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Annex to:

REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

ON THE PROGRESS OF THE RE-EVALUATION OF FOOD ADDITIVES

{COM(2007) 418 final}

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EXECUTIVE SUMMARY

Food additives are subject to a safety evaluation before they are permitted for use in the European Community. It is also a requirement that they are re-evaluated whenever necessary in light of changing conditions of use and new scientific information.

This staff working paper provides a summary of the recent additive re-evaluations undertaken by the Scientific Committee on Food (SCF) and the European Food Safety Authority (EFSA) and describes the related actions taken by the European Commission on the basis of the scientific opinions.

Some of the additive evaluations were undertaken when the SCF was first established in the 1970's. Therefore the Commission felt that it is timely to request that the EFSA undertake to review the evaluations of all currently permitted food additives. This report additionally describes the rationale and priority setting for this review by the EFSA.

This Commission staff working paper complements the Commission Report to the European Parliament and the Council[1] *by providing further details relating to the re-evaluations*

[1] [Reference to be added].

1. INTRODUCTION

The authorisation of food additives for use in foods is harmonised in the European Community. Framework Directive 89/107/EEC[2] lays down the general principles for the use and authorisation of food additives, whereas three specific directives on sweeteners (Directive 94/35/EC[3]), colours (Directive 94/36/EC[4]) and on additives other than colours and sweeteners (Directive 95/2/EC[5]) lay down the rules on which additives may be used in which foods and their conditions of use. This legal framework is complemented by three Commission Directives laying down specifications (specific purity criteria) for the authorised food additives (Directives 95/31/EC[6], 95/45/EC[7] and 96/77/EC[8]).

The authorisations are based on three criteria:

- the food additive does not pose a safety risk to the health of the consumer,
- there is a technological need for the use and,
- the consumer is not mislead by the use of a food additive.

According to the framework Directive 89/107/EEC, the Scientific Committee on Food (SCF), now replaced by the European Food Safety Authority (EFSA), must be consulted before the adoption of provisions likely to affect public health, such as the drawing up of lists of additives and the conditions for their use. Accordingly, food additives have been evaluated for their safety by the SCF or EFSA prior to their authorisation.

The framework Directive 89/107/EEC also requires that food additives must be kept under continuous observation and must be re-evaluated whenever necessary in the light of changing conditions of use and new scientific information.

Accordingly some food additives have been re-evaluated in recent years when new scientific data had been requested or became otherwise available.

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2 Council Directive 89/107/EEC of 21 December 1988 on the approximation of the laws of the Member States concerning ford additives authorized for use in foodstuffs intended for human consumption, OJ L 40, 11.2.1989, p. 27.

3 European Parliament and Council Directive 94/35/EC of 30 June 1994 on sweeteners for use in foodstuffs, OJ L 237, 10.9.1994, p. 3.

4 European Parliament and Council Directive 94/36/EC of 30 June 1994 on colours for use in foodstuffs, OJ L 237, 10.9.1994, p. 13.

5 European Parliament and Council Directive No 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners, OJ L 61, 18.3.1995, p. 1.

6 Commission Directive 95/31/EC of 5 July 1995 laying down specific criteria of purity concerning sweeteners for used in foodstuffs, OJ L 178, 28.7.1995, p. 1.

7 Commission Directive 95/45/EC of 26 July 1995 laying down specific purity criteria concerning colours for use in foodstuffs, OJ L 226, 22.9.1995, p. 1.

8 Commission Directive 96/77/EC of 2 December 1996 laying down specific purity criteria on food additives other than colours and sweeteners, OJ L 339, 30.12.1996, p. 1.

Consequently, the Commission has asked the EFSA to re-evaluate all currently permitted food additives in the EC.

2. RECENT AND ONGOING RE-EVALUATIONS

2.1. Nisin (E 234) and Natamycin (E 235)

Nisin is authorised for food preservation by Directive 95/2/EC. Nisin is permitted in ripened cheese and processed cheese, certain puddings, clotted cream and mascarpone. Specifications for nisin are laid down in Directive 96/77/EC.

The SCF previously evaluated the safety of nisin in 1990 and allocated an ADI of 0.13 mg/kg body weight[9].

Natamycin is also authorised for food preservation by Directive 95/2/EC. Natamycin is permitted for the surface treatment on cheese and on dried cured sausages.

The SCF previously evaluated the safety of natamycin in 1979 and considered that its use for surface treatment of the rind of cheese and for casings of certain sausages was acceptable. At this time the SCF recommended that the residues of natamycin in food at the time of sale, expressed in terms of surface area of the casing or rind, do not exceed 1mg/dm^2 and that they are not present at a depth of greater than 5mm.[10]

The Scientific Steering Committee adopted an opinion on antimicrobial resistance in 28 May 1999[11]. On the basis of this opinion, the Commission adopted on 20 June 2001 a Communication on a Community strategy against antimicrobial resistance[12]. Action 9 listed in the Communication is to review the use of two authorised antimicrobial agents in food: nisin and natamycin.

Therefore, in addition to the toxicological review of nisin, the issue of antimicrobial resistance has also been addressed. This re-evaluation was completed by January 2006 and the AFC Panel adopted an opinion on nisin with the following conclusions[13]:

'The available toxicity studies and its long history of use suggest that nisin can be used safely. The panel did not find any new data, which would warrant any change of the previously established SCF ADI of 0.13 mg/kg bw/day.

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9 European Commission (1992). Food-science and techniques. Report of the Scientific Committee for Food (Twenty sixth series). CEC, Luxembourg.

10 (European Commission (1979). Food-science and techniques. Report of the Scientific Committee for Food (Ninth series). CEC, Luxembourg.

11 Opinion of the Scientific Steering Committee on Antimicrobial Resistance 28 May 1999 (available from http://ec.europa.eu/food/fs/sc/ssc/out50_en.pdf)

12 COM(2001) 333 final.

13 Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the Commission related to the use of nisin (E 234) as a food additive (Question number EFSA-Q-2005-031) *The EFSA Journal* (2006) 314, 1-*16.*

Nisin has a double mode of antimicrobial action; binding to lipid II and subsequent inhibition of cell wall synthesis as well as forming pores in the cytoplasmic membrane. Nisin is used as a food preservative and has currently no therapeutic use. There are no reports of sporadic nisin resistant bacterial mutants showing cross-resistance to therapeutic antibiotics. The Panel considered that this is probably due to the differences in the antimicrobial mode of action between therapeutic antibiotics and nisin and that antibiotic resistance to nisin is not likely to be an issue in relation to its use in food.'

Similarly to nisin, the Commission has asked the EFSA to issue an opinion on the safety of using natamycin as a food additive and also to address the issue of antimicrobial resistance and the use of natamycin. This re-evaluation should be completed by mid 2007.

2.2. Sucrose esters of fatty acids (E 473)

Sucrose esters of fatty acids are food additives permitted for use as emulsifiers and stabilisers for oil/water emulsions in several processed foods by Directive 95/2/EC.

The SCF previously evaluated sucrose esters of fatty acids in 1992[14]. The SCF established a group ADI of 0-20 mg/kg bw (expressed as sucrose monostearate) for sucrose esters of fatty acids and sucroglycerides (E 474) derived from palm oil, lard and tallow fatty acids, providing that specifications would limit the presence of tetra and higher esters to 7%. Specifications for sucrose esters of fatty acids are laid down in Directive 96/77/EC.

The Commission requested a re-evaluation of this food additive in the light of new studies on short- and long-term toxicity in experimental animals as well as toxicokinetic studies in animals and humans. In addition, studies on laxative effects in humans had been provided.

The re-evaluation was completed in October 2004. The AFC Panel adopted an opinion[15] with the following conclusions:

'Sucrose esters of fatty acids have a low oral toxicity and do not raise concern of carcinogenicity. Metabolic studies in vitro and in rats, dogs and humans show that these esters are extensively hydrolysed in the gastrointestinal tract into well-known food constituents prior to absorption, that only small amounts of intact monoesters which escape hydrolysis are absorbed, and that incompletely hydrolysed sucrose esters appear to be excreted in the faeces.

Considering all the toxicity data with an overall no-observed-adverse-effect level (NOAEL) of 2000 a group ADI of 40 mg/kg bw/day can be established for sucrose esters of fatty acids (E 473) and sucroglycerides (E 474). However, in view of the

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[14] SCF (1992). Minutes of the 83rd Meeting of the Scientific Committee for Food held on 10 April 1992.

[15] Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on Sucrose esters of fatty acids, E 473 and sucroglycerides, E 474 based on a Request from the Commission related to Sucrose Esters of Fatty Acids (E 473) (Question number EFSA-Q-2003-139), *The EFSA Journal (2004) 106, 1-24.*

human tolerance studies the Panel wishes to point out that at daily doses above 2 g/day in adults these substances may cause gastrointestinal symptoms. This ADI covers products containing mono-, di- and triesters with a content of tetra and higher esters of no more than 1%.'

After considering further information from the manufacturer of this additive the EFSA issued a revised opinion in January 2006 which stated that 'The Panel therefore agrees that the ADI should cover products of sucrose esters of fatty acids with a content of up to 10% tetra and higher esters.

2.3. Para-hydroxybenzoates (E 214 – 219)

Para-hydroxybenzoates are permitted for use as preservatives in some meat coatings, potato and cereal based snacks, coated nuts, certain confectionery items and dietary food supplements in liquid form by Directive 95/2/EC.

The SCF evaluated para-hydroxybenzoates (parabens) in 1994[16] and established a temporary ADI of 0-10 mg/kg bw, as the sum of methyl, ethyl and propyl p-hydroxybenzoic acid esters and their sodium salts. The temporary ADI was based on long-term studies in rats with methyl, ethyl and propyl paraben. The ADI was made temporary because the SCF considered that the toxicological information available showed some inadequacies and uncertainties. The SCF therefore requested a new oral teratogenicity study in the rat using either free p-hydroxybenzoic acid or its methyl, ethyl or propyl ester and a cell proliferation study in the rat on the propyl ester of p-hydroxybenzoic acid given as a solution.

In 2000, the SCF reiterated its wish to review the safety of parabens. At its last meeting in April 2003, the SCF noted that no data had been submitted by the food industry in support of the parabens and drew attention to its statement of October 2000, that the temporary ADI should be withdrawn if no further data were submitted.

In addition, Directive 2003/114 requested the Commission and the EFSA to review the conditions for the use of E 214 – 219 p-hydroxybenzoates and their sodium salts before 1 July 2004.

The re-evaluation was completed in July 2004 when the AFC Panel adopted an opinion[17] with the following conclusions:

'The Panel established a full group ADI of 0-10 mg/kg bw for the sum of methyl and ethyl p-hydroxybenzoic acid esters and their sodium salts on the basis of the NOAELs of 1000 mg/kg bw/day for each compound in long-term toxicity studies and studies on sex hormones and the male reproductive organs in juvenile rats. The Panel considered that propyl paraben should not be included in this group ADI

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16 Opinion on p-hydroxybenzoic acid alkyl esters their sodium salts. Expressed on 25 February 1994. Reports of the Scientific Committee for Food, Thirty-Fifth Series. CEC, Luxembourg. p. 9-12.

17 Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on request from the Commission related to para hydroxybenzoates (E 214 – 219) (Question number EFSA-Q-2004-063), *The EFSA Journal (2004) 83, 1- 26.*

because propyl paraben, contrary to methyl and ethyl paraben, had effects on sex hormones and the male reproductive organs in juvenile rats.

The Panel is unable to recommend an ADI for propyl paraben because of the lack of a clear NOAEL. The Panel noted that human exposure resulting from the use of parabens in food in Europe has not been adequately assessed.'

Consequently, the Commission proposed in October 2004 to withdraw E 216 propyl p-hydroxybenzoate and E 217 sodium propyl p-hydroxybenzoate from Directive 95/2/EC[18]. The amendment to Directive 95/2/EC was adopted by the European Parliament and the Council on 5 July 2006[19].

2.4. Nitrites and nitrates (E 249 – E 252)

Sodium and potassium salts of nitrite and nitrate are permitted for preservation of meat products, cheese and certain fish products by Directive 95/2/EC.

The SCF had previously evaluated the safety of nitrites and nitrates (opinions expressed in 1990 and 1995). It established an ADI of 0.06 mg/kg bw expressed as nitrite ion and for nitrate an ADI of 3.7 mg/kg bw expressed as nitrate ion.

In light of the judgement of the Court of Justice in Case C-3/00, Denmark v. Commission, the Commission consulted the EFSA for advice on the current authorisations of nitrite and nitrate in meat products in relation to the effect of nitrites and nitrates on the microbiological safety of meat products, in particular related to *Clostridium botulinum*.

The re-evaluation was completed in November 2003 and the Scientific Panel on Biological Hazards adopted an opinion[20] .

The Panel confirmed that nitrite contributes to microbiological safety and also to the flavour, colour and anti-oxidative stability of meat products. Levels up to 100 mg/kg of added nitrite might suffice for preservation of many products, but some might require up to 150 mg/kg. The Panel noted that nitrate provides no direct protection against the growth of *Clostridium botulinum* in most meat products. However, the use of nitrate as a reservoir of nitrite appears necessary, in particular, in traditionally-cured meat products.

The Panel recommended that the levels of nitrite and nitrate are set down in the legislation as "added amount". It was of the opinion that the added amount of nitrite rather than the residual amount contributes to the inhibitory activity against C. *botulinum*.

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18 COM(2004)650 final.

19 Directive 2006/52/EC, OJ L 204, 26.7.2006 p. 10.

20 Opinion of the Scientific Panel on Biological Hazards on the request from the Commission related to the effects of Nitrites/Nitrates on the Microbiological Safety of Meat Products. (Question N° EFSA-Q-2003-026), *The EFSA Journal* (2003) 14, 1-31.

Furthermore, the Panel was of the opinion that monitoring of residual levels of nitrites/nitrates in the final product is of limited value. The main reason is that the rate of loss of nitrite in a product is dependent on a number of factors including the heat process used, the pH of the product, the storage temperature and the addition of ascorbic acid or other reducing agents. Consequently, the detection of low levels of nitrite will give no indication as to whether a product was recently manufactured with an initial low level of nitrite, was a product that had been stored for several months at a low temperature with an initially modest level of nitrite, or whether it was a product which additionally contained ascorbate.

In order to keep the level of nitrosamines as low as possible by lowering the levels of nitrites and nitrates added to food whilst maintaining the microbiological safety of food products, the European Parliament and the Council have adopted Directive 2006/52/EC amending Directive 95/2/EC to change the current authorisations for nitrates and nitrites. In this amendment the general principle of controlling ingoing amounts of nitrates and nitrites applies, however for certain traditionally manufactured products the use is controlled by residual amounts.

2.5. Benzoic acid and its salts (E 210 – E213)

Benzoic acid and its salts are widely used as food preservatives and permitted for use by Directive 95/2/EC.

The SCF first evaluated the safety of benzoic acid and its salts in 1994. In this opinion[21], the Committee raised questions about developmental toxicity and genotoxicity and asked for further studies in these two areas. In view of these data requests, the Committee set only a temporary ADI of 0 – 5 mg/kg bw based on an overall NOAEL of 500 mg/kg bw/day from long-term and multigeneration studies.

In September 2002, the SCF had completed the re-evaluation of its earlier opinion in the light of new information and adopted an opinion[22] with the following conclusions:

'The database is much more extensive than that considered by the Committee in 1994, both for developmental toxicity and for genotoxicity. There appear to be sufficient studies to conclude absence of teratogenic potential, with an overall NOAEL for developmental toxicity of 500 mg/kg bw/day, based on effects on fetal weight. The fact that this overall NOAEL takes into account gavage as well as dietary studies gives further reassurance. It is therefore concluded that a further teratogenicity study on benzoic acid should no longer be required.

Similarly for genotoxicity, while some of the in vitro tests have been positive or equivocal, all the results from in vivo studies have been negative. It is therefore concluded that an in vivo study for clastogenic activity on benzoic acid should no longer be required.

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[21] Opinion on benzoic acid and its salts. Expressed on 24 February 1994. Reports of the Scientific Committee for Food, Thirty-Fifth Series. CEC, Luxembourg. p. 33-39.

[22] Opinion of the Scientific Committee on Food on Benzoic acid and its salts (expressed on 24 September 2002).

On the basis of these data and the other types of study previously evaluated by the Committee, the Committee can establish a full Group ADI of 0 - 5 mg/kg bw for benzoic acid and its salts including benzyl alcohol and related benzyl derivatives used as flavourings.'

2.6. Carnauba wax (E 903)

Carnauba wax is permitted for use as glazing agent by Directive 95/2/EC for certain foodstuffs including confectionery, snacks, nuts, coffee beans, dietary food supplements and certain fruits.

Carnauba wax was first evaluated by the SCF in 1990[23] when it was found to be temporarily acceptable as a glazing agent. The acceptance was made temporary pending supplementary toxicological data and technical data on use. In 1995[24], the SCF reviewed additional data, which were still not found to be sufficient for a full acceptance and requested supplementary data on chromosome aberrations in mammalian cells in vitro and on the readiness of carnauba wax ester to hydrolyse.

In the light of the new information, the SCF completed its review of the safety of carnauba wax in July 2001. In its opinion, which was revised on April 2002, the Committee withdrew the temporary status and confirmed that the use of carnauba wax is acceptable.

2.7. Beta-carotene (E 160 a)

Carotenes are permitted for use as food colours in a wide variety of foods by Directive 94/36/EC.

In 1975[25], the SCF established a group ADI of 0-5 mg/kg b.w. for the carotenoids which includes carotenes (E160a(i) mixed carotenes and E 160a(ii) beta-carotene), beta-apo-8'-carotenal (E 160e) and ethyl ester of beta-apo-8'-carotenal (E 160 f). This group ADI was an endorsement of the ADI set by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) for a similar group of carotenoids in 1974.

In 2000, the Committee considered food additive uses of beta-carotene and its related carotenoids, in the context of the overall intake of beta-carotene from natural sources and food additives. The opinion[26] was adopted in September 2000 with the following conclusions:

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23 Scientific Committee for Food (1990). Report on a second series of food additives of various technological functions (opinion expressed on 19th October 1990). Food – Science and Techniques. Reports of the Scientific Committee for Food (26th series). EUR 13913 EN. Office of Official Publications of the European Communities, Luxembourg, 1992.

24 Scientific Committee for Food (1995). Minutes of the 95th plenary meeting held on 15/16 December 1994. Document III/5488/94-EN.

25 Scientific Committee for Food (SCF) (1975). Report of the Scientific Committee for Food on the Revision of the Directive on Colouring Matters Authorised for use in Foodstuffs Intended for Human Consumption. Reports of the Scientific Committee for Food (First Series), pp 17-29. Commission of the European Communities, Luxembourg, 31 December 1975.

26 Opinion of the Scientific Committee on Food on the safety of use of beta carotene from all dietary sources (Opinion adopted by the SCF on 7 September 2000).

'Natural food sources may contribute in Europe an average of around 2 mg/person/day and up to 5 mg/person/day in high consumers of carotenoid-rich foods, while food additives contribute 1-2 mg/person/day. The combination of these two sources represents about 3-7 mg/day (or up to 10 mg/day depending on seasonal and regional variations) of beta-carotene exposure. The Committee decided to withdraw the group ADI for beta-carotene, mixed carotenes, beta-apo-8´-carotenal and its ethyl ester of 0- 5 mg/kg b.w., which was based on rodent studies, because of the lack of relevance of these studies for human risk assessment and the adverse findings in human studies on smokers taking supplements of 20 mg/day or more of synthetic beta-carotene, amounts that are much lower than the previously established ADI. However, there are no indications that intakes of 1-2 mg/day consumed as food additives, in the context of the overall dietary intake of beta-carotene are harmful. The Committee therefore finds currently permitted food additive uses of beta-carotene and related carotenoids temporarily acceptable from a health point of view at the levels of intake quoted above. At present, there is insufficient scientific basis, either from human or experimental studies, on which to set a new ADI for beta-carotene and related carotenoids.'

2.8. Acesulfame K (E 950)

Acesulfame K is an intense sweetener, with a sweetness approximately 200 times that of sucrose. It is permitted for use in several low calorie foods and beverages by Directive 94/35/EC.

Acesulfame K was evaluated by the SCF for the first time in 1985[27]. The Committee established an ADI of 0-9 mg/kg, based on the NOAEL in a 2-year study in the dog, which was at that time regarded as the most sensitive species. This evaluation was reviewed in 1991[28], but the conclusions remained the same.

In light of additional information, the SCF re-evaluated acesulfame K again in 2000. The opinion[29] was adopted in March 2000 and concluded that acesulfame K is without mutagenic or carcinogenic potential. Furthermore, acesulfame K does not induce any other effects of toxicological significance at dietary dose levels up to 3% in the rat (equivalent to 1500 mg/kg bw/day) or in the dog (equivalent to 900 mg/kg bw/day).

In considering the request to increase the ADI from 0-9 mg/kg bw to 0-15 mg/kg bw, the Committee took into account previously available and new toxicokinetic data in a variety of species including man, however they considered that the dog remains the appropriate species on which to base the ADI and reaffirmed its previous ADI of 0-9 mg/kg bw.

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27 European Commission (1985). Food-science and techniques. Report of the Scientific Committee for Food (Sixteenth series). CEC, Luxembourg.

28 European Commission (1991). Minutes of the 79th meeting of the Scientific Committee for Food held on 20-21 June in Bilthoven. DG III, Brussels. Document III/3432/91-EN.

29 Re-evaluation of acesulfame K with reference to the previous SCF opinion of 1991 (expressed on 9 March 2000).

2.9. Cyclamic acid and its sodium and calcium salts (E 952)

Cyclamic acid and its sodium and calcium salts are intense sweeteners, with a sweetness approximately 30 times that of sucrose. They are permitted for use in several low calorie foods and beverages by Directive 94/35/EC.

The SCF evaluated the safety of cyclamate, cyclohexylamine and dicyclohexylamine in 1984[30] and established a temporary ADI of 0-11 mg/kg bw, expressed as cyclamic acid, for cyclamic acid and its sodium and calcium salts. The Committee reviewed cyclamate again in 1988, 1991 and 1995 and confirmed the temporary ADI.

In March 2000, the SCF revised its opinion[31] on cyclamate again. The Committee concluded that a full ADI for cyclamate could now be established. However, although the new epidemiological data revealed no indications of harmful effects of cyclamate on humans, the Committee decided to lower the ADI for this substance from 11 to 7 mg/kg bw. The reason for this was that new scientific evidence had shown the conversion rate of cyclamate to cyclohexylamine and dicyclohexylamine in the body to be higher than was previously thought.

Consequently, the authorisations for the use of cyclamates were revised in Directive 2003/115/EC to reflect the change in the acceptable daily intake.

2.10. Aspartame (E 951)

Aspartame is an intense sweetener with a sweetness approximately 200 times that of sucrose. It is permitted for use in several low calorie foods and beverages by Directive 94/35/EC. Aspartame is also a constituent of another additive salt of aspartame acesulfame (E 962) which is also permitted by Directive 94/35/EC. Owing to the phenylalanine content of aspartame, persons suffering from the genetic disease phenylketonuria (PKU) must take into account the consumption of aspartame into their daily intake of phenylalanine, therefore under EU legislation products containing aspartame must contain the warning 'contains a source of phenylalanine'.

The SCF initially evaluated aspartame during 1984[32] and established an ADI of 40 mg/kg bodyweight. Subsequently the SCF re-examined aspartame in 1988[33], 1997[34] and most recently in 2001 the Committee reviewed the safety of aspartame by considering over 500 papers published in the scientific literature since the earlier SCF assessment (papers published between 1988 and 2001). As a result of this

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30 Commission of the European Communities (1985). Report of the Scientific Committee for Food on Sweeteners (opinion expressed on 14 September 1984). Reports of the Scientific Committee for Food (Sixteenth Series). CEC, Luxembourg, EUR 10210 EN.

31 Revised opinion on cyclamic acid and its sodium and calcium salts (Expressed on 9 March 2000).

32 SCF (1985). Sweeteners. Reports of the Scientific Committee for Food (Sixteenth Series), EUR 10210 EN, Commission of the European Communities, Luxembourg.

33 SCF (1989). Sweeteners. Reports of the Scientific Committee for Food (Twenty-first Series), EUR 11617 EN, Commission of the European Communities, Luxembourg.

34 SCF (1997). Minutes of the 107th Meeting of the Scientific Committee for Food, held on 12-13 June 1997 in Brussels. Available at: http://europa.eu.int/comm/food/fs/sc/oldcomm7/out13_en.html

review in 2002[35] the Committee concluded that after reviewing the data available to date there was no evidence to suggest a need to revise the outcome of the earlier risk assessment or the ADI previously established for aspartame.

In June 2005, the European Commission became aware of a new study carried out at the Ramazzini research centre in Italy by Soffritti et al.[36] [37] The Commission asked the EFSA to urgently assess the new study and advise whether it is necessary to revise the previous opinion on aspartame carried out by the SCF in 2002.

After considering the data provided by the research institute in December 2005 and April 2006 the EFSA adopted an opinion on 3rd May 2006[38]. This opinion concluded that, on the basis of the data provided, there is no reason to further review the previous scientific opinion on the safety of aspartame nor to revise the ADI established by the SCF.

2.11. Beeswax (E 901)

Beeswax is permitted for use as a food additive by Directive 95/2/EC. It is permitted as a glazing agent on confectionery (excluding chocolate), small products of fine bakery wares coated with chocolate, snacks, nuts and coffee beans and for the surface treatment of certain fruits (fresh citrus fruits, melons, apples, pears, peaches and pineapples).

The SCF has previously evaluated the safety of beeswax and in 1990[39] found its use temporarily acceptable as a glazing agent until further toxicological data can be provided.

The information previously lacking in the SCF evaluation has now been made available and the Commission has asked the EFSA to provide an updated scientific opinion on the safety in use of beeswax. It is anticipated that the opinion will be made by mid 2007.

2.12. Additives with potential content of ethylene oxide

Ethylene oxide is used in the production of some food additives including polysorbates (E431-436) and may be present as an impurity in low amounts in the final product. As ethylene oxide has been classified as 'carcinogenic (Category 1)' by the International Agency for Research on Cancer [40] a maximum residue level of

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35 Opinion of the Scientific Committee on Food: Update on the Safety of Aspartame (expressed on 4 December 2002).

36 Soffritti, M., Belpoggi, F., Esposti D.D, and Lambertini, L. (2005). Aspartame induces lymphomas and leukaemias in rats. Eur. J. Oncol., 10, 107-116.

37 Soffritti, M., Belpoggi, F., Esposti, D.D., Lambertini, L., Tibaldi, E., and Rigano, A. (2006). First Experimental Demonstration of the Multipotential Carcinogenic Effects of Aspartame Administered in the Feed to Sprague-Dawley Rats. Env. Health Perspect., 114, 379 – 385.

38 The EFSA Journal (2006) 356, 1-44.

39 Report of the Scientific Committees for Food on a second series of food additives of various technological functions (expressed on 19 October 1990). Reports of the Scientific Committee for Food (Twenty sixth Series).

40 IARC (1994). IARC Monographs on the Evaluation of Carcinogenic Risk to Humans. Volume 60. Some Industrial Chemicals, pp.73-159. International Agency for Research on Cancer, Lyon, France.

less than 1 mg/kg was laid down in the specifications for these additives[41]. The SCF was asked to re-evaluate the safety in use of the food additives manufactured using ethylene oxide in view of any potential residues.

In its opinion expressed in April 2002[42] the Committee concluded that the estimated intakes of ethylene oxide from the few food additives containing it, conforming to present specifications, are very low. However, since ethylene oxide is both genotoxic and carcinogenic, intakes from food sources should be as low as possible. The Committee has been informed that the currently achievable limit of detection for ethylene oxide is well below the upper limit 1.0 mg/kg currently specified.

As a result of this opinion the Commission revised the specifications for the relevant additives and established a maximum limit for ethylene oxide of 0.2 mg/kg[43].

3. ON-GOING RE-EVALUATION OF FOOD COLOURS

The Commission has asked the EFSA to re-evaluate all currently permitted food additives in the EC and as colours were mentioned in the Nordic report with higher priority the Commission requested the EFSA to re-evaluate food colours as a priority. There are 46 currently permitted colours which can be subdivided into three groups; natural, synthetic and mineral colours. In order to collate and summarise the existing information on the colours, the EFSA published in November 2004 two calls for tenders; one for gathering information on synthetic colours[44] and one for natural colours[45]. In its call for tenders the EFSA also outlined its strategy for re-evaluation of the safety assessments (see Annex).

In 2005, the EFSA selected a contractor to prepare summary reports, including toxicity and non-toxicity data, to be used in the re-evaluation of the currently permitted natural and synthetic colours. During the first year of the contract the contractor will prepare summary reports for ten natural colours and ten synthetic colours.

The actual re-evaluation is being undertaken by the AFC Panel and commenced in 2006.

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41 Commission Directive 98/86/EC of 11 November 1998 amending Commission Directive 96/77/EC laying down specific purity criteria on food additives other than colours and sweeteners. Official Journal of the European Communities L 334/1-63. 9.12.98.

42 Opinion of the Scientific Committee on Food on impurities of ethylene oxide in food additives (expressed on 17 April 2002).

43 Commission Directive 2003/95/EC OJ L 283, 31.10.2003, p. 71.

44 Call for tender No EFSA/AFC/ADD/Tender/02/2004 for a service contract concerning the preparation of summary documents/reports including toxicity and non-toxicity data, to be used in the re-evaluation of the currently permitted synthetic colours for re-evaluation by the EFSA Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel).

45 Call for tender No EFSA/AFC/ADD/Tender/01/2004 for a service contract concerning the preparation of summary documents/reports including toxicity and non-toxicity data, to be used in the re-evaluation of the currently permitted natural colours for re-evaluation by the EFSA Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel).

ANNEX: EFSA STRATEGY FOR RE-EVALUATION OF SAFETY ASSESSMENT

The information in this annex is taken from the Call for tender n° EFSA/AFC/ADD/Tender/02/2004 for service contract concerning the preparation of Summary Documents/Reports including toxicity and non-toxicity data, to be used in the re-evaluation of the currently permitted synthetic colours for re-evaluation by the EFSA Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel)

Strategy for re-evaluation

Establishment of health based priorities for re-evaluation.

Overview

An initial screening would be conducted to determine whether full or partial re-evaluation is necessary for a particular additive. This would comprise a two stage process for establishing health based priorities for the re-evaluation of food additives comprising an information gathering stage and a decision stage. The information gathering stage will be outsourced whereas the decision stage will be undertaken by the AFC Additives Working Group, with reference to the AFC Panel, if necessary. It is expected that specification of the report of the information gathering stage will minimise the need for detailed discussion prior to a decision in the Working Group. If occasional reports require more extensive discussion, a sub-group will be formed to undertake preparatory discussions with the contractor. Following the decision stage those additives requiring re-evaluation will be prioritised in the work programme and target dates determined.

Stage 1. Information gathering

It is proposed that this comprise the following steps;

1. An examination of the original SCF opinion, working documents and (/or) dossier to ascertain what data were available and formed the basis of the conclusions

2. Brief summary and dates of any JECFA evaluations.

3. Consideration of the evaluation of the additive in the Nordic report and its comments on the substance.

4. A literature search from 2000 to date to identify relevant published literature (The Nordic report was based on updated search of the literature for papers published prior to 2000).

This information gathering process should be outsourced. The tender should contain requirements for the initial use of core search terms for the literature search [to be defined by the Additives Working Group], that additional search terms and search strategies used by the contractor will be specified and reported, that a specified report structure appropriate for insertion directly into any future opinion will be used. The relevant SCF opinions, working documents and dossiers will be provided to the contractor by EFSA. The contractor will be expected to have access themselves to relevant JECFA documents.

The report on each additive or chemically related group of additives should cover the topics set out below. If no information is available on a particular topic, this should be clearly indicated.

- background,
  - including chronology of previous assessments by the SCF and JECFA
- chemistry,
  - specifications: date set by SCF and/or JECFA; consideration of any need to review or amend
  - brief description of its manufacture
  - methods of analysis in food: indicate if methods are available (detailed description of methods not needed)
  - reaction and fate in foods: description of any available information
- uses in foods and levels of use in foods: as requested by petitioner, or as laid down in EU legislation, or as described in the SCF opinion
- exposure,
  - theoretical estimates: e.g. using worst case maximum levels of use in all foods permitted, the Budget method, etc (Note for a number of colours the maximum permitted use levels and the categories of foods in which they are permitted are identical and one set of estimates could cover them all.)
  - summarise available actual estimates and their basis: e.g. means and high percentiles in total population and in consumers only, details need to be provided on the duration of the survey and the extent to which the sample is representative.
- summary of existing SCF evaluations identifying
  - available toxicological data
  - whether the materials tested complied with the existing EU specification
  - critical end-point used in the most recent SCF evaluation
  - uncertainties in the database,
  - choice and rationale for uncertainty factors
- summary of studies published since previous evaluation
  - From Nordic 2000 Report
  - From recent (post-2000) JECFA evaluations

- o From the post-2000 literature search

∉ reference list

∉ copies of references on studies published since the previous evaluation to be supplied if in the public domain

Stage 2. Decision stage

Bearing in mind the chemical nature and origin of the additive, the outcome of the information gathering steps will be viewed alongside the current guidelines for the assessment of food additives (SCF, 2001) and used to identify whether there are:

a. Data gaps

b. Uncertainties in the existing data

c. Any new evidence of potentially harmful effects

On the basis of this screening a priority list will be established of additives requiring re-evaluation.

For additives not requiring re-evaluation, the original SCF opinion may need to be endorsed.

Criteria for a re-evaluation

In determining the extent of re-evaluation necessary the weight given to various types of information needs to be determined. The rationale for these decisions should be identifiable and transparent. In deciding whether a full re-evaluation is necessary, reported adverse effects in humans and new toxicological studies will be given greatest weight. If estimated or actual exposure data indicate that intakes are likely to exceed the ADI, further consideration will be given to the nature of the critical effect(s) used to derive the ADI and to the adequacy of the uncertainty factors used. In assessing human case reports of actual or alleged adverse effects, evidence of reproducibility of effects and results from well-designed and controlled studies will be given greater weight. Particular attention will be given to toxicological studies yielding results that differ from previous data or produce equivocal findings.

The quality of the data will also be assessed. Routine toxicological studies will be expected to conform to GLP if conducted after 1982. Special studies (e.g. those intended to explore the mechanism of adverse effects or generate hypotheses) would not normally be conducted in accordance with GLP. Studies generated before the implementation of GLP will be assessed on their own merits; lack of compliance with GLP will not necessarily imply that new studies to current guidelines are necessary. Such decisions will be taken on a case-by-case basis by consideration of the need to clearly establish safety in use, bearing in mind the need to avoid unnecessary use of animals.

Follow up

Provision of data by industry and other interested parties

For each additive identified as needing further re-evaluation, guidance will be given on a case-by-case basis describing the scope of the information required and time scale for

provision of this information. It is anticipated that the information required will be provided by the producer or user industries (or other interested parties). Risk managers should consider introducing sanctions to ensure producers provide data within the requested time limit.

Evaluation stage

Once the required data have been submitted

- six months from supply of these data is allowed for EFSA's re-evaluation,

- the regulatory status of an additive would not normally change until the evaluation is completed.

The exercise should commence by end of 2004/early 2005 with the colours since these are the oldest evaluations. Approximately 10-12 natural colours will have to re-evaluated be sub-divided for this exercise into natural and synthetic colours (approximately 20-24 in each group), the small group of mineral colours (e.g. gold, titanium dioxide) will be excluded from this initial exercise. The time-scale for the overall exercise and for groups of additives other than colours will be defined by EFSA at a later date.

The Secretariat should prepare a tender document limited initially to the colours. This will allow the process to be evaluated and modified based on the experience with colours, prior to commencing the re-evaluation of further groups of additives.