Ministry of Agriculture, Fisheries and Food
and
Department of Health

ACNFP ANNUAL REPORT 1995

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

'to advise Health and Agriculture Ministers of Great Britain and the Heads of the Departments of Health and Social Services and Agriculture for Northern Ireland on any matters relating to the irradiation of food or to the manufacture of novel foods or foods produced by novel processes having regard where appropriate to the views of relevant expert bodies'.

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FOREWORD

From this seventh annual report it is clear that 1995 was a year of continued activity for the ACNFP, with a great variety of topics to consider.

The Committee has worked hard to probe each submission carefully and thoughtfully in order to do all that it can to ensure that novel foods which are coming onto the UK market are safe for the consumer.

It is sometimes thought that the Committee is concerned solely, or predominantly with foods derived from genetic modification. While an increasing number of foods are derived from genetically modified organisms – we considered products from genetically modified oilseed rape, maize and tomatoes during 1995 – the range of topics is much wider than that. In particular, products involving novel fats are becoming increasingly important, as are new food crops such as lupins. We also continue to monitor novel foods from other areas of the world – green tea extract and guarana this year – in order to ensure that their novelty for the UK population will not cause a problem.

Thus, the Committee needs a wide variety of skills, and we have them – drawn from many British institutions. We have, in addition, a consumer representative and an ethicist to ensure a broader perspective. We comment on major issues, and work openly because we believe that this is the best way to carry the confidence of all concerned.

The experience gained in the past seven years will be invaluable when the proposed EC Novel Food Regulation is adopted. As this report goes to press it looks as if the regulation will be in place before the end of this year. When the regulation comes into effect the assessment of novel foods will move to a statutory footing. I am pleased to report that the work of this Committee has continued to make a significant contribution to the way the safety of novel foods is considered across Europe both now and in the future.

Derek C Burke
(Chairman)

INTRODUCTION

This is the seventh annual report of the work of the Advisory Committee on Novel Foods and Processes (ACNFP). It covers the specific issues discussed at the Committee meetings held during 1995, together with details of related topics which were brought to the Committee's attention. Some of the topics discussed during 1995 were continuations of previous work while others were original. For completeness, topics which were not discussed in 1995 but have data requests outstanding from previous years are identified. Brief details of the Committee's reviews of products and processes are included in the body of the report. The advice given to Ministers and other detailed material are presented in the Appendices.

The organization, remit and membership of the Committee are set out at Appendix I.

Copies of previous annual reports [1,2,3,4,5,6] can be obtained from the MAFF Secretary (see page 20). A cumulative index of all topics considered in the annual reports may be found at the back of this document (page 115).

Technical terms which are not explained in the body of the report are italicized where they appear for the first time in the text and are explained in the glossary (page 22).

1. TOPICS CONSIDERED AND FINALIZED DURING 1995

1.1 NOVEL STARTER CULTURE FOR FERMENTED DAIRY PRODUCTS

In 1995 the ACNFP received a submission seeking clearance for the use of *Enterococcus faecium* strain K77D, as a *starter culture* in the production of cultured milk products. The marketing company had already received food safety clearance for the use of this organism in Denmark and could therefore, under current EC legislation, market such products legally in all other Member States. However, the ACNFP welcomed the decision of the company, nevertheless, to approach the UK authorities to seek food safety clearance of *E. faecium* strain K77D, under the present UK voluntary scheme for novel foods and processes.

The ACNFP's evaluation of the food safety of this particular organism concentrated particularly on its history and identification and the specification and quality control criteria used to ensure a consistent product.

This particular strain of *E. faecium* was selected from *intestinal flora* isolates from people in part of the former USSR and has been demonstrated to be sensitive to a range of *antibiotics*. Information was provided from *Polymerase Chain Reaction* (PCR) analyses to demonstrate that this strain did not contain any of the recognised genetic material encoding resistance to the antibiotic vancomycin, which has been found in some other strains of *E. faecium* associated with infections in hospitals. The ACNFP noted that this particular K77D strain had been characterised and deposited in the Russian National Collection of Industrial Micro-organisms but considered it appropriate that a sample of the strain should also be deposited in a culture collection in a European Union country. The company has agreed to deposit a sample of the strain in the UK National Collection of Industrial and Marine Bacteria.

The Committee considered evidence demonstrating the lack of *pathogenicity* of this particular organism. Further reassurance on the safety of cultured milk products containing this organism was provided by data from a six-week clinical study in volunteers which showed no adverse effects and the absence of any increase in human infections with *E. faecium* in Denmark following marketing of these products in that country from 1993.

Detailed information was provided relating to the quality control checks applied to batches of this organism and these form part of an agreed specification.

The Committee concluded that *E. faecium* strain K77D was acceptable for use as a starter culture for the production of cultured milk products. A copy of the report submitted to Ministers is attached at Appendix II. Clearance of the novel starter culture was announced by Ministers on 26th February 1996.

1.2 OIL FROM OILSEED RAPE GENETICALLY MODIFIED FOR USE IN HYBRID BREEDING PROGRAMMES

Following ACNFP clearance in 1994 of oilseed rape which had been *genetically modified* (GM) for use in a breeding programme for the production of *hybrid* seed,[6]

the Committee received a second submission seeking clearance of another oilseed rape line (B94-2) which had been genetically modified to enable its use as a *fertility restorer* in the oilseed rape breeding programme. The fertility restorer line contains a *gene* which is able to counteract the arrest of pollen development in other oilseed rape lines which have been genetically modified to be male sterile so that they cannot self-pollinate. When the male sterile line is crossed with the fertility restorer line the resultant *progeny* have normal pollen development[6] (see section 1.3 for further details of genetic modification and breeding programme). The company had asked for clearance of line B94-2 and also of lines derived from B94-2 through conventional plant breeding.

This latest GM line had been developed from the same conventionally-bred variety, Drakkar, and contained the same introduced gene constructs, including an antibiotic-resistance gene and a *herbicide*-tolerance gene, as the GM fertility restorer line previously considered by the Committee. The Committee's evaluation of the food safety of the oil from the GM oilseed rape focused on the composition of the oil but other factors which could affect the safety of the oil were also considered, including the identification of any unintentional changes which may have occurred as a result of the genetic modification and confirmation that the introduced genes were stably inherited.

Extensive data on seed harvested from field trials in different countries, including the UK, satisfied the ACNFP that the composition of the oil from the GM oilseed rape did not differ from that from conventionally-bred varieties. Examination of the results of sensitive analytical tests revealed that none of the gene products from the introduced fertility restorer, antibiotic-resistance and herbicide-tolerance genes were present in the seed from the GM fertility restorer line or in the seed of lines developed from it. The processing characteristics of seed from GM hybrids and conventionally-bred hybrids were also compared and no differences were found.

Detailed information given on the genetic modification procedure indicated that there had been some rearrangement of the genes during incorporation. However, the Committee compared data from the GM lines with those from comparable conventionally-bred lines and found that despite these genetic rearrangements, there were no demonstrable differences in seed and oil composition, processing characteristics, seed digestibility and agronomic traits. Trials' data from several locations taken over successive growing seasons, demonstrated that the introduced genes had been stable for a number of generations. Molecular analysis showed that the introduced construct remained unchanged through successive generations.

The Committee concluded that oil from oilseed rape developed through conventional plant breeding methods from the fertility restorer line B94-2 and conventionally-bred varieties and breeders lines was safe for use in food and that it did not differ in composition from oil from conventionally-bred oilseed rape. As with other GM plants, the ACNFP requested that compositional data be provided at regular intervals in order to confirm the long-term stability of the GM oilseed rape. The company has agreed to provide such data.

The Food Advisory Committee (FAC) considered the labelling implications of the oil and agreed that because there was no viable genetic material in the final food to be consumed no special labelling was required.

A copy of the Committee's report to Ministers is attached at Appendix III. Ministers announced clearance of oil from further GM oilseed rape lines on 20th September 1995.

1.3 OIL FROM GENETICALLY MODIFIED OILSEED RAPE TOLERANT TO GLYPHOSATE

In 1994 the ACNFP recommended food safety clearance of processed products derived from soya beans which had been genetically modified for resistance to the herbicide glyphosate.[6] In 1995 the Committee was asked to give food safety clearance to oil from oilseed rape which had been similarly modified for glyphosate tolerance. Clearance was sought for both the original GM line and for subsequent lines derived from it using conventional plant breeding methods.

As with the soya beans, the modification procedure involved the insertion of a bacterial gene encoding an enzyme with reduced sensitivity to the herbicide[6] (see section 1.4). However, in this instance a second gene encoding an enzyme able to degrade and inactivate glyphosate was inserted into the oilseed rape.

The Committee's assessment focused upon the composition of the oil. However, other factors including the identification of any unintentional changes that had taken place as a result of the genetic modification, confirmation of the genetic stability of the introduced genes when inherited by later generations and the likelihood of transfer of the novel genetic material were also considered. The Committee compared analytical data on seed and oil from GM oilseed rape with that from conventionally-bred varieties, including the parental Westar variety and other commercial oilseed rape varieties.

Extensive data on seed from field trials in Canada satisfied the ACNFP that the composition of the oil from the glyphosate tolerant oilseed rape was similar to that from conventionally-bred varieties. The Committee was also satisfied that neither of the two inserted genes nor their gene products were present in the fully processed oil from the GM oilseed rape. The processing characteristics of the GM seed did not differ from conventionally-bred commercial varieties and there was no evidence from the agronomic characteristics of the GM oilseed rape that any unintentional changes had arisen during the genetic modification procedure. This was confirmed by molecular characterisation data. Data obtained from field trials, at a number of locations between 1992 and 1994, confirmed that the introduced genes had been stably inherited and would be stable in lines developed from the original GM line and conventionally-bred varieties.

The ACNFP concluded that the oil from the glyphosate tolerant oilseed rape was safe for use in food and was compositionally comparable to oil extracted from conventionally-bred oilseed rape already consumed as part of the UK diet. The Committee was further satisfied that oil from varieties derived from the GM line using conventional plant breeding methods would also be safe for food use.

The Company has agreed to provide, at regular intervals, appropriate data on seed composition and on the fatty acid profile of the oil from the GM line and from lines derived from it by conventional plant breeding methods, to confirm the long-term stability of glyphosate tolerant oilseed rape.

The FAC has advised that because there was no viable genetic material in the final food to be consumed, no special labelling is required for oil derived from glyphosate-tolerant oilseed rape.

A report of the ACNFP's advice to Ministers is attached at Appendix IV. Clearance for the oil was announced by Ministers on 25th January 1996.

1.4 OIL FROM GENETICALLY MODIFIED OILSEED RAPE TOLERANT TO GLUFOSINATE-AMMONIUM

In 1995, the Committee also considered a submission seeking clearance for oilseed rape that had been genetically modified for tolerance to the herbicide glufosinate-ammonium. The GM oilseed rape had been developed using conventional plant breeding methods from a GM *transformant* of the commercial variety Topas, the conventionally-bred line ACSN-3 and the conventionally-bred commercial variety Excel. In addition to the gene for tolerance to glufosinate-ammonium, the oilseed rape also contains an antibiotic-resistance gene.

As with the other oilseed rape submissions, the ACNFP concentrated its food safety evaluation on the composition of the oil and factors such as the identification of any unintentional changes that had occurred as a result of the genetic modification and confirmation that the introduced genes were stable when inherited by later generations.

Extensive data on seed from the GM oilseed rape harvested from field trials in Canada satisfied the ACNFP that the composition of the oil did not differ from that from conventionally-bred varieties. Analytical tests confirmed that neither the introduced genes nor their gene products were present in the fully processed oil from the GM oilseed rape. The processing characteristics of seed from the GM oilseed rape and a conventionally-bred commercial variety were also compared and no differences were found.

Detailed information provided on the genetic modification procedure confirmed that no unintentional changes had taken place at the molecular level. Nor was there any evidence of unintentional changes when the agronomic traits of the GM and conventionally-bred oilseed rape were compared. By examining data from several studies, including field trials, the Committee was satisfied that the introduced genes had been inherited in a stable manner during the development of the GM oilseed rape and would be stable in other GM lines developed by breeding with conventionally-bred varieties.

The ACNFP concluded that the oil from this GM oilseed rape was safe for use in food and that it did not differ in composition from oil from conventionally-bred oilseed rape already in use. In addition, the information provided indicated to the Committee that the oil from varieties derived from GM oilseed rape by conventional plant breeding methods would also be safe for use in food. The company has agreed to provide appropriate data in the future on seed composition, and on the fatty acid profile of the oil from the GM oilseed rape and lines derived from it by conventional plant breeding to confirm the long-term stability of the oilseed rape tolerant to glufosinate-ammonium.

The FAC has advised that in accordance with its own guidelines on the labelling of GM foods, because there was no viable genetic material in the final food to be consumed no special labelling is required for oil derived from this GM oilseed rape.

A copy of the Committee's report to Ministers is reproduced at Appendix V. Ministers announced clearance of glufosinate-ammonium tolerant oilseed rape on 15th May 1995.

1.5 PRODUCTS DERIVED FROM INSECT-RESISTANT GENETICALLY MODIFIED MAIZE*

Maize has a long history of use as a human food stuff and has been cultivated for several thousand years in North, South and Central America. More recently, it has become a major crop in southern Europe. Like many plants, maize is subject to attack by insect pests resulting in damage to the plant and severe yield loss. In 1995 the ACNFP received a submission seeking food safety clearance for processed products from maize that had been genetically modified for tolerance to the European corn borer (*Ostrinia nubilalis*), an important insect pest of maize in Europe and North America. Clearance was sought for products from the genetically modified maize and from inbred and hybrid lines derived from it through conventional plant breeding methods.

The GM maize contains a bacterial gene which confers resistance to the European corn borer. In addition, the maize contains selectable marker genes for tolerance to the herbicide glufosinate-ammonium and to the antibiotic ampicillin. The ampicillin resistance gene has bacterial regulatory sequences and is not expressed in the maize; it was used only in the preliminary stages of the genetic modification procedures which were carried out in bacteria.

The ACNFP's evaluation concentrated on the food safety of the processed products from the GM maize and on the genetic modification procedure. The Committee was satisfied that there were no compositional differences between grain from the GM maize and that from conventionally-bred maize. Analytical tests demonstrated that the herbicide resistance gene product was not present in freshly harvested grain from the GM maize. Some insecticidal activity was detected in the fresh grain. However, this disappeared following drying and subsequent rehydration of the grain. The Committee noted that the processing procedures would destroy any gene products present in the GM maize.

Detailed information on the genetic modification procedure satisfied the ACNFP that no unintentional changes had taken place at the molecular level. In addition, morphological studies which compared lines derived from the GM maize with conventionally-bred varieties showed no evidence of unintentional change. Data from genetic segregation studies satisfied the ACNFP that the introduced genes were stably inherited. The ACNFP was able to conclude from the information provided that the processed products from the GM maize would be safe for food use.

However, the ACNFP expressed reservations about the use of the unprocessed GM maize, including the green plant material, as an animal feedingstuff. The product of the particular ampicillin resistance gene present in the GM maize is an enzyme

* Professor Miflin declared a personal interest in this item and left the room during discussions.

which inactivates a number of antibiotics which are extremely important in clinical and veterinary medicine. The bacterial regulatory sequences on the gene could allow the gene to become functional if it were transferred from the GM maize to a bacterium, and could also allow many copies of the gene to be generated in a cell, which could lead to high levels of production of the gene product. The Committee was aware that the chance of such a transfer occurring is very low but is finite.

The ACNFP concluded that the processed products from the GM maize and from inbred and hybrid lines derived from it, were safe for use in food and did not differ in composition from those from conventionally bred maize. However, the Committee recommended that the use of the unprocessed maize as an animal feedingstuff was unacceptable at present.*

The FAC examined the labelling implications of processed products derived from the GM maize and advised that because there was no viable genetic material in the final food to be consumed, no special labelling was required for these products.

The Committee's advice will be submitted to Ministers in 1996 and its report will appear in the 1996 Annual Report.

1.6 GENETICALLY MODIFIED TOMATOES TO BE EATEN FRESH

The Committee received a submission seeking food safety clearance of genetically modified tomatoes intended to be eaten fresh. The tomatoes have been genetically modified to carry a gene which delays fruit softening and allows the tomatoes to be ripened on the plant without compromising subsequent shelf life. The tomatoes also contain a selectable marker gene which encodes for resistance to the antibiotic kanamycin and other closely related antibiotics e.g. neomycin.

In its assessment of the safety of the GM tomatoes, the ACNFP compared the composition of the fruit from ten GM tomato lines for which clearance was sought, with that from conventionally-bred tomato lines to determine whether there had been any nutritional or toxicological changes as a result of the genetic modification. The Committee also gave particular consideration to the presence of the kanamycin-resistance gene and its product in the fruit from the GM tomato lines. This was in accordance with its recommendations in its Report on the Use of Antibiotic Resistance Markers in Genetically Modified Food Organisms.[7] As kanamycin and neomycin are both in clinical and veterinary use in the UK, the ACNFP had to be satisfied that the kanamycin-resistance gene product in the fruit would not compromise the use of these antibiotics. The Committee also had to be satisfied that the resistance gene could not be transferred from the GM tomatoes to gut micro-organisms during digestion in the human gut and become functional in the gut micro-organisms.

Data reviewed by the Committee demonstrated that the fruit from the GM tomato lines was as safe in food use as that from non-GM tomato lines. Nutritionally and toxicologically there was no difference in the composition of the fruit from the GM lines and that from non-GM lines.

* Secretariat note (June 1996): In April 1996 a Commission decision to market this product under EC Deliberate Release Directive (EC 90/220) did not receive a majority vote from Member States. This issue will now be referred to the Council of Ministers.

Extensive safety information was also provided on the two introduced genes and showed that the kanamycin-resistance gene product in the fruit would be degraded rapidly by digestive fluids in the normal human gut. Further data indicated that in patients in which the digestive fluids are neutralised, the efficacy of neomycin would not be compromised by the inclusion in the diet of fruit from the GM tomato lines. The Committee was satisfied that transfer and maintenance of the kanamycin-resistance gene in human gut micro-organisms was unlikely since the gene is controlled by plant regulatory sequences and even if it did occur antibiotic therapy would not be compromised. Data from genetic segregation studies confirmed that the two introduced genes were stably inherited.

From the information submitted, the ACNFP concluded that the fruit from the ten lines of GM tomatoes that it examined was safe for use as food.

The FAC has advised that the tomatoes should be labelled to indicate that they are GM products, in line with the labelling requirements contained in the Council's Common Position on the proposed EU Regulation on Novel Foods and Novel Food Ingredients.

A copy of the Committee's report to Ministers is attached at Appendix VI. Ministers announced clearance of the GM tomatoes to be eaten fresh on 29th February 1996.

1.7 TOMATO PASTE FROM GENETICALLY MODIFIED TOMATOES

Last year, the Committee gave food safety clearance to tomato paste derived from tomatoes which had been genetically modified to improve fruit quality by reducing the levels of a pectin degrading enzyme present in tomatoes.[6] However, the Committee's clearance was limited to tomato paste from only two hybrid lines derived from one GM *inbred line*. In 1995 the Committee was asked to extend its food safety clearance to tomato paste derived from three additional GM tomato lines: two hybrid lines derived from the original GM inbred line and a new GM inbred line.

In its evaluation of the food safety aspects of paste derived from the additional GM tomato lines, the ACNFP compared analytical data on the fresh fruit from the new GM lines with that from their non-GM counterparts to confirm that, apart from the intended effects on the fruit, the genetic modification had not given rise to any untoward secondary effects which could adversely affect the composition of the paste from the new GM tomatoes. The Committee reviewed analytical and agronomic data on GM and non-GM fruit from field trials in various countries, including the UK. The Committee was satisfied that the toxicological and nutritional composition of the GM fruit, and hence the paste produced from it, was similar to that of conventionally-bred counterparts.

The genetic modification aspects involved in the development of the original GM inbred line, from which the two new hybrid lines were derived, had been considered previously and are described fully in the ACNFP's 1994 Annual Report.[6] Although the new inbred line contained the same *construct* as the original inbred line, the transformation event was different from that evaluated previously by the Committee. Data on this genetic modification event were provided in the submission.

The ACNFP concluded from data on the fresh GM fruit that paste from the three new GM tomato lines was compositionally similar to, and as safe for human consumption as, paste produced from conventionally-bred tomatoes currently consumed in the UK diet. The Committee therefore recommended food safety clearance of tomato paste produced from the two new hybrid lines and the GM inbred line. The Committee agreed to extend clearance to any hybrid line developed from the original inbred GM line. However, the ACNFP was not prepared at this stage to give clearance to every tomato line containing the construct. As with the GM tomato lines that had been cleared previously, the Company agreed to submit, at regular intervals, data confirming the genetic stability of these GM tomatoes.

Dr Rodgers declared an interest in this item and did not take part in the final decision.

The FAC has advised that because there was no viable genetic material in the final food to be consumed, the tomato paste derived from these GM tomato lines does not require any special labelling.

A copy of the Committee's report is reproduced at Appendix VII. Ministers announced clearance of the additional lines on 23rd February 1996.

1.8 LUPINS

The ACNFP's evaluation of lupins began in 1990 when it received a submission seeking food safety clearance of the seed of the narrow-leaved lupin *Lupinus angustifolius*. This particular lupin variety contains reduced levels of toxic compounds known as *alkaloids* present in other varieties of lupins. Details of the ACNFP's ongoing evaluation can be found in previous Annual Reports [2,3,4]. During its evaluation, the ACNFP sought the advice of the Committee on Toxicity (COT – see Appendix I) on the toxicological significance of liver changes found in certain rats in a ninety-day toxicity study on lupin alkaloids. As a result of the COT's considerations a second study was conducted in order to answer the question raised by the liver changes in the ninety-day study.

This second study was completed in 1995 and was considered by the COT,[10] which forwarded its advice to the ACNFP. The ACNFP has now completed its evaluation of lupins and will consider its report on this submission in the early part of 1996. The report will appear in the 1996 Annual Report.

The Committee's consideration of a submission for clearance of lupin fibre is partially dependent on the consideration of lupins in general, but is also dependent on particular data requested regarding the fibre product (see section 2.1).

1.9 OHMIC HEATING – EXTENSION OF USE

Ohmic heating or direct resistance heating is a process which sterilises foods using the heat generated by the passage of an electric current and has now been in commercial use for three years in the UK following clearance given by the ACNFP in 1992.[3] In 1995 the Committee received a submission seeking to extend the scope of the original clearance of ohmic heating technology. The submission sought

clearance for the use of ohmic heating in the sterilization of a range of particulate fruit products, such as strawberries in syrup and other fruit compote formulations.

The ACNFP's original clearance had been restricted to sterilization of prepared ready meals and similar product types.

In considering the requested extension, the ACNFP considered a range of additional data provided by the company. The Committee focused its evaluation on the microbiological, toxicological and nutritional aspects in the application of this novel sterilisation technology to the proposed new range of particulate fruit products. The Company intends to keep the conditions used for processing particulate fruit products within the range of operating conditions employed in the original application, and to employ similar quality control measures.

Since the operating conditions were similar, the ACNFP considered that any toxicological effects from possible contamination would be minimal and was satisfied that the potential for formation of toxic compounds from ohmic heating effects on high-acid foods, such as particulate fruit products, was negligible. From a nutritional standpoint, the Committee recognised that the ohmic heating process, in common with conventional cooking, could reduce the level of some heat-labile vitamins. However, data were provided which demonstrated that ohmic heating had a similar effect on the nutritional composition of whole particulate fruits in syrup, especially in terms of the folic acid, thiamin and Vitamin C content, as canning.

The Committee was therefore content that the effects of ohmic heating were equivalent to conventional processes such as canning, which are known to have an adverse effect on some vitamins, especially thiamin. Furthermore, as particulate fruit products are only a minor source of nutrients in the diet, the Committee concluded that replacement of conventionally processed particulate fruit products by ohmically heated fruit products would be of little or no nutritional significance.

The Committee therefore recommended broadening the scope of the original clearance of ohmic heating to include processing of particulate fruit products, subject to compliance with the original process specification and operating conditions.

A copy of the Committee's report to Ministers is reproduced at Appendix VIII. Ministers announced the extension of clearance on 26th June 1995.

1.10 ENZYMIC MODIFICATION OF VEGETABLE OILS – EXTENSION OF USE

In 1992, the ACNFP considered a novel enzymic *interesterification* process used to produce fats and oils. The process involved the use of immobilized *lipase* enzymes to catalyse the interesterification of glycerides derived from edible vegetable oils with *fatty acids* or triglycerides to produce an interesterified oil or fat, the composition of which can be controlled by altering the composition of the vegetable oil feedstock. The ACNFP recommended that clearance be given to the use of enzymically modified vegetable oils as ingredients in chocolate and confectionery fat and as an ingredient at up to 20% in frying fats.[3,4] Subsequently in 1994 the Committee gave clearance for oils produced using a revised process of interesterification.[5]

In 1995, the ACNFP was asked to consider extending its clearance to allow the use of enzymically interesterified fats in yellow fat spreads such as margarines. The Committee noted that the basic principles of the interesterification process were the same as those considered previously, the only difference being that the starting materials were adjusted to obtain oils suitable for use in yellow fat spreads.

Data were submitted in support of the extended clearance, including a comparison of the traditional methods of oil modification used to produce ingredients for use in yellow fat spreads and the use of enzymic interesterification. Data were also provided which indicated that the fatty acids present in the interesterified oils are found in existing natural vegetable oils or fats of commerce, and that there was no detectable enzyme activity or enzyme immobilisation support material present in the modified fat products.

The Committee also reviewed data which suggested that the use of the interesterified fats in margarines and spreads would reduce the amount of trans-fatty acids in these products and thus may have beneficial nutritional effects.

The ACNFP was satisfied that the interesterified oils were equivalent to edible oils processed by traditional methods according to good manufacturing practice and agreed to extend its original clearance to allow the use of these fats in yellow fat spreads.

A copy of the Committee's report is attached at Appendix IX. Ministers announced extension of the clearance on 1st May 1996.

1.11 HEMICELLULASE ENZYMES USED IN BREADMAKING

ACNFP advice was sought on the genetic modification aspects of two submissions the FAC had received requesting food safety clearance of *hemicellulase* enzymes for use in bread making. The enzymes are derived from *Aspergillus niger* and *Bacillus subtilis* which have been genetically modified to increase natural production of the hemicellulase or xylanase enzymes. The enzymes had been referred to the COT for food safety evaluation. However, the FAC requested ACNFP advice on the specialist area of genetic modification of the source organism.

A. niger and *B. subtilis* both have a long history of safe use in the food industry, particularly in enzyme production. In both cases, the genetic modification procedure involved the insertion of copies of a xylanase gene derived from the same strain of *A. niger* and *B. subtilis* to produce self-clones containing multiple copies of the gene, and having an increased capacity to secrete the enzyme.

The ACNFP considered data on the genetic modification procedures and on the stability of the resultant GMOs. The *plasmid* used in the genetic modification of *B. subtilis* contained an antibiotic-resistance gene, thus conferring antibiotic resistance to the GM *B. subtilis*. However, the ACNFP was satisfied that due to the way the plasmid had been constructed, the transfer of antibiotic resistance from the GM *B. subtilis* could not occur by plasmid mobilisation. Data were submitted which indicated that there was no DNA present in the final enzyme product for use in food. The Committee was also satisfied with the data provided confirming the stability of both GMOs and noted that if there was any loss of stability this would simply result in reversion to the naturally-occurring *A. niger* and *B. subtilis*.

The ACNFP concluded that there were no specific concerns arising from the genetic modification procedures used in the production of the hemicellulase enzymes. This advice was forwarded onto the FAC in December. The FAC subsequently recommended temporary clearance of both enzymes pending the submission of further data requested by the COT.

2. TOPICS ABOUT WHICH THE COMMITTEE HAS NOT CONCLUDED ITS DELIBERATIONS

The ACNFP tries to process submissions with the minimum of delay without compromising the quality of the safety assessment. However, there are times when advice needs to be sought from other Committees or proposers need to perform further studies to provide more data. In such cases the ACNFP is not able to reach final conclusions until further advice or new data are available.

2.1 REQUESTS OUTSTANDING FROM PREVIOUS YEARS

In certain instances proposers may need over a year to generate the data requested by the ACNFP or sister Committees. Additional data requested by the Committee in previous years on the topics listed below remained outstanding. However, the proposers involved have indicated that they will be acting on the requests for further data but that they may need some further time to comply. Further details may be found in the appropriate ACNFP annual reports.

(i) Sugar beet fibre[4]

(ii) Lipase ex *Aspergillus oryzae*[4,5,6]

(iii) Novel confectionery fat to replace cocoa butter[4,5,6]

(iv) Lupin fibre[2,3,4]

(v) Mycelial protein from *Polyporus squamosus*[5]

2.2 LONG-CHAIN POLYUNSATURATED FATTY ACIDS FOR USE IN INFANT FORMULAE*

The long-chain polyunsaturated fatty acids (LCPFA) arachidonic acid and docosahexaenoic acid play an important role in neural development and in visual cortical function during pre- and post-natal development. These LCPFAs are present in breast milk but generally not in infant formulae. Pre-term infants do not have the capacity to synthesize these LCPFAs from the parent *essential fatty acids* and therefore may be deficient in arachidonic acid and docosahexaenoic acid when fed formula feeds. In 1995, the ACNFP received submissions from two different infant formulae manufacturers both seeking food safety clearance for the use of oils rich in arachidonic acid and docosahexaenoic acid in infant formulae for pre-term and term infants. The oils, arachidonic acid single cell oil (ARASCO) and docosahexaenoic acid single cell oil (DHASCO), are produced during fermentation of the fungus *Mortierella alpina* and the alga *Crypthecodinium cohnii*, respectively.

In assessing the safety of these oils, the Committee considered detailed information on the production process and the controls used to ensure the quality and consistency of the oils. Acceptable specifications were agreed for ARASCO and DHASCO. The ACNFP also reviewed in detail the information provided on the taxonomy and non-pathogenicity of *M. alpina* and *C. cohnii*. In addition extensive

analytical profiling for known algal toxins and toxicity testing had been carried out on *C. cohnii*. The ACNFP was satisfied that both organisms had been correctly identified, were non-pathogenic and did not produce any toxins.

A range of toxicity data was provided on the two oils including ninety-day studies and a developmental study in rats. Several histopathological changes were reported in some of the studies and the ACNFP decided to seek specialist advice from the COT. The COT reviewed the studies concerned and was satisfied that the *histological* lesions were not caused by ARASCO and DHASCO themselves but were the result of the synthetic diet formulations used in these studies. Several nutritional and clinical studies were included in the submission and the ACNFP has referred these to COMA and its Panel on Child Nutrition for consideration of the acceptability of these oils for use in infant formulae.

The ACNFP will finalise its advice on ARASCO and DHASCO once it has received advice from COMA.

2.3 STRUCTURED TRIGLYCERIDES COMPOSED OF MIXTURES OF SHORT-CHAIN AND LONG-CHAIN FATTY ACIDS

The Committee began its evaluation of a substantial submission seeking food safety clearance of a family of structured triglycerides claimed to provide fewer calories than conventional fats. The Committee's initial discussions focused on the calorific value of the novel fats and potential effects on blood cholesterol and thrombosis. The Committee will consider toxicological and nutritional data at its meetings in 1996.

2.4 ENZYMATICALLY PARTIALLY DEPOLYMERIZED POLYSACCHARIDE

The ACNFP began its consideration of a request for food safety clearance of a soluble fibre obtained by the action of a beta *mannanase* enzyme derived from *Aspergillus niger* on guar gum. The soluble fibre is intended to be used in a wide range of processed liquid and solid foods. The Committee considered data on production of the fibre and potential intake levels. The Committee has still to consider the toxicological data provided on the fibre and further data have been requested on other aspects of the submission.

2.5 GREEN TEA EXTRACT

The Committee received a submission seeking food safety clearance for a Green Tea Extract, derived from the non-fermented leaves of the tea plant *Camellia sinesis*. It is intended to add the extract to a variety of foodstuffs, though initially it will be added only to artificial sweeteners e.g. tabletop sweeteners. The Committee has requested further data on the extract before making any decision on food safety clearance.

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* Dr Rodgers declared a personal interest in this item and left the room during discussions.

3. PROGRESS ON TOPICS CONSIDERED PREVIOUSLY

3.1 QUINOA

Quinoa is a high-protein crop native to South America. In 1990 a project was commissioned by MAFF to investigate the potential of UK-grown quinoa for use as both an animal feedingstuff and as a human food as a possible alternative to rice. As the project involved consideration of quinoa as a human food, the ACNFP was asked for advice on the food safety aspects.[2,3,4] The Committee had requested further data on the biological significance and content of some bitter-tasting detergents naturally present in quinoa. In 1995, the results of the MAFF project were submitted to the ACNFP for consideration. These indicated that quinoa lines which had been bred for cultivation under UK conditions had relatively high saponin levels in the grain which needed to be removed before the grain could be used as a food and that there may be a further antinutrient present within the grain in addition to the saponins already identified.

UK-grown quinoa is not currently available for human consumption. However, further research on UK-grown quinoa is being funded by the EU as part of a European-wide project and the Committee will continue to receive updates on the work.

3.2 GUARANA

Following the ACNFP's request in 1993, that suppliers and trade associations submit further data to support the safety in use of products containing guarana, a range of data was submitted to the Committee during 1994 and 1995. The ACNFP had previously considered the caffeine and methylxanthine levels found in guarana and found them to be similar to levels found in existing, related dietary items such as tea, coffee and colas. However, the Committee considered there to be little information available on the more general properties and safety of guarana, making it impossible to conduct a full safety evaluation.[5]

The ACNFP decided to convene a small *ad hoc* Working Group to consider the further data submitted on guarana and to identify any gaps in the data package. Although generally satisfied with the data provided on the infusate, the Working Group requested that further information on solid guarana products for non-beverage use be submitted. The Committee was subsequently informed that sale of solid guarana such as powders for sprinkling on foods has been discontinued.

A report of the Committee's considerations will be submitted to Ministers in 1996.

3.3 INTERESTERIFIED FATS FOR INFANT FORMULAE

The ACNFP received a submission in 1992 requesting clearance of Betapol, a novel fat blend made of fats which had been enzymically modified for use in infant formulae.[3,4] The Committee had previously given clearance for the use of fats produced by enzymic interesterification in confectionery and cooking fats[3,4] (see also section 1.8). The interesterification process is used to produce *triacylglycerols*

that will be added, as a blend, to infant formulae in order to make them more like breast milk. The ACNFP had indicated that while the production process itself was acceptable, the possible effects on the constituents of infant formulae should by assessed by Committee on Medical Aspects of Food Policy (COMA). The submission was therefore referred to COMA.

A number of clinical studies were included in the submission and these were considered by the COMA Panel on Child Nutrition and the Panel on Novel Foods. The Panels agreed that the addition of the novel fat blend to infant formula for *pre-term* infants offered considerable benefits, increasing the absorption of calcium and fat. The nutritional consequences of adding the fats to *term* infant formulae were also discussed. However, the Panels indicated that they would like to see further clinical trial data on term infants before giving a view on the use of the fats in formulae for term infants.

The COMA Panels advised the ACNFP that they had no objections to the use of the interesterified fats in formula for pre-term infants but requested that the company carry out post-market surveillance and investigate potential effects on the absorption of fat, soluble vitamins and iron.

4. OTHER ACTIVITIES

4.1 ANTIBIOTIC RESISTANCE MARKERS

During the year the ACNFP considered several submissions on products from GM plants containing antibiotic resistance markers (ARMs). Some of the submissions required discussion of issues which the ACNFP had previously only hypothetically considered, notably the presence of a kanamycin resistance gene in GM tomatoes to be eaten fresh (see section 1.6). Consideration of the submission on the maize genetically modified for insect resistance, led the Committee to discuss the general safety issues raised by particular ARMs in GM plants used as human food sources. In addition the ACNFP may now be asked for advice on the genetic modification aspects of GM animal feedingstuff submissions. New topics, such as the suitability of certain regulatory sequences used to control expression of the genes, and old topics, such as the risk of gene transfer to gut micro-organisms, were also discussed. A joint meeting was held between representatives of the ACNFP and the Advisory Committee on Releases to the Environment (ACRE) to discuss some of these issues.

In view of the experience the ACNFP has gained through dealing with submissions on products from several GM plants, the Committee has decided to update its report on The Use of Antibiotic Resistance Markers in Genetically Modified Food Organisms which was published in 1994.[7] In particular, the Committee has produced more detailed guidance on the criteria[11] used to assess the acceptability of particular marker genes.

4.2 DEPOSITION OF GMO AND NON-GMO CULTURES IN CULTURE COLLECTIONS

During its consideration of the submission on *Enterococcus faecium* (see section 1.1), the ACNFP discussed the issue of depositing cultures of micro-organisms in reference culture collections. The ACNFP decided that it was important that samples of cultures from both non-GM and GM organisms, used in the production of novel foods, be available for future reference, should any problems with stability or identification arise. Therefore, the ACNFP will expect samples of micro-organism cultures used in the production of novel foods to be deposited in a long-term repository, preferably in a European culture collection. The Committee noted that manufacturers of enzymes used in human food and in animal feedingstuffs are required to deposit samples of the cultures used in the production of the enzyme, as part of the approval process.

There are a number of reference culture collections in the UK that allow deposition of industrial micro-organisms for patent purposes and, also, safe deposition where the strain remains the sole property of the client: National Collection of Type Cultures, CAMA, Porton Down; National Collection of Industrial and Marine Bacteria, Aberdeen; National Collection of Food Bacteria, Reading; and, the National Collection of Yeast Cultures, Norwich.

5. DEVELOPMENTS ELSEWHERE

5.1 EUROPEAN COMMISSION PROPOSAL FOR A REGULATION ON NOVEL FOODS AND NOVEL FOOD INGREDIENTS

The controls on, and safety assessment of, novel foods vary between the Member States of the European Union and in an effort to introduce a harmonised approach, the European Commission (EC) developed proposals for a Regulation on novel foods and novel food ingredients, the first draft of which was published in July 1992.[8] Since then, various meetings have been held and revised versions of the text produced, culminating in a common position being reached at a Council of Ministers meeting in Luxembourg on 23rd October 1995.

The draft proposal has now gone back to the European Parliament for a second reading under the co-decision procedure. The European Parliament is due to vote on the proposal in March 1996.*

Details of the current position can be obtained from the MAFF Secretary (see page 20).

5.2 EUROPEAN COMMISSION PROPOSAL FOR A DIRECTIVE ON FOOD IRRADIATION

In December 1988 the EC published a proposal for a Council Directive (COMM (88) 654) on foods and food ingredients treated with ionising radiation.[9] However, despite early agreement on the technical controls in the proposal, it has not been possible to reach agreement on the range of foods to be approved for treatment at community level because of the range of attitudes to food irradiation that exists in individual Member States. Discussions have been deadlocked and there was no discussion on the proposed Directive by Member States in 1995.

Details of the current position can be obtained from the MAFF Secretary (see page 20).

* Secretariat note (June 1996): The European Parliament voted to accept six amendments to the common position text on 12th March 1996. The proposal has now been referred back to the Council of Ministers which will consider whether or not to accept the Parliament's amendments. If the amendments are accepted and the Regulation is adopted it will come into force ninety days after its publication in the Official Journal of the European Communities.

6. CONTACT POINTS

For further information about the general work of the Committee or about specific scientific points concerning individual submissions (which have been made or are being made) contact in the first instance:

The MAFF Secretary,
Mr Nick Tomlinson,
Ministry of Agriculture, Fisheries and Food,
Room 235, Ergon House,
c/o Nobel House,
17 Smith Square,
London SWIP 3JR.

Information about health or toxicological matters may be obtained by contacting, in the first instance:

The DH Secretary,
Mrs Sue Hattersley,
Department of Health,
Room 653C, Skipton House,
80 London Road,
London SE1 6LW.

7. REFERENCES

1. Advisory Committee on Novel Foods and Processes. *Annual Report 1989.* Department of Health and Ministry of Agriculture, Fisheries and Food, 1990. (Available from the ACNFP Secretariat.)

2. Advisory Committee on Novel Foods and Processes. *Annual Report 1990.* Department of Health and Ministry of Agriculture, Fisheries and Food, 1991. (Available from the ACNFP Secretariat.)

3. Advisory Committee on Novel Foods and Processes. *Annual Report 1991.* Department of Health and Ministry of Agriculture, Fisheries and Food, 1992. (Available from the ACNFP Secretariat.)

4. Advisory Committee on Novel Foods and Processes. *Annual Report 1992.* Department of Health and Ministry of Agriculture, Fisheries and Food, 1993. (Available from the ACNFP Secretariat.)

5. Advisory Committee on Novel Foods and Processes. *Annual Report 1993.* Department of Health and Ministry of Agriculture, Fisheries and Food, 1994. (Available from the ACNFP Secretariat.)

6. Advisory Committee on Novel Foods and Processes. *Annual Report 1994.* Department of Health and Ministry of Agriculture, Fisheries and Food, 1995. (Available from the ACNFP Secretariat.)

7. Advisory Committee on Novel Foods and Processes. *Report on the Use of Antibiotic Resistance Markers in Genetically Modified Food Organisms.* Department of Health and Ministry of Agriculture, Fisheries and Food, 1994. (Available from the ACNFP Secretariat.)

8. European Commission. *Proposal for a Council Regulation (EEC) on novel foods and novel food ingredients.* Official Journal of the European Communities, No.C/190/3 of 27th July 1992.

9. European Commission. *Proposal for a Council Directive on the approximation of the laws of the Member States concerning foods and food ingredients treated with ionising radiation.* Official Journal of the European Communities No. C336/7 of 31st December 1988.

10. 1995 Joint Annual Report of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment and the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment and the Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment: ISBN No 0-11-321-988-1.

11. The use of Antibiotic Resistance Markers in Genetically Modified Plants for Human Food and Animal Feed: Supplement to 1994 Report. (Available from ACNFP Secretariat.)

The Committee requests that unpublished sections of a submission are deposited with the British Library, in line with its views on the publication of available safety data. These depositions are identified in Committee reports by 'SUP Numbers' and may be obtained by contacting the British Library Document Supply Centre, Boston Spa, Wetherby LS23 7BO.

8. GLOSSARY

alkaloids: a diverse group of nitrogen-containing substances that are produced by plants and have potent effects on body function.

antibiotic: a substance, derived from micro-organisms (e.g. bacteria) that destroys or inhibits the growth of other micro-organisms. Many antibiotics are used as drugs in treating disease.

construct: gene sequence formed using recombinant DNA techniques.

enzyme: a protein produced by a living organism that changes the rate of, or promotes, a biological or chemical reaction without itself being altered or destroyed.

essential fatty acids: a group of unsaturated fatty acids that are essential for growth but cannot be synthesized by the body.

fatty acid: carboxylic acids found in fats and oils. They consist of a chain of up to thirty carbon atoms with attached hydrogen atoms and a terminal acid group.

fertility restorer line: used as the source of pollen – the male parent – in hybrid seed production. Both the female and male organs in the flowers are functional.

gene: unit of heredity composed of DNA, which forms part of a chromosome. The genetic code in a gene usually holds instructions for the manufacture of one polypeptide (protein) chain.

genetic modification: alteration of genetic material in an organism in a way that does not occur naturally by mating and/or natural recombination.

hemicellulase: an enzyme which breaks down hemicelluloses, carbohydrates which are found in wheat flour.

herbicide: a compound which is capable of either killing or severely injuring plants.

histology (-ical, *adj*): the study of the structure of tissues by means of special staining techniques combined with microscopy.

hybrid: seed produced from a cross between genetically dissimilar parents.

inbred line: a particular line of plant that has been self-pollinated over generations and is nearly genetically uniform.

interesterification: a catalytic process which alters the distribution of fatty acids in the glycerol moiety, producing fats with different properties.

intestinal flora: micro-organisms living in the gut, sometimes termed gut microflora.

lipase: a type of enzyme which can break down or synthesise components of fats and oils such as diacylglycerols and triacylglycerols.

mannanase: an enzyme which breaks down galactomannans, polysaccharides found in beans and seeds such as guar seed, locust beans and soya beans.

pathogenic: capable of causing disease.

polymerase chain reaction (PCR): a sensitive method used to amplify a specific region of DNA.

plasmid: loop of DNA found in bacteria and some other organisms, e.g. yeasts, that carries non-essential genes and replicates independently of the chromosomes.

pre-term infants: infants born before thirty-seven completed weeks of gestation.

progeny: offspring.

starter culture: a product containing live micro-organisms, often produced in a laboratory, which is used to initiate a commercial fermentation process.

term infants: infants born between thirty-eight and forty-two completed weeks of gestation.

transformant: plants derived from transformed cells.

triacylglycerols: the major component of fats and oils, also referred to as triacylglycerides or triglycerides. They consist of a glycerol backbone with three attached fatty acids. The three fatty acids can be identical, two the same, or all different.

APPENDIX I

ACNFP – REMIT, MEMBERSHIP AND LIST OF MEMBERS' INTERESTS, CODE OF CONDUCT AND INTERACTIONS WITH OTHER COMMITTEES