



**Food and Agriculture  
Organization  
of the United Nations**

**World Health  
Organization**



**JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES  
Sixty-fifth meeting  
Geneva, 7-16 June 2005**

**SUMMARY AND CONCLUSIONS**

*issued 13 July 2005*

A meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) was held in Geneva, Switzerland, from 7 to 16 June 2005. The purpose of the meeting was to evaluate certain food additives and flavouring agents.

Mrs Inge Meyland, Division of Toxicology and Risk Assessment, Danish Institute of Food and Veterinary Research, Søborg, Denmark, served as Chairman and Dr John Larsen, Danish Institute of Food and Veterinary Research, Søborg, Denmark, served as Vice-Chairman.

Dr Maria de Lourdes Costarrica, Food and Nutrition Division, Food and Agriculture Organization (7-10 June), Dr Chris Fisher, Consultant to the Food and Agriculture Organization (13-17 June), and Dr Angelika Tritscher, International Programme on Chemical Safety, World Health Organization, served as joint secretaries.

The present meeting was the sixty-fifth in a series of similar meetings. The tasks before the Committee were (a) to elaborate further principles for evaluating the safety of food additives including flavouring agents; (b) to evaluate certain food additives and flavouring agents; and (c) to review and prepare specifications for selected food additives and flavouring agents.

The report of the meeting will appear in the WHO Technical Report Series. Its presentation will be similar to that of previous reports, namely, general considerations, comments on specific substances, and recommendations for future work. An annex will include detailed tables (similar to the tables in this report) summarizing the main conclusions of the Committee in terms of acceptable daily intakes (ADIs) and other toxicological recommendations. Information on specifications for the identity and purity of certain food additives examined by the Committee will also be included.

The participants in the meeting are listed in Annex 1. Further information required or desired is listed in Annex 2. General considerations that contain information that the Committee would like to disseminate quickly are included in Annex 3. Annex 4 lists flavouring agents for which additional information is required before the end of 2007.

Toxicological monographs or monograph addenda on most of the substances that were considered will be published in WHO Food Additives Series No. 55.

New and revised specifications for the identity and purity of the compounds will be published in a proposed new 2<sup>nd</sup> Edition of the Compendium of JECFA Food Additive Specifications and in the FAO Food and Nutrition Series 52 Addendum 13.

More information on the work of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) is available at:

[www.fao.org/es/esn/jecfa/index\\_en.stm](http://www.fao.org/es/esn/jecfa/index_en.stm)

<http://www.who.int/ipcs/food/jecfa/en/index.html>

## Toxicological recommendations and information on specifications

### 1. Food additives and ingredients evaluated toxicologically or assessed for dietary exposure

Food additive	Specifications <sup>a</sup>	Acceptable daily intake (ADI) and other toxicological recommendations
Beeswax	R	No safety concern at the predicted dietary exposure (less than 650 mg/person/day), based on the long history of use and lack of toxicity observed with the major components of beeswax.
Candelilla wax	R	No safety concern at the predicted dietary exposure (less than 650 mg/person/day).
L-5-Methyltetrahydrofolic acid (L-5-MTHF), calcium salt (L-methylfolate, calcium)	N	No safety concern for the proposed use of L-5-MTHF-Ca in dry crystalline or microencapsulated form as an alternative to folic acid used in dietary supplements, foods for special dietary uses and other foods. The safety of folate fortification and supplementation as such was not evaluated.
Phospholipase A1 from <i>Fusarium venenatum</i> expressed in <i>Aspergillus oryzae</i>	N	The information provided on the enzyme phospholipase A1 was too limited to assess its safety.
Pullulan	N	ADI 'not specified' <sup>b</sup>
Quillaia extract Type 1	S	The previous ADI established for quillaia extract type 1 was converted to an ADI based on saponin content using the lower end of the specified saponin range, and established as a group ADI for quillaia extract type 1 and quillaia extract type 2. An assessment of dietary exposure considered the additional use of quillaia extract type 1 in semi-frozen carbonated and non-carbonated beverages (up to 500 mg/kg product). Using a model diet approach, high-percentile consumption was estimated to lead to an exposure of 44 to 157% of the ADI, assuming the presence of quillaia extract type 1 at 295 mg/l in all water-based flavoured drinks. Using a probabilistic exposure assessment and assuming that the frequency and amount per eating occasion are independent variables, the estimated dietary exposure was below the ADI at the 90 <sup>th</sup> percentile. Assuming 100% dependency between frequency and amount consumed, it is estimated that 100-700 individuals per million over the whole population could exceed the ADI under these conditions.
Quillaia extract Type 2	R	The previous ADI established for quillaia extract type 1 was converted to an ADI based on saponin content using the lower end of the specified saponin range, and established as a group ADI for quillaia extract type 1 and quillaia extract type 2.

<sup>a</sup> N: new specifications prepared; R: existing specifications revised; S: existing specifications maintained.

<sup>b</sup> ADI 'not specified' is used to refer to a food substance of very low toxicity which, on the basis of the available data (chemical, biochemical, toxicological and other) and the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effects and from its acceptable background levels in food, does not, in the opinion of the Committee, represent a hazard to health. For that reason, and for the reasons stated in the individual evaluations, the establishment of an ADI expressed in numerical form is not deemed necessary. An additive meeting this criterion must be used within the bounds of good manufacturing practice, i.e. it should be technologically efficacious and should be used at the lowest level necessary to achieve this effect, it should not conceal food of inferior quality or adulterated food, and it should not create a nutritional imbalance.

## 2. Food additives considered for specifications only

Food Additive	Specifications <sup>a</sup>
Aspartame acesulfame salt	R
Hexane	See below
Laccase from <i>Myceliophora thermophila</i> expressed in <i>Aspergillus oryzae</i>	R
Monomagnesium phosphate and trisodium phosphate	W <sup>b</sup>
Sucrose esters of fatty acids	R, T

<sup>a</sup>R: existing specifications revised; T: tentative specifications; W: existing specifications withdrawn.

<sup>b</sup>As no information was received on these substances, the existing tentative specifications were withdrawn.

### Hexane

As used in the food industry, 'hexane' is a mixture of hydrocarbons. Recent changes in environmental regulations have led to a change in composition of hexanes since the original specifications were established. In addition, the composition of hexanes will depend on the region of production, the source of the raw material and the site of production. Therefore, the Committee concluded that the present articles of commerce differ from those previously evaluated by the Committee and that the composition of the residues and their levels in foods may not be the same as those evaluated in the original safety assessment. The Committee also concluded that there was insufficient information available to change the current specifications, and therefore recommended a re-evaluation of hexanes.

## 3. Flavouring agents evaluated using the Procedure for the Safety Evaluation of Flavouring Agents

See also the discussion on the safety evaluation of flavouring agents in Annex 3 and Annex 4.

### A. Maltol and related substances

Flavouring agent	No.	Specifications <sup>a</sup>	Conclusions based on current intake
Maltol	1480	N <sup>b</sup>	See footnote <sup>c</sup>
Ethyl maltol	1481	N <sup>b</sup>	See footnote <sup>d</sup>
Maltyl isobutyrate	1482	N, T	No safety concern
2-Methyl-3-(1-oxopropoxy)-4H-pyran-4-one	1483	N	No safety concern (conditional) <sup>e</sup>
2-Butyl-5- or 6-keto-1,4-dioxane	1484	N	No safety concern
2-Amyl-5 or 6-keto-1,4-dioxane	1485	N	No safety concern
2-Hexyl-5 or 6-keto-1,4-dioxane	1486	N	No safety concern

<sup>a</sup>N: new specifications prepared; T: tentative specifications.

<sup>b</sup>Revised specifications for these substances in the standard additive format were also prepared.

<sup>c</sup>The ADI of 0-1 mg/kg bw established at the 25<sup>th</sup> meeting was maintained.

<sup>d</sup>The ADI of 0-2 mg/kg bw established at the 18<sup>th</sup> meeting, was maintained.

<sup>e</sup>Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

### B. Furan-substituted aliphatic hydrocarbons, alcohols, aldehydes, ketones, carboxylic acids and related esters, sulfides, disulfides and ethers

The Committee took note of the extensive positive genotoxicity data for several members of this group of flavouring agents related to furan. Furan, which is carcinogenic, is known to undergo epoxidation and ring opening to form a reactive 2-ene-1,4-dicarbonyl intermediate. Accordingly, concern arises that the observed genotoxicity may be due to formation of a reactive metabolite. Data on the potential of members of this group to form a reactive metabolite were not available and the role of metabolism in the observed genotoxicity has not been identified. Moreover, there was a paucity of *in vivo* genotoxicity data to allay concern. Also, specific *in vivo* assays to address potential carcinogenicity were lacking. Because of these concerns, the Committee concluded that the Procedure could not be applied to this group.

Flavouring agent	No.	Specifications <sup>a</sup>
2-Methylfuran	1487	N
2,5-Dimethylfuran	1488	N
2-Ethylfuran	1489	N
2-Butylfuran	1490	N
2-Pentylfuran	1491	N
2-Heptylfuran	1492	N
2-Decylfuran	1493	N
3-Methyl-2-(3-methylbut-2-enyl)-furan	1494	N
2,3-Dimethylbenzofuran	1495	N
2,4-Difurfurylfuran	1496	N
3-(2-Furyl)acrolein	1497	N
2-Methyl-3(2-furyl)acrolein	1498	N
3-(5-Methyl-2-furyl)prop-2-enal	1499	N
3-(5-Methyl-2-furyl)-butanal	1500	N
2-Furfurylidenebutyraldehyde	1501	N
2-Phenyl-3-(2-furyl)prop-2-enal	1502	N
2-Furyl methyl ketone	1503	N
2-Acetyl-5-methylfuran	1504	N
2-Acetyl-3,5-dimethylfuran	1505	N
3-Acetyl-2,5-dimethylfuran	1506	N, T
2-Butyrylfuran	1507	N
(2-Furyl)-2-propanone	1508	N
2-Pentanoylfuran	1509	N
1-(2-Furyl)butan-3-one	1510	N
4-(2-Furyl)-3-buten-2-one	1511	N
Pentyl 2-furyl ketone	1512	N
Ethyl 3-(2-furyl)propanoate	1513	N
Isobutyl 3-(2-furan)propionate	1514	N
Isoamyl 3-(2-furan)propionate	1515	N
Isoamyl 4-(2-furan)butyrate	1516	N
Phenethyl 2-furoate	1517	N
Propyl 2-furanacrylate	1518	N
2,5-Dimethyl-3-oxo-(2H)-fur-4-yl butyrate	1519	N
Furfuryl methyl ether	1520	N
Ethyl furfuryl ether	1521	N
Difurfuryl ether	1522	N
2,5-Dimethyl-3-furanthiol acetate	1523	N
Furfuryl 2-methyl-3-furyl disulfide	1524	N
3-[(2-Methyl-3-furyl)thio]-2-butanone	1525	N
O-Ethyl S-(2-furylmethyl)thiocarbonate	1526	N

<sup>a</sup>N: new specifications prepared; T: tentative specifications.

### C. *Eugenol and related hydroxyallylbenzene derivatives*

Flavouring agent	No.	Specifications <sup>a</sup>	Conclusions based on current intake
4-Allylphenol	1527	N	No safety concern (conditional) <sup>b</sup>
2-Methoxy-6-(2-propenyl)phenol	1528	N	No safety concern (conditional) <sup>b</sup>
Eugenol	1529	R <sup>c</sup>	See footnote <sup>d</sup>
Eugenyl formate	1530	N	No safety concern
Eugenyl acetate	1531	N	No safety concern
Eugenyl isovalerate	1532	N	No safety concern (conditional) <sup>b</sup>
Eugenyl benzoate	1533	N	No safety concern

<sup>a</sup>N: new specifications prepared; R: existing specifications revised.

<sup>b</sup>Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

<sup>c</sup>As this substance is used only as a flavouring agent, the Committee considered that the existing specifications in the standard food additive format should be deleted.

<sup>d</sup>The ADI of 0-2.5 mg/kg bw established at the 26<sup>th</sup> meeting was maintained.

#### D. Anthranilate derivatives

Flavouring agent	No.	Specifications <sup>a</sup>	Conclusions based on current intake
Methyl anthranilate	1534	R <sup>b</sup>	See footnote <sup>c</sup>
Ethyl anthranilate	1535	N	No safety concern
Butyl anthranilate	1536	N	No safety concern
Isobutyl anthranilate	1537	N	No safety concern
cis-3-Hexenyl anthranilate	1538	N	No safety concern (conditional) <sup>d</sup>
Citronellyl anthranilate	1539	N	No safety concern (conditional) <sup>d</sup>
Linalyl anthranilate	1540	N	No safety concern
Cyclohexyl anthranilate	1541	N	No safety concern
beta-Terpinyl anthranilate	1542	N	No safety concern
Phenylethyl anthranilate	1543	N	No safety concern
beta-Naphthyl anthranilate	1544	N	No safety concern
Methyl N-methylantranilate	1545	N	See footnote <sup>e</sup>
Ethyl N-methylantranilate	1546	N	No safety concern (conditional) <sup>d</sup>
Ethyl N-ethylantranilate	1547	N	No safety concern (conditional) <sup>d</sup>
Isobutyl N-methylantranilate	1548	N	No safety concern (conditional) <sup>d</sup>
Methyl N-formylantranilate	1549	N	No safety concern (conditional) <sup>d</sup>
Methyl N-acetylantranilate	1550	N	No safety concern (conditional) <sup>d</sup>
Methyl N,N-dimethylantranilate	1551	N	No safety concern (conditional) <sup>d</sup>
N-Benzoylantranilic acid	1552	N	No safety concern (conditional) <sup>d</sup>

<sup>a</sup>N: new specifications prepared; R: existing specifications revised.

<sup>b</sup>As this substance is used only as a flavouring agent, the Committee decided that the existing specifications in the standard food additive format should be deleted.

<sup>c</sup>The ADI of 0-1.5 mg/kg bw established at the 23<sup>rd</sup> meeting was maintained.

<sup>d</sup>Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

<sup>e</sup>The ADI of 0-0.2 mg/kg bw established at the 23<sup>rd</sup> meeting was maintained.

#### E. Miscellaneous nitrogen- containing flavouring agents

Flavouring agent	No.	Specifications <sup>a</sup>	Conclusions based on current intake
Trimethyloxazole	1553	N	No safety concern (conditional) <sup>b</sup>
2,5-Dimethyl-4-ethyloxazole	1554	N	No safety concern (conditional) <sup>b</sup>
2-Ethyl-4,5-dimethyloxazole	1555	N	No safety concern (conditional) <sup>b</sup>
2-Isobutyl-4,5-dimethyloxazole	1556	N	No safety concern (conditional) <sup>b</sup>
2-Methyl-4,5-benzo-oxazole	1557	N	No safety concern (conditional) <sup>b</sup>
2,4-Dimethyl-3-oxazoline	1558	N	No safety concern (conditional) <sup>b</sup>
2,4,5-Trimethyl-delta-3-oxazoline	1559	N,T	No safety concern
Allyl isothiocyanate	1560	N	No safety concern
Butyl isothiocyanate	1561	N	No safety concern (conditional) <sup>b</sup>
Benzyl isothiocyanate	1562	N	No safety concern (conditional) <sup>b</sup>
Phenethyl isothiocyanate	1563	N	No safety concern (conditional) <sup>b</sup>
3-Methylthiopropyl isothiocyanate	1564	N	No safety concern
4-Acetyl-2-methylpyrimidine	1565	N	No safety concern
5,7-Dihydro-2-methylthieno(3,4-d)pyrimidine	1566	N	No safety concern
1-Phenyl-3 or 5-propylpyrazole	1568	N	No safety concern
4,5-Dimethyl-2-propyloxazole	1569	N	No safety concern (conditional) <sup>b</sup>

<sup>a</sup>N: new specifications prepared; T: tentative specifications.

<sup>b</sup>Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

#### F. Epoxides

Flavouring agent	No.	Specifications <sup>a</sup>	Conclusions based on current intake
4,5-Epoxy-(E)-2-decenal	1570	N	No safety concern (conditional) <sup>b</sup>
beta-Ionone epoxide	1571	N	No safety concern (conditional) <sup>b</sup>
trans-Carvone-5,6-oxide	1572	N	No safety concern
Epoxyoxophorone	1573	N	No safety concern (conditional) <sup>b</sup>
Piperitenone oxide	1574	N	No safety concern
beta-Caryophyllene oxide	1575	N	No safety concern
Ethyl 3-phenylglycidate	1576	R <sup>c</sup>	No safety concern
Ethyl methylphenylglycidate	1577	R <sup>c</sup>	See footnote <sup>d</sup>
Ethyl methyl-p-tolylglycidate	1578	N	No safety concern

<sup>a</sup>N: new specifications prepared; R: existing specifications revised.

<sup>b</sup>Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

<sup>c</sup>As this substance is used only as a flavouring agent, the Committee decided that the existing specifications in the standard food additive format should be deleted.

<sup>d</sup>The ADI of 0-0.5 mg/kg bw established at the 28<sup>th</sup> meeting. was maintained.

#### G. Aliphatic and Aromatic Amines and Amides

##### Acetamide (No. 1592)

The Committee noted that the available toxicity data for this substance indicated that it was clearly carcinogenic in both mice and rats, and although the mechanism of tumour formation is unknown, the possibility of a genotoxic mechanism cannot be discounted. The Committee considered it inappropriate for such a compound to be used as a flavouring agent or for any other food additive purpose, and agreed that acetamide would not be evaluated according to the Procedure. No specifications were prepared.

##### Other substances in this group

Flavouring agent	No.	Specifications <sup>a</sup>	Conclusions based on current intake
Ethylamine	1579	N	No safety concern (conditional) <sup>b</sup>
Propylamine	1580	N	No safety concern (conditional) <sup>b</sup>
Isopropylamine	1581	N	No safety concern (conditional) <sup>b</sup>
Butylamine	1582	N	No safety concern
Isobutylamine	1583	N	No safety concern (conditional) <sup>b</sup>
sec-Butylamine	1584	N	No safety concern (conditional) <sup>b</sup>
Pentylamine	1585	N	No safety concern (conditional) <sup>b</sup>
2-Methylbutylamine	1586	N	No safety concern (conditional) <sup>b</sup>
Isopentylamine	1587	N	No safety concern
Hexylamine	1588	N	No safety concern (conditional) <sup>b</sup>
Phenethylamine	1589	N	No safety concern
2-(4-Hydroxyphenyl)ethylamine	1590	N	No safety concern (conditional) <sup>b</sup>
1-Amino-2-propanol	1591	N	No safety concern (conditional) <sup>b</sup>
Butyramide	1593	N	No safety concern (conditional) <sup>b</sup>
1,6-Hexalactam	1594	N	No safety concern (conditional) <sup>b</sup>
2-Isopropyl-N,2,3-trimethylbutyramide	1595	N	No safety concern (conditional) <sup>b</sup>
N-Ethyl (E)-2,(Z)-6-nonadienamide	1596	N	No safety concern (conditional) <sup>b</sup>
N-Cyclopropyl (E)-2,(Z)-6-nonadienamide	1597	N	No safety concern (conditional) <sup>b</sup>

N-Isobutyl (E,E)-2,4-decadienamide	1598	N	No safety concern (conditional) <sup>b</sup>
Nonanoyl 4-hydroxy-3-methoxybenzylamide	1599	N	No safety concern
Piperine	1600	N	No safety concern
N-Ethyl-2-isopropyl-5-methylcyclohexanecarboxamide	1601	N	No safety concern
(+/-)-N,N-Dimethyl menthyl succinamide	1602	N	No safety concern (conditional) <sup>b</sup>
1-Pyrroline	1603	N	No safety concern (conditional) <sup>b</sup>
2-Acetyl-1-pyrroline	1604	N	No safety concern (conditional) <sup>b</sup>
2-Propionylpyrroline	1605	N	No safety concern (conditional) <sup>b</sup>
Isopentylidene isopentylamine	1606	N	No safety concern (conditional) <sup>b</sup>
Piperidine	1607	N	No safety concern
2-Methylpiperidine	1608	N	No safety concern (conditional) <sup>b</sup>
Pyrrolidine	1609	N	No safety concern
Trimethylamine	1610	N	No safety concern
Triethylamine	1611	N	No safety concern (conditional) <sup>b</sup>
Tripropylamine	1612	N	No safety concern (conditional) <sup>b</sup>
N,N-Dimethylphenethylamine	1613	N	No safety concern (conditional) <sup>b</sup>
Trimethylamine oxide	1614	N	No safety concern (conditional) <sup>b</sup>
Piperazine	1615	N	No safety concern (conditional) <sup>b</sup>

<sup>a</sup>N: new specifications prepared.

<sup>b</sup>Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

#### 4. Flavouring agents considered for specifications only

Flavouring agent	No.	Specifications <sup>a</sup>
Sodium salt of 3-methyl-2-oxobutanoic acid	631.2	R,T
Sodium salt of 3-methyl-2-oxopentanoic acid	632.2	R,T
Sodium salt of 4-methyl-2-oxopentanoic acid	633.2	R,T
Sodium 2-oxo-3-phenylpropionate	1479	R,T

<sup>a</sup>R: existing specifications revised; T: tentative specifications

**Annex 1**  
**Sixty-fifth meeting of the**  
**Joint FAO/WHO Expert Committee on Food Additives (JECFA)**  
**Geneva, 7-16 June 2005**

**Members**

Prof John R. Bend, Faculty of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada  
Prof Yehia El-Samragy, Food Science Department, Ain Shams University, Cairo, Egypt  
Dr Yoko Kawamura, National Institute of Health Sciences, Tokyo, Japan  
Dr Ada Knaap, National Institute of Public Health and the Environment, Bilthoven, The Netherlands  
Dr Paul M. Kuznesof, US Food and Drug Administration, College Park, MD, USA  
Dr John C. Larsen, Danish Institute of Food and Veterinary Research, Søborg, Denmark (*vice-Chairman*)  
Dr Antonia Mattia, US Food and Drug Administration, College Park, MD, USA  
Mrs Inge Meyland, Danish Institute of Food and Veterinary Research, Søborg, Denmark (*Chairman*)  
Dr Gérard Pascal, Institut National de la Recherche Agronomique, Paris, France  
Dr Madduri Veerabhadra Rao, Central Laboratories Unit, U.A.E. University, Al Ain, United Arab Emirates  
Dr Josef Schlatter, Swiss Federal Office of Public Health, Zürich, Switzerland  
Dr Philippe Verger, Institut National de la Recherche Agronomique, Paris, France  
Mrs Harriet Wallin, National Food Agency, Helsinki, Finland  
Dr Donald Brian Whitehouse, Bowdon, Cheshire, United Kingdom

**Secretariat**

Dr Peter J. Abbott, Food Standards Australia New Zealand (FSANZ), Canberra, Australia (*WHO Temporary Adviser*)  
Dr Annamaria Bruno, Joint FAO/WHO Food Standards Programme, Secretariat of the Codex Alimentarius Commission, Food and Agriculture Organization, Rome, Italy  
Dr Richard C Cantrill, AOCS, Champaign, IL, USA (*FAO Consultant*)  
Dr Ruth Charrondiere, Food and Nutrition Division, Food and Agriculture Organization, Rome, Italy (*FAO Staff*)  
Dr Maria de Lourdes Costarrica, Food and Nutrition Division, Food and Agriculture Organization, Rome, Italy (*FAO Staff, Acting FAO Joint Secretary*)  
Dr Michael DiNovi, US Food and Drug Administration, College Park, MD, USA (*WHO Temporary Adviser*)  
Dr Christopher E Fisher, Hatfield, Herts, United Kingdom (*FAO Consultant, Acting FAO Joint Secretary*)  
Dr Charles A. Lawrie, Food Standards Agency, London, United Kingdom (*FAO Consultant*)  
Dr Catherine Leclercq, National Research Institute for Food and Nutrition, Rome, Italy (*FAO Consultant*)  
Dr Gerald Moy, Food Safety Department, World Health Organization, Geneva, Switzerland (*WHO Staff Member*)  
Dr Ian C. Munro, CanTox Health Sciences International, Mississauga, Ontario, Canada (*WHO Temporary Adviser*)  
Dr Akiyoshi Nishikawa, Division of Pathology, National Institute of Health Sciences, Tokyo, Japan (*WHO Temporary Adviser*)  
Dr Zofia Olempska-Beer, Center for Food Safety and Applied Nutrition, US Food and Drug Administration, College Park, MD, USA (*FAO Consultant – unable to attend*)  
Dr Monica Olsen, Food and Nutrition Division, Food and Agriculture Organization, Rome, Italy (*FAO Joint Secretary-unable to attend*)



Dr Sam Page, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland (*WHO Staff Member*)

Mrs Ir Marja E.J. Pronk, Center for Substances and Integrated Risk Assessment, National Institute for Public Health and the Environment, Bilthoven, The Netherlands (*WHO Temporary Adviser*)

Prof Andrew G. Renwick, Clinical Pharmacology Group, University of Southampton, Southampton, United Kingdom (*WHO Temporary Adviser*)

Prof I. Glenn Sipes, Department of Pharmacology, College of Medicine, University of Arizona, Tucson, AZ, USA (*WHO Temporary Adviser*)

Prof Lucia Maria Valenta Soares, Food Science Department, State University of Campinas, Campinas, Brazil (*FAO Consultant*)

Prof Ivan Stankovic, Institute of Bromatology, Faculty of Pharmacy, Belgrade, Serbia and Montenegro (*FAO Consultant*)

Dr Angelika Tritscher, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland (*WHO Joint Secretary*)

Dr Luis G Valerio, Jr., Center for Food Safety and Applied Nutrition, US Food and Drug Administration, College Park, MD, USA (*FAO Consultant*)

Prof Gary M Williams, Environmental Pathology and Toxicology, New York Medical College, Valhalla, NY, USA (*WHO Temporary Adviser*)

## Annex 2

### Further information required

#### 1. Need for use levels and reported poundage data for flavouring agents

For a number of flavouring agents the evaluation was made conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of these substances will be revoked if use levels or poundage data are not provided before the end of 2007. The Committee also requested use levels or poundage data to be provided for the flavouring agents it had previously assessed on the basis of an MSDI that was calculated from anticipated poundage. This includes any substances where the MSDI based on anticipated poundage for one region (EU or USA) was higher than the MSDI based on recorded poundage in the other region.

The existing assessments will be revoked if such data are not forthcoming by the end of 2007.

The Committee emphasized that use level data are requested for all flavouring agents listed in Calls for Data, and subsequent submissions that do not contain this information will not be evaluated by the Committee.

For further discussion see Annex 3. Details of all the flavouring agents for which further data are required are given in Annex 4.

#### 2. Information for specifications

##### 2.1. Flavouring agents

a. *Sodium 3-methyl-2-oxobutanoate (No. 631.2), Sodium 3-methyl-2-oxopentanoate (No. 632.2), Sodium 4-methyl-2-oxopentanoate (No. 633.2) and Sodium 2-oxo-3-phenylpropionate (No. 1479)*

The existing tentative specifications for these four flavouring agents were revised to include new information on methods of assay. However, the tentative designations of the specifications were maintained, pending more detailed information on these methods. For the first three substances, information on an assay by HPLC using an ion exchange column are required, and for flavouring No. 1479 information on an assay by HPLC is required.

b. *Maltol (No.1480) and Ethyl maltol (No. 1481)*

New specifications were prepared for these substances in the flavouring agent format. However both substances are believed to have uses in addition to flavouring agent uses, and the existing specifications in the standard food additive format were revised and made tentative. In both cases information on functional uses other than flavouring uses and on the method of assay is required.

c. *Maltyl isobutyrate (No. 1482), 3-Acetyl-2,5-dimethylfuran (No. 1506) and 2,4,5-Trimethyl-delta-3-oxazoline (No. 1559)*

New tentative specifications were prepared for these substances. In each case, further information is required on the reasons why the quoted specific gravity ranges are wider than would be expected given the level of purity of the substances. In addition, further information is required on why the refractive index range for flavouring No. 1559 is wider than would be expected given the level of purity of the substance.

##### 2.2. Sucrose esters of fatty acids

The specifications for sucrose esters of fatty acids were revised but maintained as tentative. Information is required on

- a method of analysis for the determination of free sucrose using capillary GC or HPLC;
- an alternative and less toxic solvent than pyridine for preparing the standard and sample solutions for the determinations of free sucrose and propylene glycol; and
- a method of analysis for the determination of dimethyl sulfoxide that does not require a packed column.

The tentative specifications mentioned above will be withdrawn unless the requested information is received before the end of the year 2006.

## Annex 3

*An edited version of this section will appear in the report of the sixty-fifth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). It is reproduced here so that the information is disseminated quickly. This draft is subject to extensive editing.*

### General Considerations

#### 1. The safety evaluation of flavouring agents

##### *Estimating dietary exposure to flavouring agents*

In its 46<sup>th</sup> report (1997) the Committee adopted a Procedure for the safety evaluation of flavouring agents. In developing this Procedure, the Committee recognized the need for an approach that could be efficiently applied to a large class of substances. In view of the availability of industry poundage data covering several thousand flavouring ingredients, the Committee agreed that a per capita or MSDI method using these data could be readily and efficiently applied for exposure assessments as part of the Procedure for safety evaluation. The Committee re-endorsed the MSDI approach at its 49<sup>th</sup>, 55<sup>th</sup>, 61<sup>st</sup> and 63<sup>rd</sup> meetings, noting that the estimation of dietary exposures based on production data is both a practical and realistic approach (JECFA 1998).

There have also been discussions identifying limitations in the use of the MSDI for estimation of dietary exposure. At its 55<sup>th</sup> meeting (2000), the Committee noted that the use of the MSDI might in some cases result in an underestimate of dietary exposure of those persons with high levels of consumption of specific foods. At its 61<sup>st</sup> meeting (2003) the Committee decided that flavouring agents submitted without reported poundage data would not be evaluated by the Committee and at its 63<sup>rd</sup> meeting (2004) the Committee recognized that the estimates of current dietary exposure are difficult to reconcile with reported maximum use levels of some flavouring agents in some foods.

At the current meeting, the Committee considered how better to identify and deal with cases where the MSDI estimates, as used in the Procedure, may be substantially lower than dietary exposures estimated from flavouring agent use levels.

The Committee anticipated that the existing data will, in the great majority of cases, provide assurance that there is no safety concern at these estimated exposures, even though these are expected to be higher than the MSDI, particularly for flavouring agents that are not used in a wide range of food products. However, this would need to be confirmed on a case-by-case basis.

##### *Implications for toxicological data requirements of using model diet methods for estimating exposure to flavouring agents*

Use level based (model diet) dietary exposure data would result in higher estimated dietary exposures than the MSDI estimates. As a result more flavouring agents would be likely to exceed the intake thresholds at steps A3 and B3 of the decision tree, which is a central part of the Procedure for the evaluation of flavouring agents.

The Committee at its present meeting explored the application of alternative approaches for estimating dietary exposure and obtained use levels for approximately 90% of the flavouring agents submitted for evaluation. These data made it possible to prepare conservative estimates of the dietary exposure using several methods, including a model diet. A majority of the flavouring agents had dietary exposures above the intake threshold for the respective structural class when estimated by methods based on use levels, compared with a few compounds for the MSDI. However, a preliminary comparison of the dietary exposure estimates with the NOELs for selected flavouring agents indicated that there would be very few cases where the additional, more conservative, dietary exposure estimates would suggest a possible safety concern. A comprehensive risk characterization based on the additional use level-based dietary exposure estimates for all agents was not possible at the present meeting because appropriate toxicology data were not required for assessment of safety using the Procedure, and had not been submitted.

The most appropriate approach to the safety evaluation of flavouring agents using additional conservative methods to estimate dietary exposure requires careful consideration by the Committee.

##### *Recommendation to the JECFA Secretariat to form a working group*

To address concerns raised at the 55<sup>th</sup> meeting, at the recent FAO/WHO workshop on dietary exposure assessments and in several recent publications, the Committee recommended that the Secretariat should form a small working group, shortly after the conclusion of the present meeting, to consider further all relevant aspects of the introduction of an additional use level-based screening method to complement the MSDI, the method used by JECFA for the estimation of

dietary exposure of flavouring agents. The Committee also recommended that intake experts should work with the temporary advisors during monograph development in the future.

The terms of reference for this working group will be determined by the JECFA Secretariat but might include:

- i) to make a detailed analysis of the impact of different methods for estimating dietary exposure on the safety assessment of flavouring agents, according to the Procedure;
- ii) to develop a pre-meeting approach, based on MSDI and use level-derived dietary exposure estimates, to identify flavouring agents that require special consideration at future meetings of the Committee;
- iii) to revise the dietary exposure section of the Procedure for the safety evaluations of flavourings for discussion by the Committee at its next meeting; and
- iv) to consider an approach for the estimation of combined dietary exposure for a group of substances through use level-based model diets.

#### ***Interactions with industry and requests for data***

The Committee noted that the evaluation of flavouring agents should be on the basis of complete and up-to-date information and therefore welcomed a proposal from the industry to update and extend the existing surveys of flavour usage.

The Committee recommended that poundage data should be collected for all flavourings on a regular basis so that rolling averages of poundage can be calculated. This information should be collected with attention to adequate quality control of the data.

The apparent discrepancy between dietary exposures estimated by reported poundage and those estimated by published use levels for some flavouring agents requires further investigation to ensure that safety evaluations are based on exposure estimates that reflect current and future practice in the food and flavouring industries. The Committee recommended that studies be undertaken in this area, giving priority to substances of potential toxicological concern, i.e. those where there is only a low margin of safety between the potential exposure level and the no-effect level observed in animal studies either with the same compound or with a structural analogue.

A recent analysis of flavouring agents evaluated by JECFA was made available to the Committee. It showed that of 808 substances considered, 16 substances had margins of safety of less than 100 using exposure estimates based on the model diet method, compared to only 1 (methyl salicylate) using the MSDI analysis. Considering estimates of dietary exposure and toxicity data, the Committee suggested that a subset of these flavouring substances might form a basis for prioritizing substances for future investigation. Proposed substances are p-Ethylphenol, 2,5-Xylenol, 2,6-Xylenol, 3,4-Xylenol, p-Vinylphenol, 2,3,6-Trimethylphenol, 4-Phenyl-2-butyl acetate, Heptanal dimethyl acetal, Thiamine hydrochloride, 4-[(2-Furanmethyl)thio]-2-pentanone, 4,8-Dimethyl-3,7-nonadien-2-one, 2-(Methylthio)ethanol, 2,3,5-Trithiahexane, 3-L-Menthoxyp propane-1,2-diol and 3-(1-Menthoxy)-2-methylpropane-1,2-diol).

The Committee recommended that there should be appropriate follow-up by the JECFA Secretariat so that use level data are included in submissions from sponsors for safety evaluation of flavouring agents as requested in future calls for data. The Committee noted that these data were not submitted by the sponsors at this meeting. In future, submissions that do not contain this information will not be evaluated by the Committee.

#### ***Anticipated poundage data***

The Committee noted that an increasing number of the flavouring agents submitted for evaluation in recent years had no recorded poundage data in either the EU or the USA, and MSDI values could only be calculated on the basis of an annual poundage anticipated by the manufacturer. This was the situation for 60 of 135 flavouring agents on the agenda of the present meeting, and for a number of those evaluated during the 59<sup>th</sup>, 61<sup>st</sup> and 63<sup>rd</sup> meetings. As MSDI estimates based only on anticipated poundage data contain additional uncertainty, the Committee decided that in future either the dietary exposure to such substances should be assessed using an alternative approach, or the assessment should be deferred until actual poundage data were available.

The Committee decided that the Procedure would be applied where appropriate for the safety evaluation of flavouring agents submitted to this meeting, including those where anticipated poundage data were submitted for the USA and/or the EU. The evaluation was made conditional if it was based on an MSDI derived from anticipated poundage estimates, and the Committee decided that the results of the conditional assessments will be revoked if use levels or

poundage data are not provided before the end of 2007. This decision was not unanimous, and two members registered a minority opinion.\*

The Committee also requested use levels or poundage data to be provided for the flavouring agents it had previously evaluated using MSDIs calculated from anticipated poundage. This includes any substances where the MSDI based on an anticipated poundage for one region (EU or USA) was higher than the MSDI based on a recorded poundage in the other region. The existing assessments for these flavourings will be revoked if such data are not forthcoming by the end of 2007.

Flavouring agents for which further information is required, including those evaluated at both the present meeting and at earlier meetings, are listed in Annex 4.

## 2. Safety evaluation of enzymes produced by Genetically Modified Microorganisms (GMM)

In 1987, the Committee outlined criteria for the safety evaluation of enzymes (Environmental Health Criteria 70, Annex III, 135-136). It was proposed to group enzyme preparations into 5 major groups on the basis of their origin (enzymes obtained from edible tissues of animals commonly used as foods; enzymes obtained from edible portions of plants; enzymes derived from microorganisms that are traditionally accepted as constituents of foods or are normally used in the preparation of foods; enzymes derived from non-pathogenic microorganisms commonly found as contaminants of foods; enzymes derived from microorganisms that are less well known). At the same time, the Committee envisaged three cases for the safety assessment of enzymes (added directly to food but not removed, added to food but removed; or immobilized enzyme preparations) and indicated guidelines that are appropriate for evaluation of safety in each case.

In 1987, the case of enzymes produced by genetically modified microorganisms (GMM) was not considered. Since then, the Committee has evaluated several enzymes produced by GMM, for example, laccase from *Myceliophthora thermophila* expressed in *Aspergillus oryzae* and xylanase from *Thermomyces lanuginosus* expressed in *Fusarium venenatum*. The Committee evaluated the safety of these two enzyme preparations on the basis of toxicological data that included, in both cases, a 90-day study in the rat, a test for reverse mutation *in vitro*, and a test for chromosomal aberration. The committee allocated an ADI 'not specified' to these enzyme preparations.

The present Committee evaluated an enzyme preparation of Phospholipase A1 produced by the same host strain of *A. oryzae* that had been modified to produce other enzymes. However, it could not assess the safety of Phospholipase A1 using the information available on one of the other enzymes produced by this host strain as comparators, and the Committee concluded that guidelines need to be developed for the safety assessment of enzymes produced by GMM. These guidelines should set out what information is essential for different enzyme preparations and what details of molecular characterization of the producing microbial strain are necessary to allow an adequate assessment of safety. Furthermore, the Committee reiterated the view expressed at its 57<sup>th</sup> meeting that the existing General Specifications and Considerations for Enzyme Preparations used in Food Processing should be revised, together with the elaboration of the guidelines for the safety evaluation of enzyme preparations within the Project to Update the Principles and Methods for the Risk Assessment of Chemicals in Food.

The Committee also recommended that the report from the Joint FAO/WHO Expert Consultation on Safety Assessment of Food Derived from Genetically Modified Microorganisms (2001) should constitute a starting basis for this future task.

## 3. Compendium of food additive specifications

At this meeting the Committee considered a paper describing a number of issues that had arisen as a result of an exercise to draft a new Introduction for a proposed 2<sup>nd</sup> Edition of the Compendium of Food Additive Specifications. As well as updating the current Introduction and current texts, the new Introduction is intended to serve as the basis for revising those sections of the *Principles for the Safety Assessment of Food Additives and Contaminants in Food* (Environmental Health Criteria 70) dealing with specifications.

The Committee noted that the new Introduction emphasizes that the setting of specifications is an inherent part of the risk assessment process for food additives, and that the safety evaluation of an additive should therefore always be read in conjunction with the specifications of identity and purity that describe the additive. The Committee also discussed

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\*Minority Opinion (Prof Gérard Pascal and Dr Philippe Verger):

The minority opinion states that for the 60 flavouring substances submitted to the Committee without reported poundage, the safety evaluation using the normal Procedure should not be performed, even on a conditional basis.

the conditions under which the 'tentative' designation is applied to additive specifications and the possible link with the 'temporary' ADI designation. It agreed that although there should always be a clear link between the specifications and the safety assessment, the conditions under which the 'tentative' specifications and 'temporary' ADI designations are used should continue to be judged on a case-by-case basis. The Committee also reaffirmed that these designations should be time-limited.

#### **4. Residual solvents**

At the 61<sup>st</sup> meeting, the Committee recognized the need to revise the general method for the determination of residual solvents, which is published in FNP 5, and following that meeting, a tentative general method using headspace capillary gas chromatography with flame ionisation detection for the determination of residual solvents was published in FNP 52 Add. 11.

In reviewing the responses in the call for data for comments on the tentative general method, the Committee noted that the critical parts of the determination are the liberation of the solvent residues from the food additive and their capture through headspace sampling prior to the gas chromatographic step. The Committee decided, therefore, that the critical steps should be included in future individual additive specifications rather than in the general method. The Committee also decided that there was a need to revise the tentative general method to include more solvents. The Committee further recommended that methods for the analysis of many common solvents used in the preparation of food additives should be reviewed during the revision of FNP 5.

#### **5. Application of Threshold of Toxicological Concern Approaches for Risk Characterization**

The Threshold of Toxicological Concern (TTC) is defined as the level of human exposure below which it can be anticipated that there are no significant risks to health, even in the absence of toxicological data for the substance under evaluation. Risk assessments based on TTC approaches can use a variety of scientific data, including structural information for the substance of concern; combinations of absorption, distribution, metabolism, excretion and toxicity data of compounds of the same structural class; and, most importantly, the exposure data. These pragmatic risk assessments can be used where more comprehensive evaluations are not possible to provide timely advice for risk management decisions. They are also useful in risk management prioritizations.

The TTC approach should not be used if there are sufficient chemical-specific toxicological data for hazard characterization and is applicable only to defined chemical entities of low molecular weight.

The TTC approach was developed following analyses of the relationships of chemical structures and chronic toxicity, including carcinogenicity. Additional TTC approaches have been proposed for other toxicological endpoints. JECFA has adopted a decision-tree approach that uses a series of TTC considerations for the evaluation of flavouring agents.

The Committee noted that the following considerations should be taken into account for additional applications of TTC approaches:

- TTC approaches should be applied in conjunction with conservative estimates of dietary exposure. These considerations should cover potentially susceptible subpopulations, such as children.
- Additional toxicity data for structurally-related substances may be necessary.

The Committee reaffirmed the use of the TTC approach for flavouring agents. The Committee recommended that guidance for the application of TTC approaches for other substances present in the diet in very small amounts, such as certain residues of processing aids, packaging migrants, and contaminants, should be developed for providing risk assessment advice for those substances for which full toxicological data sets are not available or not necessary. The Committee recommended that this guidance should be developed by a special task group appointed by the Joint FAO/WHO Joint Secretaries, and should be incorporated into the Principles and Methods for the Risk Assessment of Chemicals in Food.

## Annex 4

**Flavouring agents for which use level or reported poundage data are required**

The safety assessment of these flavouring agents will be revoked if use level data or reported poundage data are not provided before end of 2007 (see Annex 3).

**1. Flavouring agents evaluated at the present meeting which were assessed as of ‘no safety concern’ on a conditional basis**

No.	Flavouring agent
1483	2-Methyl-3-(1-oxopropoxy)-4H-pyran-4-one
1527	4-Allylphenol
1528	2-Methoxy-6-(2-propenyl)phenol
1532	Eugenyl isovalerate
1538	cis-3-Hexenyl anthranilate
1539	Citronellyl anthranilate
1546	Ethyl N-methylantranilate
1547	Ethyl N-ethylantranilate
1548	Isobutyl N-methylantranilate
1549	Methyl N-formylantranilate
1550	Methyl N-acetylantranilate
1551	Methyl N,N-dimethylantranilate
1552	N-Benzoylantranilic acid
1553	Trimethyloxazole
1554	2,5-Dimethyl-4-ethyloxazole
1555	2-Ethyl-4,5-dimethyloxazole
1556	2-Isobutyl-4,5-dimethyloxazole
1557	2-Methyl-4,5-benzo-oxazole
1558	2,4-Dimethyl-3-oxazoline
1561	Butyl isothiocyanate
1562	Benzyl isothiocyanate
1563	Phenethyl isothiocyanate
1569	4,5-Dimethyl-2-propyloxazole
1570	4,5-Epoxy-(E)-2-decenal
1571	beta-Ionone epoxide
1573	Epoxyoxophorone
1579	Ethylamine
1580	Propylamine
1581	Isopropylamine
1583	Isobutylamine
1584	sec-Butylamine
1585	Pentylamine
1586	2-Methylbutylamine
1588	Hexylamine
1590	2-(4-Hydroxyphenyl)ethylamine
1591	1-Amino-2-propanol
1593	Butyramide
1594	1,6-Hexalactam
1595	2-Isopropyl-N,2,3-trimethylbutyramide
1596	N-Ethyl (E)-2,(Z)-6-nonadienamide
1597	N-Cyclopropyl (E)-2,(Z)-6-nonadienamide
1598	N-Isobutyl (E,E)-2,4-decadienamide
1602	(+/-)-N,N-Dimethyl menthyl succinamide
1603	1-Pyrroline
1604	2-Acetyl-1-pyrroline
1605	2-Propionylpyrroline
1606	Isopentylidene isopentylamine
1608	2-Methylpiperidine
1611	Triethylamine
1612	Tripropylamine

No.	Flavouring agent
1613	N,N-Dimethylphenethylamine
1614	Trimethylamine oxide
1615	Piperazine

2. Flavouring agents evaluated at the 59th (2002), 61st (2003) and 63rd (2004) meetings where only anticipated poundage data were available or where the MSDI derived from anticipated poundage data from one region (EU or US) was greater than the MSDI derived from recorded poundage data of the other region

No.	Flavouring agent	Year	Note
963	Ethyl cyclohexanecarboxylate	2002	a
986	10-Hydroxymethylene-2-pinene	2002	a
1063	2,5-Dimethyl-3-furanthiol	2002	b
1065	Propyl 2-methyl-3-furyl disulfide	2002	a
1066	Bis(2-methyl-3-furyl) disulfide	2002	b
1067	Bis(2,5-dimethyl-3-furyl) disulfide	2002	b
1068	Bis(2-methyl-3-furyl) tetrasulfide	2002	a
1070	2,5-Dimethyl-3-furan thioisovalerate	2002	a
1077	Furfuryl isopropyl sulfide	2002	b
1082	2-Methyl-3,5- or 6-(furfurylthio)pyrazine	2002	b
1085	3-[(2-Methyl-3-furyl)thio]-4-heptanone	2002	a
1086	2,6-Dimethyl-3-[(2-methyl-3-furyl)thio]-4-heptanone	2002	a
1087	4-[(2-Methyl-3-furyl)thio]-5-nonanone	2002	a
1089	2-Methyl-3-thioacetoxy-4,5-dihydrofuran	2002	a
1157	4-Hydroxy-4-methyl-5-hexenoic acid gamma lactone	2003	a
1158	(+/-) 3-Methyl-gamma-decalactone	2003	a
1159	4-Hydroxy-4-methyl-7-cis-decenoic acid gamma lactone	2003	a
1160	Tuberose lactone	2003	a
1161	Dihydromintlactone	2003	a
1162	Mintlactone	2003	b
1163	Dehydromenthofurolactone	2003	b
1164	(+/-)-(2,6,6,-Trimethyl-2-hydroxycyclohexylidene)acetic acid gamma-lactone	2003	a
1167	2-(4-Methyl-2-hydroxyphenyl)propionic acid-gamma-lactone	2003	a
1174	2,4-Hexadien-1-ol	2003	a
1176	(E,E)-2,4-Hexadienoic acid	2003	a
1180	(E,E)-2,4-Octadien-1-ol	2003	a
1183	2,4-Nonadien-1-ol	2003	a
1188	(E,Z)-2,6-Nonadien-1-ol acetate	2003	a
1189	(E,E)-2,4-Decadien-1-ol	2003	a
1191	Methyl (E)-2-(Z)-4-decadienoate	2003	a
1193	Ethyl 2,4,7-decatrienoate	2003	a
1199	(+/-)-2-Methyl-1-butanol	2003	a
1217	2-Methyl-2-octenal	2003	a
1218	4-Ethyl octanoic acid	2003	a
1226	8-Ocimenyl acetate	2003	a
1228	3,7,11-Trimethyl-2,6,10-dodecatrienal	2003	a
1229	12-Methyltridecanal	2003	a
1232	1-Ethoxy-3-methyl-2-butene	2003	b
1236	2,2,6-Trimethyl-6-vinyltetrahydropyran	2003	b
1239	Cycloionone	2003	a
1245	2,4-Dimethylanisole	2003	a
1248	1,2-Dimethoxybenzene	2003	a
1265	4-Propenyl-2,6-dimethoxyphenol	2003	a
1289	erythro- and threo-3-Mercapto-2-methylbutan-1-ol	2003	b



No.	Flavouring agent	Year	Note
1290	(±)-2-Mercaptomethylpentan-1-ol	2003	b
1292	3-Mercapto-2-methylpentanal	2003	b
1293	4-Mercapto-4-methyl-2-pentanone	2003	b
1296	spiro[2,4-Dithia-1-methyl-8-oxabicyclo(3.3.0)octane-3,3'-(1'-oxa-2'-methyl)-cyclopentane]	2003	a
1299	2,3,5-Trithiahexane	2003	b
1300	Diisopropyl trisulfide	2003	b
1311	2-(2-Methylpropyl)pyridine	2004	a
1319	2-Propionylpyrrole	2004	b
1322	2-Propylpyridine	2004	a
1334	4-Methylbiphenyl	2004	b
1342	delta-3-Carene	2004	a
1343	alpha-Farnesene	2004	a
1344	1-Methyl-1,3-cyclohexadiene	2004	a
1367	trans-2-Octen-1-yl acetate	2004	b
1368	trans-2-Octen-1-yl butanoate	2004	b
1369	Cis-2-Nonen-1-ol	2004	b
1370	(E)-2-Octen-1-ol	2004	a
1371	(E)-2-Butenoic acid	2004	a
1372	(E)-2-Decenoic acid	2004	a
1373	(E)-2-Heptenoic acid	2004	a
1374	(Z)-2-Hexen-1-ol	2004	a
1375	trans-2-Hexenyl butyrate	2004	a
1376	(E)-2-Hexenyl formate	2004	a
1377	trans-2-Hexenyl isovalerate	2004	a
1378	trans-2-Hexenyl propionate	2004	a
1379	trans-2-Hexenyl pentanoate	2004	a
1380	(E)-2-Nonenoic acid	2004	a
1381	(E)-2-Hexenyl hexanoate	2004	a
1382	(Z)-3- & (E)-2-Hexenyl propionate	2004	a
1384	2-Undecen-1-ol	2004	a
1407	Dihydronootkatone	2004	b
1409	beta-Ionyl acetate	2004	a
1410	alpha-Isomethylionyl acetate	2004	a
1411	3-(1-Methoxy)-2-methylpropane-1,2-diol	2004	a
1412	Bornyl butyrate	2004	a
1413	D,L-Menthol(+/-)-propylene glycol carbonate	2004	a
1414	L-Monomenthyl glutarate	2004	a
1415	L-Menthyl methyl ether	2004	a
1416	p-Menthane-3,8-diol	2004	a
1435	Taurine	2004	a
1438	L-Arginine	2004	a
1439	L-Lysine	2004	a
1447	Tetrahydrofurfuryl cinnamate	2004	a
1457	(+/-)-2-(5-Methyl-5-vinyl-tetrahydrofuran-2-yl)propionaldehyde	2004	a
1475	Ethyl 2-ethyl-3-phenylpropanoate	2004	a
1478	2-Oxo-3-phenylpropionic acid	2004	a

<sup>a</sup>Flavourings where only anticipated poundage data were available

<sup>b</sup>Flavourings where the MSDI derived from anticipated poundage data from the US was greater than the MSDI derived from recorded poundage data of the EU.