The Advisory Committee on Novel Foods and Processes (ACNFP)

2012 Report

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Forward

I am pleased to present the 2012 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 Paul Brantom, Ms Jayam Dalal, Professor Harry Flint, Professor Paul Haggarty, Professor Stephen Holgate, Mrs Gillian Pope, Professor Peter Shewry and Professor John Warner all of whose terms of appointment came to an end during 2012.

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
May 2013

1. NOVEL FOOD APPLICATIONS SUBMITTED TO THE UK

(a) Full applications

In 2012 the ACNFP considered six 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 two of these applications during this calendar year and also completed its assessment of two applications which were carried over from previous years.

Table 1: Novel food applications made via the UK that were considered by the Committee during 2012

Novel food (Applicant)	***Meeting discussed***	***Initial opinion***	***Comment***
Chia Seed (extension of use) (The Chia Company)	Feb, Sept (postal)	Completed Annex 3(a)	A positive initial opinion was issued in March 2012
Calanus Oil (Calanus AS)	Feb	-	Evaluation continued in 2013
Clostridium butyricum (Miyarisan Pharmaceutical Company)	Feb, April, Sept, Nov	-	Evaluation continued in 2013
Methyl Cellulose (Dow)	April, Sept	Completed Annex 3(b)	A positive initial opinion was issued in October 2012
Vitamin D enriched yeast (Lallemand)	April, Sept (postal	Completed Annex 3(c)	A positive initial opinion was issued in September 2012
Isomatoligosaccharides (Bioneutra Inc)	Sept (postal)	Completed Annex 3(d)	A positive initial opinion was issued in October 2012
DHA and EPA Rich Algal Oil (DSM)	Nov	-	Evaluation continued in 2013
Chia Oil (Functional Products Trading)	Nov	-	Evaluation continued in 2013

(b) Opinions on substantial equivalence

In 2012 the ACNFP considered one request 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 this request during this calendar year.

Table 2: Applications for an opinion on substantial equivalence that were considered by the Committee during 2012

Novel food (Applicant)	*Meeting discussed*	*ACNFP Opinion*	*Comment*
DHA Rich Algal Oil (Ocean Nutrition)	Feb	Completed Annex 3(e)	The Committee agreed that substantial equivalence had been demonstrated between this oil and an existing product.

2. NOVEL FOOD APPLICATIONS SUBMITTED TO OTHER MEMBER STATES

In 2012 the ACNFP considered four 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 2012 following an initial assessment in another Member State

Novel food (Member State)	*Meeting discussed*	*UK response*	*Comment*
Methyltetrahydrofolic acid, Glucosamine salt (Irelands)	April	Annex 3 (f)	Minor comments
Citicoline (Ireland Postal)	Sept (postal)	Annex 3 (g)	Objections (Purity concerns, absence of stability data, likely to be medicinal in UK)
Rapeseed Protein (Ireland)	Nov (Postal)	Annex 3 (h)	Objections (lack of information on protein composition, potential for cross reactivity in individuals with mustard allergy, lack of precision in exposure assessment)
Nattokinase (Belgium)	Nov	Annex 3 (i)	Objections (lack of safety data, potential to act as a kinase enzyme in gut a cause for concern)

3. NOVEL FOOD APPLCIATIONS CONSIDERED IN PREVIOUS YEARS

During 2012 the ACNFP also considered a response from twq applicant companies, and an opinion from the European Food Safety Authority (EFSA) which following reasoned objections to the marketing of novel foods (Article 6(4) of regulation (EC) 258/97). 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 2011 following an initial assessment in another Member State

Applicant response or EFSA opinion	***Meeting discussed***	***Comment***
Gamma Cyclo Dextrin (Response)	Feb,	The Committee's previous objection was addressed satisfactorily
Coriander Seed Oil (Response)	Sept	The Committee's previous objections were addressed satisfactorily
Bovine Lactoferrin (EFSA opinion)	Sept, Nov	The Committee's previous objections were addressed satisfactorily

4. OTHER ISSUES

In 2012 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***
New GM Techniques (EU Working Group)	Feb	The mandate of the EU working group was to interpret the definition of a GMO in relation to the terminology used in the legislation, rather than in relation to safety considerations. The Committee found the report difficult to interpret as departures from the consensus opinion were reported ambiguously and the scientific conclusions were therefore difficult to understand
Exposure assessment	April, Sept	The Committee highlighted the tendency for under-reporting of food consumption, the under-representation of some population groups in national surveys (e.g. pregnant women and ethnic minorities), the possibility that foods formulated with novel ingredients might be consumed in different amounts to their existing counterparts and potential co-consumption of food supplements and foods supplemented with the same ingredients
Plants Developed through cisgenesis and intra-genesis (EFSA opinion)	Sept	The Committee advised that the risks associated with cisgenic and conventionally bred plants were the same and there is a need to look at new products produced by these techniques on a case by case basis. Emphasis should be on the end product and not the technology by which it is produced
ACNFP Advice	Nov	Summary of advice given to the FSA between 2010 and 11 and subsequent actions taken (refer to paper ACNFP/108/7)

ANNEX 1 – Information about the Committee

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 2012`, 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 2012 and a copy of the code of conduct for ACNFP members can be found on the following pages.

Membership of the Committee during 2012

Chairman

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

Members

Dr Paul Brantom (Until July 2012) BSc, PhD, MIBiol (Toxicologist)
Independent consultant and registered European toxicologist

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.

Jayam Dalal (Consumer affairs)
Freelance marketing consultant and Independent Public Appointments Assessor accredited by the Office of the Commissioner for Public Appointments

Dr Susan Duthie (From September 2012) BSc, MSc, PhD (Nutritionist)
Senior research Scientist in the Nutrition and Epigenetics Group of the Rowett Institute of Nutrition and Health, University of Aberdeen

Simon Flanagan (From September 2012) BSc (Quality Assurance/Food Processing)
Senior Consultant in Food Safety and Allergens for Reading Scientific Services Ltd

Professor Harry Flint (Until July 2012) BSc, PhD (Microbiologist)
Head of the Gut Microbiology and Immunology Division at the Rowett Research Institute of Nutrition and Health, University of Aberdeen

Professor Paul Haggarty (Until July 2012) BSc, PhD (Nutritionist)
Head of Nutrition & Epigenetics and Senior Lecturer, Rowett Institute of Nutrition and Health, University of Aberdeen and Honorary Clinical Scientist in Grampian NHS Trust

Professor Stephen Holgate (Until July 2012) BSc, MBBS, MD, DSc, FRCP, FRCPath, FIBiol, FMed Sci (Allergenicity expert)
Medical Research Council Clinical Professor of Immunopharmacology at the University of Southampton

Nichola Lund (From September 2012) (Consumer affairs)
Trading Standards Officer with the North East London Metrology Partnership.

Professor George Macfarlane (From September 2012) BSc,PhD (Microbiologist)
Professor of Bacteriology at the University of Dundee

Rohini Manuel (From September 2012) MB BCh BAO, MSc, MD (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 (From September 2012) (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, The University of Leeds

Professor Clare Mills BSc, PhD (Plant science and allergy expert)
Head of the Structuring Food for Health Programme at the Institute of Food Research in Norwich
Professor of Molecular Allergology, School of Translational Medicine, University of Manchester

Gillian Pope (Until July 2012) (Consumer affairs)
Company Secretary for NRC (Europe) Ltd.

Professor Christopher Ritson BA, MAgrSc (Expert in Ethics)
Professor of Agricultural Marketing and former Dean of the Faculty of Agriculture and Biological Sciences at Newcastle University

Professor Peter Shewry (Until July 2012) BSc, PhD, DSc (Plant Biochemist)
Associate Director of Rothamsted Research

Professor John Warner MB, ChB, MD, FRCP, FRCPCH, FMed Sci (Allergenicity Expert)
Professor of Child Health at the University of Southampton;
now Head of the Department of Paediatrics at Imperial College

FSA Assessors

Mr T Donohoe	Food Standards Agency
Ms H Neathey	Food Standards Agency (Wales)
Ms A Taylor	Food Standards Agency (Scotland)
Mr G McCurdy	Food Standards Agency (Northern Ireland)

ACNFP Members' Interests during 2012

Member

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Professor Peter Gregory	East Malling Research	Chief Executive	None	
	R Royal Horticultural Society	Trustee		
	Produced in Kent	Non-Exec Director		
	Rank Prize Nutrition Committee	Member		
	Informal Research Advisory Group, Dfid	Member		
Dr Paul Brantom	Advisory Committee on Animal Feedingstuffs (ACAF). Expert Committee on Pesticide Residues in Food (PRiF).	Committee Member	None	
Professor Michael Bushell	Abbott Laboratories, Chicago	Consultant	None	
Professor Andrew Chesson	None	None	European Food Safety Authority	Chair of FEEDAP panel and member of Scientific Committee
Jayam Dalal	Agricultural Wages Committee.	Vice Chair.		

Personal Interests			Non-personal Interests	
Member	Company	Interest	Company	Interest
Dr Susan Duthie	None		UK Environmental Mutagen Society Molecular Epidemiology Group (UKMEG) Rank Prize Funds Tenovus UK Scottish Government (RESAS)	Secretary Funded PhD Studentship Funded PhD Studentship Research Funding
Simon Flanagan	Reading Scientific Services Ltd Subsidiary of Mondeleze International	Employee	UK Food and Drink Federation Food and Drink Europe ILSI Europe	Member of Allergen Steering Group Member of Allergen Working Group Member of Food Allergy Taskforce
Professor Harry Flint	Shell. Syral.	Shareholder. Member of Scientific Advisory Board	Provexis Alizyme.	Research funding.

Personal Interests			Non-personal Interests	
Member	Company	Interest	Company	Interest
Dr Paul Haggarty	Smith Nephew	Shareholder	Pharmaton	Unpaid advisor on pregnancy study protocol.
	Diageo	Shareholder		
	Cafe Direct	Shareholder	Editorial consultant on the American College of Physicians' Information and Education Resource	Consultation fee contributed to research funds
			Nutrition and Health Conference and German Society for Reproductive medicine	Lecture fees contributed to research funds.
Professor Stephen Holgate	Merck Research Laboratories and MSD	Consultant	Novartis. MSD.	Research Funding.
	Novartis	Consultant	Various charities and trusts	Trustee.
	Laboratorias Almirall	Consultant	Advisory Committee on Hazardous Substances	Chair
	Amgen	Consultant		
	Synairgen (Spin out company University of Southampton).	Shareholder/ Director.		
	Southampton Asset Management.	Director		
Nichola Lund LLB DCA DTS MTSI	None		Member of the Trading Standards Institute	

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Professor George Macfarlane	None		Government Chief Scientist Office	Member
Dr Rohini Manuel	None		None	
Professor John Mathers	None		EU BBRSC MRC Governing Council of the British Nutrition Foundation Lifelong Health and well being Research Advisory Panel BBRSC DRINC Advisory Panel	Research funding Research funding Research funding Member Member Member
Professor Harry McArdle	None		SACN Nutrition Society International Copper Association	Member Honorary Secretaryr Funds to support visiting scientist
Professor Peter Meyer	None		None	

Personal Interests			Non-personal Interests	
Member	Company	Interest	Company	Interest
Dr Clare Mills	None		FSA	Occasional external reviewer. PI on FSA funded project T07062. Col on FSA funded TEXTFALL
			BBSRC	Member of DRINC steering group Core member Committee C Grant Holder
			EU funded research	CHANCE project
			University of Nebraska Food Allergy Research and Resource Programme, USA	Joint PhD student : collaborations on databasing (informaAll)
			Industry : Novartis DBV	
			Neogen Corp	Provision of challenge meals for diagnosis of food allergy
			Exponent	Protein purification
			Pepsico	expert advice
Mrs Gillian Pope	None		None	
Professor Chris Ritson	Home Grown Cereals Authority	Deputy Chairman (June 2000-March 2008)	Food Ethics Council	Director/Trustee

Personal Interests			Non-personal Interests	
Member	Company	Interest	Company	Interest
			Cereals Industry Forum	Chairman
			EU	Research Funding
Professor Peter Shewry	Journal of Cereal Science	Reviews Editor	EU	Funded research
	Various	Occasional laboratory review panel member	Fra	Funded research
	Various	Editors and other royalties	FSA	Funded research
	Association of Applied Biologists	Vice President	Rank Prize Funds	Trustee
			Alpro Foundation	Member of Advisory Committee UK
Professor John Warner	UCB Pharma Ltd	Chairman of Scientific Advisory Board.	Danone. UCB Pharma, Food & Drink Federation	Funded Research
	Merck	Member of Scientific Advisory Board.	Anaphylaxis Campaign.	Trustee
	Danone	Member of Scientific Advisory Board		
	Novartis	Scientific Advisory Board		
	Allergy Therapeutics	Scientific Advisory Board		

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 31);
- 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 XXX 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
Advisory Committee on Research
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]
Scientific Advisory Committee on Nutrition

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 – as far as is practicable	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	
6. Data from stakeholders will be considered and weighted according to		

quality by the SAC.	Yes	Secretqriat, also seeks further information and advice when required, from other Committees or individual experts.
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 example consumer behaviour and consumer activities	For complex statistical questions, the Secretariat is able to consult with specialists within the FSA. 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.
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	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.
12. When considering what evidence needs to be collected for assessment, the following points will be	Yes	

[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

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.		Novel food application dossiers include a list of references which make it clear whether or not they have been peer reviewed.
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	
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. ACNFP could usefully consider how to formalise the process of reporting on uncertainty *[DN is the last sentence still relevant]*
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	Yes	ACNFP complies with this – uncertainties and interpretations are identified clearly in the Committee's opinions.

alternative interpretations fit the same evidence.		
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 accuracy.	Yes	Items 23 -27 – Decisions and their basis are clearly communicated to all parties. The quality of the reports and opinions is good and great care is taken over accuracy. The final conclusions set out the context and history of the issue being covered.
24. It will be made clear by the SAC where assessments have been based on the	Yes	

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.		Committee papers are made publicly available at the time of each meeting. This is also the case for the detailed annexes, except where this is prevented by commercial considerations (e.g. details of manufacturing processes) or EU constraints. The Committee focuses on risks but also advises on management, notably labelling.
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 answer Board Members' questions on the science. The Chairs may also, where appropriate, be invited to provide factual briefing to Board	N/A	(Item 28 is not for the Committee itself to implement. If invited, the Committee Chair would provide the necessary input to the FSA 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	The FSA provides feedback to the Committee in a timely manner and also produces an annual paper summarising actions taken.

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 £22,008.

ANNEX 2 ACNFP Meeting Minutes

(a) Minutes of 105th meeting (Feb 2012)

Minutes of the 104th meeting DRAFT/ACNFP/104/Min

The Committee agreed, subject to minor amendments, that the minutes were a true record of the 104th meeting of the ACNFP held on Thursday 24 November 2011

3. Matters Arising

The Secretariat reported on the actions following the previous meeting:

- The Committee's finalised opinions on DHA and EPA-rich algal oil (item 4); Coriander seed oil (item 6); and Synthetic vitamin K_2 (item 7) had been submitted to the European Commission
- Members of the Secretariat had met on 23 January with their counterparts from the Scientific Advisory Committee on Nutrition, the Committee on Toxicity and the Social Science Research Committee to discuss the intake of novel ingredients from multiple food sources (item 11.3). The Secretariats agreed that a paper should be prepared that describes the possible scenarios and how they can be handled, to be discussed at the ACNFP meeting in April 2012 and the SACN meeting in June.

4. Independent Review of the ACNFP ACNFP/105/1

The Committee was asked to consider the final report of the independent review of the ACNFP which took place between November 2011 and January 2012 and to consider how it wished to respond to the recommendations that were relevant to the Committee and Committee members.

The Committee considered the report was positive and congratulated the independent reviewer on the way the interviews were conducted. The Committee noted the examples of good practice and recommendations 4, 5 and 6, which were of relevance to the secretariat.

The Committee was updated on the timing of the new EU Regulation on novel foods, which is expected to transfer primary responsibility for novel food assessments to the European Food Safety Authority. The Secretariat estimated that this would not occur before mid-2015. The Committee sought an assurance from the Secretariat that it would be able to influence any future changes to the remit of the Committee and the Secretariat assured the Committee that it would be consulted before any changes were made.

The Committee agreed to continue to undertake horizon scanning on a regular basis, both in its routine meetings and in dedicated workshops.

The Committee acknowledged the comment in the report about the wide-ranging nature of its work and that discussions were weakened if members were absent when a given topic was discussed that called for their expertise. However, Members questioned whether the turnout was low compared with other similar committees. Expert members tended to be busy and in high demand. It put

forward suggestions for increasing participation in discussions for example by the use of teleconferencing for specific agenda items.

Action: the Secretariat will draft a response to the review to be considered by the Committee

5. Gamma Cyclodextrin ACNFP/105/2

The Committee had reviewed additional information from the applicant on a number of occasions over the last 2 years but had retained its concerns regarding the potential for this ingredient to interact with fat-soluble vitamins and to interfere with their absorption.

After receiving a further response from the applicant it was agreed that the Secretariat should seek a view from officials in the Department of Health (DH) as to whether gamma cyclodextrin is likely, in practice, to cause a significant reduction in the uptake of vitamin D, particularly amongst "at risk" individuals. DH officials had referred the question to the Chair of the Scientific Advisory Committee on Nutrition (SACN) and, in the light of her conclusions, the Committee agreed that the potential to interfere with the absorption of fat soluble vitamins was minimal. The Committee did, however, highlight the general issue of vitamin D deficiency and the potential effect of dietary factors on the uptake of fat soluble vitamins, and suggested that this should be the subject of additional research.

Action Secretariat to inform the European Commission that the Agency's concerns in relation to the safety of gamma cyclodextrin have now been addressed and draft a response for the Chair to send to the Chair of SACN.

6. DHA Rich Oil from the Microalgae *Schizochytrium sp.* ACNFP/105/3

The Committee considered this application for an opinion on substantial equivalence at its meeting in November 2011 and requested additional information in relation to the taxonomic classification of the source material. Members also queried whether the observed variation in the composition of the oil was consistent with that seen in the comparator oil and requested additional information on the methods of analysis used.

The Committee was satisfied that the response from the applicant addressed their concerns, noting that the observed differences in the composition of the oil would not affect its safety. It agreed the text of a draft opinion, subject to minor amendments.

Action: the Secretariat will clear the initial opinion through Chairman's action and issue it for public consultation.

7. Chia Seed (Additional Use) ACNFP105/4

A draft initial opinion for the extension of use of these seeds was reviewed by post during summer 2011. Members had a small number of comments on the text of the draft opinion but raised concerns in relation to potential allergenicity and the effect of the more widespread use of chia seeds on consumer choice for those individuals who are, or may be, allergic to the seeds.

The Committee considered an updated draft opinion which was agreed with minor amendment. The Committee also requested that, once authorised, the FSA would highlight the potential for chia seeds to cause allergic reactions with allergy clinics and allergy support groups.

Action: Secretariat will clear the initial opinion through Chairman's action prior to a public consultation

8. Clostridium butyricum MIYARI 588 ACNFP/105/5

The Committee was asked to consider an application from the Japanese company Miyarisian Pharmaceutical Co. Ltd to the UK competent authority for the approval of *Clostridium butyricum* as a probiotic food supplement under the novel foods regulation (EC) No258/97.

Andrew Chesson and Paul Brantom informed the Committee they had been members of EFSA's FEEDAP Panel which issued favorable opinions on the use of this strain of

Clostridium butyricum as a feed additive in 2009 and 2011. The Committee agreed that this did not prevent them from taking part in this item.

The Committee considered this item in two parts 1) the intrinsic safety of the strain CBM 588 and 2) whether the production process provided sufficient reassurance to guarantee the safety of individual batches of CBM 588 supplements. .

Relating to the intrinsic safety of CBM 588, Members emphasised the need for genome sequence data in comparison to other related species and strains of Clostridium, particularly because some strains of *C. butyricum* can produce neurotoxins. The Committee requested a comprehensive bioinformatics analyses to ensure that there are no functional or partial virulence genes present in CBM 588. Members regarded the PCR studies supplied in the applicant's dossier as somewhat outdated and limited by the probes used in the assays, therefore not providing a definitive answer with regard to the presence or absence of relevant genes.

The Committee questioned the impact of CBM 588 on the composition and activities of the host microbiota and requested clarification from the applicant on whether existing evidence allowed such effects to be predicted in humans. Further information was considered necessary to rule out possible detrimental effects.

The Committee questioned the potential for effects of CBM 588 on the host immune system and gut epithelium in humans and noted that the dossier does not address this issue.

The Committee also raised the possibility of gene transfer events resulting in acquisition of toxin genes from related *Clostridium* strains and species, either during production, or in the human intestine and, although this may be considered unlikely, Members requested that this point be addressed by the applicant.

The Committee also reviewed whether quality control procedures employed during production are adequate to ensure the safety of individual batches of the novel ingredient but did not request any further information for the time being.

Members commented that surveys show a low incidence of *Clostridium butyricum* in the gut. As CBM 588 is a soil isolate the Committee did not consider it would colonise the gut.

The Committee noted that *Clostridium butyricum* was first marketed as a pharmaceutical in Japan and is also viewed as a pharmaceutical in the United States. It is widely used as a supplement in animal feed to help weight gain. The Committee recommended allergy labelling as lactose would be present in the probiotic.

Action: The Secretariat to ask the applicant for more information.

9. Calanus Oil ACNFP/105/6

The Committee was asked to consider an application from the Norwegian company, Calanus AS to the UK competent authority for the approval to market oil from the miniature shrimp *Calanus finmarchicus* as a novel food ingredient.

The Committee noted a human study in which a number of subjects appeared to suffer gastrointestinal side effects that may be due to the composition of the oil, which is predominantly wax esters that cannot be metabolised by mammals. The Committee also queried whether the presence of fatty acids as wax esters meant that the oil may have limited effectiveness as a dietary source of DHA, when compared to existing sources (other marine oils, algal oil).

The Committee sought information about the levels of dioxins present in the oil and queried the sensitivity of the protein analysis that had been carried out and the allergenic potential of the oil. The Committee also noted the potential for seasonal variations (the 'red tide effect') which, if *C. finmarchicus* is harvested throughout the year, may give rise to variability in the composition of the oil.

Action: the Secretariat to ask the applicant for more information

10. New Techniques of Genetic Modification ACNFP/105/7

The Committee was asked to consider the final report of an EU working group (WG) that was set up to address the question of whether some new plant breeding techniques result in a genetically modified organism (GMO). The WG was made up of experts from the Competent Authorities (CAs) responsible for Directive 2001/18/EC (environmental release of GMOs) and Directive 2009/41/EC (contained use of GMOs) as these Directives contain the relevant definitions of a GMO. Defra and the Health and Safety Executive are the CAs responsible for these Directives in the UK.

The Committee found the report difficult to interpret as the terms used to report departures from the consensus opinion were ambiguous and the scientific conclusions were therefore difficult to understand. However, the central criterion applied by the WG appeared to be that a technique met the definition of genetic modification if it resulted in a heritable change in the genome. The Committee noted that the mandate of the working group was to interpret the definition of a GMO in relation to the terminology used in the legislation, rather than in relation to safety considerations.

Members commented that GMOs can be regulated either according to the process by which they are produced, or in relation to the characteristics of the end product. The current EU approach is to regulate GMOs by process, although it would be preferable to regulate GMOs by product characteristics and the EU should be encouraged to move in this direction.

These comments will be sent to the ACRE secretariat in Defra for consideration at their next meeting, when the WG report will be considered in detail. ACRE, the Advisory Committee for Releases to the Environment, provides independent scientific advice to Defra on environmental issues related to GMOs.

Open Event ACNFP/105/8

The Committee was asked to consider a summary of the feedback from attendees of an Open Event which took place in November 2011.

In the light of this feedback, the Committee will consider improvements when deciding on the format of the next open event.

12. Items for Information:

12.1 EU Update ACNFP/105/9

12.2 Update on Scientific Advisory Committees (SACs) ACNFP/105/10

The Secretariat agreed to include the Food Standards Agency's Consumer Advisory Panel in future updates on SACs.

12. Any other business

The Committee was invited to suggest topics for the next horizon scanning workshop.

13. Date of next meeting

The next meeting was scheduled for Thursday 26 April 2012 in Aviation House.

(b) Minutes of 106th meeting (April 2012)

1. Minutes of the 105th meeting **DRAFT/ACNFP/105/Min**

The Committee agreed, subject to minor amendments, that the minutes were a true record of the 105th meeting of the ACNFP held on Wednesday 15 February 2012

2. Matters Arising

The Secretariat reported on the actions following the previous meeting:

3. Clostridium butyricum MIYARI 588 **ACNFP/106/1**

The Committee first reviewed this application at its meeting in February 2012. The Committee considered the response from the applicant to a number of concerns raised by the Committee at that meeting. Members noted that, in the applicant's response, the genome sequence is described as a draft and appears to be incomplete. In order to demonstrate the absence of toxin genes Members stated that it is essential to know the proportion of the genome that has been sequenced and what percentage of open reading frames are likely to have been identified, to rule out the possibility that unidentified open reading frames may encode virulence factors.

The Committee mentioned that at the previous meeting it had requested a bioinformatics analyses, of the open reading frames, giving predicted gene functions including any that have some homology to toxin sequences, but no summary of toxin gene distribution across *Clostridium* strains was provided. Members emphasised that it would be useful to see a table listing what are regarded as virulence genes, particularly in the closely related pathogenic strains of *C. butyricum*, and confirming that they are not detected in strain CBM588.

The Committee noted that several antibiotic resistance genes have been identified from the data provided so far and the genome sequence suggests there may still be others. The Committee asked what evidence is available to support the applicant's conclusion that all these resistance genes were non-functional and noted that, even if these genes are non-functional in CBM588, there is still a possibility that they could be transferred to other bacteria where they may be functional. The Committee was content with the toxicity data.

The Committee advised that the applicant's response did not fully answer its previous concerns about the novel ingredient's impact on the host microbiota, its effects on immune functions and host epithelium and the possibility of gene transfer from pathogenic Clostridia. Although they had no further questions at this time, they would consider this issue again if the applicant had any further data.

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

4. Isomalto-oligosaccharides **ACNFP/106/2**

The Committee considered this application at its meeting in February 2009. The Committee considered the response from the applicant to concerns raised by the Committee in 2009.

The Committee thanked the applicant for the time and effort it had put into carrying out a human study to answer the questions raised in 2009.

The Committee agreed that the study data provided reassurance about human tolerance. However, the Committee identified inconsistencies between these new data relating to glucose/insulin responses to this product, its stated composition, its energy value and information on the extent of absorption. Members noted that data from the human study showed that the novel ingredient and glucose placebo showed similar glycaemic responses, which was inconsistent with other data that demonstrated that 70% of the novel ingredient was resistant to digestion. The Committee requested clarification on these inconsistencies. Based on the data provided, the Committee doubted that the novel ingredient could function as a prebiotic. Members were therefore concerned that there is a potential to mislead consumers into thinking that this is a low energy prebiotic, although this assertion was not supported by the clinical data.

The Committee recommended wheat starch be included on the label of foods containing this novel ingredient.

Action: the Secretariat to ask for additional information from the applicant and draft an initial opinion for consideration at the next meeting.

5. Methyl Cellulose — ACNFP/106/3

The Committee was asked to consider a new full application from the Swiss company Dow Wolff Cellulosics for the approval of methyl cellulose as a novel ingredient.

The novel ingredient is already approved as a food additive (E461). The applicant now intends to incorporate methylcellulose into a range of foods to function as a dietary fibre to promote satiety.

The Committee noted that the fermentability of native cellulose in the human large intestine ranges from <6% (for highly crystalline purified cellulose) to around 70% for more amorphous cellulose that is present in normal diets. The applicant gave no indication as to where methyl cellulose falls within this range. The Committee requested experimental evidence of the fermentability of methyl cellulose to aid its assessment as a novel ingredient. The Committee also requested evidence for the applicant's references to satiety, as methylcellulose had no apparent effect on feed intake in the animal feeding studies.

The Committee was generally content with the data provided in the dossier on microbiology, toxicology and allergenicity but questioned the relevance of some of the data on methylcellulose analogues and how these substances relate to the novel ingredient that is to be marketed by the applicant.

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

6. Vitamin D enriched yeast product — ACNFP106/4

The Committee was asked to consider an application from the Canadian company Lallemand for the approval of a Vitamin D enriched yeast product. The novel ingredient is to be marketed as a baker's

yeast which has been subjected to ultraviolet (UV) treatment to enhance the levels of vitamin D2. The baker's yeast will be marketed primarily for use in baking and food supplements.

The Committee noted the current interest in vitamin D fortification, which might enable vulnerable groups (elderly people and pregnant women) to meet the daily requirement of 10mg/day for vitamin D intake.

The Committee noted that the enriched yeast product was produced by a non sterile process, which appeared to be the case for all bakers yeast and noted that the novel UV-treated yeast has been scrutinised by the Food and Drug Administration in the USA.

The Committee noted that UV irradiation *per se* could induce genetic changes or damage, but accepted that this effect of UV was not a cause for concern in this case. Members did, however, note that the methods employed by the applicant to identify mutants were outdated and more sensitive methods were now available.

The Committee considered whether tachysterol, a sterol produced in small quantities during the UV treatment, could intervene with vitamin D absorption. The applicant had provided evidence that tachysterol was inert, based on its presence following photochemical reactions in the skin, and the Committee sought reassurance that tachysterol was similarly inert if consumed orally.

Action: Secretariat to request further information from the applicant and draft an initial opinion for consideration at the next meeting.

7. Methyltetrahydrofolic acid, Glucosamine salt — ACNFP/106/5

The Committee was asked to review the Irish Competent Authority's favourable initial opinion on an application for authorization of the glucosamine salt of methyltetrahydrofolic acid, to be used as a source of folate in food supplements.

The Committee agreed with the Irish assessment of this product and noted that there has been considerable discussion and debate about the need for, and levels of, folate supplementation and about the possibility of a link with colorectal cancer. However, the Committee concluded that there are no special issues arising from the use of this particular salt, which would be subject to the same recommendations and controls as the existing sources of folate that it might replace.

Action: The Committee's comments will form the basis of the UK's formal response to the Irish initial opinion

8. Exposure estimation of novel foods — ACNFP/106/6

The question of how best to estimate the potential intake of novel ingredients has been raised on a number of occasions. The Secretariat had recently discussed this with the Secretariats of SACN and other committees with an interest (SSRC and GACS)[8] and had prepared an overview of the current approaches to intake estimation of novel ingredients.

[8] SACN: Scientific Advisory Committee on Nutrition;
SSRC: Social Science Research Committee;
GACS: General Advisory Committee on Science

The Committee considered that this was a useful paper which clarified the way that estimates are prepared in different scenarios, including new sources of existing ingredients and combined intake of ingredients from supplements and from foods. Members noted that it is difficult for consumers to monitor their total intake of novel ingredients that are added to multiple foods.

The Secretariat pointed out that prospective intake estimates are typically based on "worst-case" scenarios where a novel ingredient is assumed to be present in all the relevant foods at the maximum level. This provides an element of conservatism in the risk assessment and does not require individual consumers to track their consumption. In the case of phytosterols, the potential for consumers to exceed the desirable intake was identified in the original assessment and post-market monitoring was undertaken by the applicant and by some national authorities to confirm whether the resulting intake was in the acceptable range.

The Committee was concerned that knowledge of background levels of consumption of nutrients was insufficient to determine the total levels consumed from both existing and novel sources. Another issue that might require further attention was the combined intake of ingredients that have a different composition but similar biological effects, such as novel carbohydrates.

The Committee made suggestions for improving the way estimates are presented, focusing on uncertainties and background intake from the diet. Uncertainties included the tendency for under-reporting of food consumption, the under-representation of some population groups in national surveys (e.g. pregnant women and ethnic minorities), the possibility that foods formulated with novel ingredients might be consumed in different amounts to their existing counterparts and potential co-consumption of food supplements and foods supplemented with the same ingredients.

The Committee was informed that the European Food Safety Authority (EFSA) has published an opinion on identifying and reporting uncertainties in different types of intake assessments[9]. It was suggested that this approach might be helpful when assessing future novel food applications.

Action: The Secretariat will present the Committee's comments to SACN at their meeting on 12 June and report back to ACNFP on 4 July.

9. Items for Information

10.1 EU Update **ACNFP/106/7**

10.2 Update on Scientific Advisory Committees (SACs) **ACNFP/106/8**

The Chair gave a report on the GACS meeting which took place on 14 March. The meeting considered the ACNFP's response to its independent review and held a discussion on folic acid supplementation.

Jayam Dalal reported on a Consumer Advisory Panel meeting which took place on 17 April and a workshop on a Capability Review of the FSA which took place on 25 April.

[9] EFSA (2008) "Guidance of the Scientific Committee on a request from EFSA related to Uncertainties in Dietary Exposure Assessment"; EFSA Journal (2006) 438, 1-54; http://www.efsa.europa.eu/en/efsajournal/pub/438.htm

10. Any other business

Members were asked for views on their preferred route for circulating electronic copies of meeting papers. The Secretariat agreed to email as many documents as possible for the July meeting and will continue to monitor other committees' experience with web-based systems.

The Committee was given an update on the forthcoming appointment process to replace Members whose appointments end in the second half of the year.

11. Date of next meeting

The next meeting was scheduled for Wednesday 4 July 2012 in Aviation House.

(c) Minutes of 107th Meeting (September2012)

1. Minutes of the 106th meeting; Matters Arising and Postal Consultations **DRAFT/ACNFP/106/Min**

The Committee adopted the minutes of the 106th meeting, which had previously been circulated for comment by post.

The Secretariat reported on the following items which the Committee considered by post during July and August:

(a) UV Treated baker's yeast **ACNFP/107/P1**

This paper presented the applicant's response to concerns raised at the April meeting regarding the low level presence of tachysterol and also invited comments on a draft initial opinion.

Members reviewed the responses from the applicant and were satisfied that the levels of tachysterol in the novel ingredient were very low, equating to a maximum of 2.7µg tachysterol per day. Members noted that this level of exposure is below EFSA's threshold of toxicological concern[10] and no further questions were raised.

Members also agreed the text of the draft opinion, which was published on the ACNFP website on 6 August for the usual 10 day public consultation. Seven public comments were received and it was agreed through Chairman's action that none was substantive in terms of raising additional safety concerns.

The UK's initial opinion on the safety of this yeast was sent to the Commission on 31 Aug and would be available on the ACNFP website in the near future.

(b) Methylcellulose **ACNFP/107/P2**

This paper presented the applicant's response to questions raised at the April meeting regarding the extent to which methylcellulose is fermented in the large intestine, the relevance of data supplied on related compounds and the applicant's references to satiety. Members were also invited to comment on a draft opinion.

Members were satisfied with the applicant's responses to all questions raised and concluded that there were no safety concerns.

Members also agreed the text of the draft opinion and this was published on the ACNFP website on 16 August for the usual 10-day public consultation. Three public comments were received and it was agreed through Chairman's action that none was substantive in terms of raising additional safety concerns. The UK's initial opinion on the safety of methylcellulose would be sent to the European Commission very shortly.

[10] http://www.efsa.europa.eu/en/consultationsclosed/call/110712a.htm

(c) Isomaltooligosaccharide **ACNFP/107/P3**

(see Item 5 below)

(d) Citicoline **ACNFP/107/P4**

Members considered a positive initial opinion from the Irish authorities on citicoline (choline cytidine 5'-pyrophosphate) as a novel food ingredient.

Members noted that the minimum purity of the ingredient is 98% and that the applicant had not considered the safety of the other unnamed secondary components which will be present in the final product. Members also agreed that the non specific UV absorbance assay employed by the applicant was insufficiently accurate or specific for quality control purposes and should be replaced by an alternative analytical method. Members also highlighted absence of stability data for the product in food matrices and concerns about interactions with the human dopaminergic system.

As citicoline is approved elsewhere in the world as a pharmaceutical product, the Agency contacted the Medicines and Healthcare products Regulatory Agency who indicated that products containing citicoline would probably be considered medicinal in the UK. (This may not be the case in all EU member states as the determination of medicinal status is made at the level of individual national authorities).

The UK's response, which highlighted each of these concerns, was sent to the European Commission on 7 September.

The Secretariat also reported on one further item arising from the 106th meeting (april 2012):

Item 8: methyltetrahydrofolic acid, glucosamine salt

In line with the Committee's advice, the Food Standards Agency wrote to the Commission on 27 April, registering the UK's support for the favourable opinion of the Irish authorities. The applicant was currently responding to questions and concerns that were raised by other Member States.

2. Clostridium butyricum MIYARI 588 **ACNFP/107/1**

The Committee first reviewed this application at its meetings in February 2012 and April 2012. The Committee considered the response from the applicant to a number of concerns raised by the Committee.

Andrew Chesson informed the Committee he had been a member of EFSA's FEEDAP Panel which issued favorable opinions on the use of this strain of *Clostridium butyricum* as a feed additive in 2009 and 2011. The Committee agreed that this did not prevent him from taking part in this item.

The Committee found the data regarding antibiotic resistance and the associated discussion provided by the applicant to be convincing and no further information was requested on this point.

The Committee stated that, based on the history of use of this novel ingredient since the 1960s in Japan and previous authorisations as a feed additive in the EU, it appears highly unlikely that this particular strain of *Clostridium butyricum* is pathogenic. However, the Committee emphasized that a particularly cautious approach to assessment is required, given that this is the first live microorganism to be assessed as a novel ingredient, and given that some other members of this genus and species are well known pathogens.

The Committee expressed its gratitude to the applicant for providing additional information on the genome sequence but asked to view the full dataset for the sequencing exercise. The Committee requested that the applicant provide quantitative homology information for the bioinformatic comparison with the other clostridial genomic sequences, for all of the ORFs (open reading frames). Specifically, the Committee would like to review the percentage sequence identity and the associated amino acid overlap data so that an independent risk assessment can be made.

Since the novel ingredient has been marketed in Japan since the 1960s, the Committee asked to review any post market monitoring data that may be available to demonstrate the absence of adverse effects.

The Committee discussed the issue of horizontal gene transfer of chromosomally located genes (antibiotic resistance), either from CBM 588 to other gut bacteria or vice versa, and concluded that virtually all bacteria possess genes encoding antibiotic resistance and no further information need be requested on this point.

The Committee discussed the presence of the putative genes for fibronectin and two types of haemolysin in the genome of CBM 588, exploring the possibility that these genes may be expressed under certain conditions. The Committee agreed that no further information could be requested on this point.

The Secretariat agreed to draft an opinion for the next meeting.

Action: The Secretariat to ask for additional information from the applicant and draft an opinion

3. Isomalto-oligosaccharides ACNFP/107/2

The Committee considered this application at its meetings in February 2009 and April 2012, and by post in July 2012. It reviewed a draft opinion and considered the response from the applicant to the outstanding concerns raised by the Committee in the recent postal consultation.

The Committee concluded that there were no safety concerns relating to this novel ingredient, provided that it is labelled as unsuitable for diabetics. However, based on the data provided by the

applicant, the Committee was not convinced that this product has a significantly reduced energy content compared with other (digestible) carbohydrates.

The Committee noted that there are conflicting data on the digestibility of IMO preparations. However, the most recent clinical study, which was conducted with the applicant's product, showed that plasma glucose and insulin responses were very similar to those for glucose, which suggests that this product is well digested in the small intestine.

The Committee agreed the text of the initial opinion, subject to certain amendments to reflect its final position.

Action: the Secretariat to undertake a public consultation on the draft initial opinion following clearance by the Committee.

4. Coriander Seed Oil — ACNFP/107/3

In September 2011 the Committee had reviewed a favourable initial opinion from the Irish Competent Authority on an application for coriander seed oil (CSO) as a novel ingredient, and had raised some concerns.

The Committee reviewed this application and favourable Irish opinion in November 2011 and raised questions relating to the metabolism of the petroselenic acid constituent of CSO and its impact on the metabolism of other fatty acids. The Committee also requested a more sensitive protein assay method to confirm the absence of protein in CSO.

The applicant had provided responses to all the questions and objections from member states, including those raised by the ACNFP. The Committee was content that the applicant had provided suitable reassurance relating to its concerns about petroselenic acid. The Committee did however, request clarification on the way that new data were presented in Table A of the applicant's response.

The Committee was content with the new spectrophotometric assay method that the applicant used to confirm the absence of detectable protein and no further information was requested.

5. Bovine Lactoferrin — ACNFP/107/4

The Committee was asked to consider two EFSA opinions on two applications for the authorisation of bovine lactoferrin as a novel food ingredient. The Committee had previously reviewed initial opinions for the authorisation of two bovine lactoferrin ingredients from the Belgium Competent Authority (2008) and the Dutch Competent Authority (2010).

The Committee regarded the EFSA opinions to have addressed the majority of its concerns regarding bovine lactoferrin. However the Committee noted that EFSA had not investigated whether bovine lactoferrin could reduce iron bioavailability, given its reduced affinity with human intestinal receptors and increased resistance to digestion. Although this concern was raised when the Committee reviewed an earlier Belgian opinion on bovine lactoferrin in 2008 the Secretariat noted

that this first application had subsequently stalled and it was possible that this point had not been transmitted to EFSA when the Committee asked for opinions on the two subsequent applications.

Although it did not address the potential for bovine lactoferrin to reduce iron bioavailability in individuals with marginal iron status, the Committee noted that the EFSA opinions had addressed a question from another member state about whether the introduction of lactoferrin into the diet may lead to an increase in iron availability. The Committee therefore suggested that the Secretariat contact a UK specialist in iron metabolism for an expert view on the likelihood that iron bioavailability might be substantively reduced by bovine lactoferrin and on the implications that this might have for UK consumers.

Action: Secretariat to seek advice from an expert in iron metabolism

6. Intake estimation of novel foods **ACNFP/107/5**

The Secretariat informed the Committee that its earlier discussions on uncertainties in intake estimation had been reported to the Scientific Advisory Committee on Nutrition (SACN), who had asked to be kept updated. The Committee noted this paper and will return to the topic at a future date.

Action: The Secretariat to keep SACN updated

7. Plants developed through cisgenesis and intragenesis **ACNFP/107/6**

The Committee considered an opinion from EFSA's GMO Panel concerning the risk assessment of plants developed through cis- and trans-genesis. Andrew Chesson informed the Committee that, as a Member of EFSA's GMO Panel, he would be joining the New Techniques Panel that EFSA has convened to review seven new techniques designed to manipulate the genome of plants, including cisgenesis and intragenesis.

The Committee did not agree that the risks associated with cisgenic and conventionally bred plants were the same. Transposition of endogenous genes or the addition of endogenous gene copies can alter expression levels or the timing, developmental stage or tissue specificity of gene expression. There is therefore a need to characterize the DNA sequences at the point of insertion, including the flanking regions. The Committee concluded that there was a need to look at new products produced by these new techniques on a case by case basis and that the emphasis should be on the end product and not the technology by which it is produced.

8. **Items for Information**

9.1 EU Update **ACNFP/107/8**

9.2 Update on Scientific Advisory Committees (SACs) **ACNFP/107/9**

The Committee noted these two information papers without comment.

9.3 Health Claims **ACNFP/107/10**

Vivien Lund from the Department of Health introduced this paper, which summarized the situation regarding the assessment and authorisation of health and nutrition claims in the EU. Members noted that discussions were taking place about procedures for reviewing herbal products and advised that the process should be capable of picking up potential adverse effects, which could be severe for some herbal products.

9. Any other business

Members welcomed the recent electronic circulation of Committee papers. The Secretariat will continue to circulate papers both electronically and by hard copy.

As this would be her last attendance at a Committee meeting before retiring from the ACNFP at the end of the year, the Committee thanked Jayam Dalal for her work on the Committee and for representing it on the FSA's consumer panels.

The Committee received a report of the most recent meeting of the FSA's Consumer Advisory Panel, which took place on 24 July. The Secretariat agreed to pass on concerns that a large majority of people allergic to cows milk were also allergic to goats milk, which is being marketed as suitable for people with cows milk allergy.

10. Date of next meeting

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

(d) Minutes of 108h meeting (Nov 2012)

1. Minutes of the 107th meeting; DRAFT/ACNFP/107/Min

The Committee agreed that the minutes were a true record of the 107th meeting of the ACNFP held on Wednesday19 September 2012

2. Matters Arising and Postal Consultations

The Secretariat reported on Item 6 Bovine Lactoferrin **ACNFP 107/4** which the Committee considered at its meeting on 19 September. At the request of the Committee the Secretariat had contacted a UK specialist in iron metabolism. The specialist confirmed the consumption of boveine lactoferrin would not lead to a reduction in iron bioavailability.

3. Clostridium butyricum MIYARI 588 ACNFP/108/1

The Committee reviewed this application at its meetings in throughout 2012. The Committee considered the response from the applicant to the remaining questions raised by the Committee.

Andrew Chesson informed the Committee he had been a member of EFSA's FEEDAP Panel which issued favorable opinions on the use of this strain of *Clostridium butyricum* as an animal feed additive in 2009 and 2011. The Committee agreed that this did not prevent him from taking part in this item.

The Committee considered further information provided by the applicant relating to the genome sequence and bioinformatics data and was content that all its questions had been addressed.

The Committee asked for further information on the small number of suspected adverse effects reported during post market monitoring in Japan and requested details on the applicant's rationale for concluding that none of these were related to CBM 588 consumption.

The Committee discussed further the issue of horizontal gene transfer in the gut in relation to antibiotic resistance genes, but concluded that the risk of transfer of chromosomally-encoded genes is low, and in the context of the gut environment where genes are continually being swapped back and forth between bacteria, the presence of such genes CBM 588 would be of little significance.

The Committee asked for it to be noted a positive opinion on the use of this organism would not imply endorsement of any health benefits attributed to its consumption.

The draft opinion will be amended to address the Committees concerns.

Action: The Secretariat will incorporate the Committee's suggestions into the draft opinion to discuss at the next

4. DHA and EPA-Rich Algal Oil – Extension of use **ACNFP/108/2**

The Committee was asked to consider an application, from DSM Nutritional Products to the UK competent authority, to extend the existing authorisation of a DHA and EPA rich algal oil from the microalgae *Schizochytrium sp* under the novel foods regulation (EC) No258/97.

The applicant proposes that the use be extended to a high dose supplements (3000mg) and cited a recent EFSA opinion which established a 5g/day tolerable upper limit for DHA and EPA in support of the request. The Committee was broadly content with the request but questioned whether the 5g/day figure applied to children and, if not, asked the applicant for reassurance that the high dose supplements would not be targeted at children.

Action: the Secretariat to contact EFSA regarding the 5g/day limit and for the applicant's response, together with any comments from a public consultation, to be considered at the next meeting.

5. Chia Oil **ACNFP/108/3**

The Committee was asked to consider an application, from Functional Products Trading SA to the UK competent authority, to market Chia oil as a novel food ingredient for use as a supplement, in culinary oils, and in a limited range of cold beverages.

The Committee highlighted a number of contradictions in the manufacturing process descriptions and sought additional information about the propensity of the oil to oxidise, noting that one description referred to the additional of tocopherol.

The Committee also queried, whether any animals died during the acute toxicity study and sought an explanation for the observed changes in body weight in another study.

The Committee also queried the level of protein that would be typically be seen in the oil and whether the proposed uses, which included food categories which do not typically contain edible oil, may give rise to increased rate of allergy.

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

5. D-Ribose **ACNFP/108/4**

The Committee was given a summary of previous committee discussions which took place during 2008 when it requested a repeat study on the developmental effects of D-Ribose in rats. The Committee considered a small group of expert ACNFP members should be set up to review this application and to report back to the Committee.

Action: Secretariat to set up a small working group of expert members.

6. Rapeseed Protein **ACNFP/108/5**

The Committee reviewed the favourable 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 did not agree with the favourable opinion of the Irish Competent Authority on the novel food ingredient.

The Committee commented there was no history of consumption of rapeseed. The applicant had provided information on the amino acid present in their product but, to be able to evaluate the risk, the Committee expected to see analytical data on the protein composition obtained by HPLC.

.The Committee expressed significant concern that mustard allergic individuals would also be allergic to rapeseed protein. In the UK mustard is not a very prevalent allergen, but certain European countries, particularly France, have a high level of mustard allergies. The Committee was concerned about the allergy implications should this ingredient be authorised to be added at high levels to a range of different foods. The Committee concluded that unless the applicant can provide evidence to demonstrate a lack of cross-reactivity between their product and mustard allergens, it was unable to agree with the Irish favourable assessment.

The Committee considered the intake figures supplied in the dossier were vague. The Committee also stated that it would have liked to have seen more information on phytate levels and micronutrient absorption.

Action: Secretariat to forward the Committee's concerns to the European Commission

7. Nattokinase **ACNFP/108/6**

The Committee reviewed the unfavourable initial opinion of the Belgium Competent Authority on an application for the use of nattokinase in food supplements.

The Committee agreed with the Belgium Competent Authority that the product should not be authorised and noted the view from the UK Medicines and Healthcare Products Regulatory Agency that, unlike the Belgian Authority, the use of the product would not be regarded to be medicinal in the UK.

The Committee's concerns regarding the safety of nattokinase related to a lack of safety data, in particular its potential enzymic effect in the GI tract. Members noted that, despite its name, nattokinase is not a kinase but a protease enzyme and that its effect , for example, mucous membranes needed to be investigated thoroughly.

Action: The Secretariat to forward the Committee's concerns to the European Commission

8. ACNFP Advice **ACNFP/108/7**

The Committee was given an update on how its advice is used in discussions between Member States in relation on authorisation of novel foods, which was previously summarized at its November

2010 and September 2011 meetings. The update included all applications the Committee had advised on since September 2011.

The Committee welcomed the paper and thanked the Secretariat for producing it. It asked for additional information to be included in future updates regarding the purpose of each ingredient for example "as a form of fibre"

Action: Secretariat to include additional information requested by the Committee

9. **Items for Information**

10.1 EU Update **ACNFP/108/8**

10.2 Update on Scientific Advisory Committees (SACs) **ACNFP/108/9**

10.3 The Effect of Feeding GM Maize NK603 on Rats **ACNFP/108/10**

The Committee noted the information papers without comment.

Andrew Chesson declared an interest on item 10.3 as he is a member of the European Food Safety Authority's GMO panel.

The Chair provided received an update on the most recent General Advisory Committee on Science (GACS) meeting he attended on 31 October.

The Committee received a report of the most recent meeting of the FSA's Consumer Advisory Panel, which took place on 6 November.

10. Any Other Business

Members gave the Committee positive feedback of the induction workshop held on 19 November.

11. Date of next meeting

The next meeting was scheduled for Wednesday 13 February in Aviation House.

ANNEX 3 COMMITTEE ADVICE ISSUED DURING 2012

(a) OPINION ON AN APPLICATION UNDER THE NOVEL FOOD REGULATION FOR ADDITIONAL USES OF CHIA SEED

Applicant **The Chia Company (Australia)**

262-272 Lorimer Street

Port Melborne

Vic 3207

Australia

Responsible Person **April Halliwell**

EC Classification **2.1**

1. An application has been submitted by The Chia Company (Australia) to extend the currently authorised use of chia seeds (*Salvia hispanica* L*) to include* a number of additional food products that commonly contain other seeds.

2. Chia 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 that are the subject of this application.

3. In 2009 an authorisation was issued to the Columbus Paradigm Institute S.A. for the use of whole or ground chia seeds in bread products at a maximum level of 5%. (Commission Decision 2009/827/EC). The Chia Company previously satisfied the Committee that their chia seeds are substantially equivalent to Columbus Paradigm's seeds and has gained authorisation to market their seeds for use in bread products by notifying the European Commission, in accordance with Article 5 of Regulation (EC) 258/97.[11]

I Specification of the Novel Ingredient (NI)

Dossier, pp 6-8

4. The proximate composition of the chia seeds is detailed below. This, together with information regarding the presence of contaminants such as heavy metals, was considered in the original applicant's application and again when the present applicant submitted its request for the ACNFP's opinion on equivalence. As these data were reviewed by the Committee previously they are not reproduced in detail in this opinion but are available in the dossier.

Proximal Composition

Dry Matter	91-96%
Protein	20-22%
Fat	30-35%
Carbohydrate	25-41%
Crude Fibre (*)	18-30%
Ash	4-6%

[11] The ACNFP's opinion isavailable via the Committee's website http://acnfp.food.gov.uk)

*Crude fibre is the part of the fibre made mainly from indigestible cellulose, pentosans, and lignin

Discussion *The Committee accepted that the specification of the novel ingredient did not differ from that seen in previous applications and did not therefore give cause for concern.*

II Effect of the production process applied to the NI

Dossier pp8-10

5. The applicant describes the harvest and post harvest processing in detail in the dossier. In summary, the seeds, which originated from South America, are planted into prepared seedbeds and grown until the desired biomass is reached. This is achieved with the help of satellite imagery that indicates areas of higher and lower biomass so that targeted corrective measures (addition of plant nutrients) can be taken. Plant tissue tests are also taken during the growth stage to ensure the correct nutrition levels are obtained.

6. Post-harvest, the seed head is mechanically swathed to ensure even ripening and consistent oil yield in the seed. The seeds are transported to a seed cleaning facility where they are transferred into silos for fumigation with carbon dioxide, cleaned and then packed into finished products. The seeds are not further processed prior to use as a food ingredient and specific information related to post harvest handling is provided in Appendix 9 of the dossier.

Discussion *The Committee was satisfied with the proposed method of production is controlled and the post-harvest monitoring procedures offered sufficient reassurance that the applicant could ensure the quality of the product.*

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

Dossier p10-11

7. The applicant refers to evidence of chia seeds being consumed for millennia in South America but acknowledges that that more recent 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, to Australasia and Europe. (Dossier Annex C).

8. The applicant also notes that EU authorisation is currently restricted to use in bread products at levels of up to 5% and that this is solely a reflection of the original applicant's marketing intentions. The use of chia seeds outside the EU is not restricted to bread products, a fact acknowledged by EFSA who noted that the increased worldwide use of chia seeds was a particular factor when it concluded in 2009 that the consumption of chia seeds was safe at the proposed level of use[12].

Discussion *The Committee noted that there was a substantial history of consumption of chia seeds and increasing use of the seeds elsewhere in the world*

IX Anticipated intake and extent of use of the NI

Dossier p11-16

9. The applicant intends to incorporate chia seeds into a number of food categories that commonly contain seeds and nuts. The proposed level of incorporation is based upon a Recommended Daily Intake of 2g of omega-3 fatty acids that has been set by the Australian Heart Foundation and the Food Safety Authority of Australia and New Zealand. (Dossier, Appendix 1). The applicant also proposes the marketing of pre-packed whole seeds. The proposed use categories are detailed below:

Proposed Food Uses

Proposed Category	**% Inclusion / Recommended Daily Intake**	**Chia seed Consumption per portion**
100% Packaged Chia Seed	15g Recommended intake per day	15g Chia Seed
Baked products (muffins, cookies, crackers and biscuits)	10%, 10g Chia per 100g total mix 'flour weight'	- Muffin 95g with 9.5g of Chia Seed - Cookie 40g with 4g Chia Seed - Cracker 40g with 4g Chia Seed - Biscuit 40g with 4g Chia Seed
Breakfast cereal	10%, 10g per 100g total mix	45g serving with 4.5g Chia

[12] http://www.efsa.europa.eu/en/efsajournal/pub/996.htm

		Seed
Fruit, nut and seed mixes (sprinkles)	10%, 10g per 100g total mix	45g serving with 4.5g Chia Seed

10. Data from the UK National Diet and Nutrition Survey (NDNS) have been used to estimate the likely consumption of chia for the proposed range of products, and a summary of these figures are detailed below. The applicant recognised that the 2009 EFSA opinion does not highlight any toxicological issues related to the consumption of chia seeds and that the principal concern is likely to be in relation to potential allergenicity. In view of this the applicant has not carried out a highly detailed intake assessment, confining their analysis to published summary data from the NDNS database. Mean consumption is estimated to be 13.4 g/day, based on the assumption that a consumer is an average consumer of all the relevant foods, and that all these foods contain chia seed at the maximum level. The applicant suggests that "high level" consumption might be twice this figure.

Average potential Intake of Chia seed as calculated from UK NDNS for Bread, Breakfast Cereals, Baked Goods, Nuts, Savoury Snacks, and Confectionery Food Categories

All Respondents	Mean Consumption - (grams per day)							
Product Categories	Age Groups							
	19-24	25-34	34-49	50-64	All Consumers	% All Consumers	Chia % Inclusion	Grams of Chia Consumed / Day
Bread	94.3	102.7	101.6	101.4	100.9	99%	5%	5.0
Breakfast Cereal	16.4	26.4	28.1	37.6	29.0	67%	10%	2.9
Biscuits, buns, cakes, pastries & fruit pies	19.3	28.7	33.6	41.9	33.0	84%	10%	3.3
Nuts	0.9	2.3	2.3	2.1	2.1	20%	10%	0.2
Savoury snacks	12.4	9.9	7.0	3.6	7.4	56%	10%	0.7
Confectionary	15.9	12.3	12.3	8.6	11.7	62%	10%	1.2
SUM	159.1	182.3	184.9	195.1	184.1	65%		13.4

11. The applicant suggests that these figures will overestimate the consumption of seeds as it is unlikely that individuals will confine their consumption of foods within each category to those which contain chia seeds. The Committee noted that FSA experts in food chemical intake had recently advised that high level intake at the 97.5%ile can be estimated as three times the mean value, for individual foods[13]. The officials also noted however that the approach of summing the high level exposure for each food category to give an overall figure for high level consumption

[13] Initial opinion for taxifolin, available at http://acnfp.food.gov.uk

inevitably leads to overestimation because, in practice, it would not be possible for the same individuals to be high level consumers for every food category.

12. As noted above, the applicant also intends to market chia seeds *per se* to enable consumers to add chia seeds to products at home. The applicant states that this will give consumers the option of consuming chia seeds in their own choice of (for example) breakfast cereals and bakery products and intends that the level of consumption in such products will be in line with the RDI advice detailed above. In this regard the applicant will market 100% chia seed with appropriate labelling and intake advice will be clearly visible on the packaging.

13. The applicant does not consider the resulting increase in consumption to be cause for concern and notes that the products that are the subject of this application are currently available elsewhere in the world (Dossier pp17-20). The applicant acknowledges the potential for individuals who are allergic to seeds to cross react with chia but notes that there is little evidence of this happening elsewhere in the world (see section XIII below).

Discussion *The Committee noted FSA officials' comments on the approach used by the applicant to estimate intake, and agreed that it led to a significant overestimation of likely consumption levels. Members also accepted that, while there was a requirement to estimate the likely level of consumption of any novel food, accurate intake values were of limited value for risk assessment purposes in the absence of a benchmark for the safe intake level. As reported in Section XIII (below) the arguments in support of extending the range of food categories are largely based on the evidence of safe (non-EU) food use. In view of this approach, the Committee accepted that the provision of more extensive intake information would not significantly add to that already presented in support of the safety of the seeds. The Committee also noted that food consumption can be systematically under-reported in dietary surveys, including the NDNS, and there are no accepted methods of correcting for this.*

The Committee also highlighted that the proposed food categories are products that would typically include products that contain other seeds, which is important when assessing the potential risk of cross-reactivity in people with existing food allergies (see below).

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

Dossier p16-24

14. The applicant has provided a detailed review of chia-containing products that are on the market in non-EU countries, many of which are similar to those that are the subject of this application. The range of products is relatively large although it is not known how widely consumed each of these products is. Nevertheless, the relatively large number of newly launched products indicates increasing exposure to the seeds.

15. The applicant also notes that a number of products are being stocked by pan-Australian and New Zealand grocery chains and also cites data from the Australian Bureau of Statistics that, on a population basis, 30g of chia seeds were consumed by every Australia citizen during the 'last financial year'. (The applicant also mentions allergenic potential in this part of the dossier and this issue is considered in Section XIII below).

Discussion *The Committee noted that chia was becoming available in a wider range of products outside the EU, although the extent to which the seeds were consumed was not clear.*

XI Nutritional information on the novel food

Dossier p24-26

16. The applicant provides a detailed breakdown of the nutritional composition of the seed which is 20% protein and approximately one third fat, of which 80% is alpha-linoleic acid. The applicant contends that, as the seed is relatively rich in alpha-linoleic acid, it provides an important source of omega-3 fatty acids which are perceived to have health and nutritional benefits. The detailed nutritional profile can be found in the dossier (p24-25 and Appendix 2).

Discussion

The Committee observed that the omega-3 fatty acids in chia seed are in the form of alpha-linoleic acid, a nutritionally essential fatty acid that is required for synthesis of important fatty acids and eicosanoids, which has a different function to the long chain omega-3 fatty acids that are found in certain other foods e.g. in fish oils.

The Committee's assessment focuses on safety and labelling, 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 p26-27

17. The applicant's chia seeds are routinely tested for the presence of a range of microorganisms and mycotoxins. The results of these analyses, which were also reviewed as part of the applicant's earlier request for an opinion on equivalence and are not reproduced here, show only low levels of microbial contamination. According to the applicant the results are in compliance with relevant EU legislation.

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

XIII Toxicological information

Dossier p27-29

18. The applicant does not present any safety studies that have been carried out on their seeds. The lack of toxicological studies is consistent with the original 2003 dossier. EFSA has noted that the data were limited but has concluded that ''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' (See footnote 2).

19. The applicant refers to a study carried out to determine whether chia seeds have any effect on the immune system in Wistar rats. The results of this study were presented at a Workshop on Immunonutrition in 2008 and are reported in a Nutritional Society Proceedings publication, and do not give any indication that consumption of the seeds affected body weight, thymus weight, thymocyte number, and IgE levels when compared with controls.

Discussion *The Committee accepted that, given the nature of the ingredient, the use outside the EU and the views of EFSA then there was scope for the applicant to extend the use categories without provision of additional safety studies. Members agreed that increased consumption of the seeds did not give cause for toxicological concern.*

Allergenicity and Labelling

20. In line with the conditions attached to the original authorisation, any products containing chia seeds will be clearly labelled as such. As noted above, there is a possibility that existing seed allergic individuals will cross react with chia seeds. The applicant acknowledges this concern and points out that the proposed food products are likely to also contain other seeds and nuts, so that such individuals would routinely avoid consuming them.

21. The applicant has approached a number of organisations in Australia and the US[14] to determine whether the increased marketing of the seeds has coincided with an increase in reports of allergy to chia. None of these organisations was aware of any reports of allergy to chia seeds, either in existing seed allergic individuals or otherwise (Dossier, Appendices 3, 4, 5 & 8). The applicant notes that this is not necessarily because chia is less allergenic than any other seeds, as it could be due to appropriate risk management strategies, such as clear labelling and incorporation of chia seeds into products that are already associated with seeds (including the

[14] Anaphylaxis Australia, Food Allergy and Anaphylaxis Network (US), Allergy Bureau of Australia, Asthma and Allergy Foundation of America

sale of seeds in their own right). The applicant foresees that seed allergic individuals can continue to follow their normal diet if and when chia seeds are used in a wider range of foods.

Discussion. *The Committee noted that the seeds would be clearly labelled as such but the possibility of cross-reactivity in individuals who are allergic to seeds and nuts could not be discounted. This possibility was recognised during the earlier evaluation of chia seeds as a novel food. The Committee also noted that the additional food products that would incorporate chia seeds also contain other seeds or tree nuts and that, in the majority of cases, seed or tree nut allergic individuals would take care to avoid such products, even if they did not know specifically whether they should avoid consuming chia seeds. The Committee also highlighted the relative absence of studies quantifying the level of allergy to chia seeds amongst seed allergic individuals and suggested that such data could be useful in determining whether extending the use of chia seeds 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 protein, give rise to increased sensitisation in the wider population.*

CONCLUSION

The Committee considered that the only issue of concern in relation to extending the use of chia seeds to the foods listed in paragraph 9 related to potential consumption by individuals with existing seed allergy. Despite evidence of historical use, the seeds were effectively new to markets across in the world and the true extent of allergenicity was not known. The applicant had considered the possibility of allergenicity and had sought to minimise this likelihood by careful consideration of the proposed food categories and liaison with relevant support groups.

Chia seed is not a known allergen and it is not subject to EU rules on mandatory declaration of allergens in food. The existing authorisation for the authorisation of chia seeds for use in bread products requires that there is reference to chia seeds on the label. The Committee was concerned that the use of chia in a wider range of foods, all carrying the same precautionary labelling, would result in a restriction of choice for people with existing seed allergies and this might in fact be unnecessary if there is actually no cross-reactivity between chia and other seeds

However the Committee also accepted that the risk management measures described by the applicant would be adequate to address safety concerns in relation to allergic reactions amongst known ‘at risk’ individuals.

If such an approach were to be considered the Committee noted the current dietary practices of nut and seed allergic individuals could not, in all cases, be relied upon to remove all risks resulting from cross-reactivity, and suggested that there would need to be increased awareness among these individuals. In order that this 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 seeds 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.

The Committee advised that the uncertainty could be reduced by research being carried out to determine the likelihood of different seed allergic individuals cross-reacting to chia seeds. 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.

March 2012

(b) **OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION FOR METHYLCELLULOSE**

Applicant: **Dow Wolff Cellulosics**

Responsible Person: **Helen Stubbs**

EC Classification: **2.2**

Introduction

1. An application was accepted by the Food Standards Agency in April 2012 from Dow Wolff Cellulosics for the authorisation of methylcellulose (MC) as a novel ingredient in the EU. A copy of the application was placed on the Agency's website for public consultation.

2. The applicant's MC has the polymeric backbone of cellulose, a natural carbohydrate obtained from plant material that contains a basic repeating structure of anhydroglucose units joined by 1-4 linkages. Each anhydroglucose unit contains hydroxyl groups at the 2,3 and 6 positions. Substitution of these hydroxyl groups creates a range of cellulose derivatives e.g. treatment of cellulosic fibres with caustic solution followed by a methylating agent yields methyl cellulose.

3. MC is currently approved as a food additive (E461) in the EU, functioning as an emulsifier, stabiliser or thickener. E461 is authorised for use in a range of foodstuffs at levels up to 0.5%. It was last evaluated in the EU in 1994, when the Scientific Committee on Food confirmed the JECFA allocation of an ADI "not specified" to a group of modified celluloses.

4. The applicant manufactures different grades of MC that gel at different temperatures; all fall within the range specified in the purity criteria for MC that accompany the food additive authorisation. Variation in the distribution of the polymer backbone, different positions of methyl groups within the glucose units and differences in molecular weight can all have an impact on gelling temperature so MC can gel in water at a temperature as low as 31°C or as high as 60°C.

5. The applicant is now proposing to market MC as a novel food ingredient in the EU, as a source of dietary fibre. MC is proposed to be added to a limited range of foodstuffs (ice-cream, flavoured milk drinks, cold desserts, smoothie type drinks, yogurts and yogurt drinks and wet soups).

6. As MC does not have a significant history of consumption as a food ingredient in the EU, it requires a pre-market safety assessment and approval under the Novel Foods Regulation.

7. MC has been classified as a complex novel food from non-GM source, the source of the novel food has a history of food use in the EU (class 2.2) according to the scheme in Commission Recommendation 97/618 (EC).

Specification of the novel food

Information on this aspect is provided on p. 9-13 of the application dossier

8. The specification for MC can be found in the application dossier (p 13) and includes minimum purity, viscosity, moisture content and maximum limits for heavy metals. This specification matches that for the approved food additive E461 and encompasses a broad range of molecular weights from 20,000 to 380,000

9. The methyl cellulose products to be offered will encompass a range of different gelling temperatures and viscosities. Customer selection of particular product grades is expected to be food product-dependent, since food matrices can often impact the gelation properties of methyl cellulose (e.g. sugars lower the gelation temperature). Since viscosity is an important factor for mouth-feel and other food properties, a range of methyl cellulose products of differing viscosities will be offered to provide the best property options to food formulators.

10. The applicant has carried out analyses of nine independent lots of MC (p 13 of dossier) with a range of viscosities and in all cases MC meets the specifications.

***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

Information on this aspect is provided on p 13-17 of the application dossier (CONFIDENTIAL)

11. The applicant has provided details in the dossier of the production processes for the manufacture of MC with a gelling temperature of 50-60˚C and for MC that gels as low as 31˚C. The applicant indicates that the same production processes are currently used to manufacture the approved food additive.

12. MC is manufactured by grinding wood pulp, followed by treatment with alkaline solution and methyl chloride, purification, drying and packaging. Reaction steps and times vary depending on the desired gelling properties of the end product. Further details are provided in the dossier.

13. MC products which gel at different temperatures have the same average content of methyl groups but differ in the position of these groups within the glucose units. MC that gels at 31°C is prepared by changing the reaction kinetics to favour methylation in positions 2 and 6 and to disfavour position 3. The position of the methyl groups alters the interaction of the glucose units

within the polymer chain and also between the polymer chains, so that gelling can be obtained at body temperature (or lower) in a controlled way.

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

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

Annex 1, p 18

14. The applicant's MC is derived from highly purified cellulose from non-genetically modified plants e.g. softwood trees which are cultivated in a sustainable way. The same source material is also used to manufacture the approved MC food additive.

***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

Information on this aspect is provided on p 19-27 of the application dossier

15. MC is proposed for use primarily in cold, wet, medium viscosity foods such as ice-cream, flavoured milk drinks, cold desserts, smoothie-type beverages, yoghurts, yoghurt drinks and cold soups with an anticipated use level of between 1.5 and 2%.

16. The applicant has used four cross-sectional food consumption surveys in the UK and Irish Republic to estimate potential exposure to MC. The applicant has provided estimates for different age groups (ages 1.5 to 64).

17. Using a deterministic approach, assuming all foods contain a fixed concentration of the maximum 2% MC, the highest overall predicted intake (97.5th percentile) was for Irish male teenagers (4973±396 mg/day). When expressed on a body weight basis, the highest estimated intakes were for British female toddlers (326±29 mg/kg body weight/day).

18. The applicant has also provided estimates of current MC intake resulting from its existing permitted use as a food additive. The highest estimated baseline intake of MC as a food additive (97.5th percentile; assuming a highest fixed concentration for additive use of 0.5%) using a deterministic approach was observed for Irish adult males (2334±71 mg/day) when expressed as absolute intakes. On a body weight basis, highest intakes were observed for British female toddlers (70±2 mg/kg body weight/day).

19. The applicant notes that this approach is considered to be very conservative and yields "worst case" estimates; the estimates assume that MC is always present at a maximum fixed

concentration in all foods and that all foods are consumed in high amounts by the same individuals.

20. The applicant has also used a probabilistic approach to estimate intakes of MC, taking variability in the concentration of MC into account while still assuming 100% probability that MC is present in all relevant foods.

21. Using this approach, the highest predicted intakes of MC as a novel ingredient (4273±322 mg/day and 282±26 mg/kg bodyweight/day) and highest baseline intakes as a food additive (1380±44 mg/day and 42±2 mg/kg bodyweight per day) are considered by the applicant to be more plausible than those obtained using a deterministic approach.

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

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

Information on this aspect is provided on p 28 of the application dossier

22. As previously stated, MC is an approved food additive (E461) in the EU and has been consumed since the mid 1950s.

***Discussion**: The Committee did not raise any issues with this section of the dossier.*

XI. Nutritional information on the novel food

Information on this aspect is provided on p 28-29 of the application dossier

23. The applicant states that as a food ingredient, MC fits under the 2nd category of material constituting dietary fibre, as defined in Annex II of Directive 90/496/EEC on nutrition labelling:

> "edible carbohydrate polymers which have been obtained from food raw material by physical, enzymatic or chemical means and which have a beneficial effect demonstrated by generally accepted scientific evidence";

24. The intended use of MC is as an additional source of dietary fibre and MC is not intended to replace any foodstuff in the diet.

25. The applicant outlines a study of vitamin uptake in the gut of rats, which indicated that MC did not interfere with vitamin uptake (vitamin A and thiamine).

Discussion: In the original dossier, the applicant stated that MC was intended to be used as a dietary fibre to promote satiety. The Committee was not convinced that MC can function to improve satiety and could see no evidence for this from the data in the dossier (there is no evidence of reduced food consumption in the animal studies). The applicant has clarified that it is seeking approval to market MC only as a dietary fibre at present and wishes to withdraw its references to promoting satiety.

In the dossier, the applicant referred to MC as being resistant to fermentation and reducing gastrointestinal distress. The Committee noted that the fermentability of native cellulose in the human large intestine ranges from <6% (for highly crystalline purified cellulose) to around 70% for more amorphous cellulose and requested information about where MC would fall within this range. The applicant admitted that the original sentence in the dossier could have been worded in a better way and should have read "Unlike many other dietary fibres, methyl cellulose (as well as other cellulose ethers) is resistant to fermentation in the colon. Therefore, replacing other dietary fibres with methyl cellulose will help to reduce overall fermentation and subsequent gastrointestinal distress." The Committee was satisfied with the applicant's responses relating to these points. The applicant has also referred the Committee to two studies in the dossier which show that MC passes through both animals and humans essentially unchanged and supports the idea that MC is not broken down by fermentation or absorbed.

During the 21 day public consultation, a comment was received noting that many patients with diarrhoea-predominant irritable bowel syndrome (IBS) need to avoid foods containing additives with a laxative effect. The Committee agreed that, while some consumers might regard a mild laxative effect to be beneficial, this effect would be undesirable in others such as those with IBS.

The Committee noted that consumption of foods with added fibre and fibre-like ingredients by children could result in an increase in common intestinal symptoms. The Committee advised therefore that foods containing MC should not be intended for children.

XII. Microbiological information on the novel food

Information on this aspect is provided on p.30-31 of the application dossier

26. The applicant states that MC is produced without the aid of microbiological processes and therefore no microorganisms or their metabolites are anticipated. The production process of MC is strictly monitored and controlled and a HACCP hygiene procedure is followed.

27. The applicant has provided microbiological specifications for MC, taking into account a range of possible contaminating microorganisms. Analyses of four separate batches of MC showed that all batches comply with these specifications.

***Discussion**: The Committee did not raise any concerns or questions on this aspect of the application.*

XIII. Toxicological information on the novel food

Information on this aspect is provided on p. 32-48 of the application dossier

28. The applicant reports a range of toxicological studies conducted with MC, as well as studies using other modified celluloses that may be regarded as analogues of MC.

Pharmacokinetics and metabolism

29. The applicant describes three feeding studies, one in humans and two studies using radio-labelled MC in rats (single dose and for five days), all of which demonstrate that essentially all orally administered MC is unabsorbed and is cleared through the body via the faeces.

Sub-chronic toxicity

30. The applicant presents five feeding studies investigating sub-chronic toxicity in rats and dogs. MC of various viscosities was incorporated into the diets of rats at up to 10% for time periods up to eight months and very few significant abnormalities or treatment related effects were reported. One study where different viscosities of MC (10cP or 4000 cP) were incorporated into the diets of rats at up to 10% for 90 days showed that male rats consuming 10% MC (low viscosity, 10cP) exhibited slight reductions in terminal body weight relative to controls but growth was normal in all other 10cP treatment groups and in groups consuming high viscosity MC (4000cP). No other significant treatment-related effects were observed in this study.

31. Rats fed a diet of 5% MC for thirty two weeks showed no change in dietary intake, growth, reproduction or tissue morphology. A subsequent experiment where the diet was supplemented with 50% MC significantly depressed growth due to lack of nutrient intake; this effect was diminished when rats were returned to a standard diet.

32. The applicant also briefly mentions a study where dogs (sex and strain not mentioned) were given up to 100g MC daily for four weeks and no adverse effects were reported.

Chronic/carcinogenicity studies

33. The applicant presents 2 two year rat feeding studies where rats were fed diets containing up to 0.1 or 5% MC of viscosity 15, 400 or 4000 cP. No treatment related effects (including mortality or increased tumour incidence) were reported (McCollister *et al*, 1973).

Genotoxicity

34. Results from two *in vitro* bacterial reverse mutation assays using *Salmonella typhimurium* strains (with and without metabolic activation) and an *in vitro* chromosome aberration test using a Chinese hamster lung fibroblast cell line showed that MC is not genotoxic.

Reproductive and developmental toxicity

35. Several animal feeding studies have investigated reproductive and developmental toxicity. For some of the studies, side effects were observed at the highest doses tested (1600 mg/kg bw/day rats; 685 mg/kg bw/day rabbits), which the applicant reports as secondary effects due to nutritional imbalance in the dams given a very high fibre diet. Effects included significant mortality and a decrease in pregnancy rates. In one rat feeding study, extra centres of ossification in the vertebrae were observed in the high dose group (1200 mg/kg bw/day).

Human studies

36. The applicant has described several human studies investigating the effects of MC on constipation and on lowering cholesterol. While there are reports of MC being effective in relieving constipation and increasing faecal bulk (independent of MC viscosity, according to the applicant), some of the studies do report GI effects such as bloating, flatulence and cramps. One of these studies did not employ a placebo comparator while another showed that these GI effects were comparable for the placebo group.

37. The applicant states that these human studies show that up to 6g MC, administered as a bolus dose, is well tolerated. The applicant suggests that the expected effects of MC on children and adults will be comparable to those experienced by an individual on a high fibre diet.

38. The highest predicted intakes of MC (97.5th percentile) as a novel food ingredient using the deterministic approach are lower than 6g/day. However, when baseline intakes of MC as a food additive are taken into account, it is possible that combined high level consumption may exceed 6g/day.

39. Using a probabilistic approach, which takes variability in the concentration of MC into account while still assuming 100% probability that MC is present in all relevant foods, the applicant calculates that the highest predicted intakes of MC as a novel food ingredient (97.5th percentile), combined with baseline intake, would not exceed 6g/day (see paragraph 21 above).

***Discussion**: The Committee did not raise any specific toxicological concerns relating to MC. The Committee did however question the relevance of the safety data relating to MC analogues that had been supplied in the dossier.*

The applicant has pointed out that the safety of methyl cellulose and other cellulose ethers (E 460 through to E 466) has been extensively evaluated as food additives (SCF, JECFA, EFSA, US FDA) and that in all these evaluations, a group approach was used based on the similarity of their chemical structure and their toxicological and biochemical profiles, as demonstrated in animal and human studies. The applicant acknowledges that some studies used to support the safety of cellulose ethers were not conducted recently ; however, each study has been extensively reviewed for information and validity. The applicant therefore feels it unnecessary to conduct further studies with MC.

The applicant has also emphasised that the manufacturing route for its low temperature gelling MC is consistent with that for other MC products. Therefore, the historic toxicity profiles for MC products are representative across all MC products, including lower temperature gelling MC.

The Committee was content with the applicant's responses to its questions. The Committee acknowledged, that although the studies presented in the dossier are relatively old, the lack of radio-label in tissues and urine is sufficient evidence that all of the alkyl celluloses pass through the gut essentially unchanged and no further studies were requested.

XIV. Allergenicity and labelling

Information on this aspect is provided on p.38 of the application dossier

40. The applicant states that MC is a substituted polysaccharide and therefore no proteins are expected to be present in the product. To verify the absence of proteins, samples of food grade MC (Methocel A4M) were analysed using the Antek total nitrogen chemiluminescence analyser for nitrogen as a presumptive test for protein. No nitrogen was detected (LOQ 1ppm). The applicant also highlights that there are no known intolerances to cellulosic products.

41. The applicant states that MC is intended to be labelled in the ingredients list as Methyl Cellulose.

42. The Committee's assessment focuses on safety and labelling, 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.

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

CONCLUSION

The ACNFP has completed its assessment of MC as a novel ingredient to be added to a range of foods and did not have any safety concerns relating to this ingredient. The Committee did consider that the types of products to which MC is intended to be added may be particularly attractive to children which in turn may increase the potential for common intestinal symptoms in children. As with previous applications for similar novel ingredients, the Committee suggested that foods containing MC are not intended for children. The Committee raised questions relating to the extent to which MC is fermented in the human large intestine, the questionable role of MC in promoting satiety and the relevance of the applicant's safety data relating to MC analogues.

The applicant provided a response to clarify these points. The Committee was content that the applicant had addressed its questions in these areas.

October 2012

(c) **OPINION ON A UV TREATED BAKER'S YEAST**

Applicant **Lallemand**

Responsible Person **Celia Martin**

EC Classification **2.2**

Background

1. An application was submitted by Lallemand, for the use of ultraviolet (UV) treated baker's yeast (*Saccharomyces cerevisiae),* which contains enhanced levels of vitamin D2, as a novel food ingredient.

2. The applicant intends that the novel food, referred to as in this opinion **vitamin D2 yeast concentrate**, will be used for the leavening of bread, as a food supplement and in other foods which typically contain baker's yeast. The same yeast is approved for use in bread products in Canada and the US and the applicant reports the amount of vitamin D2 as either micrograms or International Units and this is reflected in this paper. 1mg vitamin D is equivalent to 40,000 IU.

3. Vitamin D2 (ergocalciferol) is produced photochemically from the precursor ergosterol in plants and fungi and is chemically distinct from vitamin D3 (cholecalciferol), which is synthesised in human skin from the precursor 7-dehydrocholesterol following exposure to sunlight. There is relatively little vitamin D present naturally in food (chiefly oily fish, eggs and liver) but a number of foods are routinely fortified with vitamin D e.g. breakfast cereals and margarine.

4. Both vitamin D2 and D3 are listed in Annexes 2 and 3 of regulation (EC) 1170/2009, which permits their addition to both foods and food supplements . In the EU, Vitamin D2 is currently found in food supplements by the UV treatment of purified ergosterol that is extracted from baker's yeast. This vitamin D2 yeast concentrate is to be marketed as an alternative to other vitamin D sources which are already permitted to be added to foods, including (in theory) bread.

5. In accordance with the Novel Foods Regulation, vitamin D2 yeast concentrate has been classified as a complex novel food from non-GM sources source (class 2.2).

I Specification of the Novel Ingredient (NI)

Dossier, p 7-15

6. The applicant has provided a specification for vitamin D2 yeast concentrate which is detailed in the Dossier (Appendix I.6.1) and summarised below. Other than containing significant levels of vitamin D2 the yeast is described as being no different to conventional, untreated yeast, which is widely used for in baking of bread.

Proposed Specification of vitamin D2 yeast concentrate	
Parameter	**Specification**
Appearance	Tan coloured, free flowing granules
Vitamin D2[1]	1,800,000 – 3,500,000 IU vitamin D /100g yeast
Coliforms[2]	<1000 / gram
E. coli[2]	<10 / gram
Salmonella[2]	Absent / 25 grams
Shelf life	3 years (sealed package)

[1]AOAC analysis [2] FDA Bacteriological Analytical Manual

7. The production of vitamin D3 *in vivo* by humans following exposure to sunlight produces two related sterols – tachysterol and lumisterol – and the applicant has carried out chromatographic analysis (HPLC) to determine whether the UV treatment of their yeast results in the production of these or other, related, sterols. The detailed results of these studies, carried out using HPLC, are available in the Dossier (Appendix I.5.1 A,B&C) and are summarised in Section 1.5.1. The results indicate that, prior to UV treatment, the only sterol present in the yeast in significant

quantities was ergosterol (7.05mg/g). Following exposure to UV, in addition to the internal standard, three sterols were observed. These were identified to be ergosterol (6.56mg/g), ergocalciferol (vitamin D2, 1.06mg/g) and tachysterol.

8. The applicant was unable to quantify the level of tachysterol present but noted that it was significantly smaller than the equivalent vitamin D2 peak (4.27% compared with 16.03%, as a proportion of total peak area). A separate exercise to quantify the levels present in two commercial lots was carried out by another laboratory, which found tachysterol levels to be 140 & 145mg/kg and vitamin D2 672 & 825mg/kg (Dossier, Appendix I.5.1 A). All other minor peaks were also present prior to UV treatment.

9. In order to determine the accuracy of the HPLC method, the level of vitamin D2 present in a single batch was analysed in duplicate on three occasions over a 24 day period. This analysis showed little variation over the study period and gave an average of 3,290,000 IU vitamin D/100g (Dossier Table 1). The same batch was also assessed using an alternative, modified, AOAC detection method giving a similar result (3,230,000 IU/100g). (Dossier, Appendices I.5.1.E,F & G).

Vitamin D2 in bread. The applicant also investigated the level of vitamin D2 present in three loaves baked using vitamin D2 yeast concentrate. In this study vitamin D2 yeast concentrate was blended with standard yeast to give 400 IU /100g bread. The levels of vitamin D in both the vitamin D2 yeast concentrate and the bread were analysed and found to be 3,440,000 and 489 IU / 100g respectively.

Discussion *The Committee agreed that the analytical data provided by the applicant were particularly thorough and was satisfied that the novel ingredient can be produced reproducibly by the applicant.*

II Effect of the production process applied to the NI

Dossier p16-26

10. Lallemand is a well established company who have been producing baker's yeast for almost 100 years. In addition to producing yeast for bread baking they also produce yeast for a range of other industrial applications e.g. brewing, oenology, animal health, and bioethanol production. They have provided extensive details of the procedures used to produce commercial quantities of yeast and the methods that they employ to ensure purity. These are detailed in the Dossier in Section II.2.1 (Confidential).

11. The yeast that is subjected to UV treatment is produced in the same manner as Lallemand's conventional baker's yeast product. To enhance the vitamin D content, the yeast (known as yeast cream) is continually pumped past UV lamps, wavelength 254nm, for 96 hours at 4°C prior to drying using a fluid bed dryer (yeast for baking) or a spray dryer or roller dryer (yeast for

supplements). The resulting product, which contains between 1,800,000 and 3,500,000 IU vitamin D/100g, is a concentrated form of vitamin D2. When used for baking, it and would be blended with conventional yeast to ensure that the end product contains the required amount of vitamin D2, as detailed in Section IX below.

12. Lallemand analyse every production lot to determine the vitamin D2 content (in triplicate) and to check compliance with the microbiological specification. All Lallemand manufacturing sites are ISO certified and operate under GMP conditions.

13. **Genetic stability of vitamin D2 yeast concentrate.** UV is widely used for sanitation or sterilisation purposes and the applicant acknowledges that non-fatal, intensive doses of UV can induce mutations in microorganisms, particularly at the wavelength that they use for vitamin D2 production (254mn). In line with its sanitising properties, the use of UV is particularly effective in inducing mutations that result in cells being unable to multiply. However, the applicant reports that the system they employ has little detrimental effect on the viability of the cells due to the constant circulation of the yeast cream, which contains concentrated amounts of cells, and the relatively poor transmission power of UV.

14. Scientific studies investigating the nature of mutations seen in yeast cells indicate that there are no gross chromosomal rearrangements and there are reports of an increase in mobile element TY transposition[15]. The applicant reports that the UV dosage that the yeast cells receive is much lower than the doses used for sanitation purposes or to induce mutations for research purposes (e.g. strain development). To demonstrate this, the applicant used RAPD-PCR and RFLP DNA fingerprinting techniques which they regard to be sufficient to identify both chromosomal rearrangements and point mutations. These techniques have previously been used to detect mutants in other organisms and, to increase the likelihood of inducing mutations, the applicant extended the time of exposure to UV from 96h to 160h. The results of the analyses can be seen (in the form of gels) on p24-5 of the Dossier. Based on these results the applicant concludes that each of the colonies subjected to UV treatment had an identical genetic profile to the control strain.

15. **Stability of the vitamin D2 yeast concentrate** Analysis of three lots of vacuum packed vitamin D2 yeast concentrate indicated that there was no significant reduction in the level of vitamin D2 over a three year period. The applicant does not indicate whether there is any reduction in the level of vitamin D2 if the yeast is incorporated into commercial products with an extended shelf life (e.g. food supplements).

Discussion *The Committee accepted that there were appropriate controls in place on the production of the NI to ensure the safety of the final product. The Committee did not regard the methods employed by the applicant to be adequate to identify potential mutants, noting that alternative*

[15] A **transposable element** (TE) is a DNA sequence which can change its position within the genome. In *S.cerevisiae* there are 5 distinct families (TY1-TY5) which are all 'retrotransposon ' type TE's

methods such as RT-PCR[16] would be more appropriate. However the Committee accepted that, although the number of mutants may increase as a result of the UV treatment, the subsequent use of the vitamin D2 yeast concentrate could not lead to a mutant becoming the dominant strain in the final product.

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

Dossier pp 27-30

16. *Saccharomyces cerevisiae* is extensively used by the both baking and brewing industries. It has a long history of safe food use across the world. EFSA has categorised *S. cerevisiae* as a microorganism that is proposed for QPS status[17]. Although EFSA acknowledges concerns in relation to invasive infection in certain compromised individuals, this appears to be related to a particular sub-species commonly referred to as *Saccharomyces boulardii*, which is not used in brewing or baking and is not a concern for the wider population.

17. The applicant also reports a number of uses of vitamin D2 rich yeast in the treatment of rickets in the early decades of the twentieth century and refers to approvals for their vitamin D2 yeast concentrate in the US and Canada (Dossier, Appendices B and C)

Discussion *The Committee accepted that baker's yeast and vitamin D2 have a long history of safe food use. Although there were reports of invasive infection of a related species, which was not used for food production purposes, this was not a cause for concern.*

IX Anticipated intake and extent of use of the NI

Dossier p 31-36

18. As detailed in paragraph 4 above, the applicant intends their vitamin D2 yeast concentrate to be an alternative to existing vitamin D2 ingredients that can be added to a range of foods and food supplements. However as vitamin D2 yeast concentrate requires assessment as a novel food the applicant has acknowledged that there is a requirement to indicate the intended uses in order to estimate likely intake and has done this based on use in bread, which is the major perceived use of the novel ingredient.

19. The applicant proposes that bread will be formulated to ensure that, irrespective of the level of vitamin D2 present in individual batches of the yeast concentrate, it would contain a maximum of 5µg vitamin D2 (200IU) per 100g[18]. 100g of this bread will provide the recommended daily

[16] **RT-PCR** Reverse transcription polymerase chain reaction
[17] EFSA Scientific Committee (2007) "Introduction of a Qualified Presumption of Safety (QPS) approach for assessment of selected microorganisms referred to EFSA" http://www.efsa.europa.eu/en/efsajournal/doc/587.pdf
[18] One slice of large loaf of white bread weighs between 25 and 38 g, dependent on thickness (MAFF, 1988).

allowance (RDA) for Vitamin D2.[19] The applicant indicates that proposed level of incorporation into food supplements will be in line with the same 5µg/day RDA figure. Based on the specification in Section II above, 5µg of vitamin D2 is equivalent to between 5.7 and 11mg of the UV-treated yeast.

20. The applicant used published data from the UK 2010 National Diet and Nutrition Survey (NDNS) to estimate intake from a number of different bread types. As the NDNS publication only provides mean consumption figures, the applicant has assumed a high level consumption (97.5th percentile) of three times the mean value. The applicant has presented the mean and high level consumption figures for each individual bread category separately, assuming that all products on the market contain 5µg vitamin D2. The highest estimates of mean and high level daily intake of vitamin D2 were 3.85µg and 11.55µg in adult males, 3.75µg (high level 11.25µg) male teenagers (age 11-18) and 2.4µg (7.2µg) in boys (age 4-10).

21. Experts in food chemical intake for the Food Standards Agency have reviewed the intake assessment data provided and noted that, although the approach used by the applicant is only an approximation of high level consumption, the estimates that the applicant provided were consistent with their own analysis. The Food Standards Agency analysis provided estimates based on the consumption of all types of bread (see table below) and would appear to confirm that individuals are unlikely to consume large amounts of different breads over the course of a day, a point noted by the applicant. The Food Standards Agency officials also noted that the differences seen in the applicant's data could, in part, be due to an acknowledged skew in the published 2010 figures (caused by over-reporting of weekend consumption patterns) which is compensated for in the FSA figures.

FSA: Estimated intake of vitamin D2 from bread baked with vitamin D2 yeast concentrate and assuming that all bread contains the vitamins D yeast concentrate

(based on 2010 and 2011 NDNS data)

	Mean intake (µg/day)	97.5th%ile Intake (µg/day)
Children(4-18)	3.6	8.6

[19] Commission Directive 2008/100/EC. This RDA for vitamin D is based on the earlier recommendations of the FAO/WHO (1988)

Adults (19-64)	4.5	10.8
Adults (65+)	4.0	10.2

22. The vitamin D2 yeast concentrate is to be used in food supplements as a direct "like for like" replacement for existing ingredients and, as such, will not significantly add to the level of vitamin D consumed by individuals via supplements.

23. Data for estimating the current intake of vitamin D from food supplements are not available but the applicant highlights three separate surveys which provide estimates of dietary vitamin D intake, all of which are significantly lower than the EU RDA figure (see para 21 above).

- In 2003 the UK Expert Group on Vitamins and Minerals reported the intake of vitamin D from dietary sources to be in the region of 3-4µg/day (based on NDNS 2003 consumption data)[20]. These figures are slightly higher than figures reported using the 2010 NDNS data set (Dossier p42-43) which indicate that mean dietary intake of vitamin D is 1.9-3.1µg/day for males and 2.0-2.7µg/day for females.

- The applicant also reports the findings of a 2007 dietary study investigating the nutritional and energy intake of 15,000 Germans between the age of 14 and 80, which indicated that the median level of vitamin D2 intake is around 2-3µg/day (Dossier p40-41) and that 82% of men and 91% of women consume less than the 5µg RDA (see para 20 above). The German figures and the 2010 NDNS data both record young men and women as having the lowest intake of vitamin D.

- In 2007 the Scientific Advisory Committee on Nutrition reported that a significant proportion of the UK population does not consume sufficient vitamin D to meet the UK 1998 Reference Nutrient Intake values of between 7 and 10µg/day[21].

24. The applicant notes that both the mean and high level intake estimates are less than the RDA set by the US Institute of Medicine in 2010 (15µg/day) and, even if background intake from other dietary sources is taken into account, significantly less than the upper limits set by the same organisation and by EFSA in 2006 (See section XIII below).

[20] http://cot.food.gov.uk/cotreports/cotjointreps/evmreport/
[21] LINK NEEDED

Discussion *The Committee noted the shortcomings in the approach used by the applicant to estimate intake, but agreed that it did provide a reasonable estimate of the mean and high level consumption of vitamin D2 yeast concentrate. The Committee thanked the Food Standards Agency officials for validating the approach taken by the applicant and noted that it should be the responsibility of the applicants to provide a rigorous assessment of the likely intake of novel foods.*

XI Nutritional information on the Novel Food

Dossier p37-45

25. The applicant comments on the intake of vitamin D from dietary sources using information presented in EFSA's 2006 report on tolerable upper intake levels for vitamins and minerals. The UK and German surveys report that vitamin D consumption is below recommended daily intake levels (see previous section). The applicant also notes that the there is extensive consumption of *S. cerevisiae.* Allergenic potential and bioavailability are covered in Section XIII below.

Discussion *The Committee noted that there is increasing evidence of vitamin D deficiency in the EU, and that increasing dietary intake is one way to address this concern.*

XII Microbiological Information

Dossier p48

26. The applicant tests every batch of their yeast to ensure that it meets its microbiological standards (see specification para 6.). Information on the reference methods is available in Dossier, Appendix I.6.1.

Discussion*: Members accepted that the production process did not give cause for microbiological concern, and that compliance with the specification would ensure that the NI is free from pathogenic microorganisms.*

XIII Toxicological information

Dossier p.48-56

27. **Bioavailability.** The applicant acknowledges that there is an ongoing debate regarding the comparative effectiveness of vitamin D2 and vitamin D3, with a number of scientific studies reporting D3 as being the more 'potent' form. The uncertainty appears to be in relation to the effectiveness of the two forms in maintaining serum levels of 25-hydroxyvitamin D (25(OH)D) the pro-hormone that is measured to assess vitamin D bioavailability and status. Although both vitamin D2 and D3 are converted to the respective forms of 25(OH)D *in vivo,* measurement techniques appear unable to distinguish between 25(OH)D2 and 25(OH)D3. A number of studies

point to the slow rate of conversion from vitamin D2 to 25(OH)D2 and a propensity for 5(OH)D2 to be metabolised quicker than the D3 variant. The applicant points to a number of recent studies, carried out in both humans and rats, which point to little or no difference in bioavailability between the two forms and also points to the use of vitamin D2 as the primary form for the prevention of vitamin D deficiency in children over the past 50 years.

28. The applicant has not carried out any toxicity studies on its vitamin D2 yeast concentrate but refers to a number of reviews which have set safe upper limits for vitamin D, which are summarised in the table below. As a variant of an existing source of vitamin D2, the applicant considers that these limits apply equally to their vitamin D2 yeast concentrate. These limits are higher than the anticipated intake of vitamin D2 from the novel ingredient (see para 19 above) which give a figure of around 15µg per day for high level consumers when the highest background sources are taken into account, plus an additional 5µg if both bread and supplements are consumed.

Published upper limits for vitamin D (µg/day)

	EFSA[1]	IoM[2]	EVM[3]
Adult	50	100	25
Child (14-18)	-	100	-
Child (11-17)	50	-	-
Child (9-13)	-	100	-
Child (3-10)	25	-	-
Child (4-8)	-	75	-

[1] EFSA 2006 [http://www.slv.se/upload/dokument/efsa/upper_level_opinions_full-part33,0.pdf]

[2] US Institute of Medicine 2010 report [http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx]

[3] UK Expert Group on Vitamins and Minerals report. Figure refers to supplementation and the general population. [http://cot.food.gov.uk/pdfs/vitmin2003.pdf]

29. The applicant has also reviewed a number of recent (since 2007) studies which confirm that long term exposure to relatively high levels of vitamin D does not, in the main, give rise to any adverse health effects. These are not detailed in this paper as they are summarised in the Dossier, pages 54-62.

Discussion. *The Committee noted that there have been a number of reviews into the safety of vitamin D and although, these give differing upper limits, they are all higher than the maximum high level of intake for vitamin D2 yeast concentrate, even if background sources are taken into account.*

30. **Tachysterol.** The applicant noted that the tachysterol is regarded to be both inert and non-toxic (Horlick, 1981; Gilchrest, 2006). However the Committee queried whether this view applied if it was taken orally. The Committee also noted that the presence of tachysterol could potentially reduce or block absorption of vitamin D *in vivo*.

31. The applicant's response noted that there is little published information available investigating the effect of tachysterol on the metabolism of other nutrients. A study by Holick *et al,* (1981) reports no effect on calcium absorption in rats which were given 0.25µg vitamin D3 and injected with 1µg tachysterol, but a small (insignificant) effect on calcium metabolism when 10µg was injected. The applicant highlighted the author's view that vitamin D binding protein has little affinity for tachysterol. The applicant also noted that tachysterol would be present in the final food at particularly low levels. To produce bread containing 200IU/100g vitamin D2 requires 6.67mg of the vitamin D2 yeast concentrate and at this level of incorporation the resulting intake of tachysterol would be 0.93µg/100g bread. As detailed in para 19 above the applicant proposes a daily intake of 200IU vitamin D2 from the novel ingredient. For high level consumers of bread who may also consume a supplement this would equate to around 15 µg of vitamin D2 and 2.8µg tachysterol.

Discussion. *The Committee reviewed the response from the applicant and was satisfied that it provided sufficient evidence that the vitamin D2 yeast concentrate (containing tachysterol) had a similar bioavailability to existing sources of vitamin D2. The Committee also accepted that the levels of tachysterol in the novel ingredient were very low, equating to a maximum of 2.7µg tachysterol per day and noted that this figure is below EFSA's threshold of toxicological concern*[22].

32. **Allergy.** The applicant advised that no allergens are used in the production of vitamin D2 yeast concentrate. The Food Standards Agency advises that food allergy to *S. cerevisiae* is extremely

[22] http://www.efsa.europa.eu/en/consultationsclosed/call/110712a.htm

rare and, although inhalant allergies to fungi and yeast such as *S. cerevisiae* are more common, they are rare when compared to other allergic conditions.

Discussion. *The Committee accepted that the allergenic risk of the vitamin D2 yeast concentrate was no greater than for other foods containing S. cerevisiae and although there is a risk of an individual with an inhalant allergy to S. cerevisiae having a severe systemic reaction after consuming the yeast, this would apply equally to other (non-vitamin D enriched) S. cerevisiae preparations.*

Overall Discussion

The Committee considered that information provided by the applicant in regard to their concern about tachysterol was sufficient to demonstrate that its low level presence was not a cause for concern. With regard to potential intake, the Committee noted the simplistic approach used by the applicant, but accepted the view of Food Standards Agency officials that this approach was a reasonable estimate of the likely consumption of the novel ingredient. The Committee also accepted that, based on these figures, there was an adequate margin of safety for all population groups.

Conclusion

The Advisory Committee on Novel Foods and Processes is satisfied by the evidence provided by the applicant, Lallemand, that the range of uses for the novel ingredient (vitamin D2 yeast concentrate) is acceptable

August 2012

(d) **OPINION ON AN APPLICATION UNDER THE NOVEL FOODS REGULATION FOR ISOMALTO-OLIGOSACCHARIDE**

Applicant: **Bioneutra Inc.**

Responsible Person: **Mohammed Qureshi**

EC Classification: **2.2**

Introduction

1. An application was submitted to the Food Standards Agency in February 2009 by Bioneutra Inc. for the authorisation of isomalto-oligosaccharide (IMO) as a novel ingredient in the EU. A copy of the application was placed on the Agency's website for public consultation in 2009.

2. IMO preparations generally consist of glucose oligomers with degrees of polymerisation of 3 to 10, depending on the method of production, along with variable amounts of monomeric and dimeric material.

3. The applicant's dossier refers to the intended use of IMO as a prebiotic dietary fibre. In subsequent correspondence the applicant clarified that they are seeking authorisation of their IMO as a general food ingredient and any references to fibre and prebiotic effects are not intended to be claims (see Section XIV below)

4. Other disaccharides have previously been considered and authorised under Regulation (EC) 258/97 which also have a sweet taste (tagatose, trehalose, isomaltulose) during which time their status as a sweetener and/or novel ingredient has been questioned. However, the regulatory framework for food additives now clarifies this issue. Article 3 of Regulation (EC) No 1333/2008 on food additives states:

   "The following are not considered to be food additives: monosaccharides, disaccharides or oligosaccharides and foods containing these substances used for their sweetening properties;"

5. IMO has been classified as a complex novel food from non-GM source, the source of the novel food has a history of food use in the EU (class 2.2) according to the scheme in Commission Recommendation 97/618 (EC).

Specification of the novel food

Information on this aspect is provided on p. 9-14 of the application dossier

6. The applicant proposes to market IMO in powder and syrup forms. The powder form is white and crystalline, while the syrup is a, pale yellow liquid. Both forms are approximately 50% as sweet as sucrose. On a dry basis, the IMO is prepared so that the content of isomaltose and larger oligoosaccharides (with 3-9 degrees of polymerisation) is not less than 90% while glucose content is no more than 5%. The IMO does not contain any detectable levels of heavy metals.

7. Batch on batch variation was assessed by analyses of different lots of IMO from the same starch source (3 separate lots of syrup and 2 separate lots of powder). The results of these analyses indicated a narrow range of variation in composition and contaminants and showed that all batches analysed met the required specification criteria for the IMO, as set out in Tables 1.7.2-1 to -4 of the dossier.

8. A number of other companies also manufacture IMO preparations, not for sale in the EU, which differ in the proportions of mono, di, tri, oligo and polysaccharide constituents.

***Discussion**: The Committee did not have any concerns relating to the general specifications of IMO. It was noted however, that the applicant had originally provided safety data based on IMO from other sources rather than its own product. The Committee highlighted that IMO preparations are variable and the data provided by the applicant were of limited value for a safety assessment. This aspect will be discussed further below under the appropriate sections.*

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

Information on this aspect is provided on p 15-24 of the application dossier

9. The applicant's IMO is produced via enzyme-catalysed hydrolysis of food grade starch from different cereal crops. Details are provided in the confidential dossier.

10. The applicant has provided confidential details of the specifications and regulatory status of the enzymes used in the production of its IMO in Appendix D of the dossier along with details of all other raw materials used.

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

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

Annex 1, p 25-28

11. The unmodified food-grade starch used as a raw material for the production of IMO is obtained from commonly available cereal crops such as barley, corn, oats, rice and other starch sources such as cassava, potato and pulses (peas, beans and lentils).

12. The applicant has advised that IMO are naturally present in foods such as honey, soy sauce, sake and miso and have been ingested by humans for hundreds of years particularly in Japan and other Asian countries. IMO have been approved in Japan for use in Foods for Specified Health Use (FOSHU) and it is now estimated that Japanese consumers intake of IMO from formulated foods now exceeds that from traditional food sources. In the US, Bioneutra's IMO product has been incorporated into foods (energy bars and beverages) for over two years.

***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

Information on this aspect is provided on p 29-35 of the application dossier

13. The applicant intends to incorporate IMO into a variety of conventional foods and also certain foods for particular nutritional uses (meal replacement bars and milk based meal replacements). The applicant states that IMO will be added to foods at maximum levels of up to 15.6 g/serving and the applicant suggests that a daily intake will not exceed 31.2g/day, assuming that a person will consume no more than two servings per day. A list of products and the proposed food uses and levels can be found below.

Summary of the individual proposed food uses, maximum use-levels, and amounts per serving of Bioneutra's IMO in the EU

Food category	Proposed food uses	Serving size (g)	Maximum use level (%)	IMO per serving (g/serving)
Beverages	Regular Soft Drinks	240	5	12
	Energy-Reduced Soft Drinks	240	6.5	15.6
	Energy Drinks	240	5	12
	Sports & Isotonic Drinks	240	6.5	15.6
	Fruit Juices	140	5	12
	Processed Vegetables and Vegetable Juices	100	5	12
Cereals products	Cereals Bars	50	10	5
	Cookies, Biscuits	40	20	8
	Breakfast Cereal Bars	50	25	12.5
Sugar confectionery	Hard Candies	10	97	9.7
	Soft Candies/Chocolate Bars	30	25	8.2
Nutritionally complete and	Meal Replacement Bars	40	20	8

fortified foods	Milk based Meal Replacement	40	20	8

14. Intakes were estimated for a range of population groups using information from the most recent publicly-available data from National Diet and Nutrition Surveys (NDNS). The tables below provide a breakdown of these estimates, as supplied by the applicant.

Summary of the estimated intake of IMO from all proposed food categories in the UK by population group (NDNS Data)

Population Groups	Age Group (years)	% Users	All-Person Consumption (g/day)				All-Users Consumption (g/day)			
			Mean	Percentile			Mean	Percentile		
				90th	95th	97.5th		90th	95th	97.5th
Children	1½ - 4½	98.3	15.3	29.5	35.3	38.3	14.2	21.6	26.8	28.3
Young People	4-10	99.6	26.7	44.8	51.8	62.1	26.7	44.8	51.8	62.1
Female Teenagers	11-18	99.3	24.8	45.5	53.7	63.3	24.9	45.5	53.9	63.3
Male Teenagers	11-18	99.5	33.4	59.5	69.2	86.7	33.5	39.5	69.2	86.7
Female Adults	16-64	88.1	8.1	19.3	25.8	34.3	9.2	20.7	26.5	36.7
Male Adults	16-64	85.3	9.0	22.5	33.1	40.8	10.6	24.4	35	41.5

Summary of the estimated intake per kilogram body weight intake of IMO from all proposed food categories in the UK by population group (NDNS Data)

Population Groups	Age Group (years)	% Users	All-Person Consumption (g/kg bw/day)				All-Users Consumption (g/kg bw/day)			
			Mean	Percentile			Mean	Percentile		
				90th	95th	97.5th		90th	95th	97.5th
Children	1½ - 4½	98.3	0.8	1.1	1.7	1.9	0.9	1.2	1.6	1.8
Young People	4-10	99.6	0.9	1.3	1.8	2.1	0.9	1.6	2.0	2.5
Female Teenagers	11-18	99.3	0.4	0.8	0.9	1.1	0.4	0.8	0.9	1.3
Male Teenagers	11-18	99.5	0.6	1.1	1.4	1.6	0.6	1.1	1.4	1.6
Female Adults	16-64	88.1	0.08	0.3	0.4	0.5	0.1	0.3	0.4	0.5
Male Adults	16-64	85.3	0.08	0.2	0.4	0.6	0.1	0.3	0.5	0.6

15. On an all-user basis, the highest mean and 97.5th percentile intakes of IMO by the UK population from proposed food uses in the EU were observed in male teenagers and estimated to be 33.5 and 86.7 g/person/day, respectively. Young people (age 4-10) consumed the greatest amount of IMO on a body weight basis with the highest mean and 97.5th percentile all-user intakes of 0.9 and 2.5 g/kg body weight/day, respectively. These are "worst-case"

estimates, based on the assumption that all possible foods contain IMO at the maximum levels given in the table above.

***Discussion**: The Committee did not raise any issues with this section of the dossier.*

XI. Nutritional information on the novel food

Information on this aspect is provided on p 36-57 of the application dossier

16. The dossier reports the results of nutritional and toxicological studies conducted with IMO preparations from different manufacturers. The applicant has provided information on the composition of Bioneutra's product compared to IMO from other sources (p 51 of the dossier). The applicant did not view the compositional differences (due mainly to differences in proportions of various oligomers) to be a concern and stated that since production of IMO mixtures occurs via natural enzymatic processes, some compositional variability between different products is expected.

17. The applicant stated in the dossier that IMO has a calorific value of 1.5-2 kcal/g based on typical values for non-digestible and poorly digestible carbohydrates compared with 4 kcal/g for fully digestible carbohydrates.

18. The applicant stated in its dossier that its IMO functions as a prebiotic dietary fibre and is closely related to fructo-oligosaccharide (FOS) in terms of functional benefits[23]. The applicant mentioned that its IMO is poorly digestible as it is resistant to digestion in the human stomach and small intestine, but it can be partially broken down in the colon by bacterial species (mainly bifidobacteria and lactobacilli).

19. Although not of direct relevance to a safety evaluation, the applicant described several studies illustrating the prebiotic effects of various IMO preparations (from other manufacturers). The majority of studies reveal that IMO consumption is associated with a significant increase in gut bifidobacteria and lactobacilli. The lowest effective dose of IMO to function as a prebiotic was reported to be 8-10g/day, compared to 1g/day for the prebiotic action of FOS.

20. The applicant also provided details of published studies investigating the fermentation of IMO (from other manufacturers) by gut bacteria. Fermentation of non-digestible oligosaccharides in the colon by gut bacteria can produce short chain fatty acids (SCFA) such as acetate, propionate and butyrate, generally thought to be beneficial to gut health, although there is conflicting evidence relating to the effects of butyrate production in the lower sections of the GI tract. Data presented in the dossier shows that SCFA were produced as a result of IMO administration in some studies but the types and amounts of SCFA varied and there was no

[23].The Committee disputed this statement, noting that IMO is chemically and structurally different to FOS and its microbiological effects in the gut are likely to be different.

evidence of butyrate production. Additional data to evaluate the nutritional quality of IMO are presented in the dossier. Animal studies generally support the partial hydrolysis of IMO in the upper intestine, with the remaining proportion passing into the lower intestine. However, one human study (Oku and Nakamura, 2003) suggested that IMO was not subject to extensive fermentation in the large intestine.

21. The applicant subsequently provided additional analytical data to show that approximately 70% of its IMO is in the form of oligosaccharides that are resistant to digestion in the small intestine. The applicant also provided a letter from Health Canada stating that the applicant's IMO has an available energy value of 2.4 kcal/g. Health Canada has also advised that approximately 80% of the applicant's IMO is digestion resistant and that IMO is regarded as a source of dietary fibre. (The applicant has explained that this 80% value was obtained by considering IMO preparations from a range of manufacturers, while the 70% value mentioned above relates solely to the applicant's IMO.)

22. In response to a request from the Committee, the applicant conducted a four week human tolerance study with their IMO preparation. Adults were given doses of 36g or 54g per day in three divided doses. No serious adverse effects were reported during the study and there were no significant changes in the frequency of bowel movements, although seven out of nineteen subjects in the high dose group reported diarrhoea. No statistically significant differences were observed relating to clinical chemistry parameters or biochemistry. The applicant concluded that the dose of 36 g/day was well tolerated, safe and did not contribute to worsening of GI symptoms.

23. The new study also investigated glucose/insulin responses to the applicant's IMO. The data indicated that IMO produces a similar blood glucose profile and insulin response to the glucose control. The study also indicated that IMO had a prebiotic effect, as determined by increases in numbers of bifidobacteria and lactobacilli in faeces (p=0.049 and p=0.058 respectively), although there were no significant changes in faecal levels of volatile fatty acids.

***Discussion**: Given the variability of IMO preparations from different manufacturers, the Committee asked the applicant to provide data from human studies on its own product in order to determine the extent of absorption and to investigate tolerance. The Committee also asked the applicant for information on the effects of its IMO preparation on serum glucose/insulin levels, bearing in mind the potential to mislead diabetics who might consume the product because they have perceived it to be a prebiotic dietary fibre rather than a mixture of carbohydrates that may be largely or fully absorbed.*

The Committee noted that plasma glucose/insulin responses following administration of the applicant's IMO were almost identical to those following the same dose of glucose, which is inconsistent with the applicant's claim that the majority of the oligosaccharides in IMO are resistant to digestion.

The applicant argues that, in order to assess the metabolic behaviour of IMO, it is essential to consider not only the glucose/insulin profiles but also the other observations in the new human study e.g. IMO administration exhibited a prominent prebiotic effect and resulted in increased short chain fatty acid production and other factors such as increased defecation frequency, indicating that part of the dose ended up in the colon for fermentation by gut microbiota,

The applicant has acknowledged that its IMO preparations are partly digestible, being a mixture of partially digestible and digestion resistant short chain carbohydrates, and an increase in blood glucose and insulin levels would be expected to occur following intake of IMO. As a significant proportion of IMO is absorbed as glucose, the applicant agreed that IMO will not be marketed as suitable for diabetics.

Based on the data provided by the applicant, the Committee was not convinced that this product has a significantly reduced energy content, compared with other digestible carbohydrates.

XII. Microbiological information on the novel food
Information on this aspect is provided on p.14, p58-59 of the application dossier

24. Microbiological specifications for IMO are presented below:

Specification parameter	**Specification**
Total aerobic plate count (CFU/g)	<10, 000
Yeast (CFU/g)	< 100
Escherichia coli (MPN/g)	< 10
Salmonella (CFU/g)	Absent (i.e. <1 CFU per gram or ml)

25. Analyses of five different batches of IMO showed that all batches complied with set specifications.

***Discussion**: The Committee did not raise any concerns or questions on this aspect of the application.*

XIII. Toxicological information on the novel food

Information on this aspect is provided on p. 60-79 of the application dossier

26. The applicant's dossier summarised a series of data relating to toxicological tests and human tolerance of IMO (from other manufacturers). A summary of these data can be found at Annex A.

***Discussion**: The Committee did not raise any toxicological concerns relating to IMO products in general, but did request that the applicant investigates human tolerance to its own IMO preparation which the applicant has addressed as above. The Committee was satisfied that the data from the applicant's new human study provide reassurance that there are no concerns relating to tolerance at the proposed intake levels.*

XIV. Allergenicity and labelling

Information on this aspect is provided on p.72 of the application dossier

27. The applicant has stated that allergenicity issues are unlikely to be a concern as IMO is subjected to extensive purification (including filtration and cation and anion exchange chromatography) as part of the production process to minimise the possibility of contamination with residual enzymes, other proteins or yeast.

***Discussion**: The Committee did not raise any concerns relating to this section of the dossier. The Committee's assessment focuses on safety and labelling, 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. IMO will need to be labelled in accordance with requirements for food allergens if it is derived from one of the allergenic crops identified in EU labelling legislation,[24] unless a specific exemption is obtained following an evaluation by EFSA.*

CONCLUSION

The Committee concluded that there were no safety concerns relating to IMO, provided that it is labelled as unsuitable for diabetics.

The Committee noted that there are conflicting data on the digestibility of IMO preparations. The most recent clinical study, which was conducted with the applicant's product, showed that plasma

[24] Directive 2000/13/EC and Regulation 1169/2011

glucose and insulin responses were very similar to those for glucose, which suggests that the product is well digested in the small intestine.

While the Committee did not regard this as a safety issue, it will have implications for the labelling of products containing IMO, particularly for the energy value of the product, and for any claims that it functions as a dietary fibre or prebiotic. The EU has adopted specific criteria for claims that a food is a "source of fibre" and the labelling of any foods containing IMO will need to comply with this legislation (i.e. Regulation 1924/2006 on nutrition and health claims). According to the same Regulation, prebiotic claims can only be made when they have been validated by the European Food Safety Authority and specifically authorised at EU level.

December 2012

(e) OPINION ON SUBSTANTIAL EQUIVALENCE OF A DHA RICH OIL FROM MICROALGAE CONSIDERED UNDER ARTICLE 3(4) OF THE NOVEL FOOD REGULATION (EC) 258/97

Applicant **Ocean Nutrition Canada Limited**
101 Research Drive
Dartmouth
Nova Scotia B2Y 4T6
Canada

Responsible Person **Hilary Lloyd**

Background

1. In November 2011 a request was submitted by Ocean Nutrition Canada Ltd to the UK for an opinion on equivalence on their DHA rich algal oil compared with the existing DHA rich algal oil from *Schizochytrium sp* marketed by Martek.

2. A number of applications have been made under the novel foods regulation (EC) 258/97 for algal oils that are rich in DHA (docosahexaenoic acid). Of particular relevance to the current request are the oils produced from microalgae of the genus *Schizochytrium* and the Committee first considered an application for the authorisation of an oil from this source in 2001-2 Following its authorisation in 2003[25], the applicant company Martek (*formerly* Omega–Tech) successfully sought an extension of use, which was authorised in 2009[26]

3. 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.

[25] 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)
[26] 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)

Evaluation

a) Composition

4. The applicant cultivates the algae (*Schizochytrium* sp ONC-T18) using a heterotrophic fermentation process, carried out in the absence of light under axenic[27] conditions, which, in their view, is broadly the same as the process employed by Martek. The applicant controls a number of operating parameters (temperature, aeration, pH, etc) to ensure maximal biomass production and the harvested biomass is dried prior to oil extraction using an EU permitted extraction solvent (propan-2-ol). The oil produced by Martek is extracted using hexane.

5. Once the crude oil is extracted from the biomass it undergoes a number of refining processes that are common to the edible oil industry. Specific details of the extraction and refining process can be found in Annex 1 of the application dossier. EU permitted antioxidants are added to the refined oil to ensure stability and the oil is packaged in airtight containers.

6. The applicant has assessed compositional equivalence in two ways: by evaluating the similarity of the production organisms from a taxonomic perspective and by comparing relative quantities of key components in each of the oils.

7. The **taxonomic** evaluation was carried out to provide reassurance that the production strain ONC-T18, originally classified in the genus *Thraustochytrium,* was sufficiently closely related to *Schizochytrium* to support a request for an opinion on equivalence. This evaluation concluded that, based on morphological, biochemical and ribosomal DNA analysis, strain ONC-T18 is more correctly classified within the genus *Schizochytrium*. This evaluation is attached at Annex 4 of the application dossier, together with an additional independent review. The Committee notes that there is an ongoing taxonomic discussion regarding classification within microalgal family *Thraustochytriaceae* but, irrespective of the eventual outcome of this discussion, the strain used by Ocean Nutrition would appear to be closely related to the organism used in the production of Martek's oil.

8. In terms of **composition** the applicant regards their oil to be within the specification for Martek's (Tables 1 & 2 and Annex 2 of the application dossier, summarised below). The applicant also refers to a proximate analysis (tabulated in Annex 2 of the application dossier, summarised below), noting that the oil is 'free' from protein and carbohydrate (limit of detection 0.1%). Although this may not provide evidence of the total absence of protein, the detection limit is consistent with that used for Martek's oil.

[27] Axenic: not contaminated by or associated with any other organisms.

Specification of DHA rich oil from Schizochytrium sp ONC-T18

	Specification	**Test Method**
Colour	Report Actual	Gardner colour
Acid Value	Max. 0.5 mg KOH/g	AOCS CD 3D-63
Peroxide Value (PV)	Max. 5 meq/kg	AOCS Cd 8-53
Moisture and Volatiles	Max 0.01%	AOCS Ca 2d-25
Unsaponifiables	Max 3.5%	AOCS Ca 6a-40
Trans-fatty acids	Max 1%	AOAC 996.06
DHA (Area %)	Min 35%	EP 2003:1352

	Min 350 mg/g	Method 2.4.29
Residual propan-2-ol	Max 1 mg/kg	POS SOP IN-LS-113
Elemental Analysis		
Arsenic	<0.1 mg/kg	US EPA 200.8
Copper	<0.05 mg/kg I	SO 8294 Equivalent
Mercury	<0.04 mg/kg	US EPA 245.6
Lead	<0.01 mg/kg	US EPA 200.8

Proximate Analysis of DHA rich oil from Schizochytrium sp ONC-T18

Nutritional Parameters	**Units**	**Average (of 3 lots) values**

Energy	KJ /100g	3765
Moisture	g/100g	ND
Ash	g/100g	ND
Fat	g/100g	100
Calories	/100g	900
Protein	g/100g	ND
Carbohydrate	g/100g	ND

ND: Not detected

9. A specification for Martek's oil was published in the original 2003 authorisation Decision (reproduced in Table 2, p9 of the application dossier). The applicant's oil meets this specification but, as it includes only a limited number of fatty acids, the applicant has provided a detailed lipid profile of the two oils in order to give additional reassurance that they are equivalent. This analysis, detailed in the Table below, was carried out on three independent batches and includes a side-by-side analysis of a sample of Martek's oil. To complete the comparison the applicant also includes the data set that was submitted in the original application (final column). The applicant concludes that the results of this analysis indicate a relatively high degree of similarity with Martek's oil.

Discussion

*In regard to the **compositional data** the Committee accepted the applicant's view that the differences between a commercial sample of Martek's oil (Column 6 in the Table) and their product was likely to be due to the effect of blending the commercial product with vegetable oil to obtain a consistent product that was within the published specification. However, Members requested additional reassurance from the applicant regarding the degree of variability seen both between the Martek and the applicant's oils and between individual batch analyses was typical. The applicant provided a further breakdown of the composition of individual samples and Members accepted that the differences observed were relatively minor..*

*In regard to the **taxonomic** evaluation the Committee questioned whether the production strain was truly a member of the genus Schizochytrium. In their response, the applicant noted that this evaluation was carried out, in line with the ACNFP guidelines, to provide reassurance that the*

production strain ONC-T18 was sufficiently closely related to Schizochytrium to enable a request for an opinion on equivalence to be considered. The applicant also noted that neither their, nor Martek's production strains have been formally assigned to the genus Schizochytrium using binomial nomenclature. The Committee accepted that, although the expert opinions did not necessarily confirm that the productions strains were members of the same genus, the applicant had provided reassurance that they were sufficiently closely related.

		Ocean Nutrition Oil*			Martek's oil*	Original application Omega–Tech(Martek) (2001)**
Fatty Acid (by Area %)	Formula	(lot) 22629	22630	22740		
Laurate	12:0	1.1	1.0	1.2	Trace	0.40
Myristate	14:0	13.9	13.2	14.2	4.5	10.11
Palmitate	16:0	26.1	27.0	26.6	13.5	23.68
Palmitoleate	16:1n7	2.0	1.7	3.7	0.2	1.76
Stearate	18:0	0.8	0.8	0.8	0.9	0.45
Oleate	18:1n9	0.7	0.3	0.3	17.1	Not Reported
Vaccenate	18:1n7	1.9	1.5	2.9	0.3	Trace – 1.36n
Linoleate	8:2n6	0.2	Trace	Trace	1.4	Trace -0.85

Octadecatetraenoate	18:4n3	0.2	0.2	0.2	0.3	Not Reported
Dihomo-gamma Linolenate*	20:3n6	0.1	0.1	Trace	0.3	2.21
Arachidonate	20:4n6	0.2	0.3	0.2	1.0	0.94
Eicosatetraenoate	20:4n3	0.5	0.5	0.4	0.8	0.87
EPA	20:5n3	0.8	1.0	0.8	1.2	2.63
Docosapentaenoate	22:5n6	8.0	8.2	7.5	15.9	13.50
DHA	22:6n3	40.8	41.3	38.6	39.6	35.00
Other		2.8	3.0	2.6	3.3	6.24
***** as measured by Ocean Nutrition Canada **** as measured by Omega-Tech**						

b), c) Nutritional Value and Metabolism

10. The applicant is of the view that, as their oil has an identical proximate analysis and a similar lipid profile, there will be negligible difference in terms of nutritional value and metabolism compared with Martek's oil.

Discussion: *The Committee noted that although there were differences in the composition of the oil compared with the existing product (e.g. EPA and arachidonic acid) these were not significant in terms of safety.*

d) Intended Use

11. The applicant intends to market their oil in accordance with the authorised uses that are specified in the two Decisions mentioned in paragraph 2, above.

Discussion: *The Committee was content that the intended use of the oil would be consistent with those permitted for the the existing product.*

e) Levels of Undesirable Substances

12. The applicant's oil is routinely tested to ensure compliance with the specification which includes limits for arsenic, copper iron, mercury, lead and trans-fatty acids. These limits, which are at least as stringent as for Martek's oil, are detailed in the specification (Tables 1 and 2 of the application dossier).

13. The applicant notes that the fermentation, extraction and refining processes minimise the risk of microbial contamination, and that tests to check for the presence of contaminating, (including pathogenic) organisms are carried out as part of the quality control regime. The microbiological limits, which are as stringent as those employed for Martek's oil, are as follows:

Coliforms	max 10 MPN/g
E. coli	negative

Aerobic Plate Count	<1000 CFU/g
Yeasts and Moulds	<100 CFU/g
Salmonella	negative/25g
S. aureus	<10 CFU/g

14. The applicant has also considered the possibility of toxin production, noting that there are no reports of toxin production in the any of the genus in *Thraustochytriaceae*. Nevertheless, the applicant has screened samples of both the oil and the algal biomass for a wide range of algal toxins. This screen indicates that none of the toxins tested was present in either test material (Annex 5 of the application dossier).

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

Conclusion

12. The Committee concluded that Ocean Nutrition has demonstrated the equivalence of their DHA rich algal oil with Martek's existing algal oil, according to the criteria set out in Article 3(4) of the Novel Foods Regulation (EC) 258/97.

13. The Committee therefore concluded that the DHA rich algal oil produced by Ocean Nutrition can be considered to be substantially equivalent to the existing DHA rich algal oil produced by Martek.

14. This opinion applies solely to the use of DHA rich algal oil as an ingredient in same products as detailed in Commission Decisions 2003/427/EC and 2009/778/EC and subject to the same maximum level of incorporation.

March 2012

(f) Methyltetrahydrofolic acid, glucosamine salt

27 April 2012

Andreas Klepsch
European Commission

Application under (EC) 258/97 for Approval of Methyltetrahydrofolic acid, glucosamine salt

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 the above product. This was discussed at the Committee's meeting on 26 April.

The ACNFP agreed with the Irish assessment of this product and noted that there has been considerable discussion and debate about the need for, and levels of, folate supplementation and about the possibility of a link with colorectal cancer. However, the Committee concluded that there are no special issues arising from the use of this particular salt, which would be subject to the same recommendations and controls as the existing sources of folate that it might replace.

In view of the ACNFPs advice, the Food Standards Agency is able to support the authorisation of this product.

Yours sincerely,

(By email only)

Chris Jones

For the UK Competent Authority

(g) Citicoline

Andreas Klepsch
European Commission

7 September 2012

Dear Mr Klepsch

As the UK Competent Authority (CA), the Food Standards Agency has sought advice from the UK Medicines and Healthcare products Regulatory Agency (MHRA) and Members of the Advisory Committee on Novel Foods and Processes (ACNFP) on the initial assessment report prepared by the Irish CA for citicoline. As the ACNFP has not met during the designated 60 day comment period, Members' views were sought by post.

Citicoline is an approved pharmaceutical in a number of EU Member States and, based on the advice of the MHRA, our initial view is that products containing citicoline would probably be considered medicinal in the UK

In regard to the Irish initial assessment the UK notes that citicoline (choline cytidine 5'-pyrophosphate) is present at a minimum level of 98% and the risk assessment does not consider the safety of the other unnamed components which will be present. The applicant should therefore provide additional information about the composition of their product and the safety of secondary components, in order for the risk assessment to be completed.

We do not regard the non specific UV absorbance assay that the applicant currently employs to be sufficiently accurate or specific for quality control purposes and this should be replaced by a an alternative analytical method.

The stability data provided by the applicant are restricted to the novel ingredient prior to its addition to food and, further information is required about possible interactions with food matrices.

The applicant also indicates that citicoline may affect the human dopaminergic system and we would like to see additional information regarding this interaction, noting that the dopaminergic system plays an important role in Attention Deficit Hyperactivity Disorder (ADHD) in children.

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 citicoline as a novel ingredient.

Yours sincerely

(By email only)

Dr Chris Jones

Novel Foods, Additives and Supplements Division

(h) Rape Seed protein

Andreas Klepsch
European Commission,

28 November 2012

Dear Mr Klepsch

Application under Regulation (EC) 258/97 for Approval of Rapeseed Protein

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 the above product.

The ACNFP raised a number of concerns and questions relating to this application, which are detailed below:

Allergenicity

- The Committee expressed significant concerns relating to the allergenicity of rapeseed protein. There is a high degree of homology between mustard proteins and rapeseed proteins and it is highly likely that individuals who are allergic to mustard will also be allergic to rapeseed protein. Although it is quite rare in the UK, mustard allergy is more common in other countries such as France. Unless the applicant is able to demonstrate a lack of cross-reactivity between their product and mustard allergens, the Committee is unable to agree with the Irish assessment, that there is a lack of allergenic potential of rapeseed protein for mustard allergy sufferers.

- The Committee also highlighted that, unlike mustard which is generally used in small amounts as a condiment, exposure to rapeseed protein is likely to be far more widespread as it is intended to be incorporated into a range of foods and allergy is therefore of more concern.

Specification of the novel ingredient

- The novel ingredient is a mixture of proteins and the Committee considered that the amino acid profile, while relevant to its nutritional properties, was not useful in terms of

toxicological assessment. The Committee considered that the applicant should identify the different (soluble) proteins present in the novel ingredient, for example by HPLC analysis.

- The Committee would like to see more data relating to phytate levels in the novel ingredient and on micronutrient absorption. Data should be provided to demonstrate that phytate levels for different batches of the novel ingredient are consistently within the specified limits.

Intakes

- The Committee pointed out that the intake estimates for rapeseed protein are based on a series of assumptions and are very approximate, but no further information was requested.

Given the Committee's concerns about allergy and the other questions set out above, the UK has reasoned objections to the authorisation of this ingredient.

Finally, if this ingredient is eventually approved as a novel ingredient then rapeseed should be considered for inclusion in the list of allergenic foods that are subject to special labelling rules, according to Directive 2000/13/EC and Regulation 1169/2011.

Yours sincerely,

(By email only)

Dr Manisha Upadhyay

Novel Foods Unit, Food Standards Agency

(i) Nattokinase

Andreas Klepsch

European Commission,

7 December 2012

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 Belgian CA for the above product. The Belgian assessment was unfavourable due, in the main, to concerns regarding the medicinal status of nattokinase.

The UK medicines authority is unlikely to regard nattokinase to be medicinal, but the ACNFP has concerns about the safety of consuming this type of enzyme and its potential effects on mucous membranes. In view of this we agree with the Belgian CA's conclusion that this product should not be approved.

We also note that, as they concluded that nattokinase was medicinal, the Belgian CA has not completed a full assessment in accordance with Article 6 of regulation 258/97. In view of this, if this nattokinase is to be considered under regulation 258/97in future, then it should be subject to a new initial assessment by a Member State competent authority

Yours sincerely,

(By email only)

Dr Chris Jones
(For the UK Competent Authority)

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