JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES
Fifty-first meeting
Geneva, 9-18 June 1998

SUMMARY AND CONCLUSIONS

A meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) was held in Geneva, Switzerland, from 9 to 18 June 1998. The purpose of the meeting was to evaluate certain food additives.

The findings of the Committee are summarized as follows:

Acceptable Daily Intakes (ADIs), other toxicological information, and information on intakes and specifications

Further toxicological studies and other information required or desired

General Consideration items

Professor R. Walker, Emeritus Professor of Food Science, School of Biological Sciences, University of Surrey, Guildford, Surrey, United Kingdom, served as Chairman. Dr. P.M. Kuznesof, Acting Deputy Director, Office of Premarket Approval, Center for Food Safety and Applied Nutrition, Food and Drug Administration, Washington, DC, USA, and Dr. Junshi Chen, Deputy Director, Institute of Nutrition and Food Hygiene, Chinese Academy of Preventive Medicine, Beijing, China, served as Vice-Chairmen.

Dr J. Paakkanen, Food Quality and Standards Service, Food and Nutrition Division, Food and Agriculture Organization of the United Nations, and Dr. J.L. Herrman, International Programme on Chemical Safety, World Health Organization, served as joint secretaries.

The present meeting was the fifty-first in a series of similar meetings. The tasks before the Committee were to (a) elaborate further principles for evaluating the safety of food additives; (b) undertake toxicological evaluations of certain food additives; (c) review and prepare specifications for selected food additives; and (d) assess the intake of selected food additives.

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.

Toxicological monographs or monograph addenda on most of the substances that were considered will be published in WHO Food Additives Series No. 42.

Specifications for the identity and purity of the compounds listed in Table 1 marked as N; N,T; R; or R,T will be published in FAO Food and Nutrition Paper Series 52, Addendum 6. Specifications for substances marked as S and S,T have been published previously in that series. However, if these specifications have not been adopted as Codex Advisory Specifications, they will be re-published in FAO Food and Nutrition Paper Series No. 52, Addendum 6.

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Table 1

Acceptable Daily Intakes (ADIs), other toxicological information, and information on intakes and specifications

1. Food additives

Substance	Specifications[1]	Acceptable Daily Intake (ADI) and other toxicological recommendations
Enzyme preparations		
alpha-Acetolactate decarboxylase	R	ADI "not specified"
Maltogenic amylase	R	ADI "not specified"
Flavouring agents		
trans-Anethole	S	0 – 2 mg/kg bw
Furfural	N	No ADI allocated[2]
Menthol	R	0 – 4 mg/kg bw
Food colours		
Curcumin	R,T	0 – 1 mg/kg bw (temporary)[3]
Riboflavin from genetically modified *Bacillus subtilis*	N	0 – 0.5 mg/kg bw (group ADI with synthetic riboflavin and riboflavin-5'-phosphate)
Glazing agent		
Mineral oil (medium- and low-viscosity)	R	
Class I[4]		0 – 1 mg/kg bw (temporary)[3]
Class II[5] and Class III[6]		0 – 0.01 mg/kg bw (group temporary ADI)[3]
Preservatives		
Calcium hydrogen sulfite[3]	S,T	
Calcium metabisulfite	O	
Calcium sulfite	O	
Potassium hydrogen sulfite	O	
Potassium metabisulfite[3]	R,T	Group ADI 0 – 0.7 mg/kg bw[7] as SO_2
Potassium sulfite[3]	R,T	
Sodium hydrogen sulfite[3]	R,T	
Sodium metabisulfite[3]	R,T	
Sodium sulfite[3]	R,T	
Sodium thiosulfate[3]	R,T	
Sulfur dioxide	R	

[1] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[2] Data were insufficient for establishing an ADI.

[3] See Table 2.

[4] Including P70(H) oil.

[5] Including N70(H) and N70(A) oils.

[6] Including P15(H), N15(H), and N10(A) oils.

[7] The Committee reiterated its recommendation made at the thirtieth meeting that, when a suitable alternative method of preservation exists, its use should be encouraged, particularly in those applications (e.g. control of enzymic browning in fresh salad vegetables) in which the use of sulfites may lead to high levels of acute exposure and which have most commonly been associated with life-threatening adverse reactions. Appropriate labelling would help to alert individuals who cannot tolerate sulfites.

Substance	Specifi-cations[8]	Acceptable Daily Intake (ADI) and other toxicological recommendations
Sweetening agent		
Stevioside	O	No ADI allocated[9]
Thickening agents		
Carrageenan	R	} Group ADI "not specified" (temporary)[10]
Processed *Eucheuma* seaweed	R	
Sodium carboxymethyl cellulose, enzymatically hydrolyzed	R	Group ADI "not specified"[11]
Miscellaneous substances		
gamma-Cyclodextrin	N	ADI "not specified" (temporary)[9]
Glucono *delta*-lactone	R	
Calcium gluconate	R	
Magnesium gluconate	R,T	} Group ADI "not specified" for glucono-*delta*-lactone and gluconates
Potassium gluconate	R	
Sodium gluconate	R	
Polyglycitol syrup	N	Group ADI "not specified"[12]

[8] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[9] An ADI could not be established because the data were insufficient and because specifications were not prepared.

[10] See Table 2.

[11] Included in the group ADI for modified celluloses: ethyl cellulose, ethylhydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, methyl cellulose, methyl ethyl cellulose, and sodium carboxymethyl cellulose.

[12] Group ADI for materials conforming to the specifications for polyglycitol syrup and maltitol syrup.

2. Substances evaluated using the Procedure for the Safety Evaluation of Flavouring Agents

A. Flavouring agents evaluated toxicologically and considered for specifications

Flavouring agent	No.	Specifications[13]	Conclusions based on current levels of intake
Saturated aliphatic acyclic secondary alcohols, ketones, and related saturated and unsaturated esters			
Acetone	0139	N	} No safety concern
Isopropyl alcohol	0277	N	
2-Butanone	0278	N	
2-Pentanone	0279	N	
2-Pentanol	0280	N	
3-Hexanone	0281	N	} No safety concern
3-Hexanol	0282	N	
2-Heptanone	0283	N	
2-Heptanol	0284	N	
3-Heptanone	0285	N	
3-Heptanol	0286	N	} No safety concern
4-Heptanone	0287	N	
2-Octanone	0288	N	
2-Octanol	0289	N	
3-Octanone	0290	N	
3-Octanol	0291	N	} No safety concern
2-Nonanone	0292	N	
2-Nonanol	0293	N	
3-Nonanone	0294	N	
3-Decanol	0295	N	
2-Undecanone	0296	N	} No safety concern
2-Undecanol	0297	N	
2-Tridecanone	0298	N	
2-Pentadecanone	0299	N,T	
3-Methyl-2-butanol	0300	N	
4-Methyl-2-pentanone	0301	N,T	} No safety concern
2,6-Dimethyl-4-heptanone	0302	N,T	
2,6-Dimethyl-4-heptanol	0303	N	
Isopropyl formate	0304	N,T	
Isopropyl acetate	0305	R	
Isopropyl propionate	0306	N	} No safety concern
Isopropyl butyrate	0307	N	
Isopropyl hexanoate	0308	N	
Isopropyl isobutyrate	0309	N	
Isopropyl isovalerate	0310	N	
Isopropyl myristate	0311	N	} No safety concern
Isopropyl tiglate	0312	N	
3-Octyl acetate	0313	N	
1-Ethylhexyl tiglate (3-octyl tiglate)	0448	N	

[13] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

Flavouring agent	No.	Specifi-cations[14]	Conclusions based on current levels of intake
Linear and branched-chain aliphatic unsaturated non-conjugated alcohols, aldehydes, acids, and related esters			
4-Pentenoic acid	0314	N	} No safety concern
cis-3-Hexen-1-ol	0315	N	
cis-3-Hexenal	0316	N,T	
3-Hexenoic acid	0317	N	
4-Hexen-1-ol	0318	N	
cis-4-Hexenal	0319	N,T	} No safety concern
4-Heptenal	0320	N	
cis-3-Octen-1-ol	0321	N	
cis-5-Octen-1-ol	0322	N	
cis-5-Octenal	0323	N	
cis-6-Nonen-1-ol	0324	N	} No safety concern
cis-6-Nonenal	0325	N	
4-Decenal	0326	N	
5&6-Decenoic acid	0327	N	
9-Decenoic acid	0328	N	
9-Undecenal	0329	N,T	} No safety concern
10-Undecenal	0330	N	
10-Undecenoic acid	0331	N,T	
Linoleic acid	0332	N	
Oleic acid[15]	0333	N	
Methyl 3-hexenoate	0334	N,T	} No safety concern
Ethyl 3-hexenoate	0335	N	
cis-3-Hexenyl *cis*-3-hexenoate	0336	N	
Methyl *cis*-4-octenoate	0337	N,T	
Ethyl *cis*-4-octenoate	0338	N,T	
Ethyl *cis*-4,7-octadienoate	0339	N	} No safety concern
Methyl 3-nonenoate	0340	N	
Ethyl *trans*-4-decenoate	0341	N,T	
Methyl 9-undecenoate	0342	N,T	
Ethyl 10-undecenoate	0343	N	
Butyl 10-undecenoate	0344	N	} No safety concern
Ethyl oleate	0345	N	
Methyl linoleate & methyl linolenate (mix)	0346	N	
2-Methyl-3-pentenoic acid	0347	N,T	
2,6-Dimethyl-6-hepten-1-ol	0348	N,T	
2,6-Dimethyl-5-heptenal	0349	N	} No safety concern Evaluation deferred[16]
Ethyl 2-methyl-3-pentenoate	0350	N,T	
Ethyl 2-methyl-4-pentenoate	0351	N	
Hexyl 2-methyl-3&4-pentenoate	0352	N,T	
Ethyl 2-methyl-3,4-pentadienoate	0353	N,T	
Methyl 3,7-dimethyl-6-octenoate	0354	N	} No safety concern
2-Methyl-4-pentenoic acid	0355	N	

[14] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[15] The ADIs "not specified" for the calcium, potassium, and sodium salts of oleic acid established at the thirty-third meeting of the Committee were maintained.

[16] The evaluation of ethyl 2-methyl-3,4-pentadienoate was deferred pending review of a 90-day toxicity study that was not available at the meeting.

Flavouring agent	No.	Specifi-cations[17]	Conclusions based on current levels of intake
Aliphatic acyclic and alicyclic terpenoid tertiary alcohols and structurally related substances			
Linalool[18]	0356	R	} No safety concern
Tetrahydrolinalool	0357	N,T	
Linalyl formate	0358	N	
Linalyl acetate	0359	R	
Linalyl propionate	0360	N	
Linalyl butyrate	0361	N	} No safety concern
Linalyl isobutyrate	0362	N	
Linalyl isovalerate	0363	N	
Linalyl hexanoate	0364	N	
Linalyl octanoate	0365	N	
alpha-Terpineol	0366	N	} No safety concern
Terpinyl formate	0367	N	
Terpinyl acetate	0368	N	
Terpinyl propionate	0369	N	
Terpinyl butyrate	0370	N	
Terpinyl isobutyrate	0371	N,T	} No safety concern
Terpinyl isovalerate	0372	N,T	
p-Menth-3-en-1-ol	0373	N,T	
4-Carvomenthenol	0439	N,T	
p-Menth-8-en-1-ol (*beta*-terpineol)	0374	N	
2-Ethyl-1,3,3-trimethyl-2-norbornanol	0440	N,T	} No safety concern Additional data required
4-Thujanol	0441	N	
Methyl 1-acetoxycyclohexyl ketone	0442	N,T	

[17] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[18] The group ADI of 0-0.5 mg/kg bw established at the twenty-third meeting for citral, geranyl acetate, citronellol, linalool, and linalyl acetate, expressed as citral,

Flavouring agent	No.	Specifi-cations[19]	Conclusions based on current levels of intake
Carvone and structurally related substances			
p-Menthan-2-one	0375	N	
p-Menthan-2-ol	0376	N	
Dihydrocarvone	0377	N	} No safety concern
Dihydrocarveol	0378	N	
Dihydrocarvyl acetate	0379	N	
(+)Carvone[20]	0380a	R	
(-)Carvone	0380b	R,T	
Carveol	0381	N	} No safety concern
Carvyl acetate	0382	N	
Carvyl propionate	0383	N	

Flavouring agent	No.	Specifi-cations[1]	Conclusions based on current levels of intake
Ionones and structurally related substances			
beta-damascone	0384	N,T	
alpha-Damascone	0385	N,T	
delta-Damascone	0386	N	} No safety concern
Damascenone	0387	N	
alpha-Ionone[21]	0388	R	
beta-Ionone[3]	0389	R	
gamma-Ionone	0390	N	
alpha-Ionol	0391	N	} No safety concern
beta-Ionol	0392	N	
Dihydro-*alpha*-ionone	0393	N	
Dihydro-*beta*-ionone	0394	N,T	
Dihydro-*beta*-ionol	0395	N	
Dehydrodihydroionone	0396	N,T	} No safety concern
Dehydrodihydroionol	0397	N,T	
Methyl *alpha*-ionone	0398	N,T	
Methyl *beta*-ionone	0399	N	
Methyl *delta*-ionone	0400	N,T	
Allyl *alpha*-ionone	0401	N	} No safety concern
1,4-Dimethyl-4-acetyl-1-cyclohexene	0402	N,T	
alpha-Irone	0403	N	
alpha-iso-Methylionone	0404	N	No safety concern

[19] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[20] The ADI of 0-1 mg/kg bw previously established for (+) carvone at the thirty-seventh meeting was maintained.

[21] The group ADI of 0.1 mg/kg bw for *alpha*-ionone and *beta*-ionone established at the twenty-eighth meeting was maintained.

Flavouring agent	No.	Specifi-cations[22]	Conclusions based on current levels of intake
Aliphatic acyclic and alicyclic *alpha*-diketones and related substances			
Acetoin	0405	N	
2-Acetoxy-3-butanone	0406	N	
Butan-3-one-2-yl butanoate	0407	N	} No safety concern
Diacetyl	0408	N	
3-Hydroxy-2-pentanone	0409	N	
2,3-Pentanedione	0410	N	
4-Methyl-2,3-pentanedione	0411	N	
2,3-Hexanedione	0412	N	} No safety concern
3,4-Hexanedione	0413	N	
5-Methyl-2,3-hexanedione	0414	N	
2,3-Heptanedione	0415	N	
5-Hydroxy-4-octanone	0416	N	
2,3-Undecadione	0417	N	} No safety concern
Methylcyclopentenolone	0418	N	
Ethylcyclopentenolone	0419	N	
3,4-Dimethyl-1,2-cyclopentanedione	0420	N	
3,5-Dimethyl-1,2-cyclopentanedione	0421	N,T	
3-Ethyl-2-hydroxy-4-methylcyclopent-2-en-1-one	0422	N	} No safety concern
5-Ethyl-2-hydroxy-3-methylcyclopent-2-en-1-one	0423	N	
2-Hydroxy-2-cyclohexen-1-one	0424	N	
1-Methyl-2,3-cyclohexadione	0425	N	} No safety concern
2-Hydroxy-3,5,5-trimethyl-2-cyclohexen-1-one	0426	N	

Flavouring agent	No.	Specifi-cations[1]	Conclusions based on current levels of intake
Menthol and structurally related substances			
Menthol[23]	0427	R	
(+)neo-Menthol	0428	N,T	
Menthone	0429	N	} No safety concern
(±)Isomenthone	0430	N	
Menthyl acetate	0431	N	
Menthyl isovalerate	0432	N	
(-)Menthyl lactate	0433	N	
p-Menth-1-en-3-ol	0434	N,T	} No safety concern
Piperitone	0435	N	
(-)Menthol ethylene glycol carbonate	0443	N	
(-)Menthol 1- and 2-propylene glycol carbonate	0444	N	
(-)Menthone 1,2-glycerol ketal	0445	N	
(±)Menthone 1,2-glycerol ketal	0446	N	} No safety concern
mono-Menthyl succinate	0447	N	

[22] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[23] An ADI of 0 – 4 mg/kg bw was established for menthol at the present meeting (see section 1 of this table).

B. Flavouring agents considered for specifications only

Flavouring agent	No.	Specifications[24]	Flavouring agent	No.	Specifications[1]
Saturated aliphatic acyclic branched-chain primary alcohols, aldehydes, and acids[25]			**Saturated aliphatic acyclic branched-chain primary alcohols, aldehydes, and acids[2]**		
Isobutyl alcohol	0251	R	5-Methylhexanoic acid	0266	N
Isobutyraldehyde	0252	N	2-Ethyl-1-hexanol	0267	N
Isobutyric acid	0253	N	3,5,5-Trimethyl-1-hexanol	0268	N
2-Methylbutyraldehyde	0254	N	3,5,5-Trimethylhexanal	0269	N
2-Methylbutyric acid	0255	N	2-Methyloctanal	0270	N
2-Ethylbutyraldehyde	0256	N	4-Methyloctanoic acid	0271	N,T
2-Ethylbutyric acid	0257	N	3,7-Dimethyl-1-octanol	0272	N
3-Methylbutyraldehyde	0258	N	2,6-Dimethyloctanal	0273	N
Isovaleric acid	0259	N	4-Methylnonanoic acid	0274	N
2-Methylpentanal	0260	N,T	2-Methylundecanal	0275	N
2-Methylvaleric acid	0261	N			
3-Methylpentanoic acid	0262	N			
3-Methyl-1-pentanol	0263	N			
4-Methylpentanoic acid	0264	N			
2-Methylhexanoic acid	0265	N			

Flavouring agent	No.	Specifications[1]	Flavouring agent	No.	Specifications[1]
Aliphatic lactones[2]			**Aliphatic lactones[2]**		
4-Hydroxybutyric acid lactone (*gamma-b*utyrolactone)	0219	N	6-Hydroxy-3,7-dimethyloctanoic acid lactone	0237	N
gamma-Valerolactone			*delta*-Tetradecalactone	0238	N
4-Hydroxy-3-pentenoic acid	0220	N	*omega*-Pentadecalactone	0239	N,T
lactone	0221	N	*omega*-6-Hexadecenlactone	0240	N
			epsilon-Decalactone	0241	N,T
			epsilon-Dodecalactone	0242	N
5-Ethyl-3-hydroxy-4-methyl-2(5H)-furanone	0222	N	4,5-Dimethyl-3-hydroxy-2,5-dihydrofuran-2-one	0243	N
gamma-Hexalactone	0223	N	3-Heptyldihydro-5-methyl-2(3H)-furanone	0244	N
delta-Hexalactone	0224	N			
gamma-Heptalactone	0225	N	5-Hydroxy-2,4-decadienoic acid	0245	N
gamma-Octalactone	0226	N	*delta*-lactone		

[24] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[25] These substances were evaluated at the forty-ninth meeting of JECFA in June 1997.

Flavouring agent	No.	Specifi-cations[1]	Flavouring agent	No.	Specifi-cations[1]
Aliphatic lactones[2]			**Aliphatic lactones[2]**		
4,4-Dibutyl-*gamma*-butyrolactone	0227	N	5-Hydroxy-2-decenoic acid *delta*-lactone	0246	N
delta-Octalactone	0228	N	5-Hydroxy-7-decenoic acid *delta*-lactone	0247	N,T
gamma-Nonalactone	0229	R			
Hydroxynonanoic acid, *delta*-lactone	0230	N	5-Hydroxy-8-undecenoic acid *delta*-lactone	0248	N,T
gamma-Decalactone	0231	N	*cis*-4-Hydroxy-6-dodecenoic acid lactone (1,4-dodec-6-enolactone)	0249	N,T
			gamma-Methyldecalactone	0250	N
delta-Decalactone	0232	N	Mixture of 5-hydroxy-2-decenoic acid *delta*-lactone, 5-hydroxy-2-dodecenoic acid *delta*-lactone, and 5-hydroxy-2-tetradecenoic acid *delta*-lactone	0276	O
gamma-Undecalactone	0233	R			
5-Hydroxyundecanoic acid lactone	0234	N			
gamma-Dodecalactone	0235	N			
delta-Dodecalactone	0236	N	4-Hydroxy-3-methyloctanoic acid *gamma*-lactone	0437	N
			5-Hydroxy-2-dodecenoic acid *delta*-lactone	0438	N

3. Food additives considered for specifications only

Food additive	Specifi-cations[26]	Food additive	Specifi-cations[1]
Acetone (extraction solvent)	R	Gum arabic	R
Aluminium powder	R	Hexane	R
Calcium propionate	S	4-Hexylresorcinol	R
Calcium sorbate	R	Isobutyl alcohol (extraction solvent)	R
Canthaxanthin	R	Methyl *p*-hydroxybenzoate	R
Carnauba wax	R	Microcrystalline cellulose	R
Carob bean gum	R	Nitrogen	R
Carotenes (algal)	R	Petroleum jelly	R
Carotenes (vegetable)	R	Polydextroses	R
Carthamus red	R	Potassium sorbate	R
Carthamus yellow	R	Propan-2-ol	R
Citric acid	R,T	Propionic acid	R
Cochineal extract	R	Propyl *p*-hydroxybenzoate	R
Diacetyltartaric and fatty acid esters of glycerol (DATEM)	R	Shellac	R
		Sodium sorbate	O
Dichloromethane	R	Sorbitan monolaurate	R
Ethyl *p*-hydroxybenzoate	R	Sucrose esters of fatty acids	R
Ferrous gluconate	R,T	Talc	R
Ferrous sulfate	R,T	Tartaric, acetic & fatty acid esters of glycerol, mixed	W
Furfuryl alcohol (flavouring agent)	N		
Guar gum	R	Thaumatin	R,T
		Xanthan gum	R

[26] N, new specifications prepared; O, no specifications prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; T, the existing, new or revised specifications are tentative and comments are invited; W, existing specifications withdrawn.

[2] These substances were evaluated at the forty-ninth meeting of the Committee in June 1997.

4. Food additives considered for evaluation of national intake assessments

Substance	Conclusions	Recommendations to CCFAC[1]
Benzoates	Intake estimates based on GSFA[2] levels and range of foods in which use is allowed integrated with national food consumption data exceed the ADI of 0-5 mg/kg bw for mean consumers for the three countries[3] submitting such data. In national data submitted from nine countries[3] mean intake estimates for consumers of benzoate did not exceed the ADI. The potential exists for high consumers of benzoate to exceed the ADI, but the available data were insufficient to estimate the number of high consumers or the magnitude and duration of intake above the ADI.	Review draft GSFA additive levels for: Category 1.6.2 Ripened cheese Category 1.6.4 Processed cheese Category 1.6.5 Cheese analogues Category 4.2.2.3 Vegetables in vinegar/brine Category 9.2.4.2 Crangon crangon/vulgaris Category 9.3 Fish products, semi-preserved Category 10.2.1 Liquid eggs Category 14.1.4.1 Carbonated water-based soft drinks
Butylated hydroxy-anisole (BHA)	Intake estimates based on GSFA[2] levels and range of foods in which use is allowed integrated with national food consumption data exceed the ADI of 0-0.5 mg/kg bw for mean consumers for the three countries[3] submitting such data. In national data submitted from ten countries[3] mean intake estimates for consumers of BHA did not exceed the ADI of 0-0.5 mg/kg bw. The potential exists for high consumers of BHA to exceed the ADI, but the available data were insufficient to estimate the number of high consumers or the magnitude and duration of intake above the ADI.	Review draft GSFA additive levels for: Category 2 Edible fats and oils Category 4.2.2.2 Dried vegetables Category 4.1.3 Cocoa products Category 8.3.1 Processed comminuted meat Category 9.2.1 Frozen fish, fillets & products Category 12.5.1 Ready to eat soup and broths Category 13.6 Food supplements
Butylated hydroxy-toluene (BHT)	Intake estimates based on GSFA[2] levels and range of foods in which use is allowed integrated with national food consumption data exceed the ADI of 0-0.3 mg/kg bw for mean consumers for the three countries[3] submitting such data. In national data submitted from ten countries mean and high intake estimates for consumers of BHT did not exceed the ADI.	Review draft GSFA additive levels for: Category 2 Edible fats and oils Category 5.3 Chewing gum Category 9.2 Fish & fish products

[1] Recommendations to the Codex Committee on Food Additives and Contaminants (CCFAC) to review additive levels for benzoates, BHA, BHT, sulfites and TBHQ in the proposed draft General Standard on Food Additives (GSFA) for specified foods.

[2] Intake estimates derived using GSFA additive levels integrated with national food consumption data will grossly overestimate actual intakes in any one country because the GSFA levels are generally compiled by adopting the highest level of use for any one food category submitted by Member States or non-government organizations. The range of food uses specified in the GSFA is also usually much wider than in national standards.

[3] Eleven countries made submissions: Australia, New Zealand, Brazil, China, Finland, Spain, India, France, USA, UK and Japan (two countries, Australia and New Zealand, made a joint submission).

Substance	Conclusions	Recommendations[1]
Sulfites	Intake estimates based on GSFA[2] levels and range of foods in which use is allowed integrated with national food consumption data exceed the ADI of 0-0.7 mg/kg bw for mean consumers for the three countries[3] submitting such data. In national data submitted from ten countries [2] mean intake estimates for consumers of sulfite did not exceed the ADI. The potential exists for high consumers of sulfite to exceed the ADI, but the available data were insufficient to estimate the number of high consumers or the magnitude and duration of intake above the ADI.	Review draft GSFA additive levels for: Category 4.1.2.2 Dried fruits Category 4.1.2.5 Jams, jellies, marmalades Category 4.1.2.8 Fruit prep, incl pulp & fruit toppings Category 4.2.2.2 Dried vegetables Category 4.2.2.5 Vegetable, nut & seed purees & spreads Category 11.1 White & semi-white sugar Category 14.1.2.3 Concentrates for fruit juice Category 14.2.3, 14.2.4 Wines, Fruit wines
tert-Butyl-hydro-quinone (TBHQ)	Intake estimates based on GSFA[2] levels and range of foods in which use is allowed with national food consumption data exceed the ADI of 0-0.7 mg/kg bw for mean consumers for the three countries[3] submitting such data. In national data submitted from six countries[3] mean intake estimates for consumers of TBHQ did not exceed the ADI. The potential exists for high consumers of TBHQ to exceed the ADI, but the available data were insufficient to estimate the number of high consumers or the magnitude and duration of intake above the ADI.	Review draft GSFA additive levels for: Category 2 Edible fats and oils Category 9.2 Fish & fish products Category 14.1.4.1 Carbonated water-based soft drinks

[1] Recommendations to the Codex Committee on Food Additives and Contaminants (CCFAC) to review additive levels for benzoates, BHA, BHT, sulfites and TBHQ in the proposed draft General Standard on Food Additives (GSFA) for specified foods.

[2] Intake estimates derived using GSFA additive leve

integrated with national food consumption data will grossly overestimate actual intakes in any one country because the GSFA levels are generally compiled by adopting the highest level of use for any one food category submitted by Member States or non-government organizations. The range of food uses specified in the GSFA is also usually much wider than in national standards.

[3] Eleven countries made submissions: Australia, New Zealand, Brazil, China, Finland, Spain, India, France, USA, UK and Japan (two countries, Australia and New Zealand, made a joint submission).

Table 2

FURTHER TOXICOLOGICAL STUDIES AND OTHER INFORMATION REQUIRED OR DESIRED

Flavouring agent

Furfural

Before reviewing the substance again, the Committee would wish to have the following:

1. *In vivo* studies investigating DNA binding or adduct formation to clarify whether furfural interacts with DNA in mice.

2. A 90-day study in rats to identify a no-observed-effect level (NOEL) for hepatotoxicity.

Food colour

Curcumin

Results of a study of reproductive toxicity on a substance complying with the specifications for curcumin and information on the need and technological justification for alternative solvents for use in the current manufacturing processes of curcumin are required for evaluation in 2001.

Glazing agent

Mineral oil (medium- and low-viscosity)

Information requested at the forty-fourth meeting of the Committee is required for evaluation in 2002. This includes information about the compositional factors in mineral oils that influence their absorption and toxicity and a study in F344 rats of at least one year duration with a reversal period of one year. In addition, research on the pharmacokinetics of mineral oils and their potential effects on immune function known to be in progress should be submitted for review at that time.

Preservatives

Calcium hydrogen sulfite

The existing specifications were maintained and designated “tentative”. Information is required regarding a modified naming of the compound to be more reflective of its physical properties; the extent of and functionality of its use as a food addtive; and the need for selenium and arsenic limits, and associated analytical methods. This information is required by 30 November 1998.

Potassium metabisulfite, potassium sulfite, sodium hydrogen sulfite, and sodium metabisulfite

Information on iron and selenium levels in commercial products and on the test method for selenium is required by 30 November 1998. The existing specifications include a selenium limit for which the test method is no longer feasible because of lack of availability of required reagents. The Committee also questioned the need for selenium limit because new processes in sulfur production as a by-product of the oil industry have replaced extraction methods from sulfur mines. The Committee noted that the selenium limit may no longer be necessary and requested information in this regard.

Sodium sulfite

Information on the sources of raw materials, on the commercial use of sodium sulfite heptahydrate in food, on iron and selenium levels in commercial products, and on test methods for selenium is required by 30 November 1998.

Sodium thiosulfate

Information on iron and selenium levels in commercial products and on test methods for lead and selenium is required by 30 November 1998.

Sweetening agent

Thaumatin

Information on a specific identification test is required by 30 November 1998.

Thickening agents

Carrrageenan and processed *Eucheuma* seaweed

Clarification of the significance of the promotion of colon cancer observed in experiments in rats is required for evaluation in 2001.

Miscellaneous substances

Citric acid

Information on the need for an oxalate test and a suitable limit is required by 30 March 1999. Comments are also invited on the new sulfate test. If no information is forthcoming, the Committee will consider retaining the specifications as they appear in the monograph to be published in FAO Food and Nutrition Paper No. 52, Addendum 6, which is expected to appear in December 1998.

***gamma*-Cyclodextrin**

A study of human tolerance known to have been conducted should be reviewed in 1999 in order to confirm the absence of adverse gastrointestinal symptoms at normal levels of intake.

Ferrous gluconate

Information on the need for maintaining the limit test for oxalic acid and the maximum limit for mercury as well as the procedure for mercury analysis, if applicable, and for the introduction of maximum limits for sulfate and chloride, is required by 30 November 1998.

Ferrous sulfate

Information on the mercury limit as well as the procedure for mercury analysis and on water content is required by 30 November 1998.

Magnesium gluconate

Information on the need for maintaining the microbiological criteria included in the specifications and on the need for introducing maximum limits for chloride and sulfate is required by 30 November 1998.

Annex 1

General consideration items

An edited version of these sections will appear in the report of the fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). They are reproduced here so that the information is disseminated quickly. This draft is subject to extensive editing.

1. Literature surveys

The Committee expects sponsors of food additives to include in their dossiers relevant published papers that are identified in literature surveys. However, it is not always clear when information is submitted to what extent the literature has been surveyed. Sponsors should perform a comprehensive literature search and indicate its origin and extent. These searches should encompass the databases scanned, the years covered and the search strategy employed including the key words used. This will permit authors of working papers and those doing independent literature surveys for the Committee to focus their own searches more productively.

2. Microbiological criteria in food additive specifications monographs

In some instances, particularly for products of natural origin, the Committee has included microbiological criteria in the specifications monograph. At the present meeting, the Committee agreed to the appropriateness of establishing a policy for setting microbiological criteria. The Committee therefore established the following policy.

Policy on microbiological criteria

Food additive manufacturers are expected in general to use good manufacturing practices and to establish microbiological controls in production processes as necessary. This is to ensure that food additives are not contaminated with pathogenic or other undesirable organisms or microbial metabolites and that the food additive is otherwise suitable for its intended use. Such a requirement will be included in the monograph when the Committee recognizes the need for microbiological criteria for an individual substance.

The committee will consider, on a case-by-case basis, the following factors when developing microbiological criteria for food additives:

- the origin of the food additive (plant, animal, microbially derived via fermentation, or natural mineral source);
- evidence of a health hazard or potential hazard based on epidemiological data, hazard analysis, or known user-specific populations that may be at risk;
- the nature of the natural and commonly acquired microflora of the food additive and the ability of the food additive to support its growth;
- the effect of further processing on the microflora of the food additive;
- the potential for microbial contamination and/or growth in a food additive during its procurement, processing, handling, storage, and distribution;
- the state in which the food additive is packaged, stored, and distributed (e.g., frozen, refrigerated, heat processed); and
- the potential for direct consumer use.

Any one of these factors may signal the need to consider establishing microbiological criteria for a food additive.

3. Specifications for flavouring agents

Specifications for 231 flavouring agents were developed at the meeting. These included 224 substances that were originally placed on the agenda (numbered 139 for acetone and 219 to 442 for

the remainder) and a further eight that were added to the agenda at the meeting. (numbered 443 to 451). No information was provided on substance 436 (3-(1-menthoxy)propane-1,2-diol), which was not considered further. The specifications included a number of substances that were previously described in separate monographs, and the new specifications have the effect of replacing these for flavouring uses of the substances.

Forty-four specifications were classified as tentative because not all the necessary relevant information had been provided. Many of the flavouring agents examined at the present meeting were more complex than those considered previously, and sponsors were asked to examine the specifications carefully to ensure that all relevant information is available and to correct any information that does not accurately represent flavouring agents that are on the market.

As at previous meetings, identification of most of the flavouring agents was based on infrared spectra. However, this may not always be the method of choice because the infrared spectra of closely related substances may be indistinguishable, even in the fingerprint region. The Committee would welcome further comments on this point, in particular on the possible merits of using more sophisticated methods such as mass spectrometry and/or nuclear magnetic resonance (NMR) spectroscopy.

4. Specifications for vitamins and minerals

At the present meeting the Committee was requested by FAO to develop food-grade specifications for ferrous sulfate for use in food fortification. Vitamins and minerals do not fall within the scope of the Committee's traditional definition of the term *food additive*;[27] nonetheless, FAO receives repeated requests for food-grade specifications for substances used in food fortification.

Although the Committee has prepared specifications for approximately 40 traditional food additives that also have incidental uses as vitamins and minerals, more than 60 substances remain for which internationally recognized food-grade specifications are lacking.[28] It was agreed that such substances would normally be on the agenda for the development of specifications only. In certain cases, however, it may be necessary to undertake toxicological evaluations as well, for example when novel forms of nutrients are involved.[29]

5. Enzyme preparations from genetically modified microorganisms

At the thirty-seventh meeting of the Committee (WHO Technical Report Series (TRS) 806, 1991) an addendum to the general specifications for enzymes used in food processing was prepared. This addendum addressed issues relating to enzyme preparations from genetically modified microorganisms. The text is published in FAO Food and Nutrition Paper (FNP) 52 as Appendix B to Annex 1 of the *General specifications for enzyme preparations used in food processing* (Annex 1, reference 96).

At the present meeting the Committee concluded that the first part of Appendix B (general considerations) should be revised as follows, which will be published as an Annex in FNP 52 Add 6 (the document in which the specifications from the present meeting will be published).

For the proper evaluation of enzyme preparations derived from genetically modified microorganisms, information should be provided on the host microorganism, the genetic material introduced into the host microorganism, and the recombinant production organism. Annex 1 of FNP

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[27] At its first meeting in 1956, the Committee defined the term *food additives* as "non-nutritive substances added intentionally to food, generally in small quantities, to improve its appearance, flavour, texture, or storage properties" (FAO NMRS No. 15, 1957; WHO TRS No. 129, 1957). The Committee later expanded its scope to include food contaminants as well as certain nutritive substances consumed in high amounts (WHO Environmental Health Criteria No. 70, 1987).

[28] CAC/GL 10-1979 (amended 1983, 1991), *Advisory Lists of Mineral Salts and Vitamin Compounds for Use in Foods for Infants and Children*.

[29] Such a case occurred at the forty-first meeting when the Committee evaluated the safety aspects of the use of sodium iron EDTA in food fortification (WHO TRS 837, 1993). The Committee expressed concern about the potential for over-fortification of food because of the enhanced bioavailability of iron in this form.

52 addresses factors relevant to all microbial sources (conventional and recombinant) used in the production of enzyme preparations and to fermentation and recovery procedures. The following points need emphasis when considering the production of enzyme preparations from genetically modified microorganisms:

1. The host microorganism should be taxonomically and genetically characterized.

2. Documentation that the host microorganism is non-pathogenic and non-toxicogenic should be provided.

3. The genetic material (i.e., the expression vector or expression plasmid) intended for introduction into the host microorganism should be characterized, and a description of its construction provided. As appropriate, it should be demonstrated that the genetic material does not contain genes coding for virulence factors, protein toxins, or enzymes that may be involved in the synthesis of mycotoxins or any other toxic or undesirable substances. The source of the DNA encoding the enzyme of interest should be identified where possible.

4. The production microorganism should be characterized with respect to the introduced DNA, its genetic stability, and its growth properties.

5. If the production microorganism is capable of producing proteins that inactivate clinically useful antibiotics, documentation should be provided that the finished enzyme preparation contains neither antibiotic-inactivating proteins at concentrations that would interfere with antibiotic treatment nor DNA that is capable of transforming microorganisms, which potentially could lead to the spread of antibiotic resistance.

6. All enzyme preparations should be evaluated for their potential to elicit allergic reactions. As a general rule, if a food is known to cause an allergic reaction in humans, its use as a source of DNA encoding the enzyme of interest should be avoided. In exceptional cases, where there is a demonstrated need to use an allergenic source of DNA documentation should be provided indicating that the enzyme is not associated with the allergic reaction. The most common allergenic foods on a world-wide basis are fish, crustacea, peanuts, tree nuts, soybeans, milk, eggs, and wheat.

Points 1-6, above cover the major issues pertinent to the development of enzyme preparations derived from genetically modified microorganisms. These issues emphasize and supplement those that must be considered in the safety evaluation of enzyme preparations containing non-recombinant enzymes, which in general relate to the avoidance of undesirable impurities.

The following properties might be useful in characterizing the recombinant enzyme: molecular weight; isoelectric point; substrate specificity; reaction kinetics; activity as a function of pH and temperature; amino acid composition; amino acid sequence; a peptide map; and DNA base sequence coding for the enzyme.

In revising the second part of Appendix B (specifications) the Committee removed the *tentative* designation. The revised section on specifications to be published in FNP 52 Add 6 focuses on the *source* section of the monographs for enzymes from genetically modified microorganisms. It notes that any microbial strain that meets the general considerations for enzymes in Annex 1 of FNP 52 should be safe and suitable host for the introduced DNA. Citation of the genus and species of the host and donor organisms is usually adequate for microorganisms that have been determined to be safe and suitable. The citation of the strain is appropriate where a non-pathogenic and non-toxicogenic strain belongs to a species that encompasses pathogenic and toxicogenic strains. Citation of the specific expression plasmids is generally unnecessary where the plasmid vector is well characterized and documentation on the production microorganism, including the introduced DNA, can be used to verify the appropriateness of the selected expression plasmid.

The Committee requested comments on the revised general considerations and specifications texts for enzymes from genetically modified microorganisms.

The Committee also amended the *General notes applying to the standards, texts and assay of the specifications* in FNP 52 that related to enzyme preparations to align the text on source with the revision of Appendix B to Annex 1 as described above.

6. Heavy metals limit test

The Committee reaffirmed the decision taken at the forty-ninth meeting (report in preparation) to replace, as appropriate, the “catch-all” heavy metals specification, with a specification for one or more of the elements of concern, such as lead, arsenic, mercury, and cadmium.

Confirmation of actual levels determined in the food additives in question is required from sponsors in order to confirm the levels.

The Committee will endeavour to establish guidelines for setting limits for individual elements and confirmed its goal for as low levels as practicable for those elements of concern.

At the present meeting, the Committee adopted lead levels in general of 2 mg/kg. When an additive was known to be used in substantial amounts, the level of 1 mg/kg was chosen. In a few cases where there was evidence that the lead content of the product cannot be reduced to lower levels, 5 mg/kg was specified.

NOTE

This document has been distributed prior to publication of the full report of the fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) to ensure the fast dissemination of information, in particular to the Codex Alimentarius Commission, to which JECFA is the scientific advisory body on matters relating to food additives and contaminants.

The FAO and WHO Joint Secretaries of JECFA request that further inquiries regarding the compounds evaluated at the meeting be made only ***after*** *the official report has been published and distributed by WHO in the name of both sponsoring Organizations, FAO and WHO. Your cooperation is very much appreciated*