Food and Agriculture Organization of the United Nations

World Health Organization

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES
Sixty-third meeting
Geneva, 8-17 June 2004

SUMMARY AND CONCLUSIONS

A meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) was held in Geneva, Switzerland, from 8 to 17 June 2004. The purpose of the meeting was to evaluate certain food additives and ingredients, flavouring agents, and a natural constituent of food.

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

Dr Manfred Luetzow, Food Quality and Standards Service, Food and Nutrition Division, Food and Agriculture Organization of the United Nations, and Dr Angelika Tritscher, International Programme on Chemical Safety, World Health Organization, served as joint secretaries.

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

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.

Toxicological monographs or monograph addenda on most of the substances that were considered will be published in WHO Food Additives Series No. 54.

New and revised specifications for the identity and purity of the compounds will be published in FAO Food and Nutrition Paper Series 52, Addendum 12.

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

www.who.int/pcs/jecfa/jecfa.htm

Toxicological recommendations and information on specifications

1. Food additives and ingredients evaluated toxicologically

Food additive	Specifi-cations[a]	Acceptable daily intake (ADI) and other toxicological recommendations
Benzoyl peroxide	R	Treatment of whey with benzoyl peroxide at a maximum concentration of 100 mg/kg does not pose a safety concern.
α-Cyclodextrin	-	α-Cyclodextrin does not pose a safety concern at the proposed use levels and resulting predicted consumption as food ingredient and food additive. The previously established ADI "not specified" for use as a carrier and stabilizer for flavours, colours, and sweeteners, as a water-solubilizer for fatty acids and certain vitamins, as a flavour modifier in soya milk, and as an absorbent in confectionery was maintained.
Hexose oxidase from *Chondrus crispus* expressed in *Hansenula polymorpha*	N	Not specified[b]
Lutein from *Tagetes erecta* L.	N	0–2 mg/kg bw (group ADI for lutein and zeaxanthin)[c]
Peroxyacid antimicrobial solutions containing 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP) *Containing HEDP and three or more of the following components: peroxacetic acid, acetic acid, hydrogen peroxide, octanoic acid and peroxyoctanoic acid.*		The peroxy compounds in these solutions (hydrogen peroxide, peroxyacetic acid and peroxyoctanoic acid) would break down into acetic acid and octanoic acid, and small residual quantities of these acids on foods at the time of consumption would not pose a safety concern. HEDP does not pose a safety concern at the levels of residue that are expected to remain on foods at the time consumption.
Acetic acid	R	
1-Hydroxyethylidene-1,1-diphosphonic acid (HEDP)	N	
Hydrogen peroxide	R	
Octanoic acid (as food additive)	N	
Steviol glycosides	N, T	0–2 mg/kg bw (temporary)
D-Tagatose	-	Not specified[b]
Xylanase from *Bacillus subtilis* expressed in *Bacillus subtilis*	N	Not specified[b]
Xylanase (resistant to xylanase inhibitor) from *Bacillus subtilis* containing a modified xylanase gene from *Bacillus subtilis*	N	Not specified[b]
Zeaxanthin	N	0–2 mg/kg bw (group ADI for lutein and zeaxanthin)[c]

[a] N: new specifications prepared; R: existing specifications revised; T: tentative specifications.

[b] 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.

[c] This group ADI does not apply to other xanthophyll-containing extracts with a lutein or zeaxanthin content lower than that cited in the specifications.

2. Food additives considered for specifications only

Food Additive	Specifications [a]
Aluminium lakes of colouring matters — General specifications	R
Aluminium powder	R
Hydroxypropyl cellulose	R
Hydroxypropylmethyl cellulose	R
Iron oxides	R
Magnesium sulfate[b]	N, T
Polyvinyl alcohol	R
Titanium dioxide	R
Zeaxanthin-rich extract from *Tagetes erecta* L	N, T

[a] R, existing specifications revised; R: existing specifications revised; T: tentative specifications.
[b] Magnesium sulfate was not evaluated at the present meeting because the intended use and use levels were not identified.

3. Revision of heavy metals limits for food additives

At its fifty-fifth meeting, the Committee began its implementation of a systematic five-year programme to replace the outdated test for heavy metals (as lead) in all existing food additive specifications with appropriate limits for individual metals of concern. At the present meeting, the heavy metals and arsenic limits of 84 additives with various technological functions were reviewed.

Comments on the Committee's new proposed limits are invited. If alternative values and supporting data are not received by the deadline for submission of data for the sixty-fifth meeting (30 November 2004), the proposed metal limits will be adopted and supersede the existing limits, replacing those published in FAO Food and Nutrition Paper 52 and its addenda 1 to 11.

Additive name	INS	Limits (mg/kg)			
		As	Pb	Cd	Hg
Aluminium ammonium sulfate	523	-	3	-	-
Ammonium chloride	510	-	2	-	-
Ammonium hydrogen carbonate	503 (ii)	-	2	-	-
Azodicarbonamide	927 a	-	2	-	-
Bees wax	901	-	2	-	-
Benzoic acid	210	-	2	-	-
Benzyl alcohol	-	-	2	-	-
Butan-1,3-diol	-	-	2	-	-
Butan-1-ol	-	-	2	-	-
Butan-2-ol	-	-	2	-	-
Butyl *p*-hydroxybenzoate	-	-	2	-	-
Calcium acetate	263	-	2	-	-
Calcium benzoate	213	-	2	-	-
Calcium carbonate	170	3	3	-	-
Calcium chloride	509	-	2	-	-
Calcium cyclamate	952	-	1	-	-
Calcium hydrogen phosphate	341 (ii)	3	4	-	-
Calcium sulfate	516	-	2	-	-
Candelilla wax	902	-	2	-	-
Castor oil	1503	-	2	-	-
Chlorine	925	-	2	-	1
Citranaxanthin	-	-	2	-	-
Cyclodextrin, beta-	459	-	1	-	-
Cyclohexane	-	-	2	-	-
Dammar gum	-	-	2	-	-
Diethyl tartrate	-	-	2	-	-

Additive name	INS	Limits (mg/kg)			
		As	Pb	Cd	Hg
Diethylene glycol monoethyl ether	-	-	2	-	-
Dimethyl dicarbonate	242	-	2	-	-
Diphenyl	-	-	2	-	-
Edible gelatin	-	1	1.5	0.5	0.15
Ferric ammonium citrate	-	-	2	-	-
Glycerol	422	-	2	-	-
Glycerol diacetate	-	-	2	-	-
Heptanes	-	-	2	-	-
Hexamethylene tetramine	239	-	2	-	-
Hydrogen peroxide	-	-	2	-	-
Isoamyl acetate	-	-	2	-	-
Isobutanol	-	-	2	-	-
Isopropyl acetate	-	-	2	-	-
Lactic acid	270	-	2	-	-
Light petroleum	-	-	2	-	-
Lysozyme hydrochloride	1105	-	2	-	-
Magnesium carbonate	504 (i)	-	2	-	-
Magnesium chloride	511	-	2	-	-
Magnesium hydrogen phosphate	343 (ii)	3	4	-	-
Magnesium lactate	329	-	2	-	-
Methanol	-	-	2	-	-
Mineral oil (high viscosity)	905	-	1	-	-

Additive name	INS	Limits (mg/kg)			
		As	Pb	Cd	Hg
Monoglyceride citrate	-	-	2	-	-
Nisin	234	-	1	-	-
Norhydroguaiaretic acid	-	-	2	-	-
Pentapotassium triphosphate	451 (ii)	3	4	-	-
Phenyl phenol, *o*-	231	-	2	-	-
Polyvinylpolypyrrolidone, Insoluble	1202	-	2	-	-
Polyvinylpyrrolidone	1201	-	2	-	-
Potassium acetate	261	-	2	-	-
Potassium benzoate	212	-	2	-	-
Potassium bromate	924 a	-	2	-	-
Potassium chloride	508	-	2	-	-
Potassium dihydrogen phosphate	501 (ii)	3	4	-	-
Potassium iodate	917	-	2	-	-
Potassium nitrate	252	-	2	-	-
Potassium nitrite	249	-	2	-	-
Potassium sodium L(+) tartrate	337	-	2	-	-
Potassium sulfate	515 (i)	-	2	-	-
Propan-1-ol	-	-	2	-	-
Propylene glycol	1520	-	2	-	-
Sodium benzoate	211	-	2	-	-
Sodium carboxy methyl cellulose	466	-	2	-	-
Sodium cyclamate	952	-	1	-	-
Sodium diacetate	262 (ii)	-	2	-	-
Sodium nitrate	251	-	2	-	-
Sodium nitrite	250	-	2	-	-
Sodium *o*-phenyl phenol	232	-	2	-	-
Sodium percarbonate	-	-	2	-	-
Sodium thiocyanate	-	-	2	-	-
Sorbic acid	200	-	2	-	-
Sucralose	955	-	1	-	-
Tannic acid	181	-	2	-	-
Tartaric acid, DL-	-	-	2	-	-
Toluene	-	-	2	-	-
Triacetin	1518	-	2	-	-
Trichlorotrifluoroethane, 1,1,2-	-	-	2	-	-
Urea	927 b	-	2	-	-

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

A. Pyridine, pyrrole and quinoline derivatives

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Indole	1301	N	No safety concern
6-Methylquinoline	1302	N	No safety concern
Isoquinoline	1303	N	No safety concern
Skatole	1304	N	No safety concern
1-Ethyl-2-acetylpyrrole	1305	N	No safety concern
1-Methyl-2-acetylpyrrole	1306	N	No safety concern
Methyl 2-pyrrolyl ketone	1307	N	No safety concern
2-Pyridinemethanethiol	1308	N	No safety concern
2-Acetylpyridine	1309	N	No safety concern
N-Furfurylpyrrole	1310	N	No safety concern
2-(2-Methylpropyl)pyridine	1311	N	No safety concern
3-(2-Methylpropyl)pyridine	1312	N	No safety concern
2-Pentylpyridine	1313	N	No safety concern
Pyrrole	1314	N	No safety concern
3-Ethylpyridine	1315	N	No safety concern
3-Acetylpyridine	1316	N	No safety concern
2,6-Dimethylpyridine	1317	N	No safety concern
5-Ethyl-2-methylpyridine	1318	N	No safety concern
2-Propionylpyrrole	1319	N	No safety concern
Methyl nicotinate	1320	N	No safety concern
2-(3-Phenylpropyl)pyridine	1321	N	No safety concern
2-Propylpyridine	1322	N	No safety concern

[a]N: new specifications prepared.

B. Aliphatic and alicyclic hydrocarbons

Flavouring agent	No.	Specifi-cations[a]	Conclusions based on current intake
Camphene	1323	N	No safety concern
beta-Caryophyllene	1324	N	No safety concern
d-Limonene	1326	N, T	ADI not specified[b]
Myrcene	1327	N	No safety concern
alpha-Phellandrene	1328	N	No safety concern
alpha-Pinene	1329	N	No safety concern
beta-Pinene	1330	N	No safety concern
Terpinolene	1331	N	No safety concern
Bisabolene	1336	N	No safety concern
Valencene	1337	N	No safety concern
3,7-Dimethyl-1,3,6-octatriene	1338	N	No safety concern
p-Mentha-1,3-diene	1339	N	No safety concern
p-Mentha-1,4-diene	1340	N	No safety concern
1,3,5-Undecatriene	1341	N	No safety concern
d-3-Carene	1342	N	No safety concern
Farnesene (alpha and beta)	1343	N	No safety concern
1-Methyl-1,3-cyclohexadiene	1344	N	No safety concern
beta-Bourbonene	1345	N	No safety concern
Cadinene (mixture of isomers)	1346	N	No safety concern
Guaiene	1347	N	No safety concern

[a]N: New specifications prepared.

[b] An ADI "not specified" was established for *d*-limonene by the Committee at its forty-first meeting (Annex 1, reference *107*), which was maintained at the present meeting.

C. Aromatic hydrocarbons

Flavouring agent	No.	Specifi-cations[a]	Conclusions based on current intake
p-Cymene	1325	N	No safety concern
Biphenyl	1332	N	No safety concern
p,alpha-Dimethylstyrene	1333	N	No safety concern
4-Methylbiphenyl	1334	N	No safety concern
1-Methylnaphthalene	1335	N	No safety concern

[a] N: new specifications prepared.

D. Aliphatic, linear α,β-unsaturated aldehydes, acids and related alcohols, acetals and esters

Flavouring agent	No.	Specifi-cations[a]	Conclusions based on current intake
Butyl 2-decenoate	1348	N	No safety concern
2-Decenal	1349	N	No safety concern
2-Dodecenal	1350	N	No safety concern
Ethyl acrylate	1351	N	No safety concern
Ethyl 2-nonynoate	1352	N	No safety concern
2-Hexenal	1353	N	No safety concern
2-Hexen-1-ol	1354	N	No safety concern
2-(E)Hexen-1-yl acetate	1355	N	No safety concern
Methyl 2-nonynoate	1356	N	No safety concern
Methyl 2-octynoate	1357	N	No safety concern
Methyl 2-undecynoate	1358	N	No safety concern
2-Tridecenal	1359	N	No safety concern
trans-2-Heptenal	1360	N	No safety concern
trans-2-Hexenoic acid	1361	N	No safety concern
2-Nonenal	1362	N	No safety concern
2-Octenal	1363	N	No safety concern
2-Pentenal	1364	N	No safety concern
trans-2-Nonen-1-ol	1365	N	No safety concern
2-Undecenal	1366	N	No safety concern
trans-2-Octen-1-yl acetate	1367	N	No safety concern

Flavouring agent	No.	Specifi-cations[a]	Conclusions based on current intake
trans-2-Octen-1-yl butanoate	1368	N	No safety concern
cis-2-Nonen-1-ol	1369	N	No safety concern
(E)-2-Octen-1-ol	1370	N	No safety concern
(E)-2-Butenoic acid	1371	N	No safety concern
(E)-2-Decenoic acid	1372	N	No safety concern
(E)-2-Heptenoic acid	1373	N	No safety concern
(Z)-2-Hexen-1-ol	1374	N	No safety concern
trans-2-Hexenyl butyrate	1375	N	No safety concern
(E)-2-Hexenyl formate	1376	N	No safety concern
trans-2-Hexenyl isovalerate	1377	N	No safety concern
trans-2-Hexenyl propionate	1378	N	No safety concern
trans-2-Hexenyl pentanoate	1379	N	No safety concern
(E)-2-Nonenoic acid	1380	N	No safety concern
(E)-2-Hexenyl hexanoate	1381	N	No safety concern
(Z)-3- & (E)-2-Hexenyl propionate	1382	N	No safety concern
(E)-2-Hexenal diethyl acetal	1383	N	No safety concern
2-Undecen-1-ol	1384	N	No safety concern

[a]N: new specifications prepared.

E. Monocyclic and bicyclic secondary alcohols, ketones and related esters

Flavouring agent	No.	Specifi-cations[a]	Conclusions based on current intake
Borneol	1385	N	No safety concern
Isoborneol	1386	N	No safety concern
Bornyl acetate	1387	N	No safety concern
Isobornyl acetate	1388	N	No safety concern
Bornyl formate	1389	N	No safety concern
Isobornyl formate	1390	N	No safety concern
Isobornyl propionate	1391	N	No safety concern
Bornyl valerate	1392	N	No safety concern
Bornyl isovalerate (endo-)	1393	N	No safety concern
Isobornyl isovalerate	1394	N	No safety concern
d-Camphor	1395	N	No safety concern
d-Fenchone	1396	N	No safety concern
Fenchyl alcohol	1397	N	No safety concern
Nootkatone	1398	N	No safety concern
1,3,3-Trimethyl-2-norbornanyl acetate	1399	N	No safety concern
Methyl jasmonate	1400	N	No safety concern
Cycloheptadeca-9-en-1-one	1401	N	No safety concern
3-Methyl-1-cyclopentadecanone	1402	N	No safety concern
2(10)-Pinen-3-ol	1403	N	No safety concern
Verbenol	1404	N	No safety concern
7-Methyl-4,4a,5,6-tetrahydro-2(3H)-naphthalenone	1405	N	No safety concern
3-Methyl-2-(n-pentanyl)-2-cyclopenten-1-one	1406	N	No safety concern
Dihydronootkatone	1407	N	No safety concern
3-L-Menthoxypropane-1,2-diol	1408	N	No safety concern
beta-Ionyl acetate	1409	N	No safety concern
alpha-Isomethylionyl acetate	1410	N	No safety concern
3-(l-Menthoxy)-2-methylpropane-1,2-diol	1411	N	No safety concern
Bornyl butyrate	1412	N	No safety concern
D,L-Menthol(+/-)-propylene glycol carbonate	1413	N	No safety concern
L-Monomenthyl glutarate	1414	N	No safety concern
L-Menthyl methyl ether	1415	N	No safety concern
p-Menthane-3,8-diol	1416	N	No safety concern

[a]N: new specifications prepared.

F. Amino acids and related substances

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
beta-Alanine	1418	N	No safety concern
L-Cysteine	1419	N	No safety concern[b]
L-Glutamic acid	1420	N	No safety concern[b,c]
Glycine	1421	N	No safety concern[b]
DL-Isoleucine	1422	N	No safety concern
L-Leucine	1423	N	No safety concern[b]
DL-Methionine	1424	N	No safety concern
L-Proline	1425	N	No safety concern[b]
DL-Valine	1426	N	No safety concern
DL-(3-Amino-3-carboxypropyl)dimethylsufonium chloride	1427	N	No safety concern
L-Phenylalanine	1428	N	No safety concern[b]
L-Aspartic acid	1429	N	No safety concern[b]
L-Glutamine	1430	N	No safety concern[b, c]
L-Histidine	1431	N	No safety concern[b]
DL-Phenylalanine	1432	N	No safety concern
L-Tyrosine	1434	N	No safety concern[b]
Taurine	1435	N	No safety concern
DL-Alanine	1437	N	No safety concern
L-Arginine	1438	N	No safety concern[b]
L-Lysine	1439	N	No safety concern[b]

[a] N: new specifications prepared. [b] Not evaluated using the Procedure for the Safety Evaluation of Flavouring Agents. The substance is a macronutrient and normal component of protein and, as such, human exposure through food is orders of magnitude higher than the anticipated level of exposure from use as flavouring agent. [c] The group ADI 'not specified' established at the thirty-first meeting for L-glutamic acid and its ammonium, calcium, magnesium, monosodium and potassium salts was maintained.

G. Tetrahydrofuran and furanone derivatives

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
2-Hexyl-4-acetoxytetrahydrofuran	1440	N	No safety concern
2-(3-Phenylpropyl)tetrahydrofuran	1441	N	No safety concern
Tetrahydrofurfuryl acetate	1442	N	No safety concern
Tetrahydrofurfuryl alcohol	1443	N	No safety concern
Tetrahydrofurfuryl butyrate	1444	N	No safety concern
Tetrahydrofurfuryl propionate	1445	N	No safety concern
4-Hydroxy-2,5-dimethyl-3(2H)-furanone	1446	N	No safety concern
Tetrahydrofurfuryl cinnamate	1447	N	No safety concern
2-Methyltetrahydrofuran-3-one	1448	N	No safety concern
2-Ethyl-4-hydroxy-5-methyl-3(2H)-furanone	1449	N	No safety concern
4-Hydroxy-5-methyl-3(2H)-furanone	1450	N	No safety concern
2,5-Dimethyl-4-methoxy-3(2H)-furanone	1451	N	No safety concern
2,2-Dimethyl-5-(1-methylpropen-1-yl)tetrahydrofuran	1452	N	No safety concern
2,5-Diethyltetrahydrofuran	1453	N	No safety concern
cis,trans-2-Methyl-2-vinyl-5-(2-hydroxy-2-propyl)tetrahydrofuran (Linalool oxide)	1454	N	No safety concern
5-Isopropenyl-2-methyl-2-vinyltetrahydrofuran (cis and trans mixture)	1455	N	No safety concern
4-Acetoxy-2,5-dimethyl-3(2H)furanone	1456	N	No safety concern
(+/-)-2-(5-Methyl-5-vinyl-tetrahydrofuran-2-yl)propionaldehyde	1457	N	No safety concern

[a] N: new specifications prepared.

H. phenyl-substituted aliphatic alcohols and related aldehydes and esters

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Ethyl 4-phenylbutyrate	1458	N	No safety concern
beta-Methylphenethyl alcohol	1459	N	No safety concern
2-Methyl-4-phenyl-2-butyl acetate	1460	N	No safety concern
2-Methyl-4-phenyl-2-butyl isobutyrate	1461	N	No safety concern
2-Methyl-4-phenylbutyraldehyde	1462	N	No safety concern
3-Methyl-2-phenylbutyraldehyde	1463	N	No safety concern
Methyl 4-Phenylbutyrate	1464	N	No safety concern
2-Methyl-3-(p-isopropylphenyl)propionaldehyde	1465	N	No safety concern
2-Methyl-3-tolylpropionaldehyde (mixed o-,m-, p-)	1466	N	No safety concern
2-Phenylpropionaldehyde	1467	N	No safety concern
2-Phenylpropionaldehyde dimethyl acetal	1468	N	No safety concern
2-Phenylpropyl butyrate	1469	N	No safety concern
2-Phenylpropyl isobutyrate	1470	N	No safety concern
2-(p-Tolyl)propionaldehyde	1471	N	No safety concern
5-Methyl-2-phenyl-2-hexenal	1472	N	No safety concern
4-Methyl-2-phenyl-2-pentenal	1473	N	No safety concern
2-Phenyl-2-butenal	1474	N	No safety concern
Ethyl 2-ethyl-3-phenylpropanoate	1475	N	No safety concern
2-Phenyl-4-pentenal	1476	N	No safety concern
2-Methyl-4-phenyl-2-butanol	1477	N	No safety concern
2-Oxo-3-phenylpropionic acid	1478	N	No safety concern
Sodium 2-oxo-3-phenylpropionate	1479	N,T	

[a] N: new specifications prepared; T: tentative specifications.

5. Flavouring agents considered for specifications only

No.	Flavouring agent	Specifications[a]
53	Citronellyl formate	63rd/R
55	Neryl formate	63rd/R
68	Rhodinyl butyrate	63rd/R
399	Methyl-beta-ionone	63rd/R
471	2,8-Dithianon-4-ene-4-carboxaldehyde	63rd/R
504	S-Methyl benzothioate	63rd/R
557	1-Mercapto-2-propanone	63rd/R
570	Propenyl propyl disulfide	63rd/R
605	1,3-Nonanediol acetate (mixed esters)	63rd/R
615	Butyl ethyl malonate	63rd/R
628	Ethyl aconitate (mixed esters)	63rd/R
631.2	Sodium salt of 3-methyl-2-oxobutanoic acid	63rd/S[b]
632.2	Sodium salt of 3-methyl-2-oxopentanoic acid	63rd/S[b]
633.2	Sodium salt of 4-methyl-2-oxopentanoic acid	63rd/S[b]
919	Glyceryl monooleate	63rd/R
1203	Ammonium isovalerate	63rd/R
1218	4-Ethyloctanoic acid	63rd/R
1263	Isoeugenyl phenylacetate	63rd/R
1273	Ethyl 5-hexenoate	63rd/R
1291	3-Mercapto-2-methylpentan-1-ol (racemic)	63rd/R
1296	spiro[2,4-Dithia-1-methyl-8-oxabicyclo(3.3.0)octane-3,3'-(1'-oxa-2'-methyl)-cyclopentane]	63rd/R

[a] R, existing specifications revised; S, existing specifications were maintained; T, the existing, new, or revised specifications are tentative and new information is required.

[b] Specifications will be withdrawn at the next meeting at which flavouring agents are discussed if no information becomes available by that time.

6. Evaluation of a natural constituent of food

Constituent	Toxicological recommendations
Glycyrrhizinic acid	Available data suggest that an intake of 100 mg per day would be unlikely to cause adverse effects in the majority of adults. In certain highly susceptible individuals, physiological effects could occur at exposure levels somewhat below this figure. The intake data indicate that consumers with a high intake of liquorice confectionery or herbal tea containing liquorice may be exposed to glycyrrhizinic acid at more than 100 mg/day.

Annex 1

Sixty-third meeting of the
Joint FAO/WHO Expert Committee on Food Additives (JECFA)
Geneva, 8-17 June 2004

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Annex 2

Further information required or desired

Magnesium sulfate

Further information is required by the end of 2006 on functional uses of magnesium sulfate, including their use levels, and on the commercial use of anhydrous magnesium sulfate.

Steviol glycosides

The Committee required additional information by 2007, on the pharmacological effects of steviol glycosides in humans. These studies should involve repeated exposure to dietary and therapeutic doses, in normotensive and hypotensive individuals and in insulin-dependent and insulin-independent diabetics. In order to be able to remove the tentative designation from the specifications, further information for commercially available products is required on:

- Analytical data on distribution and concentrations of all component steviol glycosides, including those that are not identified in these tentative specifications.
- Method of analysis for the determination of all component steviol glycosides, including those that are not identified in these tentative specifications;
- The nature and concentration of the fractions that do not contain steviol glycosides.
- The quantities of residual solvents from isolation and purification steps of the manufacturing process.
- The hydrolytic stability of the steviol glycosides in acidic foods and beverages.

Zeaxanthin-rich extract from Tagetes erecta L

Information is required on the non-zeaxanthin components in total carotenoids and on the composition of the non-carotenoid components.

Annex 3

An edited version of this section will appear in the report of the sixty-first 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. Estimating intake of flavouring agents

At its fifty-fifth meeting, the Committee considered the use of the *per capita* x 10 method for estimating the intake of flavouring agents according to the Procedure for the Safety Evaluation of Flavouring Agents, as well as alternative procedures. While the Committee concluded that its use of the method was appropriate, it acknowledged that it may, in some cases, result in an underestimate of the intake of persons with high levels of consumption of specific foods. The Committee also recognised at the forty-ninth meeting that further consideration may be required in certain cases where there is conflicting information on intake. At the present meeting, the Committee reaffirmed these conclusions.

The Committee recognized that the estimates of current intake that it uses in evaluating the safety of flavouring agents, according to the Procedure, are difficult to reconcile with reported maximum use levels for some flavouring agents in different food groups. To help understand the basis for the apparent discrepancy in the information available to the Committee, the Committee requested that industry provide precise data on the use levels of flavouring agents that may be used in food products that are not widely distributed and that may be eaten on a regular basis by specific population groups in specific regions of the world.

The Committee anticipates that estimating the intake of flavouring agents, especially those with particularly low or particularly high production volumes, will be considered at the forthcoming joint FAO/WHO workshop on exposure assessment to be held in 2004.

Combined exposure

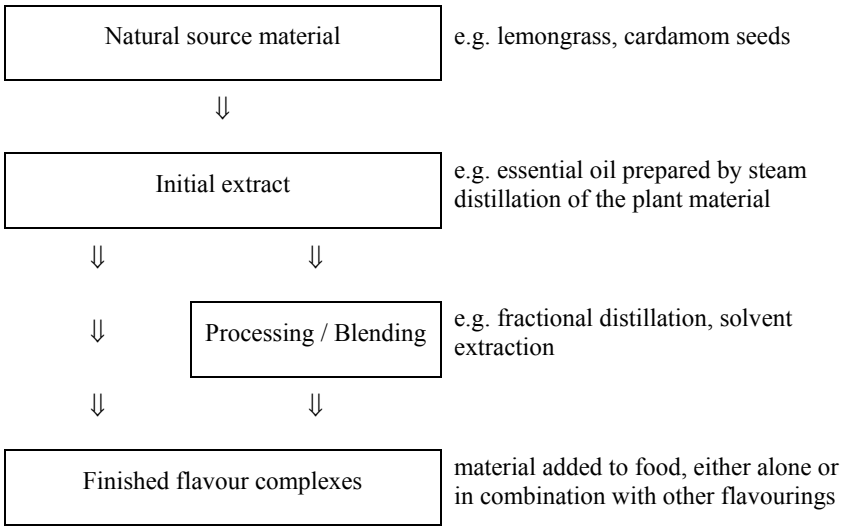
The Committee also recognised that the current procedure to estimate the combined intake for all congeners of one congeneric group of flavouring substances reflects an unlikely situation where the same individuals are consumers of all the substances. Nevertheless, this results in conservative estimates that allow evaluations to be completed. The Committee therefore recommends the establishment of a working group to develop a more adequate approach to be discussed during the next JECFA meeting that will include flavouring agents on the agenda.

2. Flavour complexes derived from natural sources

At this meeting, the Committee further considered a possible approach to the safety assessment of complex flavours derived from natural sources (usually from plant material) such as essential oils, oleoresins and solvent extracts. After considering the available data on three of the five flavour complexes originally included on the agenda – derived from essential oils of lemongrass, cardamom seed and bois de rose – the Committee defined the information that would be required in order to test the application of the revised Procedure for the Safety Evaluation of Flavouring Agents (Annex 1 Ref 131) which it had previously adopted for the safety evaluation of chemically-defined flavourings.

Background

Although these flavourings are typically named after the initial extract prepared from the source material, it is common practice for the initial extracts to be processed and refined in a variety of ways, to produce a range of flavour complexes with the specific properties desired for particular food applications. These processes might include distillation, concentration, solvent extraction and blending of extracts from different batches. Processing is generally carried out by flavour companies or, in certain cases, possibly by food manufacturers who use the finished flavours. The progression from source material to finished flavour is illustrated below:



The initial extracts are typically prepared from the plant material close to the point of production. Their composition may vary considerably at this level due to a variety of factors such as climate, geography, genotype and maturity of the source material. The flavour producer aims to supply flavour complexes with consistent technical and olfactory properties. This is primarily achieved by processing and blending to meet a target composition which is monitored by chemical analysis.

Although the finished flavour complexes are entirely derived from the original extract, using only physical processes such as those described above, their composition is likely to differ quantitatively from the initial extracts prepared directly from the source material.

The evaluation of finished flavour complexes is dependent upon:

(a) information on the composition of the material that is added to food (and hence on the elaboration of a reliable specification that covers the range of finished flavour complexes that may be derived from the initial extracts);

(b) safety evaluations of the individual components and congeneric groups

(c) estimates of intake of the finished flavour complexes and, hence of the individual components.

Compositional data necessary to support the safety evaluation of a finished flavour complex

i. General considerations

The safety evaluations of finished flavour complexes derived from natural sources would be based on the revised Procedure, with particular consideration of the major components and of congeneric groups. The analytical data should be adequate to apply the revised Procedure.

Intake should be taken into account in determining the extent to which chemical characterisation and identification of individual components is necessary, beyond those necessary to define their flavour characteristics. In applying the Revised Procedure for the Safety Evaluation of Flavouring Agents the estimated intake of the individual agent is compared with appropriate thresholds of toxicological concern to determine whether or not the intake represents a safety concern. The same numerical thresholds can be applied to the intakes of individual identified components and combinations of components, such as occur in congeneric groups, which are present in finished flavour complexes derived from natural sources. The same intake thresholds can also be used as a basis for establishing analytical requirements as described below.

The human intake thresholds of toxicological concern are of two types: thresholds of 1800, 540 and 90 µg /person per day which are applied for structural classes I, II and III, respectively, and a general threshold of 1.5µg/person per day applicable to all structural classes. The thresholds for classes I, II and III are based on the lower 5th percentile NOEL for the structural class, from toxicological studies in animals, divided by the usual 100-fold safety (uncertainty) factor. The general threshold (step B5 of the Procedure) is a pragmatic value based on an estimate of the human intake associated with a lifetime risk of cancer of less than 1 in a million calculated by linear-extrapolation from animal studies (Report of 46th Meeting). Because of the assumptions used in the derivation of this threshold, it is considered to be sufficiently conservative to cover all types of toxicity. The Committee considered that these thresholds can provide the basis for a pragmatic approach to the development of limits of sensitivity for analytical methods, when linked to reliable and validated estimates of intake, which should be derived from long-term average poundage.

ii. Consideration of individual components

Identified components

Based on step B5 of the Procedure, the Committee concluded there would be no significant safety concern if the intake for an identified component in a finished flavour complex derived from natural sources were less than 1.5 µg /person per day. This threshold can be used to establish a general limit for analytical characterization for components in a finished flavour complex under (b) below, based on the estimated intake of the complex. For example, if the estimated daily intake of the finished flavour complex is 150 µg /person per day, then there would be no safety concern for any component present at <1%. Similarly, if the estimated daily intake of the finished flavour complex is 15 µg /person per day, then there would be no safety concern for any component present at <10%. For high volume finished flavour complexes the limit for analytical characterisation would be set at 0.1-0.5% (see (b) below). Because the threshold is based on lifetime carcinogenicity data, the % should be the average value of the analyses, and not the highest single value.

Unidentified components

The chromatographic analysis of a finished flavour complex is likely to reveal the presence of a large number of unidentified minor components. Previously the Committee has not considered the general threshold of 1.5 µg /person per day for unidentified components. The Committee recognised that application of the general threshold to an unidentified component could not provide the same reassurance of safety as for structurally defined compounds, but considered that it could be incorporated into a pragmatic approach for establishing analytical requirements for finished flavour complexes derived from natural sources. This threshold combined with the estimated intake of the complex can be used to define a limit for the percentage of a chromatographic peak above which structural characterization would be necessary. For example, if the estimated daily intake of the finished flavour complex is 150µg/person per day, then chemical characterization would be required for any component present >1%, so that safety evaluation of the component could be undertaken.

Product descriptions and specifications

A key part of the safety assessment will be the preparation of appropriate specifications covering the relevant finished flavour complexes. As with all food additive evaluations, the purpose of specifications for flavour complexes is to identify the material, to ensure that it meets the criteria for safe use, and to encourage good manufacturing practice. Specifications should reflect the materials used throughout the world and should take account of existing specifications drawn up at national or international level.

The Committee noted the existence of internationally agreed specifications prepared by the International Organization for Standardization (ISO) for over 100 essential oils obtained by steam distillation of plant materials. Essential oils and derived products are numerically the largest group of flavour complexes. ISO standards describe the oils and define the acceptable ranges for various parameters, including the methods for measuring these values. Many of these standards include ranges for the key chemical components, accompanied by typical gas chromatograms that can be used to confirm the identity of the oils. The Committee concluded that these standards need to be taken into account when setting specifications for food flavourings, particularly when selecting the parameters to be included and the associated analytical methods.

In order to develop specifications for flavour complexes added to food, and to provide the data necessary for the safety evaluation to proceed, the Committee requires a full description of the range of source materials and processing conditions. Manufacturers should also provide the results of appropriate analyses carried out on samples of representative flavour complexes, accompanied by details of the analytical methods (including validation of the methods) and a full description of each sample, including the source materials and production processes. Manufacturers should also address the possible presence of undesirable compounds associated with the source material (or species with which it might be confused) and should provide sufficient information to differentiate the flavour complexes from other products with similar properties.

Standard information in the specifications for finished flavour complexes will include: descriptions of the source material(s), the derivation of the initial extract, and any subsequent processing stages; a physical description of the flavour complexes; information on solubility; and (for liquid products) specific gravity, refractive index and optical rotation.

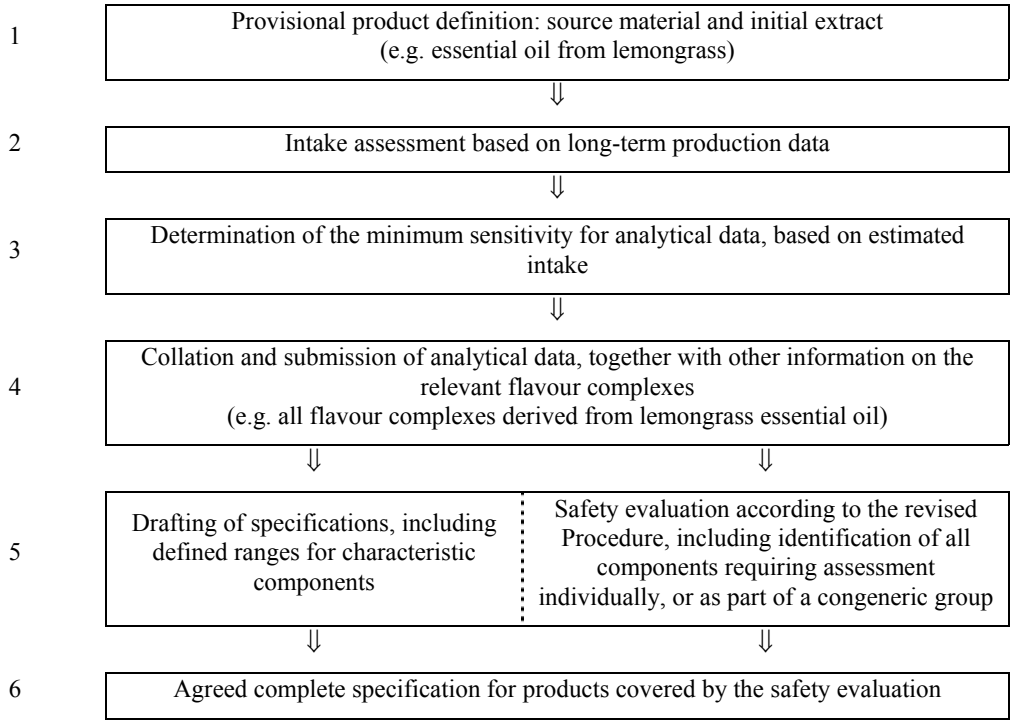
Specifications developed by the Committee will include the following information on composition, which is essential for the safety evaluation to proceed (see below).

(a) upper and lower concentrations of major characterising components, including all key constituents identified in relevant ISO standards and any other components considered to be critical for the organoleptic properties of the flavouring.

(b) a list of other components that may be present at or above a given level; the level will depend on the intake and the relevant threshold of toxicological concern (see above) in the revised Procedure for the Safety Evaluation of Flavouring Agents. Components present in the flavour complex at levels above 0.1-0.5% should be characterized if their estimated intake exceeds 1.5 µg/person per day. The need for more detailed characterization would be determined on a case-by-case basis depending on the nature of the starting material.

(c) upper limits for any other relevant components, including likely impurities and contaminants or potentially toxic components such as inherent toxins associated with any part of the source species or with related species with which it might be confused.

The overall scheme for evaluating finished flavour complexes is summarised in the following diagram:



The Committee requested data, in line with the above proposals, on examples of flavour complexes with a range of different constituents and representing different estimated intake levels in order to develop appropriate specifications and to evaluate the application of the revised Procedure to this type of flavouring agent. In particular, in the first detailed consideration of finished flavour complexes, quantitative data should be provided on the composition of representative samples of the selected flavour complexes, which allows the identification of all components present in the flavour complexes at levels above 0.1% and with an estimated intake of 1.5µg/day or more.

3. Evaluation of dietary nutrients and other ingredients

The Committee evaluated the safety of several substances that were claimed to have nutritional or health benefits. It was noted that there was increased interest in having the Committee evaluate such substances. The Committee noted that whether such products meet appropriate definitions as nutrients or are worthy of health, nutrient, or other claims was outside its remit. Therefore, the Committee only evaluated the safety of these ingredients. Moreover, the Committee expressed the view that the evaluation of the safety of these ingredients should not be interpreted to mean that the Committee endorses the use of these substances for their claimed nutritional or health benefits.

4. Determination of carotenoids

The Committee recognized that there is an increasing number of specifications for the analysis of members of the family of carotenoid compounds. Each specification prescribes the use of a different instrumental method of analysis. The Committee decided that it would be advantageous to consolidate and minimize the number of methods for the analysis of members of the carotenoid family and to publish them in FAO Food and Nutrition Paper, No. 5.

5. Revision of heavy metals and arsenic specifications

At its fifty-third meeting, the Committee agreed to implement the decision taken at its forty-ninth and fifty-first meetings, namely, to review and replace the limit test for heavy metals (as lead) and arsenic with, as appropriate, limits for the individual elements of concern in all existing specifications established by the Committee. In order to accomplish this, the Committee decided to review the existing specifications on the basis of functional use (e.g. antioxidant, preservative), and set a target of 5 years for completion of the task.

At its fifty-fifth and subsequent four meetings, the Committee reviewed all the specifications that had not been modified during previous meetings.

The principles adopted by the Committee in its reviews were as follows:

After removing the 'heavy metals (as lead)' specification, a maximum concentration of 2 mg/kg for lead and 1 mg/kg for cadmium and mercury would be established, except where there were data to support higher or lower maximum concentrations, or there were issues related to consumer exposure.

A limit for arsenic would only be included when the source from which the additive was prepared or the nature of the manufacturing method for the additive indicated that arsenic was likely to be a contaminant.

6. Core Standing Committee for JECFA

According to current procedure, JECFA is not a standing Committee. Members are selected for each meeting based on their expertise and according to the substances scheduled for evaluation. The Committee as such exists only during the actual time of the meeting which concludes with the adoption of the report.

In order to improve current working procedures and to facilitate the work of the Committee as well as of the Secretariats, the Joint Secretaries propose the establishment of a core JECFA Committee as a standing Committee for a period of three years. Chairs (one FAO and one WHO expert), rapporteurs (one FAO and WHO each) and four Members (two from FAO and WHO each) will be appointed by the secretariats according to WHO and FAO rules established for Expert Committees. The appointment of the Core JECFA Committee will be published on the JECFA websites.

The role of this standing committee is to ensure the continuity of the work of the Committee. Further responsibilities are to assist the secretariats in the following tasks: finalization of the agenda and formulation of appropriate call for data, identification of appropriate experts, and assignment of experts to specific substances for each meeting.

In addition, in agreement with the Secretariats, the Core Members may represent JECFA at specific meetings.

For each meeting additional Members will be appointed to the Committee according to existing procedures to cover all necessary expertise and to work with the Core Standing Committee in the evaluation of scheduled substances. All members of the Committee at the meeting have the same rights and responsibilities.

7. Provision of scientific advice by FAO and WHO

The Committee was informed about the advances on the consultative process carried out by FAO and WHO to enhance the procedures followed by both organizations for the provision of scientific advice to the Codex Alimentarius Commission and Member countries. In particular reference was made to the Joint FAO/WHO Workshop on the Provision of Scientific Advice to Codex and Member Countries held from 27 to 29 January 2004 which resulted in a set of recommendations on 1) essential principles, definitions and scope governing the provision of scientific advice, 2) management issues and 3) procedures and mechanism to be improved. The report of the Workshop is available on the websites of FAO (http://www.fao.org/es/ESN/proscad/index.en.stm) and WHO (http://www.who.int/foodsafety/en/).

The Committee noted that implementation of the recommendations will directly impact its work and that increased participation of experts from developing countries will require specific actions, for example, training on the operation of the Committee.

The Committee was informed that comments on the workshop recommendations received by FAO and WHO from their Member countries and international non-governmental organizations with observer status in Codex will be presented at the 27th session of the Codex Alimentarius Commission and that procedural guidelines on provision of scientific advice will be prepared and made public to increase transparency of the overall system. FAO/WHO will complete the consultative process and continue the implementation of the workshop recommendations depending on availability of resources.

8. IPCS Project on Dose–Response Modelling

The Committee was informed of the development of the project on dose–response modelling organized by the International Programme on Chemical Safety. The goal of this project is a state-of-the art review of dose–response modelling and its application in risk assessment, also harmonizing environmental and human health risk assessment. The outcome will be published in the Environmental Health Criteria document series. The Committee recognized the importance of this project with regard to chemical contaminants in food and endorsed the effort and urged its continuing support.