2013 the ACNFP considered two initial opinions from other EU Member States. These are detailed in Table 3, below. The ACNFP's advice formed the basis of the UK's comments or objections to the marketing of these novel foods. Details of the issues that were raised by the Committee can be found in the Minutes of the relevant meeting and in the responses sent to the European Commission.

Table 3: Novel foods considered by the Committee during 2013 following an initial assessment in another Member State

Novel food (Member State)	*Meeting discussed*	*UK response*	*Comment*
Pasteurised milk treated with UV light	April	Completed Annex 3h	The following objections were raised: • no information on variability of vitamin D_3 levels in the treated milk, • only limited sensory tests have been carried out

			• the formation of oxidation products should be investigated.
Synthetic resveratrol	Nov	Completed Annex 3i	The following objections were raised: • lack of information on the current production process, • potential interference with drug metabolism, • failure to take account of certain publications on the safety of resveratrol, • suitability for children, • lack of information on adverse reporting from areas where the product has already been already been marked

3. NOVEL FOOD APPLICATIONS CONSIDERED IN PREVIOUS YEARS

During 2013 the ACNFP also considered responses from two applicant companies following consideration of an initial assessment in another Member State. The ACNFP's advice formed the basis of the UK's comments or objections to the marketing of these novel foods. These are detailed in Table 4, below. Details of the issues that were raised by the Committee can be found in the minutes of the relevant meeting (Annex 2)

Table 4: Novel foods considered by the Committee during 2012 following an initial assessment in another Member State

Applicant response or EFSA opinion	***Meeting discussed***	***Comment***
Citicoline (applicant's response)	Feb	While some issues were addressed satisfactorily, the Committee maintained its concerns about effects on the human dopaminergic system and the presence of by-products.
Rapeseed Protein (applicant's response)	Feb	The Committee's concerns and questions were not resolved (micronutrient absorption, protein composition, potential for cross reactivity in individuals with mustard allergy

4. OTHER ISSUES

In 2013 the ACNFP also considered a number of other issues which related to novel foods, nanotechnology, GM plants and the functioning of the Committee. These are detailed in Table 5, below.

Table 5: Other Issues

	Meeting discussed	***Comment***
Cauliflower Mosaic Virus	Feb	The Committee noted that P35S promoters are present in most GM plants and that the virus is also found naturally in brassica species. The Committee agreed with the European Food Safety Authority that the new paper did not raise any concerns for the safety of food and feed from previously evaluated GM crops.
Toxicological study of pigs fed with GM maize and GM soya compared with non-GM equivalents	June	The Committee suggested the title of the paper was misleading as the results could not be extrapolated to animal diets containing GM crops in general. Members agreed that pigs given diets containing the GM maize and soya varieties did show a trend towards a more severe inflammation of the stomach lining which approached statistical significance when analysed by more appropriate tests. The Committee acknowledged that the paper may demonstrate some differences in the effects of the two diets but, given the uncertainties, these differences cannot be attributed to the genetically modified source of the feed ingredients.
Uncertainty in intake estimation	Sept	The Committee considered it would be useful for this analysis to be produced for each new application in future, and suggested that a semi-quantitative estimate of magnitude of the uncertainties should be included.
Transfer of DNA from food to human blood	Nov	The Committee agreed that this was a very interesting paper and that the results required confirmation. DNA contamination was only one of a number of possible explanations of the results. The Secretariat agreed to keep the Committee informed of further work that might help to clarify this point.

ANNEX 1 – Information about the Committee

ACNFP – remit, membership and list of Members' interests, code of conduct and interactions with other committees.

REMIT

The Advisory Committee on Novel Foods and Processes is an independent body of experts whose remit is:

> "to advise the central authorities responsible, in England, Scotland, Wales and Northern Ireland respectively on any matters relating to novel foods and novel food processes including food irradiation, having regard where appropriate to the views of relevant expert bodies"

Officials of the Food Standards Agency provide the Secretariat. As well as formal meetings, the Committee organises workshops on specific topics related to its remit.

MEMBERSHIP AND MEMBERS' INTERESTS

The membership of the Committee provides a wide range of expertise in fields of relevance in the assessment of novel foods and processes. A list of the membership during 2013, together with the names of the FSA assessors can be found overleaf.

In common with other independent advisory committees the ACNFP is publishing a list of its members' commercial interests. These have been divided into different categories relating to the type of interest:

Personal:	a) direct employment or consultancy; b) occasional commissions; c) share holdings.
Non-personal:	a) fellowships; b) support which does not benefit the member directly e.g. studentships.

Details of the interests held by members during 2013 and a copy of the code of conduct for ACNFP members can be found on the following pages.

Membership of the Committee during 2013

Chairman

Professor Peter Gregory BSc, PhD
Chief Executive of East Malling Research and Professor of Global Food Security at the University of Reading.

Members

Professor Michael Bushell BSc, PhD (Microbiologist)
Professor of Microbiology and Head of Microbial Sciences at the University of Surrey.

Professor Andrew Chesson BSc, MSc, PhD, CChem, FRSC (Nutritionist)
Independent Scientific Adviser and Honorary Professor at the University of Aberdeen.

Dr Susan Duthie BSc, MSc, PhD (Nutritionist)
Senior Research Scientist in the Natural Products Group, Division of Lifelong Health, Rowett Institute of Nutrition and Health, University of Aberdeen.

Simon Flanagan BSc, FIFST (Quality Assurance/Food Processing)
Senior Consultant in Food Safety and Allergens for Reading Scientific Services Ltd.

Nichola Lund LLB (Consumer Affairs Representative)
Trading Standards Officer with the North East London Metrology Partnership.

Professor George Macfarlane BSc, PhD (Microbiologist)
Professor of Bacteriology at the University of Dundee.

Dr Rohini Manuel MB BCh BAO, MSc, MD (Microbiologist and Mycologist)
Consultant Medical Microbiologist at the Public Health Laboratory London, Barts Health NHS Trust.

Professor John Mathers BSc, Dip. Nutr, PhD (Nutritionist)
Professor of Human Nutrition and Director of the Human Nutrition Research Centre at Newcastle University

Professor Harry McArdle BSc, PhD (Nutritionist)
Deputy Director of Science and Director of Academic Affairs at the Rowett Institute of Nutrition and Health, University of Aberdeen

Professor Peter Meyer BSc, PhD (Molecular Biologist)
Professor of Plant Genetics, University of Leeds

Professor Clare Mills BSc, PhD (Plant Science and Allergy Expert)
Professor of Molecular Allergology, at the School of Translational Medicine, University of Manchester.

Ms Claire Nicholson BA and MBA (Consumer Affairs Representative)
Independent Consumer Advisor to the FSA and other food industry organisations.

Dr Camilla Pease BSc, PhD (Toxicologist)
Senior Manager/Consultant Toxicologist at ENVIRON International Corporation.

Professor Christopher Ritson BA, MAgrSc (Ethicist)
Emeritus Professor of Agricultural Marketing, Newcastle University.

Dr Carina Venter BSc, Dip. Allergy PhD (Allergy)
Senior Allergy Dietician at the David Hide Asthma and Allergy Research Centre, St Mary's Hospital, Newport, Isle of Wight, and Senior Lecturer at the University of Portsmouth.

FSA Assessor

Mr Terry Donohoe	Food Standards Agency

FSA Observers

Ms Hilary Neathey	Food Standards Agency (Wales)
Ms Alison Taylor (Jan- July)	Food Standards Agency (Scotland)
Mr Stephen Hendry (July – Dec)	Food Standards Agency (Scotland)
Mr Gerry McCurdy (Jan – Aug)	Food Standards Agency (Northern Ireland)
Mr Mervyn Briggs (Aug – Dec)	Food Standards Agency (Northern Ireland)

ACNFP Members' Interests during 2013

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Professor Peter Gregory	East Malling Research	Chief Executive	BBRSC	Funding
	Royal Horticultural Society	Trustee		
	Produced in Kent	Non-Exec Director		
	Rank Prize Nutrition Committee	Member		
	Informal Research Advisory Group, Dfid	Member		
Professor Michael Bushell	Abbott Laboratories, Chicago	Consultant	None	
Professor Andrew Chesson	None		European Food Safety Authority	Chair of FEEDAP panel and member of Scientific Committee
Dr Susan Duthie	None		UK Environmental Mutagen Society Molecular Epidemiology Group (UKMEG)	Secretary
			Rank Prize Funds	Funded PhD Studentship
			Tenovus UK	Funded PhD Studentship
			Scottish Government (RESAS)	Research Funding

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Mr Simon Flanagan	Reading Scientific Services Ltd Subsidiary of Kraft Foods Inc	Employee	UK Food and Drink Federation	Member of Allergen Steering Group
			Food and Drink Europe	Member of Allergen Working Group
			ILSI Europe	Member of Food Allergy Taskforce
Mrs Nicola Lund	None		None	
Professor George Macfarlane	None		Government Chief Scientist Office	Member
Dr Rohini Manuel	None		None	
Professor John Mathers	None		EU	Research funding
			BBRSC	Research funding
			MRC	Research funding
			Governing Council of the British Nutrition Foundation	Member
			BBRSC Basic Bioscience underpinning Health	Member
			Rank Prize Nutrition Committee	Member

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
			ESRC Understanding Society Governing Board	Member
			BBRSC DRINC Advisory Panel	Member
Professor Harry McArdle	None		Scientific Advisory Committee on Nutrition (SACN)	Member
			Nutrition Society	Honorary Treasurer
			International Copper Assocation	Funds to support visiting scientists
Professor Peter Meyer	None		BBRSC	Funding
			Leverhulme Trust	Funding
			EU	Funding
Professor Clare Mills	React Biotech Ltd	Spin-out Company Director	FSA	i) Occasional external reviewer. ii) PI on FSA funded project T07062 iii) CoI on FSA funded TRACE
			BBSRC	i) Member of DRINC steering group ii) Grant Holder iii) CASE students sponsored by Campden BRI, Genon and Waters Corp

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
			TSB	Collaborative project with Waters Corp, LGC and Romer Labs on allergen analysis
			EU funded research	CHANCE and IFAAM projects
			EFSA (2012-2013)	Tender for systematic review for the GMO panel
			University of Nebraska Food Allergy Research and Resource Programme, USA	Joint PhD student
			Industry funded research Novartis DBV	
			Solazyme	
			Pepsico	Allergen expert advice
Ms Claire Nicholson			Smedvigcapital	Partner's shareholding and employment. May invest in food businesses.
Dr Camilla Pease	Environ UK Ltd	Employee	DEFRA	Consultant on C4SLS project
			Unilever – non foods related project	Research funding
Professor Chris Ritson	None		None	

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Dr Carina Venter	None		Danone (Infant and Toddler Forum)	Part funding of PhD students paid to University of Portsmouth
			Fish Mongers Association	Part funding of a PhD student paid to University of Portsmouth
			ThermoFisher	Funding to University of Portsmouth
			Mead Johnson, GSK, Abbott, Danone and Nestle (Vitaflo)	Funding for students travel and conference attendance - grant paid to University of Portsmouth

A CODE OF CONDUCT FOR MEMBERS OF THE ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES (ACNFP)

Public service values

The Members of the ACNFP must at all times:

- observe the highest standards of impartiality, integrity and objectivity in relation to the advice they provide and the management of this Committee;
- be accountable, through the Board of the Food Standards Agency and Health Ministers, to Parliament and the public for its activities and for the standard of advice it provides.

The Board of the FSA and Health Ministers are answerable to Parliament for the policies and performance of this Committee, including the policy framework within which it operates.

Standards in Public Life

All Committee Members must:

- follow the Seven Principles of Public Life set out by the Committee on Standards in Public Life (page 19);
- comply with this Code, and ensure they understand their duties, rights and responsibilities, and that they are familiar with the function and role of this Committee and any relevant statements of Government policy. If necessary members should consider undertaking relevant training to assist them in carrying out their role;
- not misuse information gained in the course of their public service for personal gain or for political purpose, nor seek to use the opportunity of public service to promote their private interests or those of connected persons, firms, businesses or other organisations; and
- not hold any paid or high profile unpaid posts in a political party, and not engage in specific political activities on matters directly affecting the work of this Committee. When engaging in other political activities, Committee members should be conscious of their public role and exercise proper discretion. These restrictions do not apply to MPs (in those cases where MPs are eligible to be appointed), to local councillors, or to Peers in relation to their conduct in the House of Lords.

Role of committee members

Members have collective responsibility for the operation of this Committee. They must:

- engage fully in collective consideration of the issues, taking account of the full range of relevant factors, including any guidance issued by the Food Standards Agency or Health Ministers;

- in accordance with Government policy on openness, ensure that they adhere to the Code of Practice on Access to Government Information (including prompt responses to public requests for information); agree an Annual Report; and, where practicable and appropriate, provide suitable opportunities to open up the work of the Committee to public scrutiny;

- not divulge any information which is provided to the Committee in confidence;

- ensure that an appropriate response is provided to complaints and other correspondence, if necessary with reference to the sponsor department; and

- ensure that the Committee does not exceed its powers or functions.

Individual members should inform the Chairman (or the Secretariat on his or her behalf) if they are invited to speak in public in their capacity as a committee member.

Communications between the Committee and the Board of the Food Standards Agency will generally be through the Chairman except where the Committee has agreed that an individual member should act on its behalf. Nevertheless, any member has the right of access to the Board of the FSA on any matter that he or she believes raises important issues relating to his or her duties as a Committee member. In such cases the agreement of the rest of the Committee should normally be sought.

Individual members can be removed from office by the Board of the FSA, if they fail to perform the duties required of them in line with the standards expected in public office.

The Seven Principles of Public Life

Selflessness

Holders of public office should take decisions solely in terms of the public interest. They should not do so in order to gain financial or other material benefits for themselves, their family, or their friends.

Integrity

Holders of public office should not place themselves under any financial or other obligation to outside individuals or organisations that might influence them in the performance of their official duties.

Objectivity

In carrying out public business, including making public appointments, awarding contracts, or recommending individuals for rewards and benefits, holders of public office should make choices on merit.

Accountability

Holders of public office are accountable for their decisions and actions to the public and must submit themselves to whatever scrutiny is appropriate to their office.

Openness

Holders of public office should be as open as possible about all the decisions and actions that they take. They should give reasons for their decisions and restrict information only when the wider public interest clearly demands.

Honesty

Holders of public office have a duty to declare any private interests relating to their public duties and to take steps to resolve any conflicts arising in a way that protects the public interests.

Leadership

Holders of public office should promote and support these principles by leadership and example.

The role of the Chairman

The Chairman has particular responsibility for providing effective leadership on the issues above. In addition, the Chairman is responsible for:

- ensuring that the Committee meets at appropriate intervals, and that the minutes of meetings and any reports to the Board of the FSA accurately record the decisions taken and, where appropriate, the views of individual members;

- representing the views of the Committee to the general public; and

- ensuring that new members are briefed on appointment (and their training needs considered), and providing an assessment of their performance, on request, when members are considered for re-appointment to the Committee or for appointment to the board of some other public body.

Handling conflicts of interests

The purpose of these provisions is to avoid any danger of Committee members being influenced, or appearing to be influenced, by their private interests in the exercise of their public duties. All Members should declare any personal or business interest that may, or may be perceived (by a reasonable member of the public) to, influence their judgement. A guide to the types of interest that should be declared can be found on page 21 of this report.

(i) Declaration of interests to the Secretariat

Members of the Committee should inform the Secretariat in writing of their current personal and non-personal interests, when they are appointed, including the principal position(s) held. Only the name of the organisation and the nature of the interest are required; the amount of any salary etc. need not be disclosed. Members are asked to inform the Secretariat at any time of any change of their personal interests and will be invited to complete a declaration form once a year. It is sufficient if changes in non-personal interests are reported in the annual declaration form following the change. (Non-personal interests involving less than £1,000 from a particular company in the previous year need not be declared to the Secretariat).

The register of interests should be kept up-to-date and be open to the public.

(ii) Declaration of interest and participation at meetings

Members of the Committee are required to declare any direct interests relating to salaried employment or consultancies, or those of close family members, in matters under discussion at each meeting. Having fully explained the nature of their interest the Chairman will, having consulted the other members present, decide whether and to what extent the member should participate in the discussion and determination of the issue. If it is decided that the member should leave the meeting, the Chairman may first allow them to make a statement on the item under discussion.

Personal liability of Committee members

A Committee member may be personally liable if he or she makes a fraudulent or negligent statement which results in a loss to a third party; or may commit a breach of confidence under common law or a criminal offence under insider dealing legislation, if he or she misuses information gained through their position. However, the Government has indicated that individual members who have acted honestly, reasonably, in good faith and without negligence will not have to meet out of their own personal resources any personal civil liability which is incurred in execution or purported

execution of their Committee functions save where the person has acted recklessly. To this effect a formal statement of indemnity has been drawn up.

Different types of interest

The following is intended as a guide to the kinds of interests that should be declared. Where Members are uncertain as to whether an interest should be declared they should seek guidance from the Secretariat or, where it may concern a particular product which is to be considered at a meeting, from the Chairman at that meeting. If Members have interests not specified in these notes but which they believe could be regarded as influencing their advice they should declare them. However, neither the Members nor the Secretariat are under any obligation to search out links of which they might reasonably not be aware. For example, either through not being aware of all the interests of family members, or of not being aware of links between one company and another.

Personal Interests

A personal interest involves the Member personally. The main examples are:

- Consultancies and/or direct employment: any consultancy, directorship, position in or work for the industry or other relevant bodies which attracts regular or occasional payments in cash or kind;
- Fee-Paid Work: any commissioned work for which the member is paid in cash or kind;
- Shareholdings: any shareholding or other beneficial interest in shares of industry. This does not include shareholdings through unit trusts or similar arrangements where the member has no influence on financial management;
- Membership or Affiliation to clubs or organisations with interests relevant to the work of the Committee.

Non-Personal Interests

A non-personal interest involves payment which benefits a department for which a member is responsible, but is not received by the member personally. The main examples are:

- Fellowships: the holding of a fellowship endowed by industry or other relevant body;
- Support by Industry or other relevant bodies: any payment, other support or sponsorship which does not convey any pecuniary or material benefit to a member personally, but which does benefit their position or department e.g.:
    - a grant for the running of a unit or department for which a member is responsible;
    - a grant or fellowship or other payment to sponsor a post or a member of staff or a post graduate research programme in the unit for which a member is responsible (this does not include financial assistance for undergraduate students);
    - the commissioning of research or other work by, or advice from, staff who work in a unit for which a member is responsible.

- Members are under no obligation to seek out knowledge of work done for, or on behalf of, industry or other relevant bodies by departments for which they are responsible, if they would not normally expect to be informed. Where members are responsible for organisations which receive funds from a very large number of companies involved in that industry, the Secretariat can agree with them a summary of non-personal interests rather than draw up a long list of companies.

- Trusteeships: any investment in industry held by a charity for which a member is a trustee. Where a member is a trustee of a charity with investments in industry, the Secretariat can agree with the member a general declaration to cover this interest rather than draw up a detailed portfolio.

Definitions

For the purposes of the ACNFP 'industry' means:

- Companies, partnerships or individuals who are involved with the production, manufacture, packaging, sale, advertising, or supply of food or food processes, subject to the Food Safety Act 1990;

- Trade associations representing companies involved with such products;

- Companies, partnerships or individuals who are directly concerned with research, development or marketing of a food product which is being considered by the Committee.

'Other relevant bodies' refers to organisations with a specific interest in food issues, such as charitable organisations or lobby groups.

In this Code 'the Secretariat' means the Secretariat of the ACNFP

FSA GOOD PRACTICE GUIDELINES FOR THE INDEPENDENT SCIENTIFIC ADVISORY COMMITTEES (Revised and updated July 2012)

GOOD PRACTICE GUIDELINES FOR THE INDEPENDENT SCIENTIFIC ADVISORY COMMITTEES

INTRODUCTION

The Government Chief Scientific Adviser's *Guidelines on the Use of Scientific and Engineering Advice in Policy Making*[1] set out the basic principles which government departments should follow in assembling and using scientific advice. The key elements are to:

- **identify early** the issues which need scientific and engineering advice and where **public engagement** is appropriate
- draw on a **wide range of expert advice** sources, particularly where there is uncertainty;
- adopt an open and transparent approach to the scientific advisory process and publish the evidence and analysis as soon as possible;
- **explain publicly the reasons for policy decisions**, particularly when the decision appears to be inconsistent with scientific advice; and
- **work collectively** to ensure a joined-up approach throughout government to integrating scientific and engineering evidence and advice into policy making.

The *Code of Practice for Scientific Advisory Committees*[2] and the *Principles of Scientific Advice to Government*[3] provide more detailed guidance on the operation of scientific advisory committees (SACS) and their relationship with their sponsor Departments.

The Food Standards Agency's Board adopted a **Science Checklist** in 2006 (updated in 2012) that makes explicit the points to be considered in the preparation of papers and proposals dealing with science-based issues, including those which draw on advice from the Scientific Advisory Committees (SACS).

These **Good Practice Guidelines** were drawn up in 2006 by the Chairs of the independent SACs that advise the FSA based on, and complementing, the Science Checklist. They were updated in 2012 in consultation with the General Advisory Committee on Science (GACS).

[1] http://www.bis.gov.uk/assets/bispartners/goscience/docs/g/10-669-gcsa-guidelines-scientific-engineering-advice-policy-making-pdf

[2] http://www.bis.gov.uk/assets/BISPartners /GoScience/Docs/C11-1382-code-of-practice-scientific-advisory-committees.pdf

[3] http://www.bis.gov.uk/go-science/principles-of-scientific-advice-to-government

The Guidelines apply to the SACs that advise the FSA and for which the FSA is sole or lead sponsor Department:

Advisory Committee on Animal Feedingstuffs
Advisory Committee on Microbiological Safety of Foods
Advisory Committee on Novel Foods and Processes
Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment[4]
Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment[5]
Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment[6]
General Advisory Committee on Science
Social Science Research Committee

For the SACs with a shared sponsorship the Guidelines apply formally to their advice to the FSA; they may opt to follow them also in advising other sponsor Departments.

These committees share important characteristics. They:

- are independent;
- work in an open and transparent way; and
- are concerned with risk assessment and/or science governance, not with decisions about risk management.

The Guidelines relate primarily to the risk assessment process since this is the main purpose of most of the SACs. However, the SACs may, where appropriate, comment on risks associated with different risk management options, highlight any wider issues raised by their assessment that they feel should be considered (distinguishing clearly between issues on which the SAC has an expert capability and remit, and any other issues), or any evidence gaps and/or needs for research or analysis.

In addition, GACS and SSRC may advise the FSA on aspects of the governance of risk management, or on research that relates to risk management.

Twenty nine principles of good practice have been developed. However, the different committees have different duties and discharge those duties in different ways. Therefore, not all of the principles set out below will be applicable to all of the committees, all of the time.

The SACs have agreed to review their application of the principles annually and report this in their Annual Reports. Compliance with the Guidelines will also be covered in the annual self assessments by Members and annual feedback meetings between each SAC Chair and the FSA Chief Scientist.

[4] Joint FSA/HPA Secretariat, HPA lead
[5] Joint FSA/HPA Secretariat, HPA lead
[6] Joint FSA/HPA, FSA lead

ACNFP self-assessment against the Good Practice Guidelines

Issue	Compliance?	Notes/Comments
Defining the problem and the approach		
1. The FSA will ensure that issues it asks an SAC to address are clearly defined and take account of stakeholder expectations in discussion with the SAC Secretariat and where necessary the SAC Chair. The SAC Chair will refer back to the FSA if discussion suggests that further iteration and discussion of the task is necessary. Where an SAC proposes to initiate a piece of work the SAC Chair and Secretariat will discuss this with FSA to ensure the definition and rationale for the work its expected use by the FSA are clear.	Yes	ACNFP does this on a routine basis
Seeking input		
2. The Secretariat will ensure that stakeholders are consulted at appropriate points in the SAC's considerations. It will consider with the FSA whether and how stakeholder views need to be taken into account in helping to identify the issue and frame the question for the committee.	Yes	The main part of the ACNFP's work is the evaluation of dossiers submitted under EU procedures for authorisation of novel foods. For applications made directly to the UK, each dossier is published for public comment and the Committee carries out a second consultation on its draft opinion before it is finalised. That level of consultation cannot be achieved for applications made via other member states, as the Committee must comply with EU rules on access to documents. For the same reason, the Committee cannot discuss the documents in public. The ACNFP does however hold an annual open event, which allows Members to discuss relevant topics with members of the public. The Committee (via the Secretariat) requests relevant information from applicants and gives an appropriate time to respond. The Committee, with the assistance of the
3. Wherever possible, SAC discussions should be held in public.	Yes	
4. The scope of literature searches made on behalf of the SAC will be clearly set out.	N/A	
5. Steps will be taken to ensure that all available and relevant scientific evidence is rigorously considered by the committee, including consulting external/additional scientific experts who may know of relevant unpublished or pre-publication data.	Yes	

		Secretariat, also seeks further information and advice when required, from other Committees or individual experts.
6. Data from stakeholders will be considered and weighted according to quality by the SAC.	Yes	
7. Consideration by the Secretariat and the Chair (and where appropriate the whole SAC) will be given to whether expertise in other disciplines will be needed.	Yes	
8. Consideration will be given by the Secretariat or by the SAC, in discussion with the FSA, as to whether other SACs need to be consulted.	Yes	
Validation		
9. Study design, methods of measurement and the way that analysis of data has been carried out will be assessed by the SAC.	Yes	The Secretariat and Committee critically review the methods and statistical treatments used in dossiers and published and seeks further information from authors and other bodies as required.
10. Data will be assessed by the committee in accordance with the relevant principles of good practice, e.g. qualitative social science data will be assessed with reference to guidance from the Government's Chief Social Researcher[7].	Yes Where relevant,	For complex statistical questions, the Secretariat is able to consult with specialists within the FSA.
11. Formal statistical analyses will be included wherever appropriate. To support this, each SAC will have access to advice on quantitative analysis and modelling as needed.	Yes	The Committee has commented on a number of occasions about the value of using detailed information on dietary habits of UK consumers, so that risk assessments of novel foods can take account of potential intake by UK consumers, including relevant at-risk groups.

[7] Quality in Qualitative Evaluation: A Framework for assessing research evidence http://www.civilservice.gov.uk/w-content/uploads/2011/09/a_quality_framework_tcm6-7314.pdf; The Magenta book http://www.hm-treasury.gov.uk/d/magenta_book_combined.pdf

12. When considering what evidence needs to be collected for assessment, the following points will be considered: • the potential for the need for different data for different parts of the UK or the relevance to the UK situation for any data originating outside the UK; and • whether stakeholders can provide unpublished data.	Yes Yes	Evaluations of novel foods are mainly based on evidence provided by the applicant, including unpublished studies and commercially-sensitive information about manufacturing processes. For applications made via the UK, the dossier (less any confidential sections) is published via the Committee's website.
13. The list of references will make it clear which references have been subject to external peer review, and which have been peer reviewed through evaluation by the Committee, and if relevant, any that have not been peer reviewed.	Yes	Novel food application dossiers include a list of references which make it clear whether or not they have been peer reviewed.
Uncertainty		
14. When reporting outcomes, SACs will make explicit the level and type of uncertainty (both limitations on the quality of the available data and lack of knowledge) associated with their advice.	Yes	ACNFP complies with items 14 to 17 – outcomes are critically evaluated and uncertainties are identified.
15. Any assumptions made by the SAC will be clearly spelled out, and, in reviews, previous assumptions will be challenged.	Yes	
16. Data gaps will be identified and their impact on uncertainty assessed by the SAC.	Yes	
17. An indication will be given by the SAC about whether the evidence base is changing or static, and if appropriate, how developments in the evidence base might affect key assumptions and conclusions.	Yes	

Drawing conclusions 18. The SAC will be broad-minded, acknowledging where conflicting views exist and considering whether alternative interpretations fit the same evidence.	Yes	ACNFP complies with this – uncertainties and interpretations are identified clearly in the Committee's opinions.
19. Where both risks and benefits have been considered, the committee will address each with the same rigour, as far as possible; it will make clear the degree of rigour and uncertainty, and any important constraints, in reporting its conclusions.	N/A	The Committee's assessment focuses on safety and labelling and it does not address any nutrition or health benefits that may be claimed for the novel ingredient or for foods that contain it. Nutrition or health claims may only be made if they are specifically authorised under EU Regulation (EC) No 1924/2006
20. SAC decisions will include an explanation of where differences of opinion have arisen during discussions, specifically where there are unresolved issues, and why conclusions have been reached. If it is not possible to reach a consensus, a minority report may be appended to the main report, setting out the differences in interpretation and conclusions, and the reasons for these, and the names of those supporting the minority report.	Yes	The final opinions are adopted by consensus, identifying the key issues and generally explaining the reasoning behind the Committee's conclusions.
21. The SAC's interpretation of results, recommended actions or advice will be consistent with the quantitative and/or qualitative evidence and the degree of uncertainty associated with it.	Yes	
22. SACs will make recommendations about general issues that may have relevance for other committees.	Yes	
Communicating SACs' conclusions 23. Conclusions will be expressed by the SAC in clear, simple terms and use the minimum caveats consistent with	Yes	

accuracy.		
24. It will be made clear by the SAC where assessments have been based on the work of other bodies and where the SAC has started afresh, and there will be a clear statement of how the current conclusions compare with previous assessments.	Yes	
25. The conclusions will be supported by a statement about their robustness and the extent to which judgement has had to be used.	Yes	
26. As standard practice, the SAC secretariat will publish a full set of references (including the data used as the basis for risk assessment and other SAC opinions) at as early a stage as possible to support openness and transparency of decision-making. Where this is not possible, reasons will be clearly set out, explained and a commitment made to future publication wherever possible.	Yes	
27. The amount of material withheld by the SAC or FSA as being confidential will be kept to a minimum. Where it is not possible to release material, the reasons will be clearly set out, explained and a commitment made to future publication wherever possible.	Yes	
28. Where proposals or papers being considered by the FSA Board rest on scientific evidence produced by a SAC, the Chair of the SAC (or a nominated expert member) will be invited to the table at the Open Board meetings at which the paper is discussed. To maintain appropriate separation of risk assessment and risk management processes, the role of the Chairs will be limited to providing an independent view and assurance on how their committee's advice has been reflected in the relevant policy proposals, and to	N/A	

answer Board Members' questions on the science. The Chairs may also, where appropriate, be invited to provide factual briefing to Board members about particular issues within their committees' remits, in advance of discussion at open Board meetings. 29. The SAC will seek (and FSA will provide) timely feedback on actions taken (or not taken) in response to the SAC's advice, and the rationale for these.	Yes	

Financial Statement

ACNFP is an independent SAC, but does not have resources of its own. The operation of the Committee is funded by the FSA. In the period of this report, costs for this support (covering Members expenses and fees and administrative cost for the meetings) were £34,098.

ANNEX 2 ACNFP MEETING MINUTES

a) Minutes of the 109th Meeting (February 2013)

Minutes of the 108th meeting; **DRAFT/ACNFP/108/Min**

The Committee agreed, subject to minor amendments that the minutes were a true record of the 108th meeting of the ACNFP held on Tuesday 20 November 2012

Matters Arising and Postal Consultations

The Secretariat confirmed that the Committee's concerns about Nattokinase were forwarded to the European Commission.

Citicoline **ACNFP/109/1**

The Committee reviewed the applicant's response to comments and objections raised by the Committee in its earlier review of the Irish Competent Authority's favourable initial opinion on an application for authorisation of Citocoline as a novel food ingredient. These related to composition, stability and potential interactions with the human dopaminergic system.

The Committee noted the European Food Safety Authority (EFSA) was to be asked by the European Commission to undertake an additional assessment.

The Committee noted that the applicant now proposed that the use of citicoline be limited to food supplements, and their concerns about stability in other foods no longer applied. The Committee considered that its concerns about potential interactions with the human dopaminergic system had not been answered by the applicant. and remained concerned about the presence of unnamed components which make up 2% of the novel ingredient and sought information on the maximum level of the three components that the applicant suggested may be present.

The Committee highlighted a contradiction in the applicant's response about xylene and noted that dizziness is a known adverse effect linked to choline but which was only reported as affecting one person in the clinical trials.

Action: The Secretariat will forward the Committee's comments to EFSA for consideration in its additional assessment of this novel ingredient.

Rapeseed Protein **ACNFP/109/2**

The Committee considered the applicant's response to a number of concerns and questions, raised at its meeting in November 2012, when it reviewed the favorable initial opinion of the Irish Competent Authority on an application for rapeseed protein to be incorporated into a range of foods as an alternative to soya protein and at similar levels, except where soya protein is explicitly specified such as in infant formula.

The Committee's concerns primarily related to the possibility of allergic cross reactivity in people with mustard allergy. although questions relating to micronutrient absorption, phytate levels and analytical data on protein composition obtained by HPLC were also raised.

The Committee reviewed the applicant's responses to its concerns and maintained that its concerns and questions had not been satisfactorily addressed. The Committee reiterated that mustard and rapeseed are highly homologous (approx. 80% allergen sequence similarity) and as such, it is

extremely important for the applicant to determine the extent of cross-reactivity between rapeseed protein and mustard to determine the likelihood of mustard allergic individuals cross-reacting to rapeseed protein.

The Committee also highlighted that many people are sensitive to airborne rapeseed pollen and questioned how these individuals would react to the consumption of rapeseed protein, a concern exacerbated by the wide range of foods to which the novel ingredient is intended to be added.

The Committee did not consider that its questions relating to micronutrient absorption had been addressed.

The Secretariat explained that the European Commission is considering three possible risk management approaches should the novel ingredient be authorized in the EU and asked the Committee for advice to inform these risk management decisions (post-market monitoring as a method to monitor adverse effects, the possibility of including rapeseed on the list of allergen sources that must be highlighted on food labels, or the need for labelling of rapeseed protein to reflect cross-reactivity to mustard allergens. The Committee advised that it is essential for data on cross-reactivity to mustard to be provided in order to identify the appropriate risk management.

The Secretariat advised the Committee that this application is likely to be referred to EFSA and that if this is the case, it will write and inform EFSA of the Committee's outstanding concerns.

Action: The Secretariat will write to the EFSA Secretariat outlining the Committee's concerns.

Clostridium butyricum **ACNFP/109/3**

The Committee reviewed the latest response from the applicant, which provided details of the small number of suspected adverse effects reported by the applicant in Japan. While Members questioned that some of these suspected adverse effects seemed to be of a concerning nature, this needs to be balanced by the fact that individuals consuming this novel ingredient are likely to have existing GI symptoms. It was also highlighted that it is unlikely that these data could be improved if further investigations were conducted. The Committee therefore concluded that it did not have any safety concerns relating to this novel ingredient but, given that this is the first live micro-organism to be assessed under the novel foods regulation, it may be useful for the applicant to consider introducing systems to monitor adverse effects, should the ingredient be approved.

The Secretariat stated that it would finalise and publish the draft opinion for a 10 day public consultation.

Action: Secretariat to finalise and publish the draft opinion for a 10 day public consultation

DHA and EPA-rich oils **ACNFP/109/4**

The Committee reviewed this application from DSM Nutritional Products at its previous meeting in November 2012 and had a number of comments The Committee accepted the applicant's explanation that the high dose supplement would not be consumed by children because the claims related to adults. The Committee also accepted that high dose supplements containing fish oils were already on the market.

The opinion, which the Committee noted would exceptionally be in the form of a letter to the European Commission, was agreed subject to minor amendments.

Action: the Chair to clear the amended draft opinion prior to a 10-day public consultation

DHA rich microalgal oil **ACNFP/109/6**

The Committee considered this new application from DSM Nutritional Products for the extension of use of this DHA-rich oil form Schyzychytrium sp. The purpose of this application is to bring the permitted uses of the DHA-rich oil into line with the company's parallel application of the DHA and EPA-rich oil (Item 7 above).

The Committee was content with this application and agreed the draft opinion.

Action: the Chair to clear a draft opinion prior to a 10-day public consultation.

Chia oil **ACNFP/109/5**

The Committee reviewed this application for chia oil at its last meeting in November 2012. The Committee considered the response to the applicant to questions raised by the Committee.

The Committee remained concerned the applicant had not fully described the production process. The Committee noted that there was measurable protein in the oil and that this could lead to allergic reactions in susceptible individuals. However the Committee also noted that the oil would be used only in culinary oils and food supplements and that it was possible that this concern could be addressed through suitable risk management.

The Committee considered some residual questions on toxicology had not been answered by the applicant and the secretariat agreed to obtain the original study report from the applicant and forward them to toxicologists for review

Action: The Secretariat will incorporate the Committee's comments into the draft opinion for discussion at the next meeting.

Sporopollenin shells from club moss **ACNFP/109/7**

The Committee was asked to consider an application from Sporomex Ltd, for authorisation of sporopollenin shells from club moss (*Lycopodium clavatum)* as a novel ingredient to be added to a range of foods in the European Union.

The shells are produced by emptying spores of their genetic, lipid and protein material to leave an empty sporopollenin shell. The applicant's intention is to fill the empty shell with functional ingredients such as fish oils or vitamin D. Sporopollenin will therefore function as a novel system to deliver functional ingredients into the body.

The Committee raised several questions and concerns relating to this application. The Committee requested a detailed specification of the novel ingredient including for example, particle size distribution, physical characterization such as surface properties and information relating to contaminants such as pesticide and heavy metal levels.

The Committee also sought further information on the production process. The Committee considered it unlikely that the production process would empty entirely the contents of the spores and requested information relating to the exact nature of the product obtained at the end of the production process. A diagram of the production process was requested to aid understanding.

The Committee requested a full report of the rodent feeding study that had been conducted on the novel ingredient.

The Committee also requested further information on the fate of the shells in the GI tract as the electron micrograph supplied in the dossier did not provide sufficient evidence that spores pass through the GI tract unchanged. The Committee requested further information on the possible implications of sporopollenin shells being lodged in intestinal villi, as was reported in the dossier.

More information on the carrier properties of the shells was requested, in terms of ingredient release for example. Although the Committee is not assessing efficacy *per se*, this information was considered important in this case, to support the safety assessment.

Relating to allergenicity, the Committee noted that pollen is a potent vehicle for allergens and advised that sporopollenin shells should not be used as carriers for proteins, which could remain intact within the shell and subsequently initiate an allergic reaction (either in the GI tract or by inhalation of the shells during manufacturing or while incorporating into foodstuffs). The Committee also enquired about the allergenic potential of the club moss source, as no reference was made to this in the dossier. The Committee requested reassurance on possible inhalation-related allergy, particularly as the novel ingredient is to be supplied to consumers in powder form.

As the dossier refers to sporopollenin consumption from mushrooms, the Committee requested information to support the comparison between sporopollenin from club moss and components found in edible mushrooms.

The Committee highlighted that club moss is regarded as an endangered species in many areas and requested further information to demonstrate that the novel ingredient is produced in a sustainable way

Action: The Secretariat to ask for additional information from the applicant

Refined oil from Buglossoides arvensis **ACNFP/109/8**

The Committee was asked whether it was content to agree substantial equivalence had been established between a refined oil produced by Technology Crops International from *Buglossoides arvensis* and the refined echium oil produced by Croda Chemicals Ltd.

The Committee highlighted significant differences in the key fatty acids that characterise the two oils. On this basis, the Committee did not regard the two oils to be substantially equivalent in terms of composition or metabolism. The Committee mentioned that it had not made any judgements on the safety of the refined oil and comments were relating solely to equivalence, as defined in the novel foods regulation.

Action: The Secretariat to inform the applicant of the Committees views.

UV Treated Milk **Oral Update**

The secretarat informed the Committee that the Food Standards Agency (FSA) had recently received an initial opinion from the Irish competent authority for pasteurised cows milk that has been treated with ultra violet light so as to increase the content of vitamin D_3 present. This treatment would also increase the shelf life of the treated milk.

The FSA is awaiting key information relating to the application, particularly in relation to the likely levels of exposure to the treated milk. The Committee will be asked to comment by post once this information is received.

Action: The Secretariat to consult members on the Irish competent authority's initial opinion.

D-Ribose **Oral Update**

This item was deferred to the following meeting.

Cauliflower Mosaic Virus promoter regions in Transgenic Plants **ACNFP/109/11**

The Committee considered a recent peer reviewed article that provides an overview of different variants of the cauliflower mosaic virus promoter regions (P35S) that have been used to produce transgenic plants and the consequences of the presence of the viral gene VI in such plants.

The Committee noted that P35S promoters are present in most GM plants and that the virus is also found naturally in brassica species. While it was possible that the inserted sequences could lead to the production of part of a viral protein in GM plants, these products may not be stable and the level of expression would be much lower than in virus-infected plants. All inserted DNA sequences are investigated as part of the safety evaluation of GM plants and the Committee agreed with the European Food Safety Authority that the new paper did not raise any concerns for the safety of food and feed from previously evaluated GM crops.

Items for Information

15.1 EU Update ACNFP/109/12
15.2 Update on Scientific Advisory Committees (SACs) ACNFP/109/13

The Committee noted the information papers without comment.

Any Other Business

Professor Harry McArdle, who is the cross-member between the Scientific Advisory Committee on Nutrition (SACN) and the ACNFP provided an update to the Committee on SACN's activities.

Date of next meeting

The next meeting was scheduled for Thursday 25 April in Aviation House.

b) Minutes of the 110th Meeting (April 2013)

Minutes of the 109th meeting; DRAFT/ACNFP/109/Min

The Committee agreed that the minutes were a true record of the 109th meeting of the ACNFP held on Wednesday 13 February 2013

Matters Arising and Postal Consultations

The Secretariat reported on progress with the following items:

(a) Citicoline (item 4) and Rapeseed protein (item 5): The Secretariat had not yet informed EFSA of the Committee's outstanding concerns but would do so shortly.

(b) Clostridium butyricum (item 6) – Two members of the public had commented on the Committee's draft opinion. The first respondent 3 detailed points, while the second raised more general concerns about quality and safety of the ingredient. The issues raised in these comments were all covered by the Committee in some detail during its evaluation of this dossier. As no further changes were required, the Secretariat would submit the opinion to the European Commission.

(c) DHA Oils (items 7 and 8) - The draft opinions for these related products were published for public comment and no comments were received. The Secretariat would therefore proceed to submit these opinions to the European Commission.

Members were consulted by post on the following item between 1 and 13 March 2013:

Pasteurised milk treated with UV light (paper ACNFP/110/P1)

The Committee was asked to consider an initial assessment report prepared by the Irish Competent Authority on an application from Dairy Crest for authorization of pasteurised milk treated with ultraviolet (UV) light as a novel food.

Members advised that the applicant ought to provide information on the extent of variation in the level of vitamin D3 both within and between batches and, if appropriate, this should

be reflected in the product specification. Also, only limited sensory tests that had been carried out on the treated milk, based on analyses of one day old samples rather than at the end of the product's shelf life, where any effect may be more apparent. As there are published reports of 'sensory defect' associated with UV treated milk, Members advised that additional reassurance was needed on this point.

Members were also concerned that the applicant did not consider whether the UV treatment may give rise to the formation of oxidation products and treatment induced aggregates, as there are published reports showing that UV treatment can induce the formation of such products in whey.

On the basis of Members' concerns, the Agency wrote to the European Commission on 15 March raising reasoned objections to the positive report of the Irish authorities.

Chia Seed Oil **ACNFP/110/1**

The Committee reviewed the applicant's response to concerns about the oil's allergenic potential, which had been raised by the Committee whilst reviewing the application at its meeting in February 2013, and considered the first draft of an initial opinion on this product..

The Committee was broadly content with the text of the opinion but requested that the specification be amended to take account of additional steps in the production process (e.g. winterising) which may be necessary if requested by customers. The Committee also agreed that the Secretariat should work with Members with expertise in food allergy to ensure that concerns in regard to allergenic potential are accurately reflected in the text.

The Committee also requested that allergy support organisations receive notification of the novel ingredient when it is authorized.

Action: The Secretariat to draft a specification of the product for inclusion in the initial opinion prior to clearance through Allergy specialists and Chairman's action.

D-Ribose **ACNFP/110/2**

The Committee considered an application for the authorisation of D-Ribose as a novel food ingredient on a number of occasions in 2008. At the time the Committee was concerned about variations in skeletal development seen in the offspring of rats given a diet containing 20% ribose. The Committee also noted that clinical studies with high bolus doses of ribose have been shown to affect glucose levels and that there is a potential link between glucose and embryo development. The Committee had requested a further developmental toxicity study to be performed. The applicant was now, after some time, considering how to respond to this request and was seeking further advice on how to proceed.

The Committee advised that it would review the position on receipt of an updated dossier, which should include any relevant information that wasn't available at the time of the original submission, particularly in relation to glucose and pregnancy, bearing in mind that young women will be part of the target population for this ingredient, and some of these may be diabetic. The dossier should also include responses to the observations that ribose can affect glucose levels and fluctuations in glucose levels are a cause for concern during pregnancy. However, the Committee considered that a further animal study along the lines of the high dose feeding study would not be useful and did not see the need, at this stage, for a new study at lower doses. Finally, it would be useful to review any additional data on elevated uric acid levels, as this issue was also highlighted during the ACNFP's original discussions.

Action: The Secretariat to ask the applicant to provide an updated dossier

Chia Seed (Inversoria Agropecuaria) Substantial Equivalence **ACNFP/110/3**

The Committee was asked whether it agreed that substantial equivalence had been established between chia seeds produced by an Argentinean company, Company Inversora AgroPecuaria and chia seeds currently marketed by the Chia Company.

The Committee was not satisfied with the data in the dossier and highlighted that, before it could carry out an assessment of substantial equivalence, it is essential that the applicant provides data on at least three batches of the product for all the parameters assayed. The Committee was not able to provide advice based on data from single measurements taken at different times and noted that, for some parameters, this particular dossier included analyses carried out over many years.

The Secretariat agreed to ask the applicant for a more robust dataset from which the Committee can carry out an assessment of this novel ingredient.

Action: The Secretariat to ask for further information from the applicant

Chia Seed (Infoods Ltd) Substantial Equivalence **ACNFP/110/4**

The Committee was asked whether it agreed that substantial equivalence had been established between chia seeds produced in Argentina by Infoods Ltd and chia seeds grown in Australia and marketed by the Chia Company

The Committee was content that substantial equivalence had been demonstrated, subject to confirmation that the data cited in the dossier correspond to the attached certificates of analysis.

The Committee also made a general comment about requests for opinions on equivalence, as recent applications had included a great deal of superfluous information. The Committee requested that, in future, any request should focus only on information relating to the five criteria detailed in Article 3(4) of Commission Regulation No. (EC)258/97. The Committee also noted that EU Member States had agreed a new common guidance document for the assessment of substantial equivalence and that this would be published in the coming months. One published, this would replace the Committee's current guidance document.

Action: the Secretariat to ask the applicant for clarification regarding the certificates, prior to clearing the opinion through Chairman's action.

Annual Report 2012 **ACNFP/110/8**

The Committee was content with the new abbreviated format for this report.

Action: Members to provide the Secretariat with updates to their personal details prior to publication of the Annual Report.

Items for Information

9.1 EU Update	ACNFP/110/5
9.2 Update on Scientific Advisory Committees (SACs)	ACNFP/110/6
9.3 GM Research Update	ACNFP/110/7

The Committee noted the information papers without comment.

Any Other Business

The Committee was notified that Members' self-appraisals were to be carried out shortly, in advance of the Chair's annual meeting with the FSA's Chief Scientist.

Date of next meeting

The next meeting was scheduled for Wednesday 26 June in Aviation House.

c) Minutes of the 111th meeting (June 2013)

Minutes of the 110th meeting (April 2013)

The Committee agreed that the minutes were a true record of the 110th meeting of the ACNFP held on Wednesday 25 April 2013

Matters Arising and Postal Consultations

The Secretariat reported on progress with the following items:

Item 3 (matters arising): the Committee's opinions on DHA-rich oils were submitted to the European Commission on 29 April and will now be reviewed by the other Member States. The opinion on *Clostridium butyricum* was likewise submitted to the Commission on 14 May and is also awaiting review by the other Member States.

Item 4 (chia seed oil): the Secretariat confirmed that the draft opinion had recently been published for public consultation and any substantive comments would be circulated to the Committee.

Item 5 (d-ribose): the applicant intends to provide an updated dossier as requested, for discussion at a future meeting.

Item 6 (chia seeds – Inversoria): the applicant is providing additional data for discussion at a future meeting.

Item 7 (chia seeds – Infoods): the Committee's opinion was finalised and issued to the applicant. It was now up to the applicant to notify the European Commission before they begin to market their seeds in the EU.

Calanus Oil **ACNFP/111/1**

The Committee considered an application for the authorisation of Calanus Oil as a novel food ingredient at its February 2012 meeting. Members had sought clarification from the applicant on a number of points and was now asked to review the applicant's responses.

The Committee reviewed the protein analysis data provided by the applicant and, although Members were critical of the quality, and reporting, of the Western Blot results, they concluded that the novel ingredient was unlikely to contain shellfish allergens. The Committee did, however, request that the applicant re-present the data with clearer, better labeled gels for completeness. The Committee was content with the applicant's response about dioxins and adverse gastrointestinal effects and it was reassured that there were unlikely to be any environmental consequences if the source material was fished in commercial quantities.

However, the Committee did not agree with the applicant that there was evidence to demonstrate that the long chain polyunsaturated fatty acids present in the oil, primarily in the form of wax esters, had a similar bioavailability to those in other marine oils. The Committee noted that the literature suggested that fatty acids in wax esters have limited bioavailability and requested that the applicant carry out appropriate studies to demonstrate that this would not be the case for calanus oil, noting that it was a key requirement that any novel food was of a similar nutritional quality to the food that it would replace in the diet.

Action: Secretariat to ask for further information from the applicant

Refined Oil from *Bugloissoides arvensis* **ACNFP/111/2**

The Committee considered an application from Technology Crops International for the authorisation of refined Bugloissoides Oil, as a novel ingredient.

In February 2013 the Committee considered whether this novel ingredient was substantially equivalent to refined Echium oil, which has previously been authorised as a novel ingredient. The Committee advised that equivalence could not be established as there were clear compositional differences between the two oils. The oil therefore did not meet the criteria for authorisation under the simplified procedure set out in the novel food regulation and the applicant submitted a full application.

The Committee requested further information on the production process of the novel ingredient, such as the seed harvesting procedure and what steps are taken to ensure the absence of other plant material. The Committee also wanted reassurance about the homogeneity of the seeds used as the source material for the refined oil.

The Committee expressed some concern relating to the lack of safety data from human studies, particularly given that the novel ingredient and its source material do not have any history of consumption globally. The Committee enquired whether any such data are available or if any clinical studies are under way.

The Committee requested to view the detailed reports from some of the toxicology studies summarised in the dossier in order to independently assess some of the findings reported by the applicant in relation to adverse effects.

Members queried the concept of employing additional processing steps for some batches of the oil until it meets the required specifications and requested further information from the applicant on this approach.

Action: Secretariat to ask for further information from the applicant

1-Methlynicontinamide Chloride (1-MNA) **ACNFP/111/3**

The Committee considered an application from the Polish company, Pharmena, for the authorisation of 1-MNA as a novel ingredient for use as supplements.

The Secretariat notified the Committee that it was awaiting confirmation from the Medicines and Healthcare products Regulatory Agency (MHRA) as to whether the novel ingredient is considered a medicine but, as the levels of 1-MNA that were being proposed were low, the Secretariat was of the view that it was appropriate to proceed with the novel food assessment pending advice from the MHRA.

The Committee noted that the metabolic pathway for 1-MNA is not fully elucidated and the levels proposed were significantly higher than would typically be present in the body (1-MNA is a metabolite of niacin). The Committee also noted that 1-MNA was structurally similar to key cellular components NADP-NAD. The Committee therefore requested further information on the possibility that the novel ingredient could interfere with the metabolism of niacin and related compounds.

The Committee noted that the half-life of 1-MNA in rats was in excess of 24 hours and, if it was of a similar duration in humans, this could lead to accumulation. The Committee requested additional information from the applicant in this regard.

The Committee also noted the presence of lesions in rats given high doses of 1-MNA in the 28 day feeding study, on which the applicant had sought an independent view regarding their significance. The Committee would review these findings and the conclusions of the expert in more detail.

The Committee queried the implications of the gender differences observed in one of the human studies and asked if the applicant had considered whether 1-MNA could interact with pharmaceutical products such as statins and whether it could be safely consumed by individuals who are also consuming high doses of niacin to reduce cholesterol.

The Committee considered the novel ingredient was unlikely to be allergenic.

Action: Secretariat to ask for further information from the applicant

Phytosterol esters – extension of use **ACNFP/111/4**

The Committee considered an application from Unilever to extend the use of phytosterol esters as a novel food ingredient. The application seeks to extend the use in margarine to include cooking and baking and to permit the addition of phytosterol esters to liquid vegetable fat based emulsions (liquid margarines) which also used for frying and baking.

Dr Camilla Pease informed the Committee that she had worked on similar products at Unilever between 2000 and 2010, however she is no longer employed at Unilever and has not been involved with these or similar products since 2010.

The Committee considered the information provided to estimate intakes, which included the results of post launch monitoring over a 12 month period, to be useful and asked the Secretariat to provide an analysis of the level of uncertainly which was associated with the different data sets.

The Committee queried whether the concerns relating to the potential atherogenic effects associated with phytosterol oxidation products had been fully investigated by the applicant. The Committee also noted that the studies looking at the safety of phytosterol oxidation products had not investigated their effects in humans and asked the applicant to clarify why this was the case.

Action: Secretariat to ask for further information from the applicant

Pasteurised milk products treated with *Bacteroides xylanisolvens* **ACNFP/111/5**

The Committee considered an application submitted to the Irish Competent Authority on pasteurised fermented milk products with heat-inactivated *Bacteroides xylanisolvens.* The favourable opinion of the Irish Competent Authority was recently finalised and would be distributed to Member States over the summer.

The Committee agreed with the favourable opinion of the Irish Competent Authority and did not raise any safety concerns relating to this novel ingredient. Members explained that *B. xylanisolvens* produces only very low levels of short-chain fatty acids, which may explain why fermentation of low fat or non-fat milk with this micro-organism could result in better tasting products than more traditional low fat/non-fat fermented milk products.

Members regarded *B. xylanisolvens* to be non-pathogenic and no concern was expressed relating to the use of this micro-organism for the purposes proposed by the applicant. The applicant had mentioned in its dossier the possibility that some *Bacteroides* species may favourably affect the immune system; the Committee disagreed with this. The Committee also pointed out that the background information supplied in the dossier relating to probiotic properties was irrelevant as the live organism would not be present in the pasteurised milk products.

While no safety concerns were expressed relating to this application, the Committee asked to see the full report of the summarized human study in order to gain further details on the exact methodology employed.

Action: Secretariat to circulate the Opinion of the Irish Competent Authority for further comment.

Toxicology study on pigs fed GM and non-GM diets **ACNFP/111/6**

The Committee reviewed a paper that had recently been published in the online *Journal of Organic Systems*, with results of a study of pigs that had been reared as livestock under commercial conditions in the USA using diets that included maize and soya from GM and non-GM varieties. The Committee was asked to consider whether this work had any implications for the safety of GM crops that have been authorised for use as food and feed.

The Committee noted that this work was not carried out to test a particular hypothesis but it involved a large number of animals and was potentially able to detect small changes in the parameters that were recorded. However, the work was a field trial carried out under normal conditions of livestock production and animal slaughter and, compared with standard toxicity tests, only limited data were available, primarily based on macroscopic examinations of the animals and their internal organs.

The Committee suggested that the title of the paper was misleading as the researchers had tested samples of specific maize and soya varieties that were genetically modified against varieties that were not genetically modified, and the results could not be extrapolated to animal diets containing GM crops in general. It would have also been useful to include an intermediate group that was given a mixture of the two diets as this would have allowed a basic dose response analysis.

The paper emphasised a small but statistically significant difference in uterine weights between the two groups of pigs. The Committee noted that there is significant variability in uterine weights in pigs and the range of values in the two groups overlapped to a considerable extent. The pigs were slaughtered around the age that females reach sexual maturity. This would have a significant effect on the size of the uterus in individual animals and might explain the relatively larger inter-individual differences in uterine weight. This issue was not apparently taken into account in the design of the study and the stage of sexual maturity in each animal was not recorded. In addition, a dietary effect which influenced the attainment of sexual maturity might explain the higher mean uterine weight in one group of animals.

The authors also reported that there was more severe inflammation of the stomach lining in pigs given diets containing the GM maize and soya varieties. While the statistical test used by the authors was not ideal, and the method of assessing inflammation has not been validated, Members

agreed that there was a trend in this direction that approached statistical significance when analysed by more appropriate tests.

The paper did not describe the agronomic practices that were used to grow, harvest and store the GM and non-GM crops, which were from different farms. As the GM varieties were insect resistant and/or herbicide tolerant, it was highly likely that they were subjected to different treatments from the conventionally-grown crops. It was also possible that there were other physical or biochemical differences in these raw feed materials that could have an influence on the severity of inflammation of the stomach lining.

The Committee acknowledged that the paper may demonstrate some differences in the effects of the two diets but, given the uncertainties, these differences cannot be attributed to the genetically modified source of the feed ingredients.

Items for Information

10.1 EU Update	**ACNFP/111/7**
10.2 Update on Scientific Advisory Committees (SACs)	**ACNFP/111/8**
10.3 GM Wheat	**ACNFP/111/9**

The Committee noted items 10.1 and 10.2 without comment.

In item 10.3 the Committee was updated on the discovery of GM wheat in a wheat field in Oregon. The Committee was informed there were no immediate consequences for UK imports as unauthorised GM material had been detected in a type of wheat the UK does not import from the USA and a part of the US that exports via the Pacific rather than the Atlantic Ocean.

Any Other Business

In preparation for the open event that was scheduled to take place in November. Members were asked to submit ideas for suitable topics by email. The Secretariat would discuss the programme with the Chair and present option to the Committee at the next meeting

Date of next meeting

The next meeting was scheduled for Thursday 12 September in Aviation House.

d) Minutes of the 112th meeting (12 September)

Minutes of the 111th meeting (26 June)	**DRAFT/ACNFP/111/Min**

The Committee agreed that subject to minor amendments the minutes were a true record of the 111th meeting of the ACNFP held on Wednesday 26 June 2013.

Matters Arising and Postal Consultations

The Committee received positive feedback from members of the Advisory Committee on Animal Feed, following circulation of the ACNFP's conclusions on the effects of GM feed and non-GM feed in pigs.

Buglossoides Oil **ACNFP/112/1**

The Committee reviewed the applicant's response to concerns raised at its previous meeting when it reviewed this application for the authorisation of refined Buglossoides Oil as a novel ingredient.

The Committee was satisfied with the applicant's response relating to production process details, in particular details about the seed harvesting procedure and the applicant's response to provide reassurance about seed homogeneity. The applicant's rationale for employing additional optional processing steps if required was also reviewed. No further information was requested on these aspects.

The Committee had requested reference papers for certain toxicology studies and, having reviewed these references, indicated that no further information was required.

The Committee reviewed the applicant's response regarding the absence of human study data. The Committee noted that there are no apparent safety concerns relating to this novel ingredient or its known constituents and was satisfied that it is not necessary for the applicant to conduct a human study.

Because neither the novel ingredient nor its source has a history of consumption anywhere in the world, the Committee considered that some type of post-market monitoring scheme (such as adverse effects monitoring) might be appropriate, should the oil be authorized and marketed in the EU. The Secretariat agreed to draft an opinion for discussion at the November meeting.

Action: The Secretariat will incorporate the Committee's comments into the draft opinion for discussion at the next meeting.

1-Methylnicotinamide Chloride (1-MNA) **Oral Update**

The Committee was given an oral update on an application for the authorisation of 1- as a novel ingredient.

The Committee was informed that the FSA had recently received confirmation from the Medicines and Healthcare products Regulatory Agency that it did not consider 1-MNA to be a medicinal product. In line with the discussion at the June meeting, toxicologists on the Committee would now be asked to complete their scrutiny of the 28 day rat feeding study and the independent review of its results. Once this was completed the Committee would review their conclusions along with with the response from the applicant to the other concerns that were raised in June.

Action: The Secretariat will consult the Committee Toxicologists.

D-β-hydroxybutyrate ester **ACNFP/112/3**

The Committee was asked to consider a new application from TDeltaS seeking authorisation for D-β-hydroxybutyrate ester as a novel food ingredient, for use in food supplements targeted at high performance athletes.

The Committee queried why the applicant had not carried out mutagenicity and genotoxicity tests, noting that this would normally be a prerequisite for obtaining ethical approval for human studies with a new substance. The Committee also noted that some of the clinical chemistry parameters

monitored during the 28 day rat feeding study showed significant differences and suggested that these findings should have resulted in a follow up 90 day study to assess their significance.

The ACNFP acknowledged that the proposed intake of D-β-hydroxybutyrate ester may be similar to the level of circulating ketone bodies seen under certain conditions where blood glucose levels are reduced, but was of the view that the production of ketone bodies is usually in response to an undesirable physiological condition and is more akin to a pathological response. The Committee also did not agree that the circulating levels of ketone bodies (including hydroxybutyrate) were a relevant comparison when considering the safety of bolus doses of D-β-hydroxybutyrate ester as a food supplement.

The Committee noted that the bodies of high performance athletes undergo severe physical stress and requested information on the typical circulating levels of ketone bodies seen during extreme exertion and whether supplementation with D-β-hydroxybutyrate ester could increase these to a level which may be a cause for concern. The Committee also noted that the long term effects of consuming D-β-hydroxybutyrate ester as a supplement had not been examined and questioned whether such exposure could have a deleterious effect on an athlete's digestive system.

Action: Secretariat to ask for further information from the applicant

DHA rich algal oil from the microalgae *Schizochytrium* **ACNFP/112/4**

The Committee considered an application from DSM for to market oils rich in polyunsaturated fatty acids obtained from a specific strain of the microalgae Schizochytrium sp as a novel ingredient. The oil is proposed for use, primarily, in infant and follow on formula.

The Committee was unsure how the extraction process worked and queried whether, compared with traditional solvent extraction, there was a greater potential for other unidentified (non-lipid) components to be present in the oil. The Committee also requested additional taxonomic information regarding the production strain and whether it had been given a specific culture collection number.

The Committee also requested additional information regarded the extent of microbial control, specifically whether any tests had been carried out investigating potential contamination by Cyanobacteria. The Committee was content with the 90 day study.

Action: The Secretariat to ask for further information from the applicant.

Phytosterol Esters – Extension of Use **ACNFP/112/5**

The Committee reviewed the applicant's response to concerns raised at its meeting in June when it reviewed this application to extend the scope of the original authorisation for phytosterol esters.

Dr Camilla Pease informed the Committee that she had worked on similar products at Unilever between 2000 and 2010, however she has not been involved with these or similar products since leaving Unilever's employment in 2010.

The Committee reviewed the data the applicant provided in relation to phytosterol oxidation products,k which provided an indication of the levels present in a range of different foods and food ingredients, including those with added phytosterol esters. However the Committee noted that these data did not quantify the increase in exposure to phytosterol oxidation products if consumers used exclusively these fortified products for cooking and baking.

The Committee also requested any relevant information on the level of consumption of similar liquid margarine products in EU Member States where they are marketed with added phytostanols.

Action:The Secretariat agreed to seek a view from the applicant and to draft an Opinion for the next meeting.

Uncertainty in Exposure Estimation **ACNFP/112/6**

The Committee considered a paper on the assessment of uncertainties following a request by the Committee at the previous meeting that the Secretariat provide an overview of the uncertainties that are associated with each of 4 intake assessments included in the application to extend the scope of the original authorisation for phytosterol esters (see previous item).

The Committee considered the table attached to the paper was useful. The table provided information on the potential sources of uncertainty and whether they would lead to under- or over-estimation of exposure. The Secretariat advise dthat the greatest influence was the assumption that all spreads are fortified, which leads to a significant over-estimation. The Committee considered it would be useful for a paper to be produced for each new application in future, and suggested that a semi-quantitative estimate of magnitude should be included.

Action: Secretariat to produce a paper assessing uncertainties for each application

Chia Seeds (Inversoria) **ACNFP/112/7**

The Committee reviewed the applicant's revised dossier and the new certificates of analyses, but indicated that it was still not satisfied with the quality of the information, for example Table 6 where figures for calcium levels for the applicant's seeds are incorrect. It also questioned whether the data had been obtained from accredited laboratories and what validated testing methods were used.

Action:The Secretariat to ask for further information from the applicant

Pasteurised milk products treated with *Bacteroides xylanisolvens* **ACNFP/112/8**

The Committee reviewed the favourable initial opinion of the Irish Competent Authority on an application for the authorisation of pasteurised milk products treated with *Bacteroides xylanisolven* as a novel food. The Committee had commented on the application dossier at its previous meeting.

The Committee was content with the Initial opinion of the Irish Competent Authority and no concerns were raised. The Secretariat agreed to send favourable UK comments to the Commission.

Action: The Secretariat will inform the Commission that the UK does not have any objections to this application.

Open Event **ACNFP/112/9**

The Committee agreed the format and the Agenda for the Open Event which is scheduled to take place on the afternoon of 20 November.

Items for Information

13.1 EU Update **Oral Update**
13.2 Update on Scientific Advisory Committees (SACs) **ACNFP/112/10**
103.3 GM Wheat **ACNFP/112/12**

The Committee was given an oral update on item 13.1. The Committee noted item 13.2 without comment.

In item 13.3 the Committee was informed of recent advice from the European Food Safety Authority (EFSA) on the design and conduct of long-term feeding studies with whole foods, which is relevant to GM foods and also to novel foods.

Any Other Business

(none)

Date of next meeting

The next meeting was scheduled for Wednesday 20 November in Aviation House.

e) Minutes of the 113th meeting (20 November)

Minutes of the 112th meeting (12 September) **DRAFT/ACNFP/112/Min**

The Committee agreed that subject to minor amendments the minutes were a true record of the 112th meeting of the ACNFP held on Thursday 12 September 2013.

Matters Arising and Postal Consultations

Matters arising from the 112th meeting:

The Secretariat confirmed that the Committee's comments on item 11 (milk products treated with *Bacteroides xylanisolvens*) had been sent to the European Commission on 25 September.

Synthetic Resveratrol (paper ACNFP/113/P1)

The Committee considered this paper by correspondence during October 2013, when they reviewed the Irish Competent Authority's Initial Assessment Report on synthetic resveratrol. As a result of Members' comments, the UK submitted reasoned objections to this opinion citing concerns over:

- Lack of information about the current production process
- Potential interference with drug metabolism
- Failure to take account of certain publications on the safety of this resveratrol
- Suitability for children
- Lack of information on adverse reporting from areas where the product has already been marketed

Buglossoides Oil **ACNFP/113/1**

The Committee considered a draft opinion following its review of the applicant's response to concerns raised at its September and June meetings when it reviewed this application for the authorisation of refined Buglossoides Oil as a novel ingredient.

The Committee agreed the wording in the draft opinion subject to some amendments. The Committee stated nonetheless, that neither the novel ingredient nor its source has a history of consumption anywhere in the world and as such recommended that the applicant should ensure that reports of adverse reactions are closely monitored after the product is introduced to the market, in order to identify any unexpected effects.

Before completing its opinion, the Committee would therefore like to see details of how the applicant intends to monitor adverse effects once foods containing the novel ingredient are launched in the EU, for example, how data will be collected and monitored by the applicant in a way that enables early detection of any unexpected reactions to the novel ingredient.

Action: Secretariat to update and publish the draft opinion for a 10 day public consultation

1-Methylnicotinamide Chloride (1-MNA) **ACNFP 113/2**

The Committee discussed the applicant's response to concerns raised at the June meeting, together with the conclusions of a sub-group of ACNFP toxicologists and nutritionists who had examined the implications of various treatment-related changes that were observed in the 90-day feeding study.

The sub-group did not agree with the interpretation provided by the applicant and indicated that the presence of liver lesions and other findings were a cause for concern. The Committee agreed with the conclusions of its sub-group and with its suggestion that a follow up 90 day animal study should carried out to investigate these observations in more detail. The Committee advised that this study should also consider potential bone mineral changes.

The Committee was not satisfied with the information provided in regard to the effect of 1-MNA supplementation on the metabolism of niacin. The Committee advised that the response described the relevant pathways in a qualitative manner but did not consider the quantitative aspects of the kinetics of metabolism. The Committee therefore requested that appropriate investigations are carried out to determine whether the proposed level of consumption of 1-MNA is likely to have a significant effect on niacin metabolism. This study should also take into account the effect of 1-MNA supplementation on high doses of niacin which are used for the treatment of cholesterolaemia. Members noted that mathematical modelling of metabolic pathways and metabolic interactions is now available and this might be one way of addressing this question.

Action: The Secretariat to ask for further information from the applicant.

D-beta-hydroxybutyrate ester **ACNFP/113/3**

The Committee reviewed the applicant's response to concerns raised at its meeting in September.

The Committee accepted that the component parts of the ester are not mutagenic and that there are no structural alerts for ketone esters. However the Committee did not regard this to offer conclusive reassurance that D-beta-hydroxybutyrate ester is not mutagenic. The Committee noted that mutagenicity and genotoxicity studies are relatively straightforward to perform and are routinely carried out for novel foods, and requested that these are carried out for this novel food.

The Committee did not agree with the applicant's view that the proposed intake of D-beta-hydroxybutyrate ester was akin to that seen during certain physiological conditions where carbohydrate intake is restricted and remained of the view that the *in vivo* production of ketone bodies is of limited relevance to modern consumers. In regard to the applicant's suggestion that statistically significant changes in certain clinical chemistry parameters were not clinically significant, the Committee also noted that the relatively low margin of safety from the animal studies was not confirmed by an appropriate human study. In view of this the Committee concluded that the significance of changes in the clinical chemistry parameters ought to be confirmed in a longer term study and the Committee toxicologists agreed to provide additional information regarding a suitable study to the Secretariat following the meeting.

The Committee noted that the novel ingredient is intended to be targeted at a particularly small subset of the population (high performance athletes) who would only use products containing D-beta-hydroxybutyrate ester during sustained periods of intense muscular activity. However, the Committee remained concerned that this limited use is at odds with information on the applicant's website and asked that the applicant provides information to reassure it that D-beta-hydroxybutyrate ester would not be widely incorporated into mainstream sports supplements. The Committee noted that, if D-beta-hydroxybutyrate ester has no conceivable benefit to the wider population, wider availability could be misleading to the consumer.[8]

Action: Secretariat to ask for further information from the applicant

DHA rich algal oil from the microalgae *Schizochytrium* **ACNFP/113/4**

The Committee reviewed and accepted the applicant's response to questions raised at its meeting in September about the extraction process and regarding the specific strain used in the production of the novel ingredient.

The Committee highlighted the absence of good quality taxonomic information on production strains of alga and microorganisms that are used in the production of novel foods as a potential area of concern. The Secretariat agreed to look into this issue, with a view to the Committee issuing guidance to assist applicants. The Committee also sought clarification from the applicant on an apparent inconsistency in the analytical results of mycotoxins and agreed the draft opinion subject to this and other amendments.

Action: Secretariat to update and publish the draft opinion for a 10 day public consultation

[8] Article 3 of EC Regulation No. 258/97 requires, *inter alia*, that novel foods must not mislead the consumer

D- Ribose **ACNFP/113/5**

The Committee had considered an application for the authorisation of D-Ribose as a novel food ingredient on a number of occasions in 2008 and 2009 when the assessment was suspended. In June 2013 the Committee confirmed to the applicant that it did not see the need for additional animal experiments at this stage and would review the situation when the applicant submitted an updated dossier.

The Committee reviewed the applicant's revised dossier and was generally content with the information provided. The Secretariat agreed to obtain specialist advice on the results from the developmental toxicity study, where the applicant reported minor variations in the offspring of the top dose group.

The Committee noted that the novel ingredient altered glucose metabolism when taken at a high dosage under fasting conditions, but was satisfied that concern was addressed by ensuring that D-ribose is only proposed for addition to foods that contain other carbohydrate energy sources. It recommended labelling 'not to be taken on an empty stomach' as a warning against possible hypoglycemic effects for food supplements containing D-ribose.

The Committee noted that the method used to assess the protein content of the ingredient (the Bradford assay) is not itself sufficient to demonstrate the absence of proteins and peptides at levels that could be allergenic. The Committee also sought further information about the performance characteristics of the method that is used to determine the purity of the ingredient.

Action: Secretariat to seek advice from a developmental toxicologist and to draft an initial opinion for the next meeting

Phytosterol Esters: Extension of Use **ACNFP/112/6**

The Committee considered the applicant's response to concerns raised at the previous meeting about the increase in exposure to phytosterol oxidation products (POPs) if consumers used margarine and the liquid margarine products with added phytosterol esters for cooking and baking purposes.

Dr Camilla Pease informed the Committee that she had worked on similar products at Unilever between 2000 and 2010, however she has not been involved with these or similar products since leaving Unilever's employment in 2010.

The Committee was broadly happy with the response from the applicant and commented on the text of a draft opinion. Before finalising the opinion, Members requested that the Secretariat circulate further background information about POPs, including a summary of the studies that resulted in the setting of a NOAEL figure when this issue was first discussed in 1999-2000.

Action: Secretariat to update the Initial Opinion and provide background information to Committee members.

Chia Seeds (Supernutrients) **ACNFP/113/7**

The Committee was asked whether it agreed that substantial equivalence had been established between chia seeds produced by Supernutrients and chia seeds currently marketed by the Chia Company.

The Committee noted that the evidence provided by the applicant was very clear and well-presented, and was content that substantial equivalence had been established.

Action: The public to be consulted on the application and the secretariat to draft an opinion

Sporopollenin Shells from Club Moss **ACNFP/113/9**

The Committee reviewed the applicants response to concerns raised at its February meeting about this application for the authorisation of sporopollenin shells from club moss (*Lycopodium clavatum*) as a novel ingredient.

The Committee accepted the preparation process at the laboratory scale and requested more information on how this would be scaled up for bulk production.

The Secretariat informed the Committee that detailed specifications will be provided by the applicant in time for the next meeting. The Committee requested that the specifications should include details of the molecular structure of sporopollenin, not only its physical characteristics and elemental composition.

The Committee again expressed concern relating to the possible effects that these small particles may have when they are in a food matrix, in terms of inhalation effects of dry particles and effects on the gut and immune system, and sought further reassurance on these points.

The Committee also requested more information relating to the range of ingredients intended to be encapsulated into sporopollenin shells. The Committee remarked that the applicant's response highlighted that the bioavailability of vitamin D is increased 2.2 fold as a result of encapsulation into sporopollenin shells, but the applicant has not considered the nutritional and safety consequences of this. It was unclear whether similar changes in bioavailability will occur in other applications, and how manufacturers will be able to ensure the safety and nutritional quality of products formulated with sporopollenin shells.

The Committee also sought evidence to support the suggestion that all ingested sporopollenin shells are egested unchanged, minus their contents. In this context, the Committee questioned the suitability and limits of detection of the methods used to test for the presence of sporopollenin shells in urine, faeces, blood and gut.

The Committee was content with the information the applicant provided relating to sustainability.

Action: Secretariat to ask for further information from the applicant

Possible Transfer of DNA from Food to Human Blood **ACNFP/113/10**

The Committee considered a recent article that reports the potential presence of plant derived DNA sequences in human blood samples.

The Committee agreed that this was a very interesting paper and that the results required confirmation. Members made a number of comments in relation to the results of the study, which were obtained using next generation sequencing, a relatively new high throughput method of DNA sequencing that generates very large numbers of DNA sequences and corresponding sequence information:

(a) Of the foreign DNA fragments identified, plant sequences seemed to be overrepresented and it was unclear why so few bacterial and mammalian sequences were found. Dietary intake did not seem to be the most likely explanation as a number of the plant species identified, such as Arabidopsis, are not consumed as part of the human diet.

(b) It was also unclear why the authors had not attempted to clone some of the longer plant DNA fragments, as this could have confirmed the indirect evidence that these fragments are in the 10 Kilobase range.

(c) The Committee were divided on the question of whether DNA contamination issues could explain the results of the study and it was only one of a number of possible explanations of the results.

The Secretariat agreed to keep the Committee informed of further work that might help to clarify this point.

Items for Information

13.1 EU Update **ACNFP/113/11**

13.2 Update on Scientific Advisory Committees (SACs) **ACNFP/113/12**

The Committee noted item 13.1 without comment.

Under item 13.2 the Chair updated the Committee on the last GACS meeting held on 8 October.

Any Other Business

Members received further information on arrangements for the open event which took place after the meeting.

Date of next meeting

The next meeting was scheduled for Wednesday 12 February in Aviation House.

ANNEX 3 COMMITTEE ADVICE ISSUED DURING 2013

a) OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION FOR CLOSTIDIUM BUTYRICUM PROBIOTIC.

Applicant: **Miyarisan Pharmaceutical Co. Ltd**

Responsible Person: **Elinor McCartney**

EC Classification: **2.2**

Introduction

1. An application was submitted to the Food Standards Agency in January 2012 by Miyarisan Pharmaceutical Co. Ltd. for the authorisation of *Clostridium butyricum* (strain CBM 588) as a probiotic food supplement under the novel foods regulation (EC) No 258/97. A copy of the application was placed on the Agency's website for public consultation.

2. Clostridium is a large bacterial genus with more than 150 species. Although the genus contains pathogenic species, notably *Clostridium botulinum, Clostridium difficile, Clostridium perfringens* and *Clostridium tetani,* the applicant points out that less than 10% of this genus produces toxins. The applicant draws attention to the fact that most clostridial species, especially gut-associated clostridial species are non-pathogenic gut commensals which form an important part of the lower gut flora of humans and animals.

3. The *C. butyricum* strain (CBM 588) intended to be marketed by the applicant is a Gram positive, spore forming, obligate anaerobic, non pathogenic, non-genetically modified bacterium.

4. The applicant's intention is to market CBM 588 as viable spores in tablet form intended for use as a probiotic food supplement to support, maintain or restore healthy gut flora physiology and/or function. The applicant intends to make a parallel application for assessment under the EU Nutrition and Health Claims Regulation.

5. The applicant has marketed preparations of CBM 588 for use as a probiotic in Japan and other Asian countries for several decades. This strain of *C. butyricum* has also received EU approval as a microbial feed additive for chickens for fattening, weaned piglets and minor avian and porcine species in 2009 and 2011, respectively.

6. This is the first time that a live microorganism has been assessed under the Novel Foods Regulation. Commission Recommendation 97/618/EC does not address the specific information

that should be supplied by applicants for this type of ingredient. However, the European Food Safety Authority (EFSA) has established a framework known as the Qualified Presumption of Safety (QPS) concept which provides a generic assessment system that can be applied to all requests received for the safety assessments of microorganisms deliberately introduced into the food chain. Microorganisms granted QPS by EFSA have been placed on a list thus avoiding the extensive investigation of organisms known not to cause concern. Microorganisms not considered suitable for QPS remain subject to a full safety assessment.

7. *C. butyricum* was considered by EFSA's BIOHAZ Panel in its 2011 update to the QPS list. EFSA concluded that "the safety of *Clostridium butyricum* is a strain-related property, therefore *Clostridium butyricum* should not be recommended for the QPS list." This conclusion was based on the observation that a minority of strains contain a gene coding for botulinum neurotoxin type E and there is only limited knowledge of human and animal exposure to this species. As QPS does not apply, the microorganism should undergo a full novel food assessment.

8. CBM 588 has been classified as a complex novel food from a non-GM source, the source of the novel food has no history of food use in the Community (Class 2.2) according to the scheme in Commission Recommendation 97/618 (EC).

I. Specification of the novel food

Information on this aspect is provided on p. 14-22 of the application dossier

9. The applicant intends to market *Clostridium butyricum* tablets in two forms, standard and strong, containing a minimum of $3x10^5$ and $4.5x10^5$ viable cells per tablet, respectively. The tablets in different strengths are intended to suit the needs of the consumer as the need for this probiotic may vary amongst individuals. Data on five individual batches indicate that the actual content of the tablets is substantially higher than the quoted minimum (standard: 5 to 7.1×10^6; strong: 1.1 to 1.7×10^7). According to a certificate of analysis the content of "strong" tablets should not exceed 4.5×10^7 CFU. The specification for tablets containing CBM 588 has been established by the applicant and can be found in the table below.

Specification	**Detail**
Appearance	Round tablet, 9mm diameter, white or pale grey, with characteristic odour and sweet taste.
Total aerobic count	$< 10^3$ CFU/g
E. coli in 1 g sample	not detected
Staphylococcus aureus in 1 g sample	not detected
Pseudomonas aeruginosa in 1 g sample	not detected
Yeasts & moulds	$< 10^2$ CFU/g

10. The applicant states that the product complies with the limits for food supplements that are set out in Commission Regulation (EC) 1881/2006 on maximum levels for certain contaminants in foodstuffs. The product specifications also comply with the Japanese Pharmacopoeia. A certificate of analysis is provided in Appendix 6 to the application dossier**.**

11. The applicant states that the original wild strain of *C. butyricum* MIYAIRI (CBM 588) was isolated in 1963 from a soil sample sourced in Nagano, Japan. This strain is deposited at the Fermentation Research Institute, Agency of Industrial Science and Technology, Japan under the strain name *Clostridium butyricum* MIYAIRI 588 strain, deposit number FERM BP-2789. The applicant has preserved their collection of *Clostridium butyricum* MIYAIRI strains by freeze-drying and freezing methods since 1986. Subculture of CBM 588 master cell banks and working cell banks is performed at appropriate intervals. The applicant has provided details of quality control procedures employed for each lot of the novel ingredient including methods to confirm strain identity.

12. Genetic and biochemical stability of CBM 588 has been accepted by EFSA in the context of its use in animal feed. The applicant states that the strain of *C. butyricum* intended to be marketed does not carry any genes encoding any toxins and virulence factors associated with clostridium or other enteropathogens

13. Absence of neurotoxin production was demonstrated by PCR and Southern blot hybridisation for type E botulinum toxin gene. The absence of genes encoding botulinum neurotoxin A,B,F and genes encoding non-toxic haemagglutinin (NTNH) and genes encoding *Clostridium perfringens* toxins (alpha, beta, epsilon and iota) was demonstrated by PCR assay. The applicant acknowledges that the presence of a single cryptic plasmid of 6.5 kb has been noted in this strain of *C. butyricum* but the nucleotide sequence of this plasmid was analysed and none of the nine putative open reading frames encoded any known virulence factor of Clostridium spp. (EFSA 2009, 2011). The applicant provided further details of these analyses in Appendices 12 and 13 to the dossier.

14. The susceptibility of this strain of *C. butyricum* to key antibiotics as recommended by EFSA was tested. The applicant reports that the minimum inhibitory concentrations of these key antibiotics were lower than the EFSA breakpoints confirming that CBM 588 is not resistant to antibiotics of human or veterinary importance (EFSA 2008, 2009, 2011).

Discussion*: The Committee was not sufficiently reassured that the data provided by the applicant conclusively demonstrated the absence of pathogenic clostridial toxins and other virulence factors in CBM 588. The Committee requested that the applicant provide a genome sequence for CBM 588 in comparison to other related species and strains, and a comprehensive bioinformatics analysis to ensure the absence of functional or partial virulence genes. The Committee emphasised that it was necessary to review the full dataset for the genome sequencing exercise, including information on the quantitative homology with other clostridial genome sequences for all open reading frames (ORFs) identified in CBM 588. The applicant had provided genome sequence data. The final assembly of the genomic sequence was initially hampered by the presence of redundant DNA sequences, for example ribosomal RNA (rRNA) genes and 200 bp direct repeat sequences, which create gaps in the deduced genomic sequence. The applicant did*

nonetheless state that 100% of the protein coding sequences of the genome (4208) had been sequenced. Subsequently, the sequences obtained were assembled into 157 contiguous sequences (contigs) which the applicant has listed. Details of the complete nucleotide sequences were also provided.

The 157 sequences were uploaded to the software "GENOME GAMBLER" and the ORFs were predicted following the procedure described by Shimizu et al., 2002. The applicant has provided BLAST (Basic Local Alignment Search Tool) search results of CBM 588 ORFs against a non redundant protein database, which includes all bacterial protein sequences. The degree of homology is reported, based on the sequence alignment between CBM588 and all bacteria and the percentage of identical aligned amino acids between the ORF of CBM588 and the most identical sequence of all other bacteria.

The applicant performed a bioinformatics comparison of genomic sequences of CBM 588 with other available bacterial genomic sequences including clostridial species, to identify known virulence factors or clostridial toxins. The applicant provided nucleic acid sequences and amino acid sequences of the three putative virulence genes identified in CBM 588 (haemolysin A, haemolysin 3 and fibronectin-binding protein) and a detailed explanation as to why these sequences are not a cause for concern, including evidence to demonstrate lack of haemolytic activity in CBM 588. The Committee was content that the putative virulence genes are non-functional in CBM 588.

The applicant has also provided bioinformatics data to show that similar or related haemolysin sequences are present in the genomes of several Lactobacillus species; thus the presence of these genes, particularly when non-functional, does not necessarily indicate pathogenicity.

The Committee was satisfied that the applicant's additional data addressed its concerns and no further information was requested.

The Committee noted that several antibiotic resistance determinants were identified in the genome sequence of CBM 588 (tetracycline, chloramphenicol, beta-lactams, vancomycin) and the genome sequence suggests there may be others. The Committee requested further clarification from the applicant.

The applicant provided updated antimicrobial resistance data on CBM 588 strains (C. butyricum FERM BP-2789 as originally deposited, and the current CBM 588 working strain), the type strain (C. butyricum ATCC 19398^T) and Bacteroides fragilis ATCC 25285 as a positive control.

Resistances to ampicillin, chloramphenicol, clindamycin, erythromycin, gentamycin, kanamycin, streptomycin, tetracycline, vancomycin, metronidazole and acriflavine were tested. Both C. butyricum ATCC 19398^T and CBM 588 were susceptible to all of the antimicrobials used except aminoglycosides (i.e. gentamicin, kanamycin and streptomycin) and acriflavine.

The applicant highlighted in its response that anaerobes are intrinsically resistant to aminoglycosides and possibly acriflavine, in addition to clarifying that acriflavine is a topical antiseptic, thus any tolerance would be of little clinical significance.

The applicant's response highlights that the specific risk of transferring non-functional antibiotic resistance genes from CBM 588 to other bacteria where they may be functional, seems low, given the well documented use in humans in Japan since the 1960s which has been supported by pharmacovigilance carried out by the applicant, the Japanese medical profession and Japanese regulatory authorities. Gene transfer issues are discussed further below in Section XIII.

The Committee was reassured by the applicant's new data relating to antibiotic resistance and no further information was requested on this point.

II. Effect of the production process applied to the novel food

Information on this aspect is provided on p 23-24 of the application dossier

15. The applicant's *Clostridium butyricum* supplement is produced by submerged anaerobic fermentation followed by centrifugation, drying, blending and packaging to produce either strong or standard tablets. The process complies with Japanese Good Pharmaceutical Manufacturing Practice and details can be found in the dossier.

Discussion: *The Committee asked whether the quality control procedures employed during production are adequate to ensure the safety of individual batches of the novel ingredient. The applicant explained that fermentation of CM588 is carried out under strict conditions of monoculture, under certified pharmaceutical-quality GMP. The purity of every lot of CBM powder concentrate is tested by appropriate traditional and molecular microbiological methods to ensure no contamination by other Clostridial strains, which ensures a low risk of gene transfer events to CBM 588 during manufacture. The Committee was satisfied with this section of the dossier.*

III. History of the organism used as a source of the novel food

Information on this aspect is provided on p 24-25 of the application dossier

16. The applicant has marketed preparations of CBM 588 for use as a probiotic in Japan and other Asian countries for several decades.

Discussion: *The Committee was reassured by the knowledge that CBM 588 preparations have been sold in Japan since the 1960s but requested further information on monitoring of side effects in Japan. The applicant has provided updated post-market monitoring data to replace the data in the original dossier to demonstrate that between 2005 and 2012, there have been no confirmed adverse effects or adverse drug reactions related to CBM 588, as defined by WHO pharmacovigilence procedures.*

IX. Anticipated intake/extent of use of the novel food

Information on this aspect is provided on p 25 of the application dossier

17. The applicant has considered historical and current consumption patterns of CBM 588 in non-EU countries in order to derive appropriate daily intakes of this food supplement in the EU. The applicant states that daily intake of CBM 588 as a food supplement in the EU as intended for market is expected to be within the range of 3×10^5 to 1.35×10^8 CFU/day (one standard tablet to three strong tablets per day). The supplement is intended for healthy adults.

18. The applicant states that the optimum daily dose may vary between adults but the appropriate daily dose is anticipated to provide gut health benefits such as improved gut transit time, improved faecal bulk and consistency and more comfortable bowel movements. The Committee's assessment focussed only on safety and labelling and does not address any nutrition or health benefits that may be claimed for the novel ingredient or for foods that

contain it. Nutrition or health claims may only be made if they are specifically authorised under the EU Nutrition and Health Claims Regulation (EC) 1924/2006.

19. The applicant states that CBM 588 does not establish permanently in the gut.

Discussion: *The Committee did not raise any concerns relating to this section of the dossier.*

XI. Nutritional information on the novel food

Information on this aspect is provided on p 26 of the application dossier

20. The applicant states that CBM 588 is not intended to replace any other foods or nutrients in the diet, and does not supply significant dietary macro or micro nutrients.

Discussion: *The Committee did not raise any concerns about this section of the dossier.*

XII. Microbiological information on the novel food

Information on this aspect is provided on p 26 of the application dossier

21. Microbiological specifications are presented above in Section I. The applicant has also acknowledged the possibility that CBM 588 may have effects on the intrinsic gut flora of animals and humans but has highlighted a number of published studies illustrating that CBM 588 has no adverse effects on beneficial gut flora of humans or animals.

Discussion*: The Committee questioned the effects of CBM 588 on the host gut epithelium, microbiome and immune system, as the dossier does not specifically address these issues and data from animal feeding studies presented in the toxicology section of the dossier indicate that CBM 588 may have immune effects. For example, the study by Yuzawa et al. 1987a refers to increased platelet and white blood cell counts in rats fed higher doses of CBM powder. The Committee also requested further information to rule out any possibility that CBM 588 has any detrimental effects on the host microbiome.*

The applicant highlighted that CBM 588, in common with other probiotic bacteria, interacts with host microbiota and immune functions, but does not exert harmful, pro-inflammatory or inflammatory effects. The genomic data confirm that CBM 588 is a typical Clostridium butyricum, closely related to the type strain, C. butyricum ATCC 19398. Wild-type Clostridium butyricum strains are common commensal inhabitants of the gut of healthy individuals.

The applicant has therefore concluded that CBM 588 consumption is not expected to adversely affect the host microbiota, drawing on the presence of strains of C. butyricum in the healthy gut and three efficacy studies which demonstrated that CBM 588 did not have any adverse effects on human microbiota.

The Committee accepted the applicant's information and no further information was requested.

XIII. Toxicological information on the novel food

Information on this aspect is provided on p. 27-29 of the application dossier

22. The applicant highlights that the safety of CBM 588 has been reviewed by EFSA in 2009 and 2011 when EFSA concluded that its use in animal nutrition is safe for animals, consumers, industrial workers/users and the environment. The applicant reiterates that CBM 588 does

not pose a risk to humans as the strain does not carry genes encoding relevant toxins and virulence factors, nor does it harbour acquired or transferable antibiotic resistance.

23. The applicant has described a series of toxicological studies using CBM powder (the dried fermentation concentrate of CBM 588). An acute oral toxicity study in rats showed that the acute oral toxicity of CBM powder is in excess of 5000 mg/kg body weight. A subacute (5 week) oral toxicity study investigating the effects of CBM powder in beagle dogs showed a NOEL (No Observed Effect Level) of 2000 mg/kg body weight/day (the highest dose tested). Chronic oral toxicity of CBM powder was investigated in SPF Fischer 344 rats over a twelve month period. Some effects (increased blood glucose and increased urine volume and kidney weights in males) were observed at the highest dose tested (50 g/kg diet) but macroscopic and microscopic pathological examinations revealed no differences between treated and untreated rats. The NOEL was therefore determined to be 5 g/kg diet (equivalent to 241 mg/kg body weight/day in male rats and 288 mg/kg body weight/day in female rats).

24. The applicant highlights that the optimum CBM 588 intake may vary between individuals but emphasises that the maximum intake envisaged in healthy adults in the EU is 100 fold less than the NOEL calculated from toxicological studies in laboratory animals. The lowest NOEL for CBM powder was determined as 241 mg/kg bodyweight per day in male rats. From these data, the NOEL can be extrapolated to a 60 kg human as 14.46 g/day (0.241 g x 60 = 14.46 g). CBM powder contains $\geq 1 \times 10^9$ CFU CBM 588 per g, so the NOEL is equivalent to a dose of 1.45×10^{10} CFU/day for a 60 kg adult. The highest anticipated dose of CBM 588 (3 Strong Tablets per 60 kg adult per day, each containing up to 4.5×10^7 CFU) is 1.35×10^8 CFU/adult/day. This is 107 times less than the human equivalent of the NOEL.

25. The applicant also details a study looking into mutagenicity of CBM powder by way of reverse mutation assays and chromosome aberration assays; the study highlights that CBM 588 did not exhibit any mutagenicity or clastogenicity in this study.

26. Although CBM 588 does not have a history of consumption as a food ingredient in the EU, the applicant draws attention to other examples of previous human exposure to *Clostridium butyricum*. The applicant refers to studies which show that *C. butyricum* strains are commensals in the gut of humans and may colonise the gut of infants after birth.

27. The applicant has sold preparations of CBM 588 in Japan and other Asian countries for both human and animal use since the 1960s and the applicant states that there have been no confirmed adverse effects related to CBM 588 consumption nor any reports of allergenicity.

Discussion: *The Committee was satisfied that the toxicology data presented in the dossier did not give cause for concern. The Committee however, discussed the possibility of transfer of any possible virulence genes from CBM 588 to other bacteria in the gut or vice versa and requested further reassurance from the applicant on this aspect.*

The Committee highlighted that some toxin-encoding genes have been reported to reside on chromosomally-located conjugative transposons in Clostridia and such transposons can mediate efficient transfer to bacteria.

The applicant submitted additional data from bioinformatic analyses illustrating that CBM 588 does not harbour any chromosomally-encoded toxins of concern, so such genes cannot be transferred to other bacteria. Only three putative virulence genes were identified for CBM 588 which are non-functional in CBM 588 (the Committee was relatively content with the applicant's BLAST analyses data demonstrating that the putative haemolysin genes are non-functional and likely encode other proteins such as channel or membrane proteins or be involved in tRNA synthesis and FtsJ-like methyltransferase activity and are also found in gut commensals such as Lactobacillus spp).

The Committee considered that it is largely unknown whether these sequences and partial sequences could be transferred to other bacteria in the gut where they could become functional. However, to put the matter in perspective, the Committee highlighted that many gut bacteria harbour a multiplicity of pathogenicity determinants, which are being swapped back and forth (at least those borne on plasmids) and, in this environment, the non-functioning chromosomal sequences detected in CBM 588 would be an irrelevance.

The Committee noted that CBM 588 has been marketed in Japan for several decades and requested further information on any adverse effects monitoring data that the applicant may hold. Following a response from the applicant to this, the Committee requested further details relating to the small number of suspected adverse effects mentioned in the applicant's response and the rationale for concluding that none were related to CBM 588 consumption.

The applicant categorised suspected adverse effects or adverse drug reactions into different groups in order to provide the Committee with more details. The applicant states that in most cases, no probable causal relationships between the reported adverse effect and CBM 588 was determined. In other cases, not enough information was provided to evaluate the possible relationship. The applicant therefore concluded that there are no confirmed adverse drug reactions related to its novel ingredient. The applicant emphasised that the number of adverse effect reports represent a tiny proportion of the total sales of CBM 588.

The Committee was satisfied with the applicant's response. The Committee suggested that, given that this is the first live micro-organism to be assessed as a novel ingredient, it could be useful for the applicant to establish a mechanism for monitoring adverse effects, should the novel ingredient be authorised in the EU for use in food supplements.

CONCLUSION

The ACNFP has completed its assessment of Clostridium *butyricum* CBM588 as a novel ingredient to be added to supplements and concluded that it did not have any unanswered safety concerns relating to this novel ingredient.

These conclusions are based on the information in the applicant's dossier, supplemented by additional information that the applicant provided, relating to:

- Verification of the absence of toxins and other virulence factors in CBM588 to be demonstrated by genome sequence and bioinformatics data

- Verification that the antibiotic resistance determinants identified CBM 588 are non-functional
- Impact of CBM 588 on host gut epithelium, microbiome and immune system
- Reassurance that any toxin or virulence-encoding genes will not be transferred to other bacteria in the gut
- Further details on the small number of suspected adverse effects reported

May 2013

b) OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION ON DHA RICH MICROALGAL AND EPA-RICH OILS (EXTENSION OF USE).

Andreas Klepsch
European Commission
DG SANCO
Brussels B-1049

29 April 2013

Ref NFU 795

Dear Mr Klepsch

Initial Opinion: DHA and EPA-rich algal oil from *Schizochytrium sp* (Extension of use)

On 19 November 2012 the UK Competent Authority accepted an application from DSM Nutritional Products to extend the use of their novel food, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) rich algal oil, in accordance with Article 4 of Regulation (EC) 258/97.

This oil was evaluated in 2011 for use in the EU as a novel food ingredient and there were no objections to the initial assessment report that the UK transmitted to the Commission on 9 December 2011 (ref NFU 786, attached). The UK wrote to the applicant confirming the authorisation of the oil for a range of uses on 6 July 2012.

The new application follows the publication of two positive EFSA opinions in 2012 which establish a cause and effect relationship between dietary intake of EPA and DHA and the reduction of blood pressure and blood triglycerides. These opinions have resulted in approved health claims[9] which, due to the doses of DHA and EPA required, are likely to be restricted to high dose food supplements.

The Advisory Committee on Novel Foods and Processes (ACNFP) has reviewed this new application and noted that the only change is an increase in the amount of algal oil in food supplements from 250 mg DHA+EPA per day to a maximum of 3000 mg per day. In all other respects the Committee's 2011 opinion applies to this request.[10]

In its 2011 opinion, the intake of the oil was estimated using data from the UK National Diet and Nutrition Survey data. This indicated that male teenagers potentially have the greatest high level (97.5th percentile) intake of DHA and EPA from fortified foods at 1.72g per day.

[9] Expected early 2013
[10] A copy of this opinion is available at http://www.food.gov.uk/multimedia/pdfs/inopdhamartek.pdf

These estimates did not include intake from food supplements but, in the event that high level consumers of fortified foods also consumed high dose supplements providing the maximum proposed dose of 3000mg/day, this would result in a maximum consumption of DHA and EPA of 4.72g/day. The ACNFP noted that this combined estimate is below 5g/day, a level of intake that EFSA do not regard to cause safety concerns (EFSA 2012[11]) and accepted that this provides sufficient reassurance of the safety of this extension of use.

The 5g/day figure applies specifically to adults but the ACNFP accepted that high dose food supplements will not be targeted at children, as EFSA has established a cause and effect relationship between high dietary intake of EPA and DHA and the reduction of blood pressure and blood triglycerides, which are not relevant to younger age groups.

In view of the ACNFP's advice, the UK Competent Authority considers that this algal oil, at levels of up to 3000 mg EPA and DHA per day in food supplements, and not exceeding the maximum use levels previously described for other foods, meets the criteria for acceptance of a novel food defined in Article 3(1) of regulation 258/97.

I have also attached a copy of the specification for this oil, which was included in my letter of 6 July 2012 that authorised the use of this oil.

Yours sincerely

by email

Dr Chris Jones
UK Competent Authority

[11] http://www.efsa.europa.eu/en/efsajournal/pub/2815.htm

SPECIFICATION OF DHA (DOCOSAHEXAENOIC ACID) AND EPA (EICOSAPENTAENOIC ACID)–RICH OIL FROM MICROALGAE *SCHIZOCHYTRIUM SP.*	
Test	**Specification**
Acid value	Not more than 0.5 mg KOH/g
Peroxide value (PV)	Not more than 5.0 meq/kg oil
Moisture and volatiles	Not more than 0.05%
Unsaponifiables	Not more than 4.5%
Trans-fatty acids	Not more than 1%
DHA content	Not less than 22.5%
EPA content	Not less than 10%

c) OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION ON DHA – RICH ALGAL OIL (SECOND EXTENSION OF USE).

Andreas Klepsch
European Commission
DG SANCO
Brussels B-1049

29 April 2013

Reference NFU 796

Dear Mr Klepsch

Initial Opinion: DHA-rich algal oil from *Schizochytrium sp* (Second Extension of use)

On 16 January the UK Competent Authority accepted an application from DSM Nutritional Products to extend the use of their novel food, docosahexaenoic acid (DHA) rich algal oil, in accordance with Article 4 of Regulation (EC) 258/97.

This oil was evaluated in 2003[12] for use in the EU as a novel food ingredient and the company successfully sought an extension of the use in 2009.[13]

This application is to bring the use categories into line with their DHA and EPA rich oil which is produced from the same algal source and was approved as a novel food in July 2012. The application includes an increased use level in food supplements, which is in line with the company's parallel request for the DHA and EPA rich oil to be added to supplements at levels providing up to 3000 mg DHA and EPA per day. The UK's initial opinion on the latter request was also sent to the European Commission on 29 April (ref NFU 795).

Both applications follow the publication of two EFSA opinions in 2012 which establish a cause and effect relationship between dietary intake of EPA and DHA and the reduction of blood pressure and blood triglycerides. These opinions have resulted in approved health claims[14] which, due to the level of DHA and EPA required, are likely to be restricted to high dose food supplements.

The ACNFP's 2011 opinion for the DHA and EPA rich oil[15] assessed the estimated intake of the oil using data from the UK National Diet and Nutrition Survey data and the results are also applicable to

[12] Commission Decision of 5 June 2003 authorising the placing on the market of oil rich in DHA (docosahexaenoic acid) from the microlagae *Schizochytrium sp.* as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council (2003/427/EC)
[13] Commission Decision of 22 October 2009 concerning the extension of uses of algal oil from the micro-algae *Schizochytrium sp*. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council (2009/778/EC)
[14] Expected early 2013
[15] A copy of this opinion is available at http://www.food.gov.uk/multimedia/pdfs/inopdhamartek.pdf

this oil. This estimate indicated that male teenagers potentially have the greatest high level (97.5th percentile) intake of DHA and EPA from fortified foods at 1.72g per day. This estimate applies equally to the present application for the extension of use of the DHA rich oil, which would bring its uses in line with that of the second oil.

This intake assessment did not consider intake from food supplements. In the event that high level consumers of fortified foods also consumed high dose supplements providing the maximum proposed dose of 3000mg/day, this would result in a maximum consumption of DHA of 4.72g/day. When assessing the DHA and EPA oil the ACNFP noted that this combined estimate is below 5g/day, a level of intake that EFSA do not regard to cause safety concerns (EFSA 2012[16]) and accepted that this provides sufficient reassurance of the safety of this extension of use.

The 5g/day figure applies specifically to adults but the ACNFP accepted that high dose food supplements will not be targeted at children, as EFSA has established a cause and effect relationship between high dietary intake of EPA and DHA and the reduction of blood pressure and blood triglycerides, which are not relevant to younger age groups.

In view of the ACNFP's advice, the UK Competent Authority considers that this algal oil, at levels of up to 3000 mg DHA per day in food supplements, and not exceeding the maximum use levels previously described for other foods, meets the criteria for acceptance of a novel food defined in Article 3(1) of regulation 258/97.

I have also attached a copy of the specification for this oil, which was included in the 2003 Commission Decision,

Yours sincerely

by email

Dr Chris Jones
UK Competent Authority

[16] http://www.efsa.europa.eu/en/efsajournal/pub/2815.htm

SPECIFICATION OF DHA (DOCOSAHEXAENOIC ACID) RICH OIL FROM MICROALGAE *SCHIZOCHYTRIUM SP.*	
Test	**Specification**
Acid value	Not more than 0,5 mg KOH/g
Peroxide value (PV)	Not more than 5,0 meq/kg oil
Moisture and volatiles	Not more than 0,05%
Unsaponifiables	Not more than 4,5%
Trans-fatty acids	Not more than 1%
DHA content	Not less than 32%

d) OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION ON CHIA OIL

Applicant	**Functional Products Trading**
Responsible Person	**Sebastián Romero Melchor (K&L Gates) on behalf of Functional Products Trading**
EC Classification	**2.1**

An application has been submitted by Functional Products Trading SA of Chile for the use of chia seed oil as a novel food ingredient.

Chia (*Salvia hispanica* L) is a summer annual herbaceous plant belonging to the Labiatae family. It grows from a seedling to develop lush green foliage before it produces long flowers which are purple or, less commonly, white. These flowers develop into seed pods which ultimately contain the seeds which are the source of the oil. Chia seeds typically contain around 250-390g oil/kg. This is the first application for chia seed oil and follows the authorisation for chia seeds which was originally issued in 2009 and extended in January 2013.

In accordance with the novel food regulation chia seed oil has been classified as a complex novel food from non-GM source (Class 2.1).

I Specification of the Novel Ingredient (NI)

Dossier p 7-17

1. A specification of the oil is set out in the attached Annex. The applicant has provided analyses of 7 batches of the oil, each of which complies with the specification (Dossier, Table 2). The applicant has also carried out additional analyses to which further characterise the oil (see Dossier Tables 3 and 4). This includes an extensive fatty acid analysis which indicates that, in addition to the predominant fatty acids detailed in the specification (alpha linolenic acid (ALA) and linoleic acid), a number of other fatty acids are also present at low, but measurable levels. These include palmitic acid, stearic acid and oleic acid (See Dossier, Table 5).
2. The applicant has also carried out a number of analyses to determine whether environmental contaminants (pesticides, heavy metals, hazardous air pollutants, PCBs and dioxins) are present. Where detectable quantities were found these were in compliance with relevant EU food contaminants legislation.

Discussion *The Committee was content with this information (refer to Section II and XIII for a commentary regarding manufacturing method and protein analyses respectively).*

II Effect of the production process applied to the NI

Dossier pp17-18

3. The oil is produced under HACCP conditions by cold pressing the seeds. Cold pressing is a technique that is widely used in the production of edible oils and is regarded to be the 'best' technique to preserve the nutritional value and flavour of oils. The low temperature allows the removal of high molecular weight waxes after which the oil is filtered to remove solid material.

The final oil is stored in steel drums and the applicant notes that tocopherols, naturally present in the oil, inhibit oxidation. A detailed diagram of the methods employed is presented in the Dossier (Appendix 9).

Discussion *The Committee was content that the production process did not give cause for concern, but noted that the flowchart in Appendix 9 included additional steps which were not described in the dossier. This flowchart also indicated that tocopherols may also be added as required, implying that the oil may be prone to oxidation.*

In response, the applicant explained that the additional steps that are highlighted in Appendix 9 (e.g. winterising, deodorising) are commonly used in the production of vegetable oils and may be used as required. The applicant noted that the oil is as prone to oxidation as other cold pressed oils with a similar peroxide index value (measured at 7.2 mEqO_2/kg anhydrous fatty acids). In addition the applicant pointed out that the low level presence of copper and iron, which catalyse oxidation reactions, indicates that oxidation will be slow. The Committee was reassured that the oil was comparable to other cold pressed oils in terms of oxidation and manufacturing processes. Members were concerned by the apparent ad hoc approach to the use of additional processing steps, but accepted that this may be because the oil is not yet being produced in commercial quantities for the EU market. The Committee advised that the list of manufacturing steps should be included in the authorisation decision for this novel ingredient, should it be approved.

III History of the organism used as the source of the NI

Dossier p19 & Section 5

4. The applicant refers to evidence of chia seeds being consumed for millennia but acknowledges that that their use appears to have been restricted to local markets in rural South America until the 1990s, when increased commercialisation led to exports to North America and, latterly, Australasia and Europe.

5. There has been a marked increase in the availability of chia seeds in a wide range of food products across the world in recent years. The seeds have been authorised as a novel food in the EU for use, at defined levels, in bread and other baked products, breakfast cereals and various seed mixes.[17]

Discussion *Members accepted that there was a history of use of chia seeds and noted that both the original application for chia seeds and the subsequent request to extend the use received favourable risk assessments from the Committee.*

IX Anticipated intake and extent of use of the NI

Dossier p20-22

6. The applicant intends to market chia seed oil in vegetable oils (blended at a maximum level of 10%) and as a food supplement. The proposed levels are consistent with approved reference intake values for omega-3 fatty acids. EU rules require at least 0.3 g alpha-linolenic acid per 100 g (and per 100 kcal) to be present in products that claim to be a source of omega-3 fatty acids and at least 0.6 g alpha-linolenic acid per 100 g to be present in order for a claim that a food is high in omega-3 fatty acids. The proposed use categories and level of incorporation are detailed below. It should be noted that the category 'Non-alcoholic beverages' was deleted by the applicant due to concerns raised by the Committee as seed-allergic individuals would not expect to find seeds in these foods and were unlikely to check the ingredient lists.

[17] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:021:0034:0035:EN:PDF
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:294:0014:0015:EN:PDF

Proposed Category	% Inclusion / Recommended Daily Intake
Fats and Oils	10%
Food Supplements	2g/day

7. The applicant provided data from the 2002 UK National Diet and Nutrition Survey (NDNS) for UK consumers aged 19-64 years old to estimate the likely consumption of chia seed oil for the proposed range of products. In the light of the applicant's decision to drop the use in beverages the tables in the dossier have been amended as follows:

Estimated mean and high level (97.5th%ile) intake of chia seed oil as calculated from UK NDNS survey data

Product Category	Age Groups (Mean consumption, g/day)				% Chia seed oil	Chia seed oil g/day	ALA g/day
	19-24	25-34	34.49	50-64			
Fats and Oils	11.4	11.1	10	13.9	10	1.2	0.7

Product Category	Age Groups (97.5th%ile consumption, g/day)				% Chia seed oil	Chia seed oil /day	ALA g/day
	19-24	25-34	34-49	50-64			
Fats and Oils	22.8	22.2	24	27.8	10	2.5	1.5

8. The amended figures indicate that the high level consumption for chia seed oil will be 2.5g per day (containing 1.5g alpha linolenic acid), which equates to consuming 6-7g of the seed, assuming an oil concentration of 30-35%[18]. The applicant does not include intake of chia seed oil from supplements (2g/day) or intake of alpha linolenic acid from other dietary sources in this estimate. EFSA has recognised that recommended intakes of alpha linolenic acid, for nutritional purposes, is of the order of 1% of energy intake, which equates to 2–3 grams/day for the typical diet, but has not identified a tolerable upper intake level.

Discussion *The Committee was content with the projected levels of intake for the oil.*

X. Information from previous human exposure to the NF or its source

Dossier p23-24

9. The applicant has identified chia seed oil containing products which are on the market in non-EU countries, highlighting products which are similar to those that are the subject of this application. The Mintel Global New Product Database lists over 350 chia seed and chia seed oil

[18] The recent application to extend the use of chia seed estimated that the average consumption of chia seeds would be around 13g/day see http://www.food.gov.uk/multimedia/pdfs/chialetop.pdf

products which entered the market worldwide between 2009 and 2011. Although it is not known how widely consumed these products are, the number of newly launched products indicates increasing exposure to chia seed and chia seed oil internationally. The applicant also mentions allergenic potential in this section and this issue is considered in detail in Section XIII below.

Discussion *The Committee noted that products containing chia seed oil were available elsewhere in the world and, following a recent decision authorising the use of chia seeds in a wider range of products, chia seeds were increasingly available in the EU.*

XI Nutritional information on the novel food

Dossier p24-28

10. The applicant provided a basic fatty acid profile which is compared with two other vegetable oils – canola (rapeseed) and flax. The applicant notes that chia seed oil contains around 82% polyunsaturated fatty acids, including around 63% alpha linolenic acid, significantly more than the other oils. A more comprehensive comparison of the oil compared with flax oil is also provided (Dossier, Appendix 8). The applicant also provides an extensive commentary on the function and metabolism of alpha linolenic acid in humans. As alpha linolenic acid is already found in the diet, and the novel ingredient is a new source of this essential fatty acid, this aspect is not discussed in this opinion.

Discussion *The Committee observed that the omega-3 fatty acids in chia seed are mainly in the form of alpha linoleic acid, a nutritionally essential fatty acid that is required for synthesis of important fatty acids and eicosanoids. Alpha linoleic acid therefore has a different function to the long chain omega-3 fatty acids that are found in certain other foods and chia seed oil is not a "like-for-like" substitute for other sources of omega-3 fatty acids, such as fish oils.*

The Committee's assessment focuses on safety and labelling and it does not address any nutrition or health benefits that may be claimed for the novel ingredient or for foods that contain it. Nutrition or health claims may only be made if they are specifically authorised under EU Regulation (EC) No 1924/2006.

XII Microbiological Information

Dossier p31

11. The applicant's chia seed oil is routinely tested for the presence of a range of micro-organisms and mycotoxins. The results of these analyses are tabulated on page 32 of the Dossier and show extremely low levels of microbial contamination.

Discussion *The Committee accepted that there was adequate provision to ensure that the oil would not contain significant quantities of pathogenic or spoilage microorganism and that there was adequate testing to ensure the absence of mycotoxins*.

XIII Toxicological information

Dossier p32-37

12. The applicant has carried out a 14 day acute toxicity study in rats, carried out to OECD standards, in which their chia seed oil was administered to 50 rats at doses up to 9000mg/kg body weight. The rats were monitored throughout and at the end of the study. The LD_{50} was determined to be >5000mg/kg; the full study report is attached to the Dossier (Appendix 14)**.**

13. All other studies that are reported in the dossier examined the perceived beneficial effects of consumption of chia in both rats and humans, with the exception of a 30 day dietary exposure study in rats. In this study, carried out using a chia seeds and chia oil of unspecified origin, the authors reported that 5% chia seed oil (and 15% seed) reduced serum triglyceride levels by 60% and increased the levels of HDL cholesterol.

14. The paucity of toxicological studies carried out on chia seed oil is consistent with the previous chia seed dossiers that the Committee reviewed in 2003 and 2011. The first dossier was also reviewed by EFSA[19], who concluded that, although the data were limited, ''experience gained from previous and current use of chia seeds in non-EU countries can be regarded as supportive evidence of the safety of chia seeds."

Discussion *The Committee noted that it has previously established the safety of chia seeds, when consumed at levels that could result in the consumption of chia seed oil at levels greater than are proposed here. The Committee queried the results of the 30 day feeding study with the applicant, noting that there were small changes in weight gains in the control and test animals but, having reviewed the raw data concluded that this was not a cause for concern.*

Allergenicity and Labelling

15. The applicant does not propose special labelling for products that contain the oil but, in line with EU food labelling requirements, it will appear on ingredient lists as 'chia seed oil'.

16. In response to a request from the Committee the applicant provided additional information detailing the level of protein present. The Committee regarded the level of protein present (typically 0.5%) to be consistent with other unrefined oils, which would be sufficient to elicit a reaction in any individual who may be allergic to chia seeds.

Discussion *The Committee noted similarities between this application and the recent application to extend the use of chia seeds[20]. The Committee accepted that chia seed oil would be clearly labelled but reiterated its view that IgE-mediated reactions in individuals who are allergic to other seeds and nuts could be possible. The Committee again highlighted the relative absence of studies defining the extent to which seed allergic individuals might react to chia seeds. Such data could be useful in determining whether increasing use of chia seed, and derived products such as the oil, would restrict the choice of seed allergic individuals. The Committee also noted that chia seeds have little history of consumption in the European Union and it was therefore possible that extending the range of uses could, like any novel food containing new proteins, give rise to increased sensitisation in the wider population.*

CONCLUSION

17. The Committee considered that the main concern in relation to the use of chia seed oil related to its consumption by individuals with existing seed allergy. Despite evidence of historical use in South America the seeds are effectively new to markets across in the world and the true extent of allergenicity, including cross-reactivity with allergens in other seeds and nuts, is not known. The applicant is aware of this and, following concerns raised by the Committee during this evaluation, deleted one of the proposed food categories (non-alcoholic beverages) because these foods do not typically contain seeds and could lead to inadvertent consumption of chia seed protein by seed and nut allergic individuals.

[19] http://www.efsa.europa.eu/en/efsajournal/pub/996.htm
[20] Paragraphs 20, 21 and conclusion of UK initial opinion http://www.food.gov.uk/multimedia/pdfs/chialetop.pdf

18. Chia seed is not a known allergen and it is not subject to EU rules on mandatory declaration of allergens in food. The existing authorisations for chia seeds are limited to products that typically contain seeds and require that there is reference to chia seeds on the label, which should also apply to this oil.

19. The Committee accepted that clear labelling would be adequate to address safety concerns in relation to allergic reactions amongst known "at risk" groups and suggested that this should be accompanied by a programme to raise awareness among these individuals. In order that information is widely disseminated the Committee recommended that the applicant should proactively seek to work with consumer groups, allergy support groups and the relevant competent authorities in each Member State when they are seeking to place new products containing chia on the market. It would also be advisable to inform allergy clinics so that they can report any cases of chia allergy to the relevant national authorities.

20. The Committee remains concerned that the use of chia in a wider range of foods could result in a restriction of choice for people with existing seed allergies. This might be unnecessary if chia seeds do not cause reactions in individuals with allergies to other seeds (so-called cross-reactive allergies). The Committee advised that the uncertainty could be reduced by research into the likelihood of different seed allergic individuals cross-reacting to chia seeds

21. In relation to potential changes in sensitisation across the population the Committee advised that the company should be proactive in reporting allergic reactions and specifically highlight any that occurred in individuals who had not previously demonstrated any symptoms of allergy to seeds.

July 2013

Annex

Product Specification

Description

To produce the oil from Chia (*Salvia hispanica* L) the seeds (99.9% pure) are cold pressed. No solvents are used and, once pressed, the oil is held in decantation tanks and a three-phase filtration process employed to remove impurities. The filtered oil may be subjected to additional processing steps (winterising and deodorising) which are widely used in the production of edible oils. Antioxidants may also be added in conformity with EU food additives legislation.

Parameter	**Limits**	**Test Method**
Acid Value	<2% Oleic Acid	AOCS Ca 5a-40
Peroxide Value	<10 mEq/Kg	NF EN ISO27107
Insoluble Impurities	<0.001%	AOCS Ca 3a-46
Alpha Linolenic Acid	>60%	AOCS Ce 1e-91
Linoleic Acid	>15%	AOCS Ce 1e-91

f) OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION FOR REFINED OIL FROM BUGLOSSOIDES ARVENSIS

Applicant:	**Technology Crops International.**
Responsible Person:	**Peter Lapinskas**
EC Classification:	**2.2**

Introduction

On 26 June 2013, the Food Standards Agency accepted an application from Technology Crops International for refined oil from *Buglossoides arvensis* as a novel ingredient. A copy of the application was placed on the Agency's website for public consultation.

The applicant states that refined oil from the seeds of *Buglossoides arvensis* (RBO) is a rich source of omega-3 and omega-6 fatty acids, including the omega-3 fatty acid stearidonic acid (SDA), which is an intermediate in the synthesis of eicosapentaenoic acid (EPA) in the body from dietary alpha-linolenic acid (ALA). SDA is more efficiently converted to EPA than ALA and so dietary sources of SDA are important for individuals who are unwilling or unable to consume EPA directly (for instance from oily fish or fish oil supplements). There are other possible significant sources of SDA, but these are either more expensive and less concentrated (e.g. Echium oil) or not yet commercially available (e.g. SDA-rich oil from genetically modified soya beans). The applicant therefore considers that RBO has the potential to improve the nutritional status of a significant subsection of the population at a lower cost than currently available products.

RBO is closely taxonomically related, and is similar in composition, to Echium oil, which was approved as a novel food ingredient in the EU in 2008[21]. The applicant highlights that the fatty acid profiles of the two oils are similar, but with RBO having a higher concentration of SDA and ALA and a lower concentration of gamma linoleic acid (GLA).

The applicant intends that RBO will be incorporated into a range of foods and also in food supplements.

RBO has been classified as a complex novel food from non-GM source, the source of the novel food has no history of food use in the EU (class 2.2) according to the scheme in Commission Recommendation 97/618/EC.

[21] Commission Decision 2008/558/EC of 27 June 2008,authorising the placing on the market of refined echium oil as novel food ingredient

I. Specification of the novel food

The applicant has provided detailed specifications for its RBO as below. Analytical data show that three separate batches of RBO comply with their proposed specifications:

Parameter	**Proposed specification**	**Buglossoides oil batches**		
		NZ00053 Batch 4	NZ00056 Batch 5	NZ00058 Batch 6
Description	Buglossoides oil is the pale yellow product obtained by refining oil extracted from the seeds of *Buglossoides arvensis* (L.) I.M.Johnst.	Confirmed	Confirmed	Confirmed
Stearidonic acid content	Not less than 15% w/w of total fatty acids	20.5	19.7	20.8
Trans fatty acids	Not more than 2% w/w of total fatty acids	<1.0	<1.0	<1.0
Acid value	Not more than 0.6 mg KOH/g	0.22	0.12	0.34
Peroxide value	Not more than 5 meq O_2/kg	2.03	1.55	1.22
Unsaponifiable content	Not more than 2%	0.28	0.43	0.73
Protein content (total nitrogen)	Not more than 20 µg/mL	1.3	1.0	1.3
Pyrrolizidine alkaloids	Not detectable with a detection limit of 4 µg/kg	<1	<1	<1

RBO consists primarily of triglycerides (about 90%) with smaller proportions of diglycerides, monoglycerides and free fatty acids (2 – 6%, 2 – 4% and <0.3% respectively). The remaining part of the oil consists of the non-saponifiable fraction (<2%) which contains a range of sterols and tocopherols.

The applicant states that pyrrolizidine alkaloids (PAs) have been found to occur in a number of species in the Boraginaceae family, including *Buglossoides arvensis*. The applicant highlights that PAs are water-soluble and therefore the majority of any PAs present in *Buglossoides*

arvensis seed would be expected to remain in the seed meal on extraction, and the level in the oil will be further reduced during refining. The applicant reports that a sample of unrefined Buglossoides oil was analysed and found to contain 44 µg/kg of PAs, but refining reduced this level to below 1 µg/kg.

The applicant has also considered other inherent constituents which might potentially give rise to toxicity (oxidation products, hydrolysis products, trans fatty acids and erucic acid). Based on analyses data, the applicant concludes that all were found to be present at well below regulatory limits. Additionally, no significant external contaminants were detected in RBO from analyses for pesticides, elemental contaminants, dioxin and dioxin-like polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), melamine and cyanuric acid.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

II. Effect of the production process applied to the novel food

The applicant has provided details of the production process. RBO is extracted from the seeds of *Buglossoides arvensis* by mechanical pressing and solvent extraction or solvent extraction alone with hexane or isohexane. Extraction is followed by a series of refining steps such as degumming, addition of sodium hydroxide to neutralise free fatty acids, bleaching and filtration. Some refining steps such as deodorisation after bleaching are optional and are carried out to ensure that RBO batches meet the required specifications.

The applicant has acknowledged the issue of stability of RBO, particularly focusing on oxidative stability. A study was conducted to assess the stability of RBO at different temperatures (4, 22 and 60°C) for twelve weeks, using peroxide value as a measure of stability. Results show that the oil remains within specification for peroxide value over the twelve weeks at all temperatures. The applicant concludes that RBO is stable, even when stored under extreme conditions and that the oil is sufficiently stable to be used in consumer products with appropriately calculated shelf lives.

***Discussion**: The Committee requested further details on the seed harvesting procedure that is used and the steps that are taken to ensure the absence of other plant material. The applicant reported that stringent procedures are in place to ensure the purity of planted seed (the total amount of impurities is limited to 2%, the same level that has been widely adopted for other crops in the UK such as rapeseed). Harvesting is carried out in a similar manner to other oilseed crops and using the same equipment. The harvested seed is cleaned to remove other plant fragments prior to oil production.*

The Committee additionally requested reassurance about the homogeneity of the seeds used as the source material for the refined oil. The applicant noted that inhomogeneity of seeds could arise from genetic variability or environmental factors. The first of these is minimised by sowing a uniform genetic strain. The latter is normal for all crops and can result in differences between batches of the oil that require further processing, for example to adjust colour or acid value.

The Committee also queried the concept of employing additional optional steps in processing RBO until it meets the required specifications, the main concern being whether this allows a potentially unsafe product to be re-processed to make it fit for consumption. The applicant pointed out that the manufacturing and refining process for RBO is equivalent to the processes that are used for all major food oils and is designed to use the minimum number of steps which will provide a product that meets the required specifications. Additional processing can be used to standardise colour and acid value, or to reduce levels of waxes or minerals. The applicant clarified that any batches that cannot be brought up to the specification standards are rejected and destroyed.

The Committee was satisfied that all its questions had been addressed and no further information was requested.

III. History of the organism used as a source of the novel food

The applicant states that *Buglossoides arvensis* was first described and classified as *Lithospermum arvense* by Linnaeus (1753). It has been described more recently by Clapham et al. (1961). The plant is native to the UK and is found in many parts of Europe and North America.

The applicant states that the safety of RBO is supported by consideration of the safety of its constituents, which are found in a wide range of other food products and which have been tested in both animals and humans, as well as by studies on the whole oil in animals.

The applicant also highlights that refined Echium oil, which is also a triglyceride vegetable oil and which contains all the fatty acids present in RBO, in similar proportions, has been approved as a novel food ingredient in the EU since 2008.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

IX. Anticipated intake/extent of use of the novel food

RBO is similar in composition to Echium oil with the exception that the proportions of SDA and ALA are higher in RBO. Echium oil has been approved as a novel food in the EU and estimates of the anticipated intake were provided in the dossier which accompanied the application made by Croda Chemicals Ltd.

The applicant proposes that RBO should be used in exactly the same foods and in such proportions as to give the same maximum quantities of SDA as are already approved for Echium oil. As such, the applicant has used the intake estimates provided for refined Echium oil as a basis to estimating RBO intake. The applicant's aim is to provide approx. 200mg of SDA per daily serving.

Male adults were calculated to have the greatest mean and 97.5th percentile intakes of SDA at 1128 and 2175 mg/day, while children had the lowest at 719 and 1351 mg/day. On a body weight basis, children were calculated to have the highest intakes, with daily SDA intakes of 51

mg/kg body weight (mean) and 103 mg/kg body weight (97.5th percentile). Female adults had the lowest intakes at 13 and 26 mg/kg body weight/day. These figures represent an overestimate of the likely consumption of SDA, because not all of the food groups used in compiling the original estimates were included in the final approval for Echium oil.

In the group with the highest intake (male adults), estimated consumption of SDA did not exceed 2200 mg SDA/person/day, equivalent to 11 servings of food at the maximum level of incorporation of the oil. Mean consumption was estimated at 1128 mg SDA/person/day, equivalent to 5-6 daily servings. This is likely to be a significant overestimate of actual intakes as it would be extremely unlikely for a person to choose so many products, all with the maximum levels of incorporation of the oil.

The applicant states that the safety studies discussed in the dossier (where intakes of up to 4200 mg SDA/person/day were tested) indicate that it is safe to consume SDA at the highest estimated consumption level of 2200 mg/person/day.

The applicant has explained that both SDA and ALA levels will be comparable in RBO-containing foods and in foods containing Echium oil, but the added quantity of RBO will be lower as it contains higher concentrations of both fatty acids.

RBO is intended to be added to the following foods at levels of incorporation up to the specified maxima.

Table: Intended uses and incorporation levels of refined Buglossoides oil (Food categories are consistent with Part E of Annex II to Regulation 1333/2008 on Food Additives)

Use group	Maximum level of stearidonic acid
Dairy products and analogues (Category 1)	250 mg/100 g; 75 mg/100 g for drinks
Cheese and cheese products (Category 1.7)	750 mg/100 g
Butter (Category 2.2.1) and other fat and oil emulsions including spreads (Category 2.2.2)	750 mg/100 g
Breakfast cereals (Category 6.3)	625 mg/100 g
Food supplements as defined in Directive 2002/46/EC of the European Parliament and of the Council excluding food supplements for young children (Category 17).	500 mg/daily dose as recommended by the manufacturer

Dietary foods for special medical purposes as defined in Directive 1999/21/EC excluding dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC (Category 13.2)	In accordance with the particular nutritional requirements of the persons for whom the products are intended
Dietary foods for weight-control diets intended to replace total food daily intake or an individual meal (Category 13.3).	250 mg/meal replacement

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

XI. Nutritional information on the novel food

The applicant intends that RBO will primarily be a replacement for Echium oil as it will be cheaper (due to the higher yielding nature of the crop). RBO also has a higher proportion of SDA, so that less oil is required to provide the same intake of SDA.

The applicant states that both RBO and Echium oils are more expensive than fish oils, so it is unlikely that consumption of fish oils as a source of omega-3 fatty acids will be significantly reduced by introduction of RBO onto the EU market. The applicant points out that RBO is most likely to be consumed by those looking to increase their intake of long-chain omega-3 fatty acids but who are unwilling or unable to consume fish oils either for dietary reasons (e.g. vegetarians) or because they do not like the taste of fish or are concerned about the possible presence of marine pollutants.

The applicant suggests that both Echium oil and RBO may be preferable to other current plant-based sources of omega-3 fatty acids such as linseed and hempseed, as they contain significant levels of SDA in addition to ALA. The conversion of ALA to EPA is much less efficient than the conversion of SDA, requiring greater quantities of these other oils to be consumed to achieve equivalent EPA production in the body.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

XII. Microbiological information on the novel food

The applicant states that microbiological contamination of RBO is unlikely to be of concern. The processes used to extract and refine RBO include temperatures in excess of 90°C under vacuum for tens of minutes, and filtration at the micron level. The oil itself has a very low water content and activity and so does not support subsequent microbial growth. The applicant has presented microbiological analyses confirming the absence of microbial contamination (yeasts, moulds, Enterobacteria, *S.aureus*) in three separate batches of RBO.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

XIII. Toxicological information on the novel food

The applicant has summarised a number of toxicological studies on a range of different oils. The three most relevant studies relate to the applicant's own RBO.

Two sub-chronic mouse feeding studies (28 days and up to 56 days) are described, where the applicant's RBO (3.9 mg/kg body weight per day) was incorporated into the diet of mice. The applicant states that there were no treatment related adverse effects.

A sub-chronic (56 day) toxicity study conducted with salmon fry where the applicant's RBO was incorporated into the diet at 11.5%. No adverse effects were reported.

The applicant states that the metabolic fate of RBO is well understood and does not give any cause for concern. The component fatty acids are released from the glycerides upon digestion and are used primarily as an energy source. The essential fatty acids can also be metabolised to longer chain or more unsaturated fatty acids. ALA and SDA can be elongated and desaturated to EPA, the omega-3 fatty acid typically found in fish oils. SDA has not been found to accumulate in human or animal tissues.

Discussion: The Committee requested full study reports for certain studies summarised in the dossier that highlight "no compound related adverse effects", in order to evaluate these data independently: Surette & Matar, 2012 (using the applicant's RBO); Engler, 1993 and Harris et al., 2007 (using other SDA-containing oils). The applicant has clarified that it does not have access to the original data or unpublished material from these studies so only the published papers were evaluated.

Similarly, full study reports were requested for two rodent feeding studies with substances other than RBO, to evaluate some of the reported findings and their implications for humans (Engler, 1993 and Wainwright et al., 2003). Additionally, the applicant has provided further reassurance in its response as to why reported findings from the study by Wainwright et al., 2003 are not a cause for concern with respect to the gamma-linoleic acid (GLA) component of RBO.

Given that neither RBO nor its source material has any history of consumption, the Committee enquired whether any human study data are available or whether any clinical studies are underway. The applicant confirmed that no human study data are available and no clinical studies are underway and provided the following reasoning as to why such data are not necessary.

- *RBO is a highly purified vegetable oil with a restricted number of components, which have been well characterised and all appear in common foods that are widely consumed in the EU.*
- *RBO is extremely similar in composition to refined Echium oil (which is approved in the EU as a novel ingredient).*
- *The applicant has obtained GRAS (Generally Regarded As Safe) status for its RBO in the USA and the Expert Panel involved in this assessment concluded unanimously on the safety of this novel ingredient for the same intended uses described in this application.*

- *The applicant proposes to launch RBO-containing foods onto the US market in the first instance, with a view to expanding to the EU market at a later stage. The applicant mentions that it is likely there will be a significant level of experience with human intake of RBO before it is introduced onto the EU market.*

The Committee was satisfied that there are no apparent safety concerns relating to this novel ingredient or its known constituents and was content that it is not necessary to conduct a human study to obtain further data.

The Committee noted that neither the novel ingredient nor its source has a history of consumption anywhere in the world. The Committee therefore recommends that the applicant should ensure that reports of adverse reactions are closely monitored after the product is introduced to the market, in order to identify any unexpected effects. The Committee has discussed the details of post-launch adverse effects monitoring with the applicant and is satisfied that their proposed methodology is thorough and robust.

Allergenicity and labelling

Pollen from *Echium vulgare* has been reported to contain cytochrome C allergenic proteins. In order to ensure that Echium oil would not provoke an allergic reaction in sensitive individuals, a limit on the total protein content of 20 µg/ml was included in the 2008 authorisation decision. The applicant states that no allergens have been reported in *Buglossoides arvensis*, which suggests that it may not have the same allergenic potential. However, the applicant proposes that the protein content of RBO should also be limited to 20 µg/ml, in order to avoid possible unexpected allergic reactions.

The applicant assessed protein levels in RBO using a combustion / chemiluminescence method, which failed to find any protein at the level of detection (<10 µg/ml total N).

The applicant also conducted further analyses using the borate extraction method and the CBQCA analytical procedure using a commercial analytical kit as described by Rigby et al. 2011. The results from the analyses of three separate batches show that the protein content of RBO is 1-1.3 µg/ml, substantially below the proposed limit of 20 µg/ml.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier.*

CONCLUSION

The ACNFP has completed its assessment of RBO as a novel ingredient to be added to a range of foods and did not identify any significant safety concerns relating to this ingredient. On request, the Committee received further information from the applicant on the following:

- The production process
- The potential implications of optional processing steps
- Further details on certain toxicology studies
- Whether human study data are available

After reviewing the applicant's response to these issues, the Committee did not have any outstanding safety concerns.

The Committee noted that neither the novel ingredient nor its source has a history of consumption anywhere in the world and as a result recommended that the applicant should ensure that reports of adverse reactions are closely monitored after RBO-containing products are introduced onto the market.

The ACNFP therefore concluded that RBO meets the criteria set out in Article 3(1) of Regulation (EC) No 258/97, namely it does not:

- present a risk to the consumer
- mislead the consumer
- differ from foods or food ingredients which it is intended to replace to such an extent that its normal consumption would be nutritionally disadvantageous for the consumer.

January 2014

f) OPINION ON SUBSTANTIAL EQUIVALENCE OF ARGENTINIAN CHIA SEED CONSIDERED UNDER ARTICLE 3(4) OF THE NOVEL FOODS REGULATION 258/97

Applicant Infoods Ltd

Unit 2,
Selbury Drive,
Leicester,
LE2 5NG
United Kingdom

Responsible person Imran Mohammed

Introduction

1. In April 2013 a request was submitted by Infoods Ltd to the UK Competent Authority for an opinion on the equivalence of their chia seed grown in Argentina, compared with the existing chia seed cultivated in Australia, and marketed in the EU by The Chia Company.
2. Chia (*Salvia hispanica* L) is a summer annual herbaceous plant belonging to the Labiatae family. It grows from a seedling to develop lush green foliage before it produces long flowers which are either purple or, less commonly white. These flowers develop into seed pods that contain chia seeds.
3. In 2003 an application was submitted to the UK for the use of chia seeds in certain types of bread but, following a positive UK initial opinion, a number of concerns were raised by other EU Member States regarding the safety of the seeds. The applicant subsequently provided additional data that were scrutinised by EFSA before the seeds were authorised in 2009[22]. An application from The Chia Company, to extend the use of the seeds into products including baked goods and breakfast cereals was authorised in January 2013 following a positive opinion by the UK in 2012[23]. Novel food authorisations are granted on an applicant specific basis, so other companies seeking to market the same ingredient must gain separate approval.
4. The current request addresses substantial equivalence according to the five criteria set out in Article 3(4) of Regulation (EC) 258/97: composition, nutritional value, metabolism, intended use and the level of undesirable substances.

[22] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:294:0014:0015:EN:PDF
[23] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:021:0034:0035:EN:PDF

Evaluation

a) Composition

1. The dossier states that Infoods' chia seeds are grown and harvested in South America, and the applicant subsequently advised that they will be grown in Argentina. The seeds and are not processed in any way prior to use as a food ingredient. If fertilisers are used these are restricted to 'natural fertilisers' and the applicant also advises that any irrigation systems employed are used carefully to minimise soil erosion. No pesticides are used and the applicant has carried out screens to confirm their absence (Dossier, Appendix 1). In their 2011 request for an opinion on equivalence, The Chia Company advised their seed stock were originally imported from Mexico and Bolivia.

2. The applicant has compared the published composition of the approved chia seed with 3 batches of their seed. (Dossier, p 6 and Appendix 1). This is summarised in the table below.

Nutrient (%)	**Infoods' Seed**	**The Chia Company Seed**
Dry matter	91.7 – 93.4	95.0 – 96.8
Protein	21.2 – 24.3	17.4 – 22.4
Fat	27.4 – 31.1	28.5 – 34.7
Carbohydrate	36.1 – 38.5	37.1 – 42.6
Fibre	35.3 – 41.7	32.8 – 40.2
Ash	4.6	4.5 – 5.6

3. The applicant has also compared the mineral content of their chia seed with the approved chia and this is summarised in the table below. The applicant has not provided a comparison of the amino acid content of their chia seed with the Chia Company's chia but states that the overall nutritional value is consistent with the approved chia.

Mineral (mg/100g)	Infoods' Seed	The Chia Company Seed
Sodium	2.48 – 5.17	<0.1 – 6
Potassium	639 – 750	510 – 710
Calcium	510 – 581	500 – 640
Iron	5.91 – 7.37	5.70 – 15
Magnesium	298 – 360	310 – 430
Phosphorus	817 - 925	600 – 870

4. The applicant notes that some of the components analysed fall slightly outside of the range of the approved chia seed but does not regard these differences to be substantive.

5. The applicant has also included a comparison of the fatty acid profile of their chia seed with the approved chia. (**Annex 1**, Table 4, p8). Small differences in some of the fatty acids are also seen but the applicant does not highlight these as a cause for concern.

6. In all of the above analyses, it should be noted that the applicant's data are being compared with published data on the approved product. It is therefore possible that the reported differences could be due, in part, to different methods of analysis. This pragmatic approach is in line with a previous request for an opinion on equivalence between two sources of chia seed[24].

Discussion: *The Committee was satisfied that minor differences observed between the seeds were likely to be due to differing growing conditions and agreed that that the data provided were sufficient to conclude that Infoods' Argentinian chia seed and the Australian chia seed show that they have an equivalent composition.*

b) c) Nutritional Value and Metabolism

11. The applicant states that their chia seed contains around 20% protein and has an oil content of approximately one third of its weight, about 80% of which is alpha linolenic acid, making this ingredient a source of omega 3 fatty acids. The seeds contain about 5% soluble fibre and are a good source of vitamin B, minerals and antioxidants. These figures are similar to the existing product.

Discussion: *The Committee was content with information provided on the nutritional value of the chia seed, compared with the existing product.*

[24] http://www.food.gov.uk/multimedia/pdfs/chiacompdraftopinion.pdf

d) Intended Use

12. The applicant will limit the use of chia seed to bread products (max 5%), baked products (max 10%), breakfast cereals (max 10%), fruit, nut and seed mixes (max 10 %), pre-packaged Chia seed (max 15 g per day). This is consistent with the authorisation given to Columbus Paradigm in 2009 and to The Chia Company in 2013.

Discussion: *The Committee was content that the intended uses of the chia seed are consistent with those permitted for the existing product.*

e) Level of undesirable substances

Chemical and Microbial Content

7. The applicant is of the view that the production process are sufficient to ensure that the levels of undesirable substances are below the specified limits and equivalent to the approved chia seeds. The applicant has carried out a heavy metal and mycotoxin screen to support this statement. (Dossier, Table 6 and Appendix 1). Results of tests for microbial content are also provided and these are at or below those seen for The Chia Company's seeds (Dossier, Table 7 and Appendix 1).

Discussion *The Committee was content that the applicant had quality control procedures in place to minimise the risk of contamination of the chia seeds*

(f) Additional information

Toxicity and Safety Studies

15. The applicant notes that the safety of chia seeds when used in bread at a maximum of 5% has been confirmed by EFSA. EFSA's 2009 opinion took into consideration a number of trials to assess the nutritional quality of chia, its effect on selected markers of coagulation and immune function in humans, and its potential allergenicity. The applicant regards the safety of chia seeds to have been reaffirmed when EU Member States assessed, and accepted, The Chia Company's 2011 request to extend the use of the seeds.

Conclusion

16. The Committee concluded that Infoods Ltd has demonstrated the equivalence of their chia seed with the existing chia seed according to the criteria set out in Article 3(4) of the Novel Foods Regulation (EC) 258/97.

17. The Committee therefore concluded that the chia seed produced by Infoods Ltd can be considered to be substantially equivalent to the existing chia seed produced by The Chia Company.

June 2013

g) OPINION ON SUBSTANTIAL EQUIVALENCE OF ARGENTINIAN CHIA SEED CONSIDERED UNDER ARTICLE 3(4) OF THE NOVEL FOODS REGULATION 258/97

Applicant **Nutrisure Ltd (Supernutrients),**

North Barn
Manor Farm
Southstoke
Bath

Responsible person Glenn Turner

Introduction

5. In November2013 a request was submitted by Nutrisure Ltd to the UK Competent Authority for an opinion on the equivalence of their chia seed grown in Argentina, compared with the existing chia seed cultivated in Australia, and marketed in the EU by The Chia Company.

6. Chia (*Salvia hispanica* L) is a summer annual herbaceous plant belonging to the Labiatae family. It grows from a seedling to develop lush green foliage before it produces long flowers which are either purple or, less commonly white. These flowers develop into seed pods that contain chia seeds.

7. In 2003 an application was submitted to the UK for the use of chia seeds in certain types of bread but, following a positive UK initial opinion, a number of concerns were raised by other EU Member States regarding the safety of the seeds. The applicant subsequently provided additional data that were scrutinised by EFSA before the seeds were authorised in 2009[25]. An application from The Chia Company, to extend the use of the seeds into products including baked goods and breakfast cereals was authorised in January 2013 following a positive opinion by the UK in 2012[26]. Novel food authorisations are granted on an applicant specific basis, so other companies seeking to market the same ingredient must gain separate approval.

8. The current request addresses substantial equivalence according to the five criteria set out in Article 3(4) of Regulation (EC) 258/97: composition, nutritional value, metabolism, intended use and the level of undesirable substances.

Evaluation

a) Composition

Nutrisure Ltd chia seeds are grown and harvested in Argentine. The seeds and are not processed in any way prior to use as a food ingredient. The seeds used for cultivation have been selected for

[25] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:294:0014:0015:EN:PDF
[26] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:021:0034:0035:EN:PDF

resistance to pests and are not processed in any way prior to use as a food ingredient. In their 2011 request for an opinion on equivalence, The Chia Company advised their seed stock were originally imported from Mexico and Bolivia.

The applicant has compared the published composition of the approved chia seed with 3 batches of their seed. (Dossier, p 6 and Appendix 1). This is summarised in the table below.

Nutrient (%)	**Nutrisure Seed**	**TCC Seed**
Dry matter	91.2-92.7	95.0 – 96.8
Protein	19.5 – 22.6	17.4 – 22.4
Fat	27.3 -28.8	28.5 – 34.7
Carbohydrate	36.9 – 39.2	37.1 – 42.6
Fibre	28.8 – 33.0	32.8 – 40.2
Ash	4.5 – 4.7	4.5 – 5.6

The applicant has also compared the mineral content of their chia seed with the approved chia and this is summarised in the table below. The applicant has not provided a comparison of the amino acid content of their chia seed with the Chia Company's chia but states that the overall nutritional value is consistent with the approved chia.

Mineral (mg/100g)	**Nutrisure Seed**	**TCC Seed**
Sodium	<50	<0.1 – 6
Potassium	460 - 520	510 – 710
Calcium	430 - 460	500 – 640
Iron	5.5 – 6.6	5.70 – 15
Magnesium	230 - 270	310 – 430
Phosphorus	520 - 640	600 – 870

The applicant notes that some of the components analysed fall slightly outside of the range of the approved chia seed but does not regard these differences to be substantive.

The applicant has also included a basic comparison of the fatty acid profile of their chia seed with the approved chia. (Dossier, Table 2 and Appendix). Small differences in some of the fatty acids are also seen but the applicant does not highlight these as a cause for concern.

In all of the above analyses, it should be noted that the applicant's data are being compared with published data on the approved product. It is therefore possible that the reported differences could be due, in part, to different methods of analysis. This pragmatic approach is in line with a previous request for an opinion on equivalence between two sources of chia seed[27].

Discussion: *The Committee was satisfied that minor differences observed between the seeds were likely to be due to differing growing conditions and agreed that that the data provided were sufficient to conclude that Nutrisure's Argentinian chia seed and the Australian chia seed show that they have an equivalent composition.*

b) c) Nutritional Value and Metabolism

The applicant states that their chia seed have comparable levels of protein and an oil content of approximately one third of its weight, about 60% of which is α-linolenic acid, making this ingredient a source of n-3 fatty acids. The seeds have similar mineral and vitamin profiles to the existing product.

Discussion: *The Committee was content with information provided on the nutritional value of the chia seed, compared with the existing product.*

d) Intended Use

13. The applicant will limit the use of chia seed to bread products (max 5%), baked products (max 10%), breakfast cereals (max 10%), fruit, nut and seed mixes (max 10%), pre-packaged Chia seed (max 15 g per day). This is consistent with the authorisation given to Columbus Paradigm in 2009 and to The Chia Company in 2013.

Discussion: *The Committee was content that the intended uses of the chia seed are consistent with those permitted for the existing product.*

e) Level of undesirable substances

Chemical and Microbial Content

The applicant is of the view that the production process are sufficient to ensure that the levels of undesirable substances are below the specified limits and equivalent to the approved chia seeds. The applicant has carried out a heavy metal and mycotoxin screen to support this statement. (Dossier, Table 5 and Appendix 1). Results of tests for microbial content are also provided and these are at or below those seen for The Chia Company's seeds (Dossier, Table 6 and Appendix 1).

Discussion *The Committee was content that the applicant had quality control procedures in place to minimise the risk of contamination of the chia seeds.*

[27] http://www.food.gov.uk/multimedia/pdfs/chiacompdraftopinion.pdf

Conclusion

18. The Committee concluded that Nutrisure Ltd has demonstrated the equivalence of their chia seed with the existing chia seed according to the criteria set out in Article 3(4) of the Novel Foods Regulation (EC) 258/97.

19. The Committee therefore concluded that the chia seed produced by Nutrisure Ltd. can be considered to be substantially equivalent to the existing chia seed produced by The Chia Company.

January 2014

h) Pasteurised milk treated with ultra violet light as a novel production process

Andreas Klepsch
European Commission
DG SANCO
Brussels B-1049

15 March 2013

Application under Regulation (EC) 258/97 for Approval of Pasteurised Milk treated with Ultra Violet Light as a Novel Production Process

Dear Mr Klepsch

As the UK Competent Authority (CA), the Food Standards Agency has sought advice from the Advisory Committee on Novel Foods and Processes (ACNFP) on the initial assessment report prepared by the Irish CA for pasteurised milk treated with ultraviolet (UV) light. As the correct dossier was not available in time for the ACNFP's meeting on 13 February, Members' views were sought by post. Please note that these comments are based not on the version of the dossier that was made available via NF-Net, but on the final dosser that was the basis for the Irish report, which we obtained from the Irish CA.

The UK notes that there is no information detailing the variability of vitamin D_3 levels in the treated milk and requests that the applicant provide information on the extent of variation in the level of vitamin D_3 both within and between batches and, if appropriate, this should be reflected in the product specification. The sensory tests that have been carried out are limited. While the information provided by the applicant does not indicate any changes as a result of UV treatment, this is based on analyses of one day old samples where any effect of the treatment may be less apparent than at the end of the product's shelf life. As there are published reports[28] of 'sensory defect' associated with UV treated milk the UK is of the view that the applicant should provide additional reassurance on this point.

The UK is also concerned that the applicant has not considered whether the UV treatment may give rise to the formation of oxidation products and treatment induced aggregates. There are published reports showing that UV treatment can induce the formation of such products in whey[29] the applicant should investigate whether these may be present in their treated milks, and whether these have any implications for the consumer.

[28] Rossitto PV *et al* (2012) J. Food Prot. 75 (12), 2197 – 2207
[29] Kristo E *et al.* (2012) J Agric. Food Chem. 60, 6204-6209

On the basis of the concerns detailed above, the UK is unable to agree with the positive opinion of the Irish CA and has reasoned objections to the authorisation of pasteurised milk treated with UV light as a novel production process.

Yours sincerely
(By email only)

Dr Chris Jones
UK Competent Authority

i) Synthetic Resveratrol

Sirkku Heinimaa
European Commission, DG SANCO
Brussels B-1049

4 November 2013

Dear Sirkku

Application under Regulation (EC) 258/97 for Approval of Synthetic Resveratrol

As the UK Competent Authority (CA), the Food Standards Agency has sought advice from members of the Advisory Committee on Novel Foods and Processes (ACNFP) on the initial assessment report prepared by the Irish CA for the above product. Given that the deadline for submitting comments/objections to the Commission is 4 November and is in advance of the next meeting of the ACNFP, advice was sought from Members of the Committee via postal consultation.

Members raised a number of questions relating to this application, which require addressing by the applicant before the UK can support the authorisation of this novel ingredient. The UK therefore wishes to raise objections to the authorisation of synthetic resveratrol until reassurance can be provided by the applicant on these points, outlined below:

a) Production process

While it is stated in the dossier that synthetic resveratrol is currently produced using a new process, no details are provided by the applicant about this new process and how it differs from the previous manufacturing process.

This information is important because the test materials used in various safety studies were produced with the “old” process and it is essential to know how this might differ from the current product.

b) Potential of synthetic resveratrol to interfere with the efficacy of certain medications

Resveratrol given to human volunteers (1000mg/day for 4 weeks) had a significant effect on several key cytochrome P450s that play a primary role in xenobiotic metabolism. These effects occurred at 50% of the intended dose outlined in the application. Resveratrol has the potential to modify both Phase 1 and Phase 2 drug metabolism and to interfere with the effectiveness of pharmaceuticals taken concomitantly with the resveratrol supplement. This may be a significant concern for high-dose consumers or consumers taking this supplement over an extended period.

This is particularly important since resveratrol is likely to be taken by those seeking to improve cardiovascular health and who are likely to be taking prescribed medication for diabetes, hypertension, hyperlipidaemia etc.

c) Toxicology / clinical studies

In order to carry out a complete risk assessment all relevant data should be evaluated. The applicant's dossier presents data from several animal studies but it does not discuss the findings of all the published clinical studies.

A recent review of the safety and efficacy of resveratrol by C-H Cottart et al. (Mol Nutr Food Res. 2013 Jun 6. doi: 10.1002/mnfr.201200589) reviewed results from 25 studies published between 2009 and 2012, including 13 studies in humans, and concluded:

> "Toxicological data confirm that RVT (resveratrol) is well tolerated. Any adverse effects (mainly concerning the abdomen), at doses of ≥0.5 g/day for long periods, remain moderate and reversible. Nevertheless, the efficacy and safety of RVT need to be further investigated."

The applicant should therefore provide reassurance that they have taken all the available clinical studies into account and that they have addressed the uncertainties expressed in this review.

d) Estimated Intake

A No Observable Adverse Effect Level (NOAEL) of 750mg/kg/day appears well established from rodent studies and this provides a margin of safety of approximately 100 over the suggested dose of supplementation (450mg/day, equivalent to 7.5 mg/kg bodyweight/day in a 60 kg adult). The applicant suggests that this level of consumption will not be achieved by most people in the medium to long-term as many users do not consume supplements regularly. However, no evidence is presented to support this suggestion.

If a child were to consume this supplement (either intentionally or by misadventure), the 450 mg daily dose in a 15 kg child would equate to 30 mg/kg bodyweight which would result in a margin of safety of only 25. Members appreciated that the NOAEL is the top dose in the pivotal study and it is not based on a significant adverse effect, so the true margins of safety could be higher. Members nonetheless asked whether the applicant intends to label these supplements as not suitable for children.

e) Information on adverse effects of existing resveratrol preparations

Given that this and other preparations containing the proposed dose of resveratrol have been marketed for several years, it is surprising that no information about reported adverse effects of existing commercial products has been provided by the applicant.

Yours sincerely,

(By email only)

Dr Manisha Upadhyay

Novel Foods

Cumulative index (1989-2012)