The Advisory Committee on Novel Foods and Processes (ACNFP)

2010 Report

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NOVEL FOOD APPLICATIONS SUBMITTED TO THE UK

(a) Full applications

In 2010 the ACNFP considered two 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 did not conclude its assessment of any of these applications during this calendar year but 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 2010

Novel food (Applicant)	***Meeting discussed***	***Initial opinion***	***Comment***
Dihydrocapsiate (Ajinomoto)	Sept, Nov	-	Positive initial opinion was issued in 2011
Taxifolin (Ametis JSC)	Sept, Nov	-	Positive initial opinion was issued in 2011
Bee Venom for addition to honey (Nelson Honey)	Feb, April	Completed Annex 3(a)	Unfavourable opinion was issued in July 2010
Magnolia Bark Extract (William Wrigley Jr. Co.)	Feb, April	Completed Annex 3(b)	Positive opinion was issued in July 2010
Phosphated Distarch Phosphate (MGP Ingredients)	Feb, July	-	Positive initial opinion was issued in 2011

(b) Opinions on substantial equivalence

In 2010 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 Committee 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 2010

Novel food (Applicant)	*Meeting discussed*	*ACNFP Opinion*	*Comment*
Chia Seeds (The Chia Company)	Feb,April	Completed Annex 3(c)	Equivalence demonstrated in July 2010

NOVEL FOOD APPLICATIONS SUBMITTED TO OTHER MEMBER STATES

In 2010 the ACNFP considered five 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 2010 following an initial assessment in another Member State

Novel food (Member State)	*Meeting discussed*	*UK response*	*Comment*
Yeast Beta Glucans (Ireland)	Feb	Annex 3 (d)	Objections (material used in safety studies, possible immune stimulatory effects)
Guar Gum (France)	July	Annex 3 (e)	Minor comments raised
Phosphatidyl serine (Finland)	July (Postal)		No comments
Lactoferrin	July	Annex 3 (f)	Objections (Iron availability,

	(Postal)		insufficient toxicological data)
Gamma Cyclo Dextrin	September (post)	Annex 3 (g)	Objections raised (possible formation of complexes with vitamin D)

NOVEL FOOD APPLICATIONS CONSIDERED IN PREVIOUS YEARS

During 2010 the ACNFP also considered two responses from applicant companies, and four opinions from the European Food Safety Authority (EFSA) 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

Table 4: Novel foods considered by the Committee during 2010 following an initial assessment in another Member State

Applicant response or EFSA opinion	***Meeting discussed***	***Comment***
Liquorice Root Extract (Response)	Feb	Objections addressed
Rev 7 chewing gum base (Response)	Feb	Objections addressed
Conjugated Linoleic Acid (EFSA, additional EFSA Response)	July, Nov	Objections sustained (lipid oxidation and the need to address the long term effects of consumption insulin sensitivity had not been adequately addressed)
Sardine Peptide Product (EFSA)	Nov	Objections sustained (need for a 90-day toxicity study before the safety of this product could be determined expressed concern about the potential for sardine peptide product to interfere with medication (such as ACE inhibitors) likely to be taken by hypertensive individuals)

Chitin Glucan (EFSA)	Nov	Objections sustained (immune reactions to *A.niger,* and potential cross reactivity in individuals who were sensitive to *A. fumigatus*, a major respiratory and skin allergen).
Phosphated DiStarch Phosphate (EFSA)	Nov	EFSA did not agree with the Committee's conclusions regarding GI intolerance and the need to include an advisory label for children. The Committee considered that a new study, seen by EFSA, was of limited relevance as it concerned a different type of resistant starch

OTHER ISSUES

In 2010 the ACNFP also considered a number of other issues which related to novel foods, cloning, nanotechnology, GM plants and the functioning of the Committee. These are detailed in Table 5, below.

Table 5 Other Issues	***Meeting discussed***	***Comment***
EFSA assessment of allergy of GMO's (draft)	Sept	Noted
Update on Regulatory Approval of Genetically Modified Salmon for Food use in the USA	Sept	Noted
House of Lords Nanotechnology Report	Feb, April	The Committee suggested that it should be made clear that the Food Standards Agency leads on food research involving nanoparticles
Effects of 3 GMO's on the safety of mammals: CRIIGEN review	Feb	Noted

Principles of scientific advice to Government	April	The Committee commended the Board of the Food Standards Agency for its prompt acceptance of the Principles for the Treatment of Independent Scientific Advice . Members suggested that, in cases where the Government decided not to accept the advice of a scientific advisory committee, the relevant Minister should always meet with the chair.
ACRE New techniques of GM	July	The Committee agreed ACRE report that a decision needed to be made as to whether in future it was the 'process' or the 'product of genetic modification (GM) that was regulated and agreed that the product shouldn't be analysed on the basis of the technology. The Committee also considered that epigenetic changes had less potential to be of concern than current methods of genetic modification as mutations arising from epigenetic effects are fewer..
ACNFP Guidance for low level protein analysis	July, Sept	Ongoing work (See minutes)
Cloned animals (Update)	Sept	Noted
ACNFP Assessment of meat and milk from cloned cattle and their progeny (mock assessment)	Nov	Members commented that the available data did not show any differences in the composition of meat and milk from cloned animals and their conventionally bred counterparts however compositional data were limited to a small number of breeds reared under relatively controlled conditions Members agreed with the conclusions of both the FDA and EFSA that safety concerns arising as a result of epigenetic reprogramming were unlikely.

ANNEX 1 INFORMATION ABOUT THE ACNFP

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 2010, 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 2010 and a copy of the code of conduct for ACNFP members can be found on the following pages.

Membership of the Committee during 2010

Chairman

Professor Peter Gregory BSc, PhD

Chief Executive of the Scottish Crop Research Institute

Members

Dr Paul Brantom 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.

Professor Harry Flint BSc, PhD (Microbiologist)
Head of the Gut Microbiology and Immunology Division at the Rowett Research Institute.

Dr Paul Haggarty 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 BSc, MBBS, MD, DSc, FRCP, FRCPath, FIBiol, FMed Sci (Allergenicity expert)
Medical Research Council Clinical Professor of Immunopharmacology at the University of Southampton.

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

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.

Gillian Pope (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 , BSc, PhD, DSc (Plant Biochemist)
Associate Director of Rothamsted Research.

Kevin Swoffer (Resigned Nov 2010) BSc, FIFST (Food chain expert)
Independent food safety consultant

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

Dr A Gleadle

Ms J Downes Food Standards Agency

Mr T Donohoe

Mr P Morgan Food Standards Agency (Wales)

Ms A Taylor Food Standards Agency (Scotland)

Mr G McCurdy Food Standards Agency (Northern Ireland)

ACNFP Members' Interests during 2010

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Professor Peter Gregory	Scottish Crop Research Institute	Chief Executive	None	
	Royal Horticultural Society	Trustee		
Dr Paul Brantom	Elanco Animal Health.	Consultant.	None	
	Veterinary Products Committee (VPC).	Committee Member		
	Veterinary Residues Committee (VRC).			
	Advisory Committee on Animal Feedingstuffs (ACAF).			
	EFSA Panel on Additives & Products or Substances used in Animal Feed (FEEDAP).			

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
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.		
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.

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Professor Stephen Holgate	Merck Research Laboratories. Novartis. Laboratorias Almirall. Pfizer. Altana Pharm. Centecor. Ferring. Wyeth. Amgen. Synairgen (Spin out company University of Southampton). Cambridge Antibody Technology. Kyowa Hakko. York Laboratories.	Consultant.	Novartis. MSD. Wyeth. Avantec.	Research Funding.
	Synairgen.	Shareholder/ Director.	Various charities and trusts.	Trustee.

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
	Southampton Asset Management.	Director.	Advisory Committee on Hazardous Substances	Chair

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Professor John Mathers	none		EU FSA BBSRC Welcome Trust MRC Governing Council of the British Nutrition Foundation Lifelong Health and well being Research Advisory Panel DRINC Advisory Panel	Research Funding Research Funding Research Funding Research Funding Research Funding Member Member Member
Professor Peter Meyer	None		None	

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Professor Clare Mills			FSA.	External reviewer of Food Allergy and Intolerance Research Programme.
			BBSRC	Member of DRINC steering group Core member Committee C
			IFRExtra.	Analysis of Proteins in Oils. Starch work.
			Various.	Member of IFR Food and Health Network (Allergy cluster).
			Various.	EuroPrevall (EU funded) Industry partner.
				Funded Research

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
Mrs Gillian Pope	None		None	
Professor Chris Ritson	Home Grown Cereals Authority	Deputy Chairman (June 2000- March 2008)	Food Ethics Council Cereals Industry Forum EU	Director/Trustee Chairman Research Funding
Mr Kevin Swoffer	None		none	
Professor John Warner	UCB Pharma Ltd. Merck.	Chairman of Scientific Advisory Board. Member of Scientific Advisory Board.	Danone UCB Pharma. Food & Drink Federation. Anaphylaxis Campaign.	Funded Research Trustee

	Personal Interests		Non-personal Interests	
Member	Company	Interest	Company	Interest
	Danone	Member of Scientific Advisory Board Research Funding		
	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 33 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

GOOD PRACTICE GUIDELINES FOR THE INDEPENDENT SCIENTIFIC ADVISORY COMMITTEES

PREAMBLE

Guidelines 2000: Scientific Advice and Policy Making[1] set out the basic principles which government departments should follow in assembling and using scientific advice, thus:

- think ahead, identifying the issues where scientific advice is needed at an early stage;
- get a wide range of advice from the best sources, particularly where there is scientific uncertainty; and
- publish the scientific advice they receive and all the relevant papers.

The *Code of Practice for Scientific Advisory Committees*[2] (currently being updated) provided more detailed guidance specifically focused on the operation of scientific advisory committees (SACs). The Agency subsequently commissioned a *Report on the Review of Scientific Committees*[3] to ensure that the operation of its various advisory committees was consistent with the remit and values of the Agency, as well as the Code of Practice.

The Food Standards Agency's Board has adopted a Science Checklist (Board paper: FSA 06/02/07) to make explicit the points to be considered in the preparation of papers dealing with science-based issues which are either assembled by the Executive or which draw on advice from the Scientific Advisory Committees.

The Board welcomed a proposal from the Chairs of the independent SACs to draw up Good Practice Guidelines based on, and complementing, the Science Checklist.

THE GOOD PRACTICE GUIDELINES

These Guidelines have been developed by 9 advisory committees:

Advisory Committee on Animal Feedingstuffs[4]
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[5]

1 Guidelines on Scientific Analysis in Policy Making, OST, October 2005. Guidelines 2000: Scientific advice and policy-making. OST July 2000

2 Code of Practice for Scientific Advisory Committees, OST December 2001

3 Report on the Review of Scientific Committees, FSA, March 2002

4 Joint FSA/Defra Secretariat, FSA lead

5 Joint FSA/HPA Secretariat, HPA lead

Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment[6]
Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment[7]
Scientific Advisory Committee on Nutrition[8]
Spongiform Encephalopathy Advisory Committee[9]

These committees share important characteristics. They:

- are independent;
- work in an open and transparent way; and
- are concerned with risk assessment not risk management.

The Guidelines relate primarily to the risk assessment process since this is the committees' purpose. However, the Agency may wish on occasion to ask the independent scientific advisory committees whether a particular risk management option is consistent with their risk assessment.

Twenty seven 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

This list of principles will be reconsidered by each committee annually as part of the preparation of its Annual report, and will be attached as an Annex to it.

Principles

<u>Defining the issue</u>

1. The FSA will ensure that the issue to be addressed is clearly defined and takes account of stakeholder expectations. The committee Chair will refer back to the Agency if discussion suggests that a re-definition is necessary.

<u>Seeking input</u>

[6] Joint FSA/HPA Secretariat, HPA lead

[7] Joint FSA/HPA, FSA lead

[8] Joint FSA/DH Secretariat

[9] Joint Defra/FSA/DH Secretariat

2. The Secretariat will ensure that stakeholders are consulted at appropriate points in the committee's considerations and, wherever possible, SAC discussions should be held in public.

3. The scope of literature searches made on behalf of the committee will be clearly set out.

4. 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.

5. Data from stakeholders will be considered and weighted according to quality by the committee.

6. Consideration by the secretariat and the Chair will be given to whether expertise in other disciplines will be needed.

7. Consideration will be given by the Secretariat or by the committee to whether other scientific advisory committees need to be consulted.

Validation

8. Study design, methods of measurement and the way that analysis of data has been carried out will be assessed by the committee.

9. If qualitative data have been used, they will be assessed by the committee in accordance with the principles of good practice, e.g. set out in guidance from the Government's Chief Social Researcher[10].

10. Formal statistical analyses will be included wherever possible. To support this, each committee will have access to advice on quantitative analysis and modelling as needed.

11. When considering what evidence needs to be collected for assessment, the following points will be considered:

12. 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

13. whether stakeholders can provide unpublished data.

10 There is of guidance issued under the auspices of the Government's Social Research Unit and the Chief Social Researcher's Office (Quality in Qualitative Evaluation: A Framework for assessing research evidence. August 2003. www.strategy.gov.uk/downloads/su/qual/downloads/qqe-rep.pdf and The Magenta Book. www.gsr.gov.uk/professional_guidance/magenta_book/guidance.asp).

14. The list of references will make it clear which references have either not been subject to peer review or where evaluation by the committee itself has conducted the peer review.

Uncertainty

15. When reporting outcomes, committees 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.

16. Any assumptions made by the committee will be clearly spelled out, and, in reviews, previous assumptions will be challenged.

17. Data gaps will be identified and their impact on uncertainty assessed by the committee.

18. An indication will be given by the committee about whether the database is changing or static.

Drawing conclusions

19. The committee will be broad-minded, acknowledging where conflicting views exist and considering whether alternative hypotheses fit the same evidence.

20. Where both risks and benefits have been considered, the committee will address each with the same rigour.

21. Committee 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.

22. The committee'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.

23. Committees will make recommendations about general issues that may have relevance for other committees.

Communicating committees' conclusions

24. Conclusions will be expressed by the committee in clear, simple terms and use the minimum caveats consistent with accuracy.

25. It will be made clear by the committee where assessments have been based on the work of other bodies and where the committee has started afresh, and there will be a clear statement of how the current conclusions compare with previous assessments.

26. The conclusions will be supported by a statement about their robustness and the extent to which judgement has had to be used.

27. As standard practice, the committee secretariat will publish a full set of references (including the data used as the basis for risk assessment and other committee 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.

28. The amount of material withheld by the committee 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.

29. Where proposals or papers being considered by the Board rest on scientific evidence, the Chair of the relevant scientific advisory committee (or a nominated expert member) will be invited to the table at Open Board meetings to provide this assurance and to answer Members' questions on the science. To maintain appropriate separation of risk assessment and risk management processes, the role of the Chairs will be limited to providing an independent view on how their committee's advice has been reflected in the relevant policy proposals. The Chairs may also, where appropriate, be invited to provide factual briefing to Board members about particular issues within their committees' remits, in advance of discussion at open Board meetings.

Financial Statment

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 £24,582

MINUTES OF ACNFP MEETINGS DURING 2010

(a) Minutes of 96th meeting (February 2010)

1. Minutes of the 95th meeting **DRAFT/ACNFP/95/Min**

Subject to minor amendments members agreed that the minutes were a true record of the 95th meeting of the ACNFP held on Thursday 26 November 2009.

2. Matters Arising and Postal Consultations

The Secretariat reported back on matters arising from the 95th meeting and on the consultation on the EFSA draft opinion on allergenicity testing of GM foods, which was circulated in December for the Committee to consider by post (paper ACNFP/96P/1). Members' comments had been incorporated into a formal response submitted via the EFSA website.

The Committee noted that there are no definitive methods for predicting allergenic potential of new substances and that this has implications for novel foods as well as GM foods. Members suggested that it would be useful to draw up a short statement on its approach to the allergenicity assessment of novel foods.

3. Bee Venom for addition to honey **ACNFP/96/1**

The Committee was asked to further consider the text of the draft opinion and conclude whether it is content to approve venom as a novel ingredient. The application had previously been discussed by the Committee in September and November 2009. Members are asked to specially consider whether the uncertainty over sensitisation represents a risk that is greater or lesser than that from products that are accepted as part of the existing diet.

The Committee noted that honey contains venom. However, this product has significantly higher levels.

The Committee expressed some concern about the concept of deliberately adding a toxic substance to food, particularly as the data from the clinical study did not provide convincing evidence that bee venom has any clear benefits.

The Committee's main concerns with this application related to potential allergenicity. While it was felt that strong warning labeling could protect individuals who are already sensitised to bee stings/bee products, the Committee remained concerned that there may be a possibility that bee venom may cause allergic reactions in individuals who are not aware they are allergic to bee stings or bee products, and that oral consumption of bee venom may have the potential to sensitise non-venom allergic individuals to bee stings. Relating to these two points, the Committee stated that it could not be certain that there was no risk to consumers as any potential risk could not be quantified. The Secretariat agreed to amend the initial opinion and circulate it to the Committee as a postal consultation.

4. Magnolia Bark Extract **ACNFP/96/2**

The Committee initially considered this application at the September and November meetings and had two outstanding concerns relating to this application. The Committee requested that the applicant provides further data to demonstrate the absence of protein in magnolia bark extract (MBSE) preparations. The Committee stated that the Bradford assay method was not an appropriate method for protein detection for this purpose and requested the applicant uses a more specific detection method such as mass spectrometry. The Committee highlighted the need for such data to be obtained from an accredited laboratory. Members also had concerns about the gender-specific, statistically significant increases in blood total bilirubin levels (TBBL) observed during the 90 day rodent study and requested a copy of the original study report to investigate this further.

The Committee was informed that the applicant is carrying out additional protein analysis data which the Secretariat agreed to circulate upon receipt. The Committee was satisfied that the 90 day rodent feeding study contained all relevant data and that the observed increases in TBBL were not dose-related. The Committee stated that increases in TBBL levels in the treatment group were deemed significant because TBBL levels in the control group were aberrantly low rather than as a result of any dose-related effect.

Members also discussed whether cholestasis may be a reason for the observed increases in TBBL in females. Members discussed the seriousness of this disease during pregnancy (cholestasis during pregnancy can increase the risk of foetal death). However, based on reviewing the original study report, the Committee agreed that the observed increases in TBBL in females were not of toxicological concern and were not attributable to cholestasis.

The Committee noted that the dossier describes studies showing that magnolol and honokiol may have pharmacological effects on gastrointestinal function in humans, but the applicant states that exposure to magnolol and honokiol from MBSE-containing mints or gum is limited so such effects

would not be expected. The Committee was unable to assess the validity of this argument without information on levels in the GI tract of the compounds tested in the relevant studies and how these relate to exposure to MBSE from confectionery and requested that the applicant provides this information.

The Committee was asked to review the text of the draft initial opinion and suggest any amendments.

The Secretariat agreed to request further information from the applicant and to incorporate this information into the draft opinion for review at the next meeting.

5. Phosphated Distarch Phosphate **ACNFP/96/3**

Phosphated distarch phosphate is a chemically modified resistant starch derived from high amylose vegetable starch. The Committee had issued a positive opinion for phosphate distarch phosphate (from maize) in 2009 and this new application, considered for the first time at the November meeting, concerned the use of phosphate distarch phosphate (from wheat), also as a source of fibre in a range of low moisture foods.

The Committee was asked to consider whether the concerns raised at the November meeting, related to the stability of the product and the relevance of the intake assessment, were adequately addressed by the additional information provided by the applicant.

The Committee accepted the applicants' intention to modify their proposed food categories and level of incorporation to replicate those proposed by a previous applicant meant that a new intake assessment was not required because the assessment carried out by the previous applicant applies would now also apply to their product. It was possible that the entry to the market of a second company producing the same ingredient would result in more widespread use, possibly at a lower price, but the intake assessment based on "worst case" consumption scenarios remained valid.

The Committee was not satisfied with the additional information provided in relation to the stability of the product and requested that the applicant provide further data to demonstrate that the physico-chemical structure of the starch does not alter over time and indicated that the use of infrared spectroscopy could be considered in this regard. The Secretariat agreed to seek this information from the applicant, as well as information on particle size.

6. Chia Seed (The Chia Company) **ACNFP/96/4**

The Committee were asked whether it is content to agree the substantial equivalence has been established between the chia seed from The Chia Company and the authorised chia that is currently

marketed in the EU. The Committee was also asked what additional information the applicant should supply in order to demonstrate equivalence.

The Committee were generally content with this application with only two issues requiring clarification. Firstly, the Committee requested more information on the variety of chia seed grown in Australia in order to see how it differs from the South American variety that is currently on the market. Secondly, the Committee asked for more detailed information on the growing conditions in Australia, compared with the conditions for cultivation of the South American product.

7. REV-7 Chewing Gum Base **ACNFP/96/5**

The Committee initially considered this application in Summer 2009. At this time the Committee did not agree with the positive opinion issued by the Dutch CA and concluded that additional information was required before the assessment of the safety of the NI could be concluded. Concerns related to a significant underestimation of the consumption of chewing gum (and as a consequence the novel ingredient) and a lack of human studies to determine its fate during transit through the human gastrointestinal (GI) tract. Members also expressed concern that the new ingredient would not be identified on food labels.

The Committee was asked to consider additional information provided by the applicant in response to each of these concerns. Members accepted that the in vitro study carried out by the applicant addressed questions related to transit through the GI tract if the gum was swallowed, but requested clarification as to the extent to which this study was being relied upon to support the safety of the product. Members therefore sought confirmation that the other safety studies carried out by the applicant were adequate.

The Committee accepted that the there was no legal requirement to indicate the presence of this type of ingredient on the label of chewing gum products, but their view was that the applicant's proposed name "REV-7" to be inadequate if it were to appear on food labels.

The Secretariat agreed to forward the safety studies to toxicologists on the Committee for review, and to ask the applicant to consider an alternative, more descriptive, name for the ingredient.

8. Yeast beta-glucans ACNFP/96/6

The Committee was asked to consider a positive initial opinion from the Irish Competent Authority (CA) on an application submitted by Biothera Incorporated, for the authorisation of two insoluble (BWGP and WGPD) and one soluble (WGPS) yeast beta-glucan preparations as novel food ingredients.

The novel ingredients are derived from the cell wall of baker's yeast, Saccharomyces cerevisiae, which has a long history of safe use in the production of bread, beer and wine. The ingredients are intended to be used as food supplements and food ingredients.

The Committee was asked whether it agreed with the Irish CA's positive opinion, that yeast beta-glucans be granted authorisation as a novel food ingredient.

The Committee considered that a proper definition of the ingredients was required. In particular it noted that no information on the composition of the soluble product was provided, and there may be significant differences in this form due to the solubilisation steps involved in the production process.

The Committee noted that the safety data presented in the application were not clearly cross-referenced to the correct product. As there are likely to be significant differences between 1,3 and 1,4 beta-glucans, more information was required on which products the safety data corresponds to.

The Committee requested further information on the immunostimulatory effects of the ingredients and whether they have significant effects on the gut flora.

The Committee also noted some inconsistencies between the information reported by the Irish CA and the information presented in the application dossier.

The Secretariat agreed to transmit the Committee's comments to the European Commission as part of the UK's formal response to the Irish opinion.

9. House of Lords Science and Technology Committee Report on Nanotechnologies in foodACNFP/96/7

The House of Lords select committee announced this inquiry in February 2009 and gathered written and oral evidence from a range of interested parties. The inquiry covered a wide range of topics regarding the current and future use of nano-technologies in relation to food.

The Committee noted the report and suggested that the Food Standards Agency should take the lead on any research requirements that are specific to food, as food research does not feature high on the priorities of the Research Councils.

10. Open Meeting **ACNFP/96/8**

The Committee was asked to review the format and programme for the annual ACNFP workshop which is to be held on 21 April 2010.

The Committee agreed the format and the topics to be discussed in the meeting. The Secretariat agreed to proceed with the organisation of the meeting and would contact individual members directly about specific topics.

11. Items for information

12.1 EU Update *ACNFP/96/9*

12.2 Update on Scientific Advisory Committees *ACNFP/96/10*

12.3 Novel Food Notifications *ACNFP/96/11*

12.4 Effects of Three GMOs (MON810, MON863 and NK603) on the Health of Mammals *ACNFP/96/12*

12.5 Food Standards Agency's Protective Marking System *ACNFP/96/13*

On paper ACNFP/96/12, the Committee commented that the nutrient composition of animal diets can be a critical factor in feeding trials, particularly those involving a high proportion of the test material. There appeared to be some confusion over assessing the significance of any differences that are observed in these types of studies and there was a role for advisory committees in explaining this more clearly to the public.

The Committee noted the other information papers without comment.

12. Any other business

Three members reported on an event hosted by the Government Office of Science and the Food Standards Agency for non-specialist (lay) members of Government's scientific advisory committees, which they had found to be interesting and worthwhile.

The Members and Secretariat agreed to set up a small working group regarding guidance for applicants on methods for protein analysis.

Action: Secretariat to work with Members in order to set up working group

The Committee and Secretariat also suggested to consider a planning day to examine work that the Committee wish to undertake.

13. Date of next meeting

The next meeting was scheduled for Thursday 22 April 2010 in Aviation House**.**

(b) Minutes of 97th meeting (April 2010)

14. Minutes of the 96th meeting **DRAFT/ACNFP/96/Min**

Subject to minor amendments members agreed that the minutes were a true record of the 96th meeting of the ACNFP held on Wednesday 10 February 2010.

15. Matters Arising and Postal Consultations

The Secretariat reported back on matters arising from the 96th meeting.

Item 6 - Phosphate Distarch Phosphate:

The applicant had not yet provided the additional information requested by the Committee

Item 8 - REV-7 Chewing Gum Base:

The Secretariat confirmed that the ACNFP's expert in toxicology was satisfied with the safety studies which were included in the original dossier. The applicant confirmed they had registered the name of the product as "REV-7". While this was not very informative, they were planning to design a consumer facing website that would provide information on the novel chewing gum base.

Item 9 – Yeast beta-glucans:

The Secretariat has forwarded the Committee's comments to the European Commission.

4. Open Workshop **Oral Update**

The open workshop that had been planned for the previous day had been postponed due to the General Election. See item 9 below.

5. Bee Venom for addition to honey **ACNFP/97/1**

The Committee was asked to review the text of the draft opinion in the light of responses to a public consultation. The application had previously been discussed by the Committee in September and November 2009 and in February 2010.

The Committee considered in detail the forty seven public comments received during the ten day public consultation and noted that the number of comments received suggested that these people had a strong wish to consume the novel ingredient, and believed that they could be adversely affected if the novel ingredient is not authorised. However, the Committee recognised that its remit was to assess novel ingredients for safety and not to consider pharmacological properties and potential benefits.

A Member observed that the NHS was reported to use Manuka honey in the treatment of patients. The Secretariat confirmed this may possibly be the case but that this did not include the addition of the novel ingredient, bee venom.

In light of a public comment received relating to allergy and the likelihood of bee stings, the Committee agreed an amendment to the draft opinion to highlight published reports of an increase in incidence of allergic reactions to insect bites (in particular bee stings), possibly linked to population susceptibility

The Committee also highlighted that its comment relating to sugar intake was not a reason to reject the novel ingredient, but it wished it to note that the extra sugar content would have a possible effect on dental caries.

The Committee further agreed that the conclusion to the opinion should draw attention to the large number of public responses received during the consultation of its draft opinion.

6. Magnolia Bark Extract **ACNFP/97/2**

The Committee initially considered this application in September and November 2009 and in February 2010. At the February meeting the Committee requested that the applicant provide further data from protein analysis using a more precise detection method. The Committee also requested information to help rule out any possibility that components of magnolia bark may have pharmacological effects on gastrointestinal function.

The Committee was satisfied with the applicant's response relating to gastrointestinal effects. The Committee noted that the applicant had carried out protein analysis of magnolia bark extract using three detection methods but requested that the applicant provide the raw data from these analyses in order to be satisfied that its concern had been adequately addressed.

The Secretariat agreed to circulate the additional protein analysis data to the Committee by post.

7. Chia Seed (The Chia Company) **ACNFP/97/3**

The Committee considered this application for an opinion on substantial equivalence in February 2010, when Members requested additional information on the cultivation conditions and the botanical origins of the Australian chia.

The Committee was satisfied that the applicant had provided sufficient information to adequately address the Committee's concerns and agreed that substantial equivalence had been established. The Committee agreed with the text of the draft initial opinion subject to minor amendments.

8. Principles of Scientific Advice to Government **ACNFP 97/4**

The Committee considered these Principles, which had been recently published by the Government's Chief Scientific Adviser.

The Committee commended the Board of the Food Standards Agency for its prompt acceptance of the Principles for the Treatment of Independent Scientific Advice issued by senior scientists and scientific advisers in November 2009.

The Committee noted that the Government's Principles apply not only to Ministerial appointments (which are regulated by the Commissioner for Public Appointments), but also to non-Ministerial appointments and other appointments made by relevant organisations, some of which nevertheless follow OCPA guidance as best practice.

A member gave an example of how outcomes can be linked to advice, taken from another public committee that logs the various stages from the request for advice, the production of advice, and the way that this advice was used. As this committee's advice was sometime used in court, it had adopted a press protocol to avoid court proceedings being compromised.

Members suggested that, in cases where the Government decided not to accept the advice of a scientific advisory committee, the relevant Minister should always meet with the chair, although the document implied that this was optional. The Committee noted that the Agency's scientific

committees operate with a high degree of openness and that committee chairs will attend Board meetings in person where their committee's advice is being presented and discussed.

9. Open Workshop and Horizon Scanning Meetings **Oral Updates**

The Committee considered an update on the postponed Open Meeting and the responses of prospective participants to the discussion topics. It agreed to finalise the agenda for the re-arranged meeting later in the year.

The Committee also considered an update on a proposed Horizon Scanning meeting and considered ideas for possible formats and the topics which could be discussed in this meeting. These were:

- Nanotechnology (differentiating between inorganic nanoparticles and "bionanotechnology")
- Consumers' use of food labelling information
- Intake Estimation – particularly from multiple sources

The Committee considered the Horizon Scanning Meeting and Open Meeting could both be scheduled along with the November business meeting.

10. Items for information

10.1 Update on Nanotechnology **ACNFP/97/5**

10.2 Update on Protein Subgroup **Oral Update**

10.3 EU Update *ACNFP/97/7*

10.4 Update on Scientific Advisory Committees *ACNFP/97/8*

10.5 GM Update *ACNFP/97/9*

The Committee noted that the Secretariat had begun discussions with members of the Protein Subgroup and that a proposal for guidance to novel food applicants was being prepared. The Committee noted the remaining information papers without comment.

11. Any other business

The Chairman gave an update on the General Advisory Committee of Science (GACS) meeting he attended on 4 March, which included a presentation on the Committee on Toxicity's development of an approach to handling uncertainty

Action: Secretariat to liaise with Committee to identify examples for COT to consider

12. Date of next meeting

The next meeting was scheduled for Wednesday 7 July 2010 in Aviation House.

(c) Minutes of 98th meeting (July 2010)

13. Minutes of the 97th meeting **DRAFT/ACNFP/97/Min**

Subject to minor amendments members agreed that the minutes were a true record of the 97th meeting of the ACNFP held on Thursday 22 April 2010.

14. Matters Arising and Postal Consultations

The Secretariat reported back on matters arising from the 97th meeting.

Item 6 - : Magnolia Bark Extract:

No comments were received on the draft Opinion during the recent public consultation. The opinion would therefore be finalised and submitted to the European Commission.

Item 11 - Committee on Toxicity's (COT) development of an approach to handling uncertainty:

COT has published a paper -TOX/2010/19 on its website which was discussed at its meeting on 22 June. The paper can be located at http://cot.food.gov.uk/cotmtgs/cotmeets/cotmeet2010/cotmeet22jun2010/cotagendapapers22jun10

The Secretariat summarised the responses to the two postal consultations that took place after the April meeting:

Phosphatidyl serine (postal paper ACNFP/98/P1)

Only one comment was received from Members and this was not substantive. The UK had sent a nil return to the European Commission's request for comments and objections

Lactoferrin (postal paper ACNFP/98/P2)

The Committee confirmed that its concerns over a previous application for lactoferrin still applied. The Agency had relayed this to the European Commission.

4. Licorice root extract **ACNFP/98/1**

The Committee considered the Belgian Competent Authority's initial opinion in April 2009. The Committee was asked to consider further information received from the applicant in response to a number of comments and concerns which had been raised by the Committee.

The Committee questioned the average licorice intake level as it seemed very high for the UK, but accepted that consumption is significantly higher in some other European countries. The Committee also questioned the evidence for the claim that the novel ingredient was comparable to existing licorice extracts, as the applicant had not provided data on how the production process changes the composition of the product.

The Committee considered that their concerns about children's intake levels had not been answered. This was particularly relevant as it was intended to add the novel ingredient to yoghurt and fruit drinks which were widely consumed by children. The Committee noted that the novel ingredient would not be suitable for children under 12.

The Committee also considered that the applicant had not addressed their concerns on haematological effects. It was particularly concerned that when the novel ingredient was consumed there was prolongation of PT (prothrombin time) and APTT (activated partial thromboplastin time). This was a significant concern, even although the effect was reversible and values rapidly returned to normal once consumption had stopped.

The Committee agreed that its concerns on oestrogen receptors had been addressed by the applicant.

The Committee's comments will inform the UK's position in future discussions regarding this novel ingredient at meetings of the Standing Committee on the Food Chain and Animal Health.

5. Phosphated Distarch Phosphate **ACNFP/98/2**

The Committee previously considered this application in September and November 2009 and in February 2010. In February the Committee requested that the applicant provide additional

information to reassure Members that the product remained stable for the duration of its shelf life. The applicant had questioned the need for additional studies, pointing out that a previous application for a similar product which had not provided detailed stability data, but had relied upon compliance with a European starch industry standard.

The Committee understood the rationale for the applicant's question but as it dealt with ingredients that, by their nature, were new there was a strong possibility that new issues of concern could emerge. The Committee might therefore need to ask for more information than they had requested for previous applications. In the case of this product it considered that there was greater awareness that processing and shelf life of ingredients can affect their chemical properties and it concluded that the additional information it requested following the February 2010 meeting was still required.

6. Guar Gum **ACNFP98/3**

The Committee considered the French Competent Authority's initial opinion on this application for authorization of Guar Gum as a novel food ingredient.

Professor Paul Brantom confirmed he did not have an interest in the company BIBRA which had prepared a report that was included in the application. Whilst he had been previously employed by BIBRA, he was not associated with the company involved in the current application, which was a new company that had started up following the demise of the original BIBRA.

The Committee noted that, although it is stated in the application dossier that the guar plant has no history of consumption in the EU, guar beans are consumed in the UK by the Indian community. However, the Committee was not aware of consumption of guar gum derived from the beans.

The Committee recognized there was a possibility that the novel ingredient may cause obstructions in the GI tract (oesophageal and intestinal obstruction) as it will swell significantly on exposure to water. Members shared the French authorities' concern that some consumers may eat the cereal component of the proposed cereal/dairy bi-component product without mixing with the dairy component and stressed that such products should be clearly labelled so that the cereal component is not consumed on its own. The committee advised there was little risk in consuming the product provided this risk was addressed.

7. Conjugated Linoleic Acid (CLA) **ACNFP/98/4**

The Committee considered two opinions from the European Food Safety Authority (EFSA) on two separate applications for CLA-rich oils, which had initially been assessed by the Irish and Spanish Competent Authorities. The Committee had considered the two opinions in July 2008 and September 2008 respectively.

The Committee confirmed that their previous concerns had not been satisfactorily resolved.

The Committee agreed with EFSA's conclusion that the long term effects of CLA intake on insulin sensitivity had not been adequately addressed. The Committee considered that a study longer than eight weeks was necessary to address its concerns that people might be put at risk of developing

type 2 diabetes if they consumed this novel ingredient. The Committee considered that both animal and human studies should be considered when evaluating the effects of CLA. The Committee also agreed with EFSA that the products were unsuitable for type 2 diabetics, noting the high prevalence of type 2 diabetes in the UK and the fact that many cases are undiagnosed. It recommended that food containing CLA-rich oils, if authorised, should carry a warning label that it should not be taken by diabetics and those at risk of diabetes, by pregnant women or by children or babies.

The Committee re-iterated its concern about oxidative effects of high level intake of polyunsaturated fatty acids (PUFA) at the arterial wall, which had led the Committee on Medical Aspects of Food and Nutrition Policy (COMA) to recommend an upper limit of 10% for the ratio of PUFA to total fat intake. Consumption of the recommended amounts of CLA-rich oil would significantly increase PUFA intakes. The EFSA opinion confirmed that this issue has not been addressed by the applicants.

The Committee expressed disappointment that EFSA had not considered the implications of CLA consumption by children and also noted that the intake estimates reported in the EFSA opinions did not take account of the total intake of CLA from all sources. One member observed that surveys of food consumption may underestimate real rates of consumption, as judged by energy balance studies, and that this could lead to underestimation of the intake of added components such as CLA.

The Committee could not therefore agree with EFSA's conclusion that the safety of these ingredients has been demonstrated (for limited periods of exposure), given the significant uncertainties over oxidative stress and effects on glucose control (in non-diabetic subjects), combined with the lack of data on the stability of CLA in food products.

From a risk management perspective, the the Committee questioned how it would be possible to implement advice that a novel ingredient was safe for a period of six months continuous exposure but safety beyond this had not been established. Whilst recognizing that risk management issues were outside the remit of the Committee, it noted that advice in this format may cause practical difficulties for risk managers.

8. New Techniques of Genetic Modification **ACNFP 98/5**

The Committee considered the techniques detailed in the Advisory Committee on Releases to the Environment (ACRE) draft report entitled *"New Techniques used in plant breeding".* The ACRE report is in response to a Brussels working group addressing the question of whether new techniques, now being employed or under development, result in a genetically modified organism (GMO) as defined in European Union (EU) legislation.

The Committee agreed with the thrust of the ACRE report that a decision needed to be made as to whether in future it was the 'process' or the 'product of genetic modification (GM) that was regulated. EU legislation currently defines GM as a process or technique whereas many countries define it as a product and the definition of GM needs to be rethought so it is consistent with state of the art techniques of GM. The Committee agreed that the product shouldn't be analysed on the basis of the technology. All ethical issues identified by the Committee were concerned with the product rather than the technology.

The Committee considered that epigenetic changes had less potential to be of concern than current methods of genetic modification as mutations arising from epigenetic effects are fewer.. It considered it was arguable whether, contrary to popular belief, transgenesis is more dangerous than cisgenesis, e.g. changing the spatial or temporal pattern of endogenous gene expression.

The Committee commented that a rigorous risk assessment was required before GMO's could be placed on the market whereas products derived from traditional cross breeding techniques required no risk assessment even though allergenicity levels may be altered or toxic compounds expressed. The Secretariat agreed to keep the Committee informed as to future drafts of the ACRE report and any outputs that arise from the Commission working group ahead of discussions by EU Member States in Brussels.

9. ACNFP Guidelines for low-level Protein Analysis **ACNFP/98/6**

The Committee reviewed a draft guidance note regarding the detection of proteins in novel foods, which was prepared by the Protein Sub-group, a working group of the ACNFP. The guidance note was intended to assist applicants with the provision of appropriate information on the presence of proteins in novel ingredients.

The Committee thanked the members of the Sub-group for their input into the draft guidance. It noted that the draft guidance aimed to help applicants identify the appropriate methods fo protein detection, quantification and identification when seeking authorisation for novel foods.

The Committee agreed that all products should be evaluated on a case by case basis and that the technique used for the protein analysis should based on optimal performance rather than availability.

The Committee also viewed the decision tree approach to be very useful as made it clear the importance of critical review of the methods employed.

10. Preparation for Horizon Scanning Meeting **Oral Update**

The Committee considered the format and potential speakers for a forthcoming fact finding meeting on nanotechnology, to be held in November.

The Committee considered that the objective of the meeting should be clearly set out so that the meeting's success would be measurable. It agreed that the main objective was that the Committee would be better informed on nanotechnology and able to deal with any future issues related to nanomaterials The Committee was particularly interested in the effect of nanoparticles in the gut and where nanotechnology may be applied in the future in food.

The Committee was of the view that discussions would be more useful than lengthy presentations, providing more opportunity to question invited experts. It would be useful to be given papers in

advance of the meeting including key discussion points so that there was a focus. It also considered it helpful if they could see the UK Nanotechnology Strategy, which had been published by the Government in March 2010.

The Committee was informed there would be a debate the following week in the House of Lords on the House of Lords Science and Technology Committees report on Nanotechnologies and Food. It was suggested that an organisation which had given evidence to the enquiry should be invited to speak to the Committee as the people giving evidence had shown they were very knowledgeable. Some organisations, such as Unilever, had experience in engagement with the public as well as with food applications and the Committee and Secretariat suggested additional experts who might join this meeting.

The Committee considered whether labelling issues should be discussed at a separate meeting in the evening but concluded that a discussion which should include all members of the Committee may be difficult over dinner and it would be better to concentrate on one topic during the Horizon Scanning meeting.

11. Items for Information

11.1 EU Update **ACNFP/98/8**

11.2 SAC Update **ACNFP/98/9**

11.3 Update on G03 research programme **ACNFP/98/10**

11.4 Improving engagement across SAC secretariats **ACNFP/98/11**

The Committee noted these information papers without comment.

12. Any other business

The Committee was given an update on the FSA's engagement with a representative Hindu group which was founded following a visit of FSA officials to a Temple. The Committee was informed that a Chair for a meeting with the catering industry had been identified. The FSA would bring others into the group. The FSA had reaffirmed that it was committed to engage with various communities, such as the Indian community, to take forward food issues which were specific to that community.

The Committee was reminded about the new FSA policy on refunding travel and other expenses. The Committee asked the Secretariat to note that they would need early notice of events, particularly those outside the normal ACNFP meeting times, in order to take advantage of the cheapest fares.

Members were invited to stay after the meeting for a presentation on nanomaterials by a representative from Food Standards Australia New Zealand, who was visiting the Food Standards Agency.

13. Date of next meeting

The next meeting was scheduled for Thursday 23 September 2010 in Aviation House

(d) Minutes of 99th meeting (Sept 2010)

15. Minutes of the 98th meeting **DRAFT/ACNFP/97/Min**

Subject to amendments members agreed that the minutes were a true record of the 98th meeting of the ACNFP held on Wednesday 7 July 2010.

16. Matters Arising and Postal Consultations

The Secretariat reported back on matters arising from the 98th meeting and

summarised the outcome of the postal consultation that took place after the July meeting on gamma-cyclodextrin (postal paper ACNFP/99/P1). Members raised a number of questions concerning:

- The use of n-decane to separate the complexant from the formed gamma-cyclodextrin, as n-decane is not included in the list of permitted extraction solvents (EC Directive 88/344);
- The intestinal fate of gamma-cyclodextrin, and whether the ingredient truly is a slow release source of glucose, as stated in the application dossier;
- The potential effect on absorption of fat-soluble vitamins, particularly vitamin D;
- The intended use and estimated intakes;
- Labelling and the need to avoid any misunderstanding that the product is a source of glucose.

A letter itemising the Committee's concerns was sent to the Commission on 17 September.

17. Dihydrocapsiate **ACNFP/99/1**

The Committee was asked to consider this application from the Japanese Company Ajinomoto to the UK competent authority for the approval of synthetic dihydrocapsiate (DHC) as a novel food ingredient.

DHC is found naturally in chilli peppers and according to the applicant can enhance energy expenditure and fat oxidation. Extracting DHC from peppers is not sustainable and the applicant has chosen to produce synthetic DHC.

The Committee had no major concerns with the toxicity data but questioned why the product was being produced as it didn't appear to have any particular nutritional value. The Committee was concerned that no information was provided about what happens to the metabolites of DHC. It questioned the effects on blood pressure that were seen in clinical trials and also requested more data on the pharmacological effects of DHC or its breakdown products on its interaction with the cardiovascular system and its accumulation in adipose and brain tissues.

The Committee questioned the NOAEL of 1000mg/kg bw/day that the applicant had derived from the animal feeding studies and considered that it should be should be lower at 300mg/kg bw/day, noting that this still provided a significant margin of safety compared with the potential intake of DHC.

The Committee considered the points raised in the 21 day public consultation.

18. Taxifolin **ACNFP/99/2**

The Committee was asked to consider this application that had been submitted by the Russian company Ametis to the UK competent authority for the approval of a taxifolin rich extract as a novel food ingredient which is to be added to a range of foods.

Taxifolin is a flavonoid extracted from the wood of dahurian larch, a species of larch native to eastern Siberia and adjacent regions of Mongolia and northeastern China.

As the batch analyses comfortably exceeded the specification, the Committee queried whether these batches were truly representative and also noted a lack of detail regarding the unidentified components present in the extract. The Committee also questioned whether the test material used in the toxicological studies was the same as, or directly comparable to, Ametis' product and whether the studies were carried out in accordance with relevant OECD guidelines. Finally, the Committee queried the potential environmental impact of felling *Larix gmelinii* for food production purposes and asked whether there are any programmes in place to ensure that the trees are sustainably farmed.

19. ACNFP guidelines for low-level protein analysis **ACNFP99/3**

The Committee was asked to consider guidelines for low-level protein analysis. Following a useful discussion in the July meeting the Committee was asked to comment on the text of the revised document. The Committee suggested minor amendments prior to it being finalised and asked to see the final draft prior to it being finalised.

20. **Preparation for horizon scanning meeting and the Open Event** **ACNFP/99/4**

The Committee was asked to consider the proposed organisation and programme for the ACNFP open event to be held on Thursday 25 November at Aviation House and to further consider the programme for the horizon scanning meeting on 24 November.

The Committee agreed the format of the Open Event. Preparation for the horizon scanning meeting will be taken forward by the Secretariat and the Chair of the Committee.

21. Items for Information

8.1 Cloning Update	**ACNFP/99/5**
8.2 EFSA Opinion on the Assessment of Allergenicity of GMOs	**ACNFP/99/6**
8.3 EU Update	**ACNFP/99/7**
8.4 Scientific Advisory Committees (SACS) Update	**ACNFP/99/8**
8.5 Regulatory Approval of Genetically Modified Salmon for Food use in the USA.	**ACNFP/99/9**

The Committee noted these information papers without comment.

22. Any other business

Stephen Holgate gave feedback on a meeting of Chairs of Scientific Advisory Committees held by the Chief Scientific Advisor to HM Government, Sir John Beddington. The meeting had been mainly

concerned with developing an updated code of practice for Scientific Advisory Committees. A public consultation on the code of practice was launched on 17 September.

Jayam Dalal provided an update on the FSA's engagement with a representative Hindu group which followed from a visit of Agency officials to a Hindu temple. A joint meeting between Defra and the FSA has been arranged to take forward various concerns of the representive Hindu group.

The Committee thanked the Secretariat for the quality of the ACNFP papers.

23. Date of next meeting

The next meeting was scheduled for Thursday 25 November 2010 in Aviation House

(e) Minute of 100th meeting (Nov 2010)

24. Minutes of the 99th meeting **DRAFT/ACNFP/99/Min**

The Committee agreed the minutes were a true record of the 99th meeting of the ACNFP held on Thursday 23 September 2010.

25. Matters Arising and Postal Consultations

The Secretariat reported back on matters arising from the 99th meeting:

Item 6: The Secretariat will contact the Protein Subgroup after the meeting with a view to finalising the guidelines on low-level protein analysis

26. Conclusions from the Nanotechnology Briefing Session

The Committee considered that the previous day's briefing session had been a useful orientation discussion on the topic. Products of nanotechnology need to be looked at on a case by case basis, and could be considered in one of three categories: (1) insoluble and persistent nanomaterials, (2) soluble and biodegradable nanomaterials and (3) nanostructured foods.

The Committee agreed to have a more detailed discussion on nanotechnology in May 2011.

27. Dihydrocapsiate **ACNFP/100/1**

The Committee initially considered this application in September 2010. The Committee was requested to consider further information supplied by the applicant on: (1) the purpose of adding dihydrocapsiate (DHC) to food, (2) the pharmacological and nutraceutical effects of DHC or its metabolites, and information supplied by the secretariat on (3) blood pressure-related effects for human tolerance studies.

The Committee considered that the applicant's stated purpose of adding DHC to foods was very vague, although this was not a safety related issue. The Committee had previously questioned the intake data, in view of the apparent broad range of foods to which DHC could be added, but was reassured on this point by advice from the Agency's intake experts that the applicant's approach to intake estimation was sound. The Committee considered that the novel ingredient could potentially be regarded as a food additive (flavouring) rather than a novel ingredient, but noted that the applicant did not regard the flavour of DHC to be significant.

Members considered that the information relating to the interaction of DHC with TRPV1 receptors along the GI tract was unclear but acknowledged that DHC is likely to interact with these receptors in different ways along the GI tract. However, the Committee requested further information to support the statement that DHC metabolites (vanillyl alcohol and 8 methyl nonanoic acid) were also not expected to have pharmacological effects.

The Committee concluded there were no other concerns about the safety of the ingredient and that its earlier questions had been dealt with. The Committee emphasised that its approval of the novel ingredient was based soley on safety and that it should not be seen as endorsement of any health/well being claims made by the applicant.

28. Taxifolin **ACNFP/100/2**

The Committee initially considered this application in September 2010. The Committee was asked to consider further information supplied by the applicant, regarding the specification, test material, laboratory accreditation and environment impact, for the approval of Taxifolin as a novel food ingredient.

The Committee considered its concerns over the purity of the novel ingredient had been largely answered by the additional information supplied. Members considered that the level of reproducibility was acceptable, recognising that it was generally more difficult to produce an ingredient to an exact specification if it came from a 'natural' source material. One member undertook to review the High Performance Liquid Chromatography data to see whether these gave sufficient indication of the likely nature of the unidentified components.

The Committee accepted that the studies complied with the Russian GLP standard but questioned what this meant in practice. The Committee also accepted that, as the raw material (larch tree stumps) was a by-product of the logging industry, the production of the novel ingredient could not be said to have a high environmental impact. In regard to the test materials used in the safety studies, the Committee accepted that sufficient number of studies had been carried out using the novel ingredient, or a comparable counterpart, for there to be sufficient reassurance that the novel ingredient did not present a risk at the levels proposed by the applicant.

29. Sardine Peptide Product **ACNFP100/3**

The Committee was asked to consider a favourable European Food Safety Authority (EFSA) opinion on a sardine peptide product (SPP), which had been assessed by the Committee in April 2009.

The Committee again noted that SPP is regarded as a medical product in the UK. The Committee reaffirmed its earlier opinion that the 28 day feeding study in rats showed there were potential clinical effects and therefore it would be useful for the applicant to undertake a 90 day study. It was concerned that EFSA had not taken account of these effects in its conclusions.

The applicant has not applied for an exemption and therefore the novel ingredient would need to be labeled as being derived from fish, according to EU legislation on allergen labeling.

The Committee advised that the EFSA opinion had not dealt with the concerns previously raised by the Committee and that EFSA had not justified some of the statements it made about the novel ingredient.

The Committee's advice will help to determine the UKs voting position at the Standing Committee on Food Chain and Animal Health

30. Chitan-Glucan **ACNFP/100/4**

The Committee was asked to consider the favourable EFSA opinion on chitin-glucan which is extracted from *Aspergillus niger*.

During its review of the product in April 2009 the Committee highlighted published reports of immune reactions to *A.niger,* and noted that the consumption of the chitin-glucan could lead to cross reactivity in individuals who were sensitive to *A. fumigatus*, a major respiratory and skin allergen.

The Committee expressed concern that the EFSA Opinion was dismissive of these issues, given the relatively high level of protein present in the novel ingredient. The Committee was also concerned that insufficient reassurance could be drawn from the limited number of *A.niger* products on the market. Members noted that current dietary exposure to *A.niger* components was very limited, either because the derived product itself was present in food at very low levels (e.g. bakery enzymes) or it was highly purified (e.g. citric acid). The Committee also viewed the presence of *A.niger* in food as an environmental contaminant to be irrelevant as consumers would not be aware of its presence. The Committee was not reassured by the allergenicty studies reviewed by EFSA.

The Committee's advice will help to determine the UK's position when the application for approval of this ingredient is discussed at EU level.

31. Phosphated Distarch Phosphate **ACNFP/100/5**

The Committee was asked to consider an EFSA opinion and additional study on Phosphate Distarch Phosphate which had received a positive Opinion from the Committee in 2009. The EFSA opinion was also positive but the EFSA Panel did not agree with the Committee's conclusions regarding GI intolerance and the need to include an advisory label for children.

The Committee considered that the new study was of limited relevance as it concerned a different type of resistant starch. Committee Members had a range of views on the possibility that PDP could have undesirable laxative effects in children and would continue their discussion at the next meeting.

32. Conjugated Linoleic Acid **ACNFP/100/6**

The Committee was asked to consider EFSA's response following a number of concerns raised at the July 2010 meeting regarding EFSA's risk assessment of conjugated linoleic acid rich oil (CLA). The Committee assessed CLA in July and September 2008.

The Committee remained concerned about lipid oxidation during storage and considered that the testing conditions were unrealistic. The advice from EFSA, that stability had been demonstrated under these conditions was correct but was not very relevant to the commercial use of the ingredient. The Committee reiterated its earlier views that insufficient data had been provided about stability and was concerned with the implication that the absence of data meant there was no risk.

The Committee noted that EFSA's response had referred to issues being "for risk management", but considered that a rigid division between risk assessment and risk management was unhelpful.

Action: The Secretariat will inform EFSA of the Committee's views

Item 11 and the remainder of the agenda items were taken in open session, as advertised on the Agency's website the previous week. Four members of the public and one Agency official were in attendance.

33. Meat and Milk from Cloned Animals and their Progeny **ACNFP/100/7**

Members considered a hypothetical application for the authorisation of meat and milk from cloned cattle and their descendants. The paper had been prepared by the Secretariat following a request from the FSA Board that the ACNFP be asked to consider the safety of food from cloned animals and their descendants.

Introducing the paper, the Secretary highlighted an error in paragraph 14, as the FDA had highlighted individual data points lying outside the control range, rather than statistically significant differences. At paragraphs 29 and 32 the reference to "cloned animals" should read "cloned animals and their descendants".

Members commented that the available data did not show any differences in the composition of meat and milk from cloned animals and their conventionally bred counterparts. However, Members noted that the compositional data were limited to a small number of breeds reared under relatively controlled conditions and that it would be useful if additional studies were carried out which investigated potential differences under a wider range of environmental conditions. On the basis of the limited information on composition, Members agreed with the conclusions of both the FDA and EFSA that safety concerns arising as a result of epigenetic reprogramming were unlikely, but as there were reports that environmental factors could exert an influence on epigenetic status, additional data from the progeny of clones under a range of production conditions would provide reassurance on this point.

In relation to allergenicity, Members noted that epigenetic effects on post-translational modification could theoretically influence the allergenic potential of expressed proteins in meat and milk but that there was no evidence for such effects in the offspring of clones.

Members agreed that epigenetic effects could potentially occur in cloned animals and their immediate offspring, through effects on imprinting in particular, but current understanding of epigenetic inheritance suggests that these effects were unlikely to persist in subsequent generations produced using traditional breeding practices.

The Committee advised that, in view of the level of public concern, particularly with respect to animal welfare, the provision of effective labelling on products from cloned animals and their immediate descendants was important, but there was a need to define how many generations this should apply to.

34. Items for Information:

12.1 EU Update **ACNFP/100/8**

12.2 Novel Food Applications **ACNFP/100/9**

The Committee noted these information papers without comment.

35. Date of next meeting

The next meeting was scheduled for Wednesday 9 February 2011 in Aviation House

COMMITTEE ADVICE ISSUED DURING 2010

(a) OPINION ON BEE VENOM FOR ADDITION TO HONEY

Applicant: **Nelson Honey New Zealand Ltd.**

Responsible Person: **Grant MacDonald**

EC Classification: **2.1**

Introduction

1. An application was submitted to the Food Standards Agency in June 2009 by Nelson Honey New Zealand Ltd. for the authorisation of bee venom as a novel food ingredient. A copy of the application was placed on the Agency's website for public consultation.

2. Venom is harvested from honey bees (*Apis mellifera*) before adding to honey at a concentration of 20 µg/g. The applicant states that honeybee venom helps to relieve arthritic symptoms. The UK regulatory authority for medicinal products (the Medicines and Healthcare products Regulatory Agency) has confirmed that honey with added bee venom would not be regarded as a medicinal product. The marketing of such a product is therefore regulated under food law.

3. The application for authorisation of bee venom was prepared pursuant to Commission Recommendation 97/618/EC of 29 July 1997 concerning the scientific aspects and presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients. Bee venom has been classified as a complex novel food from non-GM sources. The source of the novel food has a history of food use in the Community (class 2.1).

I. Specification of the novel food

Information on this aspect is provided on p. 8-11 of the application dossier

4. The applicant states that the composition of venom has been studied extensively and has been found to be reasonably consistent. Relating to the specification for dried venom, the applicant has addressed three main specification parameters, namely the concentrations of melittin (the principal active component of bee venom) and the enzyme phospholipase A_2, which in their view are of the most toxicological significance, and moisture.

Component	Concentration or Activity
Melittin	≤ 45%
Phospholipase A_2	≤ 100 µmol/mg/min
Moisture content	≤ 5%

***Discussion**: The Committee noted the applicant's proposed specification for the novel ingredient and expressed concern about the idea of deliberately incorporating a known toxin into food, noting that the efficacy studies described by the applicant did not show sufficiently objectively any clear benefits for consumers (Section XIII.c).*

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

Information on this aspect is provided on p.12-14 of the application dossier

5. Venom is harvested from healthy bees (*Apis mellifera*). The harvesting of venom is achieved by using an electrical milking apparatus which is placed into hives and uses low amperage electrical impulses to stimulate worker bees to sting through a latex film onto a glass collector plate. The applicant proposes that the use of a latex film excludes contaminating substances. Harvested venom is then gently air-dried to a final moisture content of 5% (± 2.0%). Venom is added to a small amount of pre-warmed honey prior to slow addition of this concentrate to the bulk honey and thorough mixing for twenty four hours. The final concentration is 20 µg added bee venom per gram of honey.

***Discussion**: A number of public comments were received expressing concern about the welfare of honey bees as a result of venom production and these concerns were also echoed by the Committee. The applicant has confirmed that venom production using an electrical milking apparatus does not confer any harm to bees.*

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

Information on this aspect is provided on p.15-17 of the application dossier

6. The applicant states that although for the purposes of this application, bee venom is intended to be added to honey (20 µg venom per gram of honey), ordinary honey can also contain small amounts of bee venom (see table below):

Honey variety	Bee venom (µg/ml)
Uncreamed Manuka	1.3
Creamed Manuka	1.7
Active Manuka	1.5
Multifloral	1.1

7. The applicant has explained that venom immunotherapy is practised in certain European countries and the US and it is effective in reducing allergic sensitivity (local and systemic) and can result in almost complete protection against allergic reactions from stings.

8. The applicant further states that sublingual immunotherapy (introduction of bee venom under the tongue prior to swallowing) is also used in many European countries.

***Discussion**: Members viewed it inappropriate to use evidence relating to venom immunotherapy (subcutaneous and sublingual) to demonstrate a history of use for bee venom. Members stated that when bee venom is given by subcutaneous injection there is a very high frequency of both local and systemic reactions meaning that bee venom can only be administered under careful supervision with at least one hour's observation after each dose. Members stated that even for sublingual immunotherapy there is a necessity for the first dose and any dose increases to be administered under observation. Therefore, the Committee concluded that the information in this section of the dossier provides a further reinforcement to the main concerns expressed in relation to those with bee venom allergy (Section XIV below).*

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

Information on this aspect is provided on p 18 of the application dossier

9. The applicant suggested that consumers start with ¼ teaspoon per day of honey with added bee venom and increase daily intake to one or two teaspoons per day as required (this information will appear on the product label). The Committee considered that it may be possible for certain individuals to exceed the recommended 20g of honey per day and were also concerned about the possible effects that consumption of honey may have on dental caries. The applicant estimates that two teaspoons are equivalent to 20g of honey with added bee venom, and the maximum consumption of venom would therefore be 400 µg per

day. Honey with bee venom is not intended as a general replacement for ordinary table honey and is intended for use by individuals suffering from arthritic conditions.

***Discussion**: The applicant highlighted that honey (particularly Manuka honey) has been reported to reduce dental caries by inhibiting bacterial growth and acid and dextran production. Additionally, the applicant estimates that consumption of the suggested two teaspoons per day of honey with bee venom would provide approximately the same amount of sugar as many individuals would consume in two cups of tea or coffee per day. Members were not convinced by the applicant's response and noted that much of the available literature highlights the cariogenic properties of honey. The Committee advised that honey with bee venom should be labelled as a replacement for other dietary sugars so as not to increase total intake of sugars by consumers, in line with general dietary advice. The Committee additionally did not consider it acceptable to label a foodstuff in the way suggested by the applicant: "consumers start with ¼ teaspoon per day of honey with added bee venom and increase daily intake to one or two teaspoons per day as required".*

X. Information from previous human exposure

Information on this aspect is provided on p.19-20 of the application dossier

10. Honey with venom has been marketed in New Zealand since 1996 and the reported incidence of adverse reactions has been extremely low. Only one report, a case of anaphylaxis, has been solely attributed to bee venom (see Section XIV below).

***Discussion**: The Committee agreed that the reported incidence of adverse reactions during this thirteen year period is low but did express concerns that a more widespread use of bee venom, such as in the EU, may result in an increase in adverse effects. The Committee's comments relating to allergenicity are discussed further in section XIV below.*

XI. Nutritional information on the novel food

Information on this aspect is provided on p.21-22 of the application dossier

11. Venom when added to honey is consumed in very small amounts and is likely to have little or no nutritional value.

***Discussion**: The Committee did not raise any concerns or questions on this aspect of the application. Concerns over the potential increase in sugar consumption are discussed above.*

XII. Microbiological information on the novel food

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

12. The applicant suggests that venom may impart increased antimicrobial properties to honey but has not provided data illustrating levels of any bacterial spores or vegetative cells in typical batches of venom. The applicant proposes to label the product "*honey should not be given to infants under 12 months of age*". This advice is consistent with that of the Food

Standards Agency and many honey products in the UK already carry a similar warning, which is provided on a voluntary basis as a precautionary measure against infant botulism.

***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. 4 and p.24-30 of the application dossier

13. Two rodent studies on bee venom (acute and sub-acute) and a human clinical trial were carried out by the applicant. The human study was primarily an efficacy-based study designed to measure the improvement of patients suffering from rheumatoid arthritis and osteoarthritis as a result of consuming honey with bee venom. These studies are summarised below.

(a) Acute toxicity study

14. Forty mice received venom in either a liquid honey or freeze-dried form (0, 5, 50 or 500 mg/kg) by gavage and were observed for 48 hours. The applicant states that no animals showed any signs of overt toxicity and inspection of internal organs did not reveal any abnormalities even at the highest dose tested.

(b) Sub-acute toxicity study

15. Venom (in either honey form or freeze dried form) was dissolved in drinking water to a final concentration of 100 µg/ml. Assuming the mice consume 2 ml water per day, this is equivalent to a daily dose of 200 µg venom or 6.67 mg/kg bodyweight/day for a 30 gram mouse (equivalent to 500 mg/day for a 75 kg human). Mice were allowed *ad libitum* access for three months. The applicant reports that animals gained weight, were observed to behave normally and showed no signs of change in internal organ form or function.

16. The applicant also refers to a published rodent study (Kim *et al*., 2004) where venom was administered by injection to mice, rats and rabbits at doses up to 1000 µg/kg body weight and no significant effects on the central nervous system, blood pressure, heart rate or respiratory rate were observed.

(c) Human study

17. Ninety four patients suffering from osteoarthritis or rheumatoid arthritis were treated in two six week treatment phases, separated by a four week wash out period. Patients took two teaspoons (20g) of honey with bee venom per day, or a placebo consisting of honey without added bee venom. No serious adverse events occurred and minor effects were recorded for seven (7.4%) of the patients (four taking the venom and three taking placebo honey). Skin rash occurred in both active and placebo patients but the overall occurrence of side effects was low and there were no abnormal laboratory findings. The applicant concludes that

venom is safe, providing bee and bee product allergy is excluded, and that the side effect profile is similar to the placebo. In terms of efficacy, overall the trial indicated a small improvement only in pain score and only in patients with osteoarthritis.

***Discussion**: Although the evaluation of efficacy is not part of the risk assessment for novel foods, the Committee were not convinced of the proposed ability of bee venom to alleviate symptoms of arthritis (based on the data generated from the clinical study provided by the applicant) and noted that statistical significance in one or two endpoints does not necessarily signify clinical significance especially with such a heterogeneous patient population selected for the trial. The applicant acknowledged that the magnitude of the observed improvement lay within the expected placebo response range and is likely to be of marginal or no clinical significance. The applicant also explained that placebo honey used in the trial may also have contained a low level of bee venom, which could attenuate any positive result for the active product. The applicant highlighted that above all this human study showed that bee venom was safe for patients who are not allergic to bee products and the Committee agreed that the available data did not suggest that the proposed doses of bee venom would result in general toxicity. Allergenicity is discussed below.*

XIV. Allergenicity and labelling

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

18. Honey with bee venom has been marketed in New Zealand since 1996, during which time three adverse reaction reports have been made to the NZ Centre for Adverse Reactions Monitoring (CARM). The applicant states that honey with added bee venom is specifically implicated in only one of these three reports, where there is likely to be a strong causal association (the individual had a known allergy to bee products and suffered anaphylaxis after consuming honey with bee venom). In the other two reports a number of other products were co-administered and it was not possible to determine whether the effects were due to the consumption of honey with added bee venom.

19. The applicant has acknowledged that consumption of venom may pose a risk to individuals allergic to bee products and proposes to manage this risk by appropriate labelling.

***Discussion**: Members expressed substantial concern that the consumption of bee venom has the potential to cause serious allergic reactions, including anaphylaxis as reported in the dossier, and that the dose proposed by the applicant (400 micrograms) is within the range that is associated with significant allergic responses to other ingested allergens. Public comments received during the consultation also expressed concerns relating to potential allergenicity of bee venom.*

The applicant acknowledges that bee venom, used as a food ingredient, has the potential to cause severe allergic reactions in a small proportion of the population and highlights that this also applies to ordinary honey which can naturally contain small amounts of venom. The Committee noted the applicant's view but remained concerned that levels of venom intended to be added to honey will be at least 12 times higher than those found in natural honey varieties (see paragraph 6 above), resulting in a substantial increase in the risk of allergic reactions.

The applicant reported that, since 1996, other bee products such as pollen, propolis and royal jelly have caused more allergic reactions in New Zealand than honey with added bee venom. Additionally, the New Zealand Authorities require these other products to carry mandatory warning labels but warnings are not required for bee venom products. Nonetheless, the applicant has proposed to label honey with bee venom products as "Special Manuka Honey with added bee venom" and to include a prominent statement: "WARNING: people with allergies to honey or bee venom should seek medical advice prior to use". The applicant also proposed that, to reduce the risk of side effects, the label will state: "Directions for use: Start with ¼ teaspoon per day and increase to one to two teaspoons per day as required".

Members considered that as medical advice to those with such allergies would inevitably be not to ingest the product, the applicant's proposed labelling was not appropriate. The Committee concluded that a stronger warning label along the lines "Not to be consumed by those with allergy to honey or bee venom" would be needed. Members viewed this warning to be more concise, clear and simple for consumers.

Members were also concerned that the consumption of bee venom may sensitise previously non-allergic but genetically susceptible individuals to allergens in bee venom.

The Committee advised that concerns relating to sensitisation are unlikely to be resolved by the provision of more data by the applicant and the issue is one of risk management.

The Committee also drew attention to reports of an increased incidence of allergic reactions to insect bites (in particular bee stings), possibly linked to population susceptibility.[11],[12],[13]

The Committee also considered the possibility that the novel ingredient may pose a risk for latex allergic individuals as a result of the carry-over of latex allergens from the production process, in which bee venom is harvested by stimulating worker bees to sting through a latex film onto a glass collector plate. However, the amount of bee venom consumed is likely to be around 0.4mg/day and the amount of latex allergen consumed would be extremely small and unlikely to pose an allergenic risk. In addition, research published by the Food Standards Agency has failed

[11] Liew *et al*., 2009. Anaphylaxis fatalities and admissions in Australia.

J Allergy Clin Immunol. 2009 Feb;123(2):434-42.

[12] Sheikh *et al*.,2008. Trends in national incidence, lifetime prevalence and adrenaline prescribing for anaphylaxis in England. J R Soc Med. 2008 Mar;101(3):139-43.

[13] Sheikh *et al*., 2000. Hospital admissions for acute anaphylaxis: time trend study. BMJ. 2000 May 27;320(7247):1441).

to detect residues of allergens in foods as a result of transfer from latex-containing food contact materials[14].

CONCLUSION

The Committee's main concerns about this novel ingredient were related to allergenicity, as the ingestion of bee venom demonstrably has the ability to cause anaphylaxis in individuals who have previously been sensitised to bee stings.

The Committee agreed that strongly worded warning labelling could minimise the risk to consumers who are aware that they are allergic to bee stings. The Committee was concerned, however, that a proportion of the population with this allergy may be unaware of it (it was noted that it is an uncommon occurrence for most people to be stung by a bee) and warning labelling would not protect these consumers.

Members also noted that the consumption of bee venom may have the ability to sensitise previously non allergic but genetically susceptible individuals to allergens in bee venom and it is unlikely that this uncertainty could be addressed by additional studies.

The Committee therefore concluded its initial assessment of bee venom as an ingredient to be added to honey and stated that it was unable to advise with any certainty that bee venom, used as a food ingredient, is safe for consumers. It was unable to quantify the likelihood of potential risks relating to the two issues described above, namely:

- The risk of immediate and serious allergic reactions, including anaphylaxis, in individuals who are unknowingly allergic to bee venom (for example from earlier bee stings) and who later become consumers of the novel ingredient.

- The possibility that the ingredient may sensitise some genetically susceptible individuals so that they suffer serious allergic responses on later exposure to bee venom, for example via bee stings.

If, notwithstanding this initial assessment by the Committee, bee venom were to be authorised for addition to honey, the Committee remained concerned about the cariogenic properties of honey and that the proposed use of the novel ingredient in honey could lead to an increased risk of dental caries. Therefore, the Committee stated that honey with bee venom would need to be labelled with advice that it should be consumed as a replacement for other sugars, so as not to increase total sugar intake by consumers of the product.

The Committee reviewed the numerous public comments received during the public consultation on its draft opinion. These comments reported the efficacy of bee venom in the management of

[14] http://www.food.gov.uk/science/research/researchinfo/contaminantsresearch/contactmaterials/a03prog/a03projlist/a03056/

arthritic symptoms but the Committee emphasised that its remit is to assess novel ingredients for safety and not to provide a judgement on efficacy. The Committee's assessment is carried out in the context of the EU regulation on novel foods (Regulation (EC) 258/97), which requires that any novel food ingredient does not present a danger for the consumer and does not allow for the type of risk/benefit analysis that would be undertaken for a medicinal product.

July 2010

(b) OPINION ON MAGNOLIA BARK EXTRACT

Applicant: **William Wrigley Jr. Company**

Responsible Person: **Marion Balz**

EC Classification: **2.2**

Introduction

1. An application was submitted to the Food Standards Agency in September 2009 by William Wrigley Jr. Company for the authorisation of magnolia bark extract as a novel ingredient in the EU. A copy of the application was placed on the Agency's website for public consultation.

2. Magnolia bark extract is obtained from the bark of the plant *Magnolia officinalis*. This plant is native to the mountains and valleys of China and, according to the applicant, has been used for centuries as part of traditional Asian remedies. Magnolia bark supercritical carbon dioxide extract (MBSE) is mainly composed of two phenolic compounds, magnolol and honokiol. The applicant intends to incorporate MBSE into two confectionery products (chewing gum and mint confectionery products) at a maximum use level of 0.2% for breath freshening purposes.

3. The application for authorisation of magnolia bark extract was prepared pursuant to Commission Recommendation 97/618/EC of 29 July 1997 concerning the scientific aspects and presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients. Magnolia bark extract has been classified as a complex novel food from non-GM source, the source of the novel food has no history of food use in the EU (class 2.2).

I. Specification of the novel food

Information on this aspect is provided on p. 4-8 of the application dossier

4. The applicant states that MBSE contains two major 'active' components which comprise at least 94% of the product. The primary component is magnolol (5,5'-diallyl-2,2'dihydroxybipenyl) and the extract also contains smaller amounts of honokiol (5,3'-diallyl-2,4'-dihydroxybiphenyl). MBSE is a light brownish powder, soluble in alcohol and insoluble in water. The specification for MBSE can be found in the table below.

Parameter	**Specification**
Appearance	Light Brownish Powder

Magnolol	92.5% min
Honokiol	0.5% min
Magnolol + Honokiol	94% min
Total Eudesmol	2% max
Moisture	0.5%
Impurities	
Arsenic (ppm)	0.5 max
Lead (ppm)	0.5 max
Total Heavy Metals (ppm)	10 max
Methyleugenol (ppm)	50 max
Turbocurarine (ppm)	2 max
Total Alkaloid (ppm)	100 max

***Discussion**: Members noted that compositional data from analyses of multiple batches of MBSE did not total 100% (range 95.7 -100.6%) and requested clarification of the identity of the remaining components. Members also requested confirmation of the absence of protein in MBSE and reassurance that quality control procedures are sufficiently robust to ensure product consistency. The applicant provided additional batch analyses data for fifteen lots of MBSE and stated that most of these batches are characterised to a consistently high purity of between 98 and 100%. The applicant also stated that individual batch analysis indicates that the majority of the product is accounted for by magnolol, honokiol and moisture content. At the Committee's request , the applicant analysed a sample of MBSE in duplicate for protein using three different methods (SDS-PAGE with Coomassie blue R250®, SDS-PAGE with silver staining and LC-MS/MS). The applicant stated that no detectable*

levels of protein were found in the MBSE analysed using any of the above methods. The Committee reviewed the raw data from these analyses and was reassured that protein is effectively absent from the novel ingredient.

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

Information on this aspect is provided on p 9-12 of the application dossier

5. MBSE is obtained from the bark of *Magnolia officinalis* L, which is washed and oven dried to reduce moisture content before being crushed and extracted with supercritical carbon dioxide. The extract is dissolved in medical-grade ethanol and re-crystallised yielding MBSE.

6. MBSE is produced in accordance with Good Manufacturing Practice. The applicant states that a Hazard Analysis and Critical Control Point (HACCP) program has been implemented for the manufacture of MBSE.

7. The applicant carried out stability analyses of MBSE in chewing gum and mints over a 12 week period under accelerated storage conditions and concluded that the results demonstrate the stability of MBSE in chewing gum and mints, with minimal loss over the 12 week test period. At the request of the Committee, the applicant also provided real-time stability data for MBSE-containing gum (different flavours) over a ten month period. Magnolol content was assessed as a measure of stability and was shown to be stable within each flavour and there was no detectable degradation over 10 months of shelf-life.

***Discussion**: The Committee was satisfied with this section of the dossier and the additional data provided by the applicant.*

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

Information on this aspect is provided on p.13-15 of the application dossier

8. MBSE is obtained solely from the bark of *Magnolia officinalis* subsp. biloba. It is a species of Magnolia native to the mountains and valleys of China at altitudes of 300-1500m and it belongs to the family *Magnoliaceae*.

9. The applicant states that traditional herbal remedies containing magnolia bark, such as Banxia Houpo Tang, Saiboku-To, Hsiao-Cheng-Chi-Tang and Wuu-Ji-San, have been used for centuries as part of Asian remedies. The applicant also also states that various magnolia bark derived products are available, and these would all be regarded as traditional medicinal products. In view of this, the applicant sought clarification from the Medicines and Healthcare products Regulatory Agency (MHRA) on the medicinal status of MBSE and its proposed use in confectionery. The MHRA concluded that use of MBSE in chewing gum would not be medicinal, providing that it was limited to claims regarding breath freshening, and that the amount of MBSE did not exceed 3mg per stick. This limit is based on the potential medicinal function of the extract as an antibacterial agent and is not a safety limit.

***Discussion**: The Committee was generally content with this section of the dossier but requested an explanation for the rationale of incorporating 3 mg of MBSE into mint/gums. The applicant stated that a published study by Greenburg et al., 2007 reported that MBSE at a concentration of 0.2% displayed breath freshening properties and a 0.2% incorporation level was employed on this basis. Based on this use level and a maximum gum/mint size of 1.5 g each, each gum or mint serving would contain 3 mg of MBSE. The applicant also explains that there is also a technical limit on the use of MBSE in gum/mints because MBSE imparts unacceptable flavour characteristics to the product which are difficult to mask at incorporation levels above 0.2%. The Committee was satisfied with the applicant's response.*

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

Information on this aspect is provided on p 16-24 of the application dossier

10. The applicant intends to incorporate MBSE into gum and mints at a maximum level of 0.2%. Based on a maximum gum and mint size of 1.5g, each serving would contain up to 3mg of MBSE.

Proposed Food Use	Serving Size	MBSE (mg/serving)	Use-Level (%)
Mints	1.5g	3	0.2
Chewing Gum	1.4g	2.8	0.2

Summary of the individual proposed food-uses and use levels for MBSE in the UK

11. The applicant has indicated that MBSE will be added solely to mint and chewing gum products which are marketed for breath freshening purposes. MBSE will not therefore be added to bubble-gum type products or to other mint based confectionery such as 'Everton Mints'

12. The applicant has provided intake data from a range of population groups using information from the NDNS surveys which are available to the general public. On an absolute basis highest exposure to MBSE was observed in teenagers with 95th percentile estimates of 28 and 23 mg/person per day for gum and mints, respectively. On a mg/kg basis, exposure to MBSE in the diet was highest in children (age 4-11) at 0.6 and 1.04 mg/kg body weight per day for gum and mints, respectively.

***Discussion**: The Committee was satisfied with this section of the dossier.*

X. Information from previous human exposure

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

13. The applicant does not view the limited use of magnolia bark products as traditional remedies to be indicative of widespread exposure to the principal components of MBSE. The applicant reports that MBSE has GRAS (Generally Recognised as Safe) status in the United States**.** MBSE-containing gum and mints have been marketed in US since June 2008 and Oct 2008, respectively. Post market monitoring for adverse reactions in the USA (2008-2009) indicated that there was one adverse report for every 11 million units sold.

14. As MBSE-containing gum and mints have been marketed in the US**,** the Committee requested details on the way in which these products are marketed. The applicant has provided details from Wrigley's US website to illustrate the way in which MBSE products are marketed in the US. While for the EU application the applicant intends to limit claims to breath freshening properties, this appears not to be the case in the US where claims relating to antibacterial properties of the gums and mints are being made. Such claims would be illegal under EU legislation, as they would be regarded as medicinal.

***Discussion**: The Committee was satisfied with the applicant's response and did not raise any further questions/concerns on this aspect of the application.*

XI. Nutritional information on the novel food

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

15. The addition of MBSE to mints and gum is solely for the purposes of breath freshening and exposure to the novel ingredient is not expected to have a nutritional impact on the diet.

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

XII. Microbiological information on the novel food

Information on this aspect is provided on p.7-8 of the application dossier

The applicant has provided microbiological analyses data for four different lots of MBSE which were shown to be demonstrably free from microbial contamination (*Clostridium*, coliforms, *Salmonella*, Staphylococci, mould and yeast).

***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. 27-66 of the application dossier

Subchronic toxicity

16. The applicant conducted a 21 day toxicity study on MBSE in male and female Sprague-Dawley rats (Liu *et* al, 2007). This study was primarily a pilot dose-ranging study for a subsequent 90 day study. Animals consumed MBSE in the diet at doses of 0, 60, 120, 240 or 480 mg/kg body weight per day. Although differences in certain haematological parameters were observed, the applicant notes that these were of a low magnitude and were not dose responsive or consistent between sexes, and concludes that they are therefore not of biological relevance. Serum urea nitrogen and urine sodium values were significantly higher in the 120 mg/kg body weight/day females and males, respectively. Absolute and relative thyroid weights and relative kidney weights were slightly but significantly increased in females of the high dose group. Relative spleen weight was slightly but significantly increased in males of the 60 mg/kg bodyweight/day group. The applicant states that organ weights were within the historical range of control weights and were not accompanied by clinical, gross or pathological effects, and therefore were not toxicologically relevant. The applicant states no treatment-related side effects were observed during this study. A NOAEL of 480 mg/kg body weight was determined (the highest dose administered).

17. The applicant also provides details of a 90 day study in which male and female Sprague Dawley rats consumed MBSE in the diet at doses of 0, 60, 120 or 240 mg/kg body weight per day. Although some differences in body weight, body weight gain and food consumption were observed, the applicant states that these effects were not dose related or toxicologically significant. Differences in certain haematological parameters (total bilirubin and sodium) were observed and urinalysis revealed significantly lower potassium levels in female animals dosed at 60 mg/kg body weight per day. The applicant states these differences were not dose dependent, not observed in both sexes and not biologically relevant. The applicant concludes that a NOAEL of 240mg/kg body weight was established.

Mutagenicity and genotoxicity

18. Ames tests conducted with and without metabolic activation were negative and MBSE was non-genotoxic in Chinese hamster ovary cells with and without metabolic activation. The applicant indicates that MBSE is non-genotoxic *in vivo* as no evidence of micronucleus induction was observed in Swiss Albino (CD-1) mice receiving MBSE doses up to 2,500 mg/kg body weight. The applicant considers that these studies indicate that MBSE is not mutagenic or genotoxic.

Human studies

19. The applicant has provided details of two double-blind human studies conducted to investigate the efficacy of MBSE. The results obtained from these studies indicated that consumption of MBSE-containing peppermint mints or gum was effective in reducing oral

malodour. The applicant and the study investigator stated that the MBSE-containing products were well tolerated and that use/consumption of MBSE-containing mints did not result in any adverse effects in any of the study participants in either study. Headache was reported by one of the sixty two subjects in one of the studies, which the investigators judged was possibly related to the test product.

Toxicity studies and other studies conducted with magnolol, honokiol and crude magnolia bark preparations

20. Crude magnolia bark preparations have long been used as a component of traditional Asian remedies and the majority of published studies on the properties of magnolia bark have used the crude powdered bark or extracts produced using various solvent extraction processes. The applicant acknowledges that the test articles used in these studies are not representative of MBSE, and states that the available literature on these materials has been reviewed for completeness. This review includes a reference to mortality in animals fed 'large doses' of Houpo, a decoction (water extract) of magnolia bark that is produced for muscle relaxing purposes. The applicant notes that although the composition of this decoction is poorly defined, the findings are likely to be due to the presence of a water extracted alkaloid magnocurarine, which may have been present at concentrated levels in the extract.

21. Available data from acute and short-term animal toxicity studies carried out using these magnolia bark preparations are summarised below:

Species/Strain/No. of Animals per Group per Sex	Study Duration	Route	Dose Levels and Test Item (mg/kg body weight/day)	Observations	Reference
Mice					
Male ICR	Single dose	Gavage & i.p.	Ethanolic extract of Magnolia bark extract	Oral LD_{50} > 50 g/kg bw i.p $L.D_{50}$ = 8.5 g/kg bw	Yang and Chen, 1997
*NS	Single dose	Gavage	Houpo 60 g/kg bw	No fatalities	Murakami *et al.*, 1933
*NS	Single dose	i.p.	Houpo deconcoction	i.p. LD_{50} = 6.12 g/kg bw	Basic Medical Sciences Department, 1973
Rats					
Sprague-Dawley Male (200-250g) N=8-15/group	14 day	Gavage	- Houpo dried powder 5 g/kg bw - Houpo aqueous suspension for higher dose 10 g/kg bw	- No effect on behaviour, food/water intake or, body weight. - ↓ ALA, and Creatine - ↑ BUN - ↑ urine protein	Yang and Chen, 1997
Rabbits					
*NS	Single dose	i.v.	n/a	No Mortality	Chang and But, 1986
Dogs					
*NS	Single dose	i.v.	Houpo 1 g/kg	No mortality	Chang and But, 1986
Cats					
*NS	Single dose	i.v.	Houpo deconcoction	Minimum Lethal Dose (MLD) = 4.25 mg/kg bw	Basic Medical Sciences Department, 1973

*NS = Not Stated

The applicant acknowledges that various magnolia bark preparations or components thereof are reported in the literature as having claimed therapeutic effects and reported clinical actions including: anxiolytic and central depressant activity, muscle relaxation, vasorelaxation, thermoregulatory and antipyretic effects and protective properties on gastrointestinal mucosal membranes. The applicant also describes studies showing that magnolol and honokiol (the principal components of MBSE) may have beneficial effects on gastrointestinal function. The application dossier suggests that exposure to magnolol and honokiol resulting from the use of MBSE-containing gum and mints is limited and therefore effects on gastrointestinal function in humans are not expected.

In order to assess the validity of this conclusion, the Committee asked the applicant to provide data comparing levels of these compounds in the GI tract in the published studies and following exposure to MBSE from confectionery. The applicant reported that the observations described in the dossier were obtained from an uncontrolled study (Oikawa *et al.*, 2005) on a herbal concoction containing many ingredients, one of which was a crude magnolia bark preparation.

As such the applicant advised that there is no credible clinical evidence to support any pharmacological effects of magnolol and honokiol on the GI tract. The applicant's response also highlighted that no GI effects were seen in the 90 day toxicity study where rats were administered MBSE in the diet at doses around 500 times higher that the estimated intake for frequent MBSE product users. The applicant's response also highlighted that post-market monitoring data also supported the lack of any pharmacological activity of MBSE.

The applicant also stated that the other studies mentioned above are for completeness and are not considered relevant to the proposed use of MBSE in gums and mints.

The Committee was satisfied that the applicant's response addressed its concerns on this point.

22. The applicant has also detailed a number of clinical trials investigating the use of Asian herbal remedies containing magnolia bark preparations that are not necessarily representative of MBSE. The applicant states that these studies suggest that the herbal preparations are well tolerated, although only one of these studies (Garrison and Chambliss, 2006) evaluated safety using clinical and haematology endpoints. In the study by Kelman *et al.,* 2008, one of forty two subjects reported side-effects which included heartburn, hands shaking and thyroid dysfunction. However, the applicant considers that these effects were not significant test-article-related effects. Similar side effects were also reported for one of forty two subjects in the study of Garrison and Chambliss, 2006, although these authors concluded that the treatment was well tolerated. These studies are summarised below and detailed in the dossier (p50-60).

Component	Source	Species	Route of Administration	Duration	Dose (mg/kg body weight)	Effect	Reference
Magnolol	Dietary supplement (Saiboku to) containing amongst other ingredients, magnolol	Human	Not reported	104 weeks	2.5 g Saiboku to 3 times daily (after meals); equivalent to 3.15 mg magnolol daily	Decrease in frequency of corticosteroid administration in responding bronchial asthmatics. No reduction in the frequency of corticosteroid administration among the non-responding subjects was reported. 'Responders' to Saiboku-To treatment exhibited higher free magnolol excretion rates than non-responders.	Homma *et al.*, 1993a
Extract of *M. officinalis*	Dietary supplement containing amongst other ingredients, *M. officinalis*	Human	Oral	3 times a day for 6 weeks	250 mg of supplement (amount of extract of *M. officinalis* not reported)	Well tolerated. Significant weight gain for placebo group but no weight gain for treatment group. (tested in overweight females age 20 to 50)	Garrison and Chambliss, 2006; Kalman *et al.*, 2006.
Magnoliae cortex bark	Dietary supplement Hange-koboku-to which also contained *Hoelen, Perillae herba* and *Zingiberis rhizoma*	Human	Oral	10 days	60 (of supplement)	Decrease in frequency of choking episodes caused by sleep apnoea	Hisanaga *et al.*, 2002.
Magnolia bark	Dietary supplement Hange-koboku-to which also contained *Hoelen, Perillae herba* and *Zingiberis rhizoma*	Human	Oral	4 weeks for patient 1, 6 months for patient 2 and 2 years for patient 3	7.5 g of supplement/day	No effect in patient 1, a 59-year-old women suffering from a panic disorder and agoraphobia. Patient 2: symptoms of agoraphobia disappeared after 12 weeks treatment, no return of symptoms 2.5 years after discontinuation of supplement. Patient 3: relief of panic disorder and agoraphobia after 2 weeks treatment. Attempted discontinuation caused return of symptoms so treatments was continued.	Mantani *et al.*, 2002.

Component	Source	Species	Route of Administration	Duration	Dose (mg/kg body weight)	Effect	Reference
Magnoliae cortex	Supplement Hange-koboku-to which also contained *Hoelen, Perillae herba* and *Zingiberis rhizoma*	Human	Oral	2 weeks	7.5 g of supplement/day	Gastric emptying rate increased in healthy volunteers but after a 2-week washout returned to normal. Gastric emptying rate increased in functional dyspepsia patients and a decrease in scores for abdominal pain, indigestion and constipation but not reflux or diarrhoea.	Oikawa *et al.*, 2005.
-	Banxia Houpo tang, which contains among other ingredients magnolia	-	Oral	4 weeks	4.5 g/day of herbal medicine	Decreased cough threshold in patients with aspiration pneumonia.	Iwasaki *et al.*, 2002
Extract of *M. officinalis*	Proprietary blend of patented extracts of the bark of *M. officinalis* (1.5% honokiol/capsule) and *Phellodendrom amurense* (0.1% berberine/capsule)	Human	Oral	6 weeks	750 mg of Relora® per day (approximately 11.25 mg/day of extract of *M. officinalis* was consumed)	Relora® reduced self-perceived stress and anxiety as well as temporary, transitory anxiety. No treatment-related safety concerns or significant adverse events were reported.	Kalman *et al.*, 2008

Safety of other phenolic and alkaloid constituents

23. In addition to the two biphenol compounds, magnolol and honokiol, magnolia bark provides essential oils containing alpha, beta and gamma-eudesmol. Magnolia barks contain small amounts of plant alkaloids (magnocurarine and tubocurarine) and methyleugenol. MBSE is produced using supercritical carbon dioxide chemical extraction so that the content of essential oils and contaminants is significantly reduced.

24. The applicant states that although beta-eudesmol has been reported to display antihypertensive effects in rats, such effects required intravenous or intraperitoneal doses of at least 10 or 30 mg/kg body weight respectively and no effects were observed at lower doses. The applicant's view is that, as MBSE is intended for food use, these observations are not relevant to the current evaluation. The applicant remarks that beta-eudesmol has also been

reported to have curare like action in rodents but these findings were not consistent in the literature. The specification for MBSE limits the total eudesmol content to 2% and the applicant highlights that MBSE intake from mints and gum would be several thousand to a million fold lower than doses reported to elicit significant biological effects and would therefore not be a safety concern.

25. The applicant states that several batches of MBSE were analysed for levels of methyleugenol, noting that a 20 ppm limit of this compound that has recently been set in EU flavourings legislation for its presence ready to eat savoury products[15]. The applicant estimates that, based on the proposed consumption of MBSE in gum and mints, 90th percentile intakes in the highest consumers (teenagers) would result in daily exposures of 375 ng/person and would not appreciably increase the dietary intake of this compound relative to background exposure from food (17 micrograms to 18,000 micrograms/person).

26. Given the very low concentration of curine alkaloids magnocurarine and tubocurarine that are expected to be present in the extract (the specifications limit alkaloids to a maximum of 100 ppm) and the fact that these compounds are poorly absorbed, the applicant concludes that these compounds will not be of toxicological concern as a result of consuming MBSE in mints and gum.

***Discussion**: The Committee sought an explanation for the gender-specific statistically significant increases in total blood bilirubin levels (TBBL) observed during the 90 day rodent feeding study. Noting that these increases were apparently not accompanied by other signs of liver toxicity, the Committee requested a copy of the original study report in order to be satisfied about this finding. The Committee reviewed this report and was satisfied that the 90 day report contained all relevant data and that the observed increases in TBBL were not dose-related. The Committee concluded that TBBL levels in the treatment group were significantly higher because TBBL levels in the control group were aberrantly low rather than as a result of any treatment-related effect.*

The Committee also requested further information on the metabolism of magnolol in the liver and reassurance as to whether there may be a risk of interaction with other pharmaceutical products metabolised in the liver.

The applicant states that the principal constituents of MBSE, magnolol and honokiol, are primarily metabolised by the liver in rodents via conjugation with glucuronic acid and the main elimination route is excretion in the bile. The applicant also states that there is limited information on the metabolism of magnolol and honokiol in humans, but based on available evidence glucuronidation appears to be the main metabolic route. The applicant states that a complete absorption, distribution, metabolism, excretion (ADME) profile of magnolol in humans is not available and neither are detailed metabolic data for honokiol (although given the structural

[15] The flavourings legislation defines limits for a range of food types to which flavourings containing methyleugenol might be added. This list does not include chewing gum or other confectionery and "ready to eat savoury products" is probably the closest surrogate for comparison.

similarity to magnolol the compound is expected to be metabolised similarly via conjugation of the free hydroxyl group with glucuronic acid and subsequently excreted in the bile).

The maximum level of MBSE consumption is a fraction of the exposure to other natural dietary components that undergo similar metabolic conjugation processes e.g. polyphenols which are found in chocolate, red wine, coffee, tea and many fruits and vegetables. The applicant considers that potential adverse drug interactions with MBSE and pharmaceuticals will be extremely unlikely. The Committee was satisfied with the information provided by the applicant relating to magnolol metabolism and potential interaction with pharmaceutical products.

XIV. Allergenicity and labelling

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

27. The applicant has indicated that the product will be labelled as appropriate and in accordance with EU legislation relating to the labelling presentation and advertising of foodstuffs. Claims will be limited to its breath freshening capability and that products containing MBSE will not have any medicinal or associated health or nutrition claims.

28. The applicant states that as MBSE is isolated using supercritical carbon dioxide extraction, it does not contain protein and therefore allergy concerns are not warranted.

***Discussion**: As noted above, the applicant provided data from additional protein analyses to support their statement that MBSE does not contain measurable amounts of protein and as such it is unlikely to pose a concern with respect to allergenicity. The Committee was satisfied with the applicant's response to this point.*

CONCLUSION

The Committee has reviewed the dossier and the additional information it requested from the applicant on a number of areas:

- Improved protein analyses
- Clarification of MBSE compositional data
- Gender-specific increases in total blood bilirubin levels observed during the 90 day rodent feeding study.
- Information on the metabolism of magnolol in the liver
- Information on the shelf-life of MBSE

- Details on how MBSE products are marketed in the US
- Further information on MBSE use levels.
- Information on ecology relating to the bark stripping process of magnolia trees.

The Committee was satisfied with the information provided by the applicant in addressing all its questions or concerns and was satisfied that MBSE for use in gums and mints at the specified use level of 0.2% is unlikely to pose a risk for consumers.

July 2010

(c) OPINION ON SUBSTANTIAL EQUIVALENCE OF AUSTRALIAN CHIA SEED

Applicant The Chia Company

Responsible person April Helliwell

Introduction

1. In January 2010 a request was submitted by The Chia Company to the UK Competent Authority for an opinion on the equivalence of their chia seed grown in Western Australia, compared with the existing chia seed cultivated in South America, and marketed in the EU by the Columbus Paradigm Institute S.A.

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

3. A novel food application for whole and ground chia seeds was submitted by R. Craig & Sons to the UK in 2003. Following a number of concerns raised by Member States, regarding the safety of chia seed, responsibility for the dossier was transferred to the Columbus Paradigm Institute S.A. in 2006. The new applicant provided additional information to address these concerns and, following a favourable opinion from the European Food Safety Authority (EFSA) in 2009, authorisation to market chia seed as a novel food ingredient at a level of up to 5% in bread products was issued on 13 October 2009 (Commission Decision 2009/827/EC).

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

Evaluation

a) Composition

5. The applicant sows chia into prepared soil beds where it grows until the desired biomass is reached. Plant tissue tests are carried out throughout 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 and to prevent seed loss through shedding onto the ground. The seeds are then transported to a seed cleaning facility where they are transferred to silos for fumigation with carbon dioxide before cleaning and packaging.

7. The applicant has compared the published composition of the approved chia seed in the EFSA opinion in 2009 with their own chia seed. See table below.

Nutrient (%)		TCC Seed	Approved Chia
Dry matter		95.0 – 96.8	91 – 96
Protein		17.4 – 22.4	20 – 22
Fat		28.5 – 34.7	30 – 35
Carbohydrate		37.1 – 42.6	25 – 41
Fibre	Soluble	5.3 – 7.1	NA
	Insoluble	30.9 – 33.0	18 – 30
Ash		4.5 – 5.6	4 – 6

NA: Not available

8. The applicant has also compared the mineral content of their chia seed with the approved chia seed. This is summarised in the table below.

Mineral (mg/100g)	TCC Seed	Approved Chia

Sodium	<0.1 – 6	0.94 – 12
Potassium	510 – 710	660 – 809
Calcium	500 – 640	557 – 770
Iron	5.7 – 15	6.3 – 9.9
Magnesium	310 – 430	325 – 390
Phosphorus	600 – 870	751 – 780

9. The applicant has included a comparison of the amino acid content of their chia seed with the approved chia. This is summarised in the table below.

Amino acid (% of protein)	TCC Seed	Approved Chia
Isoleucine	3.05 – 3.53	3.21 – 3.98
Leucine	5.47 – 6.34	5.89 – 7.30
Lysine	3.87 – 4.42	3.60 – 5.50
Methionine	1.00 – 1.14	0.36 – 0.45
Phenylalanine	4.19 – 4.71	4.73 – 5.86
Threonine	2.90 – 3.42	3.23 – 4.25

Tryptophan	0.89 – 1.04	NA
Valine	3.86 – 4.56	5.10 – 6.32

NA: Not available

10. The applicant also compared the fatty acid profile of their chia seed with the approved chia. Although they acknowledge that there are small but measurable differences, the applicant does not view this to be a cause of concern.

Discussion: *The Committee was satisfied that the data comparing the Australian chia seed and the existing chia seed show that they have an equivalent composition. The Committee requested information on the botanical origins of the Australian chia seed to determine whether there were any differences when compared to seeds produced in South America. The applicant confirmed that the original source of the chia seed grown in Australia was seed stock from Mexico and Bolivia and that they had not carried out any programme of plant breeding. The Committee also sought information on the conditions in which chia seed is grown in Australia. The applicant advised that the Australian chia seed is grown under very similar climatic conditions to the South American variety at a latitude of 15 degrees south of the equator. The applicant also stated that unlike chia grown in South America, which is harvested using a chemical desiccant, they employ mechanical harvesting techniques. The Committee considered that the additional information regarding the seed stock and growing conditions provided sufficient reassurance that there were no significant differences between the two seeds.*

b) c) Nutritional Value and Metabolism

11. The applicant states that chia seed contains around 20% protein and an oil content of approximately one third by weight, of which about 80% of which is α-linolenic acid. The seeds possess about 5% soluble fibre and measurable quantities of vitamin B, minerals and antioxidants. These figures are consistent with those for the existing product.

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

d) Intended Use

12. The applicant will limit the use of chia seed to bread products at a maximum level of 5%, in accordance with the authorisation given to Columbus Paradigm in 2009.

Discussion: *The Committee was content that the intended use of the chia seed in bread products at a maximum level of 5% is consistent with the existing product.*

e) Level of undesirable substances

Chemical Contamination

13. The applicant is of the view that the production process ensures that the levels of undesirable substances are equivalent to the approved chia. The applicant has provided data from four separate batches for the heavy metal screen. See table below.

Heavy metal	TCC Seed (ppm)	Approved Chia (ppm)
Arsenic	<0.1	<0.1 - <0.2
Cadmium	<0.1	0.018 - <0.2
Mercury	<0.01 - <0.02	<0.01 - <0.03
Lead	>0.5 - <1	<0.004 - <0.12

Microbial Contamination

14. The chia seeds have been tested for microbiological contamination as part of the applicant's HACCP quality control system at accredited laboratories in Australia. Analyses include detection of yeasts and moulds, *E.coli*, *Salmonella*, *Listeria* and *Clostridium perfringens*.

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

f) Additional information

15. The applicant states that they have in place a Quality Management System based on the Codex Hazard Analysis Critical Control Point (HACCP) system. The applicant also states that their Quality Management System has been designed to meet the requirements of the Safe Quality Food (SQF) 2000 code. The applicant provided a certificate of compliance with the HACCP system.

16. The applicant included a number of bioavailability studies relating to the uptake and metabolism of chia in rats, hens and cows. Two of the studies describe an increase in blood levels of α-linoleic acid after introducing chia through controlled feeding studies in rats and cows.

17. In order to demonstrate the stability of the seed, the applicant re-tested their 2006 harvest in 2009 and found that the nutritional content did not change over this 3 year period and no deterioration in taste or smell was evident. The microbial status remained constant throughout this period of time

Conclusion

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

19. The Committee therefore concluded that the chia seed produced by The Chia Company can be considered to be substantially equivalent to the existing chia seed produced by Columbus Paradigm Institute S.A.

20. This opinion applies solely to the use of chia seed as an ingredient in bread products at a maximum level of 5%.

July 2010

(d) Insoluble and Soluble Yeast beta-glucans

Andreas Klepsch
European Commission
By email

8 March 2010

Dear Mr Klepsch

As the UK Competent Authority (CA), the Food Standards Agency has sought advice from the Advisory Committee on Novel Foods and Processes (ACNFP) on the initial assessment report prepared by the Irish CA for the above product. This was discussed at the Committee's meeting on 10 February.

The Committee considered that a clearer definition of the ingredients is required. In particular it noted that no information was provided on the composition of the soluble product and, due to the various solubilisation steps involved in the production process, there may be significant differences between this and the insoluble form.

The Committee noted that the safety data presented in the application are not clearly cross-referenced to the correct product. It considered there are likely to be significant differences between 1,3- and 1,4-beta-glucans and therefore more information is required on which substances the safety data corresponds to.

The Committee also noted some inconsistencies in the information reported by the Irish CA and the information presented in the application dossier. It noted that the ingredients are likely to be fermented rather than excreted as reported by the Irish CA on p.4 of its opinion. On page 5 of the opinion, the Irish CA states that due to the low absorption rate of beta-glucans, it is difficult to determine whether the addition of the novel ingredients would have much, if any immunostimulatory effect. However the Committee is of the view that beta-glucans are absorbed in the epithelial cells and therefore requested further information on the immunostimulatory effects of the ingredients and whether this has significant effects on the gut flora.

In view of the ACNFPs advice, the Food Standards Agency would not be able to support the authorisation of this product until these issues have been addressed,

Yours sincerely,

(By email only)

Shuhana Begum

(e) Guar Gum

Andreas Klepsch
European Commission
by email

9 July 2010

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 French CA for the above product.

The UK is in general agreement with the French initial opinion and does not raise objections to the authorisation of this novel ingredient, subject to certain specific risk management procedures being adopted.

The ACNFP has echoed the French concerns relating to the potential of guar gum to cause oesophageal and intestinal obstruction and emphasised that, if guar gum is authorised as a novel ingredient, very clear labelling should be employed for the two component dairy/cereal products to ensure that these components are mixed prior to consumption and that the cereal component is not consumed alone, as mentioned in the initial opinion of the French CA.

Additionally, the ACNFP has highlighted that Danone's study using simulated intestinal digestion does not cover the potential for oesophageal obstruction which is more likely to be a real issue for children. This will need to be addressed through risk management by providing clear information to consumers of the relevant products.

If the ACNFP has any additional general comments, the UK will inform the Commission shortly.

Yours sincerely,

Dr Manisha Upadhyay

Novel Foods Unit, Food Standards Agency

(f) Lactoferrin

Andreas Klepsch European Commission

11 June 2010

Dear Mr Klepsch

As the UK Competent Authority under regulation (EC) 258/97 on novel foods and novel food ingredients, my Agency has consulted members of the Advisory Committee on Novel Foods and Processes (ACNFP) on this application and on the initial assessment report provided by the Dutch Competent Authority.

The Committee notes that the issues raised in response to the previous application for Bovine lactoferrin in September 2008 also apply to this application.

We are therefore unable to support the authorisation of this product until we have received additional information regarding:

1. Whether the rat is a suitable species for demonstrating the safety of this ingredient, as 60% of bovine lactoferrin survives passage through the stomach. A study to demonstrate that a similar proportion survives intact in the rat would provide the necessary justification for accepting rat data.

2. In the previous application, we noted that the 90-day study with 12 animals per sex per group is less than is recommended for food additives and related substances. The design is generally adequate, but given that this product naturally raises questions about allergy and immune response it is surprising that the mesenteric lymph node was not sampled and/or weighed.

   We also noted the following observations which were not picked up in the 4-week range-finding study:

   a. The death of a single high-dose animal from malignant lymphoma is surprising in a 90-day study and although a 1985 reference is cited as evidence that such tumours do occur in this strain it would have been more reassuring to see reference to current incidence in the animals form the specific source used.

   b. The pancreas in males shows an increased incidence of islet fibrosis in all treated groups (4/12, 6/12, 6/12) compared with control (1/12). This is not considered to be of concern by the authors but is difficult to ignore since it seems to be present at all doses. Evidence for a higher historic control incidence of such changes might provide

some reassurance on this. However it is possible that we are seeing some interaction with normal pancreatic lactoferrin production and if this is the case it would be useful to review additional data on the chronic consequences of this and relevance to consumer exposure levels.

c. Thyroid weight and weight relative to body weight, is reduced in both sexes compared with the controls but only statistically significant in females. This is viewed to be within historical control values but as this occurs in change in both sexes additional confirmation was required.

3. Lactoferrin is involved in various aspects of reproduction and this justifies a more thorough investigation of this aspect of toxicity.

Yours sincerely

Sandy Lawrie

Novel Foods Unit

Food Standards Agency

(g) Gamma Cyclo Dextrin

Mr Andreas Klepsch

European Commission

By email

17 September 2010 Reference: NFU 780

Dear Mr Klepsch

Application under (EC) 258/97 for Approval of Gamma-cyclodextrin

As the UK Competent Authority under regulation (EC) 258/97 on novel foods and novel food ingredients, the Food Standards Agency has consulted members of the Advisory Committee on Novel Foods and Processes (ACNFP) on this application and on the initial assessment report provided by the Irish Competent Authority.

We consulted ACNFP members by post and their comments are provided in the attached document. Due to time constraints this document has not been endorsed by the whole Committee. However, it contains sufficient detail to explain that the UK has reasoned objections to the authorisation of this novel ingredient.

In view of these comments, the UK would not be able to support the authorisation of this ingredient until these issues have been addressed.

Yours sincerely,

Dr Sandy Lawrie

Chemical Safety Division

GAMMA-CYCLODEXTRIN

COMMENTS FROM ACNFP MEMBERS

a) Use of n-decane

The Committee notes that n-decane is used as a solvent to separate the complexant from the formed gamma-cyclodextrin. Although residues of n-decane in the NI will typically not exceed 5 ppm, the Committee notes that n-decane is not included in the list of extraction solvents (EC Directive 88/344); it is therefore not permitted to be used in the EU irrespective of residue level seen.

b) Intestinal fate of gamma-cyclodextrin

The intestinal fate of gamma-clyclodextrin is not clear. The intended target consumer group includes diabetics, those with impaired glucose tolerance and others who may "benefit" from a slow release form of glucose. From the evidence presented, we cannot be sure that gamma-cyclodextrin has this characteristic because it is claimed that gamma-cyclodextrin is hydrolysed rapidly by salivary and pancreatic enzymes. In contrast, the cited studies in rodents and humans indicate that some of the carbohydrate in gamma-cyclodextrin may reach the large bowel as evidenced by the observations of e.g. caecal enlargement, flatulence and stool softening. It is therefore not clear if the ingredient truly is a slow release source of glucose.

c) Effect on absorption of fat-soluble vitamins

The core of cyclodextrin is lipophilic and has the potential to trap fat soluble vitamins. We already have a community in the UK which is commonly Vitamin D insufficient. Anything which has the potential to worsen this situation must be studied in more detail before approval. In addition, one each of sub-acute, chronic and long term dosing studies in mice were associated with rises in alkaline phosphatase. These were dismissed as not relevant to liver toxicity as other liver markers were normal. However, this could have originated from bone which was not considered.

A paper by Munro et al (2004)[16] argues that interaction of gamma-cyclodextrin with lipophilic nutrients is not to be expected as the formation of inclusion complexes is a reversible process and this ingredient is readily digested in the small intestine (but see comments above on intestinal fate). This paper refers to studies with the related substance beta-cyclodextrin, which show that the bioavailability of vitamins A, D and E is not affected. It would be reassuring to have some good human studies on gamma-cyclodextrin.

d) Intended use and estimated intakes

It is not clearly indicated how the product is going to be used and the estimated daily intake - all of which is necessary to indicate how and where the product will end up, and who the consumers are likely to be.

This product is to be promoted as a nutriceutical with benefits for diabetics, yet there are no human studies on the relevant target population.

d) Labelling

If, metabolically, gamma-cyclodextrin is simply a source of glucose, then we need rigorous consideration of how this product will be labelled so that the proposed target consumer group (diabetics, those with impaired glucose tolerance and others who may "benefit" from a slow release form of glucose) is not misled. There is a risk that diabetics and others may consume products containing gamma-cylcodextrin in the mistaken belief that this is "low sugar".

UK Food Standards Agency

September 2010

16 (Munro IC, Newberne PM, Young VR, Bär A. Safety assessment of gamma-cyclodextrin. Regul Toxicol Pharmacol. 2004 Jun;39 Suppl 1:S3-13.)

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