



Food and Agriculture
Organization of the
United Nations



World Health
Organization

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES
Eighty-seventh meeting
Rome, 4–13 June 2019

SUMMARY AND CONCLUSIONS

Issued 26 June 2019

A meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) was held in Rome, Italy, from 4 to 13 June 2019. The purpose of the meeting was to evaluate certain food additives.

Dr R. Cantrill served as Chairperson, and Dr A. Mattia, Center for Food Safety and Applied Nutrition, United States Food and Drug Administration, served as Vice-Chairperson.

Dr M. Lipp, Agriculture and Consumer Protection Department, Food and Agriculture Organization of the United Nations (FAO), and Mr K. Petersen, Department of Food Safety and Zoonoses, World Health Organization (WHO), served as Joint Secretaries.

The present meeting was the eighty-seventh in a series of similar meetings. The tasks before the Committee were (a) to elaborate principles governing the evaluation of food additives, (b) to undertake safety evaluations of certain food additives, (c) to review and prepare specifications for certain food additives and (d) to establish specifications for certain flavouring agents.

The Committee evaluated the safety of six food additives (including one group of food additives) and revised the specifications for five other food additives (including one group of food additives). The Committee also revised the specifications for nine flavouring agents.

The report of the meeting will be published 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 and other toxicological, dietary exposure and safety recommendations. Information on the specifications for the identity and purity of certain food additives examined by the Committee and on the specifications for the nine flavouring agents will also be included.

The participants in the meeting are listed in Annex 1. Items of a general nature that the Committee would like to disseminate quickly are included in Annex 2. Future work and recommendations are listed in Annex 3.

Toxicological and dietary exposure monographs or monograph addenda on most of the substances that were considered will be published in WHO Food Additives Series No. 78. New and revised specifications for the identity and purity of the compounds will be published in FAO JECFA Monographs 23.

More information on the work of JECFA is available at:

<http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/en/>

and

http://www.who.int/foodsafety/areas_work/chemical-risks/jecfa/en/

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Toxicological and dietary exposure information and information on specifications

Food additives evaluated toxicologically and assessed for dietary exposure

Food additive	Specifications	Acceptable daily intakes (ADIs) and other toxicological and dietary exposure conclusions
Black carrot extract	N ^a , T ^b	<p>The Committee concluded that the effects observed with one anthocyanin-containing test material cannot be extrapolated to another anthocyanin-containing test material. This is because the test articles used in metabolism and toxicity studies are very heterogeneous and often not fully described and/or the anthocyanin content of the test material is too low and variable.</p> <p>Only one genotoxicity study was available for black carrot extract. Owing to the lack of toxicological data on black carrot extract, the Committee was not able to draw conclusions on its safety. To proceed with its assessment, at least a 90-day toxicological study on a well-characterized extract representative of the material of commerce would be required.</p> <p>The Committee concluded that the total mean dietary exposure to anthocyanins from naturally occurring sources and added black carrot extract ranges from 0.1 to 1.9 mg/kg body weight (bw) per day for adults (18+ years) and from 0.1 to 5.3 mg/kg bw per day for children (<18 years). The Committee noted that the contribution of the use of the food colour itself to the total mean dietary exposure to anthocyanins including from naturally occurring sources is as high as 25%.</p> <p>The Committee noted that the ADI for grape skin extract established by the previous Committee in 1982 was not reconsidered as part of this assessment and remains unchanged.</p>
Brilliant Black PN	R ^c	<p>The Committee concluded that the newly available information does not give reason to revise the previously established ADI of 0–1 mg/kg bw based on a short-term toxicity study in pigs. The Committee therefore retained the ADI for Brilliant Black PN.</p> <p>The Committee noted that the range of estimated dietary exposures for Brilliant Black PN was below the upper end of the ADI and concluded that dietary exposure to Brilliant Black PN does not present a safety concern.</p>
Carotenoids (provitamin A)	R ^d	<p>The Committee reaffirmed the conclusion from the eighty-fourth meeting that rats are not an appropriate model for deriving an ADI for β-carotene due to the relatively low bioavailability of β-carotene in rats compared with humans. Therefore, the Committee withdrew the two group ADIs of 0–5 mg/kg bw for (1) the sum of the synthetic carotenoids β-carotene, β-apo-8'-carotenal and β-apo-8'-carotenoic acid methyl and ethyl esters and (2) synthetic β-carotene and β-carotene derived from <i>Blakeslea trispora</i>^e, which were based on a no-observed-adverse-effect level (NOAEL) from a rat study.</p> <p>The Committee considered that no adverse health effects were observed in the general population in large, well-conducted human intervention studies in which healthy participants were administered 20–50 mg β-carotene per day for up to 12 years, in addition to background exposure from the diet.</p> <p>An additional elevated risk of lung cancer and total mortality was seen in heavy smokers (at least one pack per day) and asbestos workers in intervention studies in which participants were administered 20 mg β-carotene per day for 5–8 years or 30 mg β-carotene per day and 25 000 IU vitamin A for 5 years. The Committee noted that a generally accepted explanation for the cause of these effects has not been identified. The Committee was unable to reach any conclusion about risk from β-carotene exposure in heavy smokers.</p> <p>For the remainder of the general population, the Committee concluded that the estimated high exposure to β-carotene of 9 mg/day for a 30 kg child and 6 mg/day for a 60 kg adult from its current uses as a food additive, in addition to background exposure from the diet, would not be expected to be a safety concern. This conclusion includes synthetic β-carotene, β-carotene derived from <i>B. trispora</i> and β-carotene-rich extract from <i>Dunaliella salina</i>.</p>

Food additive	Specifications	Acceptable daily intakes (ADIs) and other toxicological and dietary exposure conclusions
		<p>The Committee was unable to establish a group ADI for synthetic β-carotene, β-carotene derived from <i>B. trispora</i>, β-carotene-rich extract from <i>D. salina</i>, and β-apo-8'-carotenoic acid methyl and ethyl esters because a group ADI is applicable to the general population, which includes heavy smokers. The Committee noted that it is very unlikely that it will ever be possible to establish a group ADI because further data from the population of heavy smokers cannot be gathered ethically.</p> <p>Because β-apo-8'-carotenoic acid methyl and ethyl esters were previously evaluated on the basis of β-carotene and because no new data were submitted, the Committee was unable to complete an evaluation on β-apo-8'-carotenoic acid methyl and ethyl esters.</p> <p>The present Committee established an ADI of 0–0.3 mg/kg bw for β-apo-8'-carotenal on the basis of a NOAEL of 30 mg/kg bw per day in a 13-week study in rats and application of an uncertainty factor of 100. An additional uncertainty factor to take into account the short duration of the study was not considered necessary because kidney and liver effects observed in the 13-week study at 100 mg/kg bw per day were not observed in a 2-year study at 40 mg/kg bw per day, the single dose tested.</p> <p>Estimated dietary exposure to β-apo-8'-carotenal of 0.3 mg/kg bw per day was at the upper end of the ADI established by the Committee (i.e. 0–0.3 mg/kg bw per day). The Committee noted that the estimated dietary exposure is overestimated and concluded that the current use of β-apo-8'-carotenal as a food additive will not pose a safety concern.</p>
Gellan gum	R ¹ , T ⁹	<p>Available studies confirm the absence of any adverse effects arising from exposure to gellan gum. The Committee retained the previously established ADI “not specified”^h for gellan gum.</p> <p>The Committee evaluated low-acyl clarified gellan gum for use in formulas for special medical purposes for infants. Based on a NOAEL of 100 mg/kg bw per day, the highest dose of low-acyl clarified gellan gum tested in a 21-day neonatal pig study, which modelled the 0- to 12-week period of development in human infants, and the high estimate of dietary exposure of infants to gellan gum of 13 mg/kg bw per day (based on the requested maximum concentration of gellan gum of 50 mg/L and the high level of consumption of infant formula of 260 mL/kg bw per day), a margin of exposure of 7.7 was calculated.</p> <p>The Committee concluded on the basis of several considerations (e.g. the low toxicity of gellan gum, the NOAEL being the highest dose tested, clinical studies in preterm infants and post-marketing surveillance data showing that gellan gum is well tolerated) that the margin of exposure of 7.7 calculated for the use of gellan gum in formulas for special medical purposes for infants and liquid fortification products for addition to human milk or infant formula at a maximum level of 50 mg/L in the fed product indicates low risk for the health of infants, including preterm infants, and that its proposed use is therefore of no safety concern. This conclusion applies only to the use of low-acyl clarified gellan gum. The Committee recognizes that there is variability in medical conditions among infants requiring these products and that these infants would normally be under medical supervision.</p>
Potassium polyaspartate	N	<p>In vitro data suggest that the systemic bioavailability of potassium polyaspartate is low and that potassium polyaspartate would not be cleaved in the stomach or the intestine. The NOAEL in a 90-day rat study on potassium polyaspartate was 1000 mg/kg bw per day, the highest dose tested. There was no concern for genotoxicity.</p> <p>Potassium has been evaluated by the Committee in the course of its previous evaluation of potassium hydroxide, and the result of the evaluation was an ADI “not limited”ⁱ. Exposure to potassium that results from the use of potassium polyaspartate in wine would be within normal daily variation of background potassium exposure from the diet.</p> <p>Should microbial fermentation in the human colon occur, there would be potential exposure to L- and D-aspartic acid. L-Aspartic acid is a normal constituent of dietary protein, and systemic exposure to L-aspartic acid from the diet is much higher than potential exposure from the use of potassium</p>

Food additive	Specifications	Acceptable daily intakes (ADIs) and other toxicological and dietary exposure conclusions
		<p>polyaspartate in wine.</p> <p>There are no relevant toxicological data on D-aspartic acid. In three studies, rats exposed to around 130 mg/kg bw per day showed effects on sex hormone levels. However, NOAELs have not been identified in these studies due to the use of single doses. The Committee noted that there is a margin of exposure of more than 100-fold between the potential human dietary exposure to D-aspartic acid of up to 0.8 mg/kg bw per day and the effect level of 130 mg/kg bw per day.</p> <p>The estimated dietary exposure to D-aspartic acid from typical use of potassium polyaspartate in wine (up to 0.8 mg/kg bw per day) would be expected to be lower than the exposure from non-added sources in the diet. The Committee noted that it had limited data on concentrations of D-aspartic acid in food, but that food processing (e.g. heat treatment of protein, fermentation) will result in partial conversion of L-aspartic acid to D-aspartic acid.</p> <p>The Committee concluded that the use of potassium polyaspartate in wine at the maximum proposed use level of 300 mg/L is not of safety concern.</p>
Rosemary extract	R ⁱ	<p>The Committee concluded that the new studies provided evidence for the absence of reproductive toxicity, but not for the absence of developmental toxicity. The Committee retained the temporary ADI of 0–0.3 mg/kg bw, pending the submission of studies on the developmental toxicity of rosemary extract and studies to elucidate whether the effects noted on rodent pup thyroid hormone levels can be replicated. The temporary ADI will be withdrawn if the requested studies are not submitted by the end of 2021.</p> <p>Estimated mean and high-percentile dietary exposures to carnosic acid plus carnosol from use of rosemary extract as an additive for all countries assessed based on typical use levels did not exceed the upper end of the temporary ADI (0–0.3 mg/kg bw per day). The Committee noted that when dietary exposures from naturally occurring sources are combined with dietary exposures from added sources at typical use levels, the estimated dietary exposures for children were up to 0.42 mg/kg bw per day, which exceeds the ADI. The Committee also noted that the temporary ADI is based on the highest dose tested in a short-term toxicity study in rats and that in the newly submitted reproductive/developmental toxicity screening study, no effects on reproductive toxicity or on parental animals were observed at 316 mg/kg bw per day, the highest dose tested. Therefore, the Committee does not consider the slight exceedance of the ADI to be a safety concern.</p>

N: new specifications; R: existing specifications revised; T: tentative specifications

^a For the spray-dried powder form of black carrot extract.

^b The specifications were made tentative pending further information on the material of commerce, including a full characterization of the proteins, carbohydrates, lipids, fibre, minerals and non-anthocyanin polyphenol components in five lots each of the liquid and powder forms of black carrot extract.

^c Analytical methods for determining subsidiary colouring matters and organic compounds other than colouring matters were replaced with more specific and sensitive high-performance liquid chromatography methods. The existing titrimetric method for the assay of Brilliant Black PN was replaced with a visible spectrophotometric method.

^d The specifications for synthetic β -carotene, β -carotene from *B. trispora* and β -apo-8'-carotenol were revised to replace an identification test for carotenoids with additional spectrophotometric requirements. Based on the arsenic levels from several batches of the product of commerce for β -carotene-rich extract from *D. salina*, the existing specifications for arsenic were revised from 1 mg/kg to 3 mg/kg.

^e The Committee was aware that two group ADIs for carotenoids had been established at previous meetings and that synthetic β -carotene had been included in both group ADIs. The Committee speculated that the Committee at the fifty-seventh meeting did not recognize that synthetic β -carotene was already part of a group ADI and included it in a new group ADI.

^f The Committee concluded that the use of ethanol in the manufacturing of gellan gum is not a safety concern when used according to good manufacturing practice. The specification for ethanol was removed.

^g The specifications were made tentative, pending submission of new methods for characterizing the three forms of gellan gum in commerce by 2021.

^h ADI "not specified" is used to refer to a food substance of very low toxicity that, on the basis of the available data (chemical, biochemical, toxicological and other) and the total dietary exposure to 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.

ⁱ Now called an ADI “not specified” (see table note h).

^j The Committee removed the specification for ethanol, and the tentative status of the specifications for rosemary extract was removed.

Food additives considered for specifications only

Food additive	Specifications
Cassia gum	T ^a
Citric and fatty acid esters of glycerol (CITREM)	R ^b
Metatartaric acid	R ^c
Mannoproteins from yeast cell walls	R ^d
Steviol glycosides	See note e

R: existing specifications revised; T: tentative specifications

^a At the eighty-sixth meeting, the Committee updated the specifications for cassia gum by including the high-performance liquid chromatographic method received and removed their tentative status. Based on comments received about the method performance, the present Committee reviewed the method again and noted that additional investigations were required. Therefore, the Committee decided to make the specifications tentative until ongoing investigations are completed.

^b The Committee received a suitable validated replacement method for an obsolete packed column gas chromatographic method for the determination of total citric acid content, along with performance characteristics of the method and data on the total citric acid content in products currently available in commerce, determined using that method. The Committee included the new method in the specifications and deleted the previous method. A new high-performance liquid chromatography method for the analysis of glycerol, supported by validation data, was provided and included in the revised specifications. The limit for glycerol was maintained. Data on the use of additional neutralizing salts in CITREM manufacture were received and added to the specifications. The lead limit for use of CITREM in infant formula was corrected to 0.5 mg/kg according to the previous evaluation. Data on the sulfated ash levels and the content of minerals in neutralized CITREM products were provided. The limit for sulfated ash was maintained for non-neutralized CITREM, and new limits were set for partially neutralized and for wholly neutralized CITREM. The tentative status of the specifications was removed.

^c The Committee received information on optical rotation, infrared identification, free tartaric acid content, degree of esterification and molecular weight distribution, together with the analytical methods. The Committee revised the specifications for free tartaric acid, optical rotation, molecular weight and molecular weight distribution and included a specification for polydispersity index. The tentative status of the specifications for metatartaric acid was removed.

^d The Committee revised the specifications monograph and noted that a change in the name of the additive from “Yeast extracts containing mannoproteins” to “Mannoproteins from yeast cell walls” was appropriate. The Committee noted that all mannoproteins, regardless of the range of molecular weights, were included in the same specifications monograph and therefore specifying a range of average molecular weight and a method for measuring it was not essential. Data were also received for metallic impurities. The Committee reviewed the information received and decided that only a limit for lead was required. The tentative status of the specifications was removed.

^e A framework was adopted for developing specifications for steviol glycosides by four different methods of production. Specifications for steviol glycosides produced by different production methods were included as annexes, as below:

- Annex 1: Steviol Glycosides from *Stevia rebaudiana* Bertoni (**revised** from the specifications monograph for Steviol glycosides from *Stevia rebaudiana* Bertoni prepared at the eighty-fourth meeting of JECFA (INS 960a)).
- Annex 2: Steviol Glycosides from Fermentation (specifications for Rebaudioside A from multiple gene donors expressed in *Yarrowia lipolytica* (INS 960b(i)) prepared at the eighty-second meeting of JECFA were **revised** to include other steviol glycosides from *Saccharomyces cerevisiae* and *Yarrowia lipolytica*).
- Annex 3: Enzyme Modified Steviol Glycosides (new specifications).
- Annex 4: Enzyme Modified Glucosylated Steviol Glycosides (**new** specifications, **tentative** pending further information concerning the analytical methods).

For more information, see General considerations below.

Flavouring agents considered for specifications only

Flavouring agent	No.	Specifications
Methyl propionate	141	R ^a
Ethyl oleate	345	R ^b
alpha-Methyl-beta-hydroxypropyl alpha-methyl-beta-mercaptopropyl sulfide	547	R ^c
Vanillin	889	R ^d
Ethyl vanillin	893	R ^e
2,2,3-Trimethylcyclopent-3-en-1-yl acetaldehyde	967	R ^f
alpha- and beta-Cyclocitral (50:50 mixture)	979	R ^g

Flavouring agent	No.	Specifications
Sodium 2-(4-methoxyphenoxy)propanoate	1029	R ^h
2,2,6-Trimethyl-6-vinyltetrahydropyran	1236	R ⁱ

R: existing specifications revised

^a The Committee revised the specific gravity to 0.912–0.918.

^b The Committee revised the assay minimum to not less than 75% ethyl oleate. Specifications for the secondary components were also established: ethyl linoleate (3.4–11.5%), ethyl palmitate (0.4–5.1%), ethyl stearate (0.5–2.5%), ethyl laurate (1–2%) and other fatty acid ethyl esters.

^c The Committee revised the refractive index to 1.512–1.522, the specific gravity to 1.040–1.050 and the assay minimum to 95%.

^d The Committee revised the melting point to 81–84 °C.

^e The Committee revised the melting point to 76–79 °C

^f The Committee revised the assay minimum to 93%, with a secondary component of up to 2% of gamma-campholenic aldehyde.

^g The Committee revised the specifications to include the Chemical Abstracts Service (CAS) numbers for alpha-cyclocitral (CAS No. 432-24-6) and for the mixture of alpha- and beta-cyclocitral (CAS No. 52844-21-0). The Flavis and Council of Europe (COE) numbers for alpha- and beta-cyclocitral were also included. The refractive index range was revised to 1.4986–1.4991.

^h The Committee revised the CAS number (150436-68-3) and Flavis number (08.127) to reflect the salt form. The melting point was revised to 184–190 °C. Identifiers and synonyms associated with the free acid were removed.

ⁱ The Committee changed the minimum assay to 95%, the refractive index to 1.442–1.452 and the specific gravity to 0.863–0.873.

Annex 1**Eighty-seventh meeting of the
Joint FAO/WHO Expert Committee on Food Additives**
Rome, 4–13 June 2019**Members**

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Annex 2

General considerations

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

Application of group ADIs

At the Fiftieth Session of the Codex Committee on Food Additives (CCFA), the Codex Secretariat noted that some food additives – such as provitamin A carotenoids (i.e. synthetic β -carotenes, β -carotenes from *Blakeslea trispora*, β -apo-8'-carotenal and methyl and ethyl esters of β -apo-8'-carotenoic acid); chlorophylls and chlorophyllins, copper complexes; and polyoxyethylene sorbitan esters (i.e. polyoxyethylene (20) sorbitan esters of lauric, stearic, palmitic and oleic acids and triesters of stearic acid) – were listed under the same food additive heading in the Codex General Standard for Food Additives (GSFA), despite not being included in a group acceptable daily intake (ADI). The Codex Secretariat sought clarification from the present Committee on the application of group ADIs.

In making recommendations on the safety of food additives, the Committee takes into consideration the principles regarding group ADIs contained in the publication *Principles and methods for the risk assessment of chemicals in food* (Environmental Health Criteria No. 240 [EHC 240]).

The Committee noted that most of the food additives about which CCFA had sought advice had been last considered as groups at several meetings up to and including the twenty-third meeting in 1980 and that the Committee did not explicitly use the term group ADI at those early meetings. For these food additives, the Committee was able to confirm that the chlorophylls and chlorophyllins (copper complexes), polyoxyethylene sorbitan esters (polysorbates), ascorbyl esters, ethylenediaminetetraacetates, thiodipropionates, ferrocyanides, tartrates, stearyl lactylates and iron oxide food additives should have been allocated group ADIs.

For nitrates and nitrites, the respective ADIs are expressed as the ions and therefore encompass the different salts. The group ADI for steviol glycosides, expressed as steviol, includes the whole family of steviol glycosides. The Committee was also able to confirm that the provisional tolerable weekly intake (PTWI) of 2 mg/kg body weight (bw) for aluminium and its salts, when expressed as aluminium, refers to all aluminium salts used in food additives, as well as other sources of aluminium.

An “unconditional” ADI of 0–0.2 mg/kg bw for 2-phenylphenol was first established by JECFA at its eighth meeting in 1964. According to FAO documents, 2-phenylphenol and sodium o-phenylphenate were first evaluated by the 1962 JECFA for their use as a post-harvest treatment of fruits and vegetables to protect against microbial damage during storage and distribution. The current FAO specifications still refer to this use. In 1999, the Joint FAO/WHO Expert Meeting on Pesticide Residues (JMPR) established an ADI of 0–0.4 mg/kg bw for 2-phenylphenol; an ADI was not established for the sodium salt because it rapidly dissociates to 2-phenylphenol. 2-Phenylphenol has a minor use as a flavouring agent, and, during its evaluation at the fifty-fifth meeting of JECFA, the Committee cited the most recent ADI established by JMPR for its risk assessment. In view of its major use as a post-harvest treatment of fruits and vegetables, the Committee is seeking advice from Codex on its current usage as a food additive.

The Committee noted that provitamin A carotenoids were evaluated at the current meeting (see above).

Clarification of ADI “not specified”

Codex requested clarification of the use of the term “ADI ‘not specified’” by JECFA, particularly with respect to the addition of food additives to Table 3 of the GSFA (Additives permitted for use in food in general, unless otherwise specified, in accordance with GMP).

The Committee confirmed its definition of “ADI ‘not specified’” (from EHC 240):

A term applicable to a food substance of very low toxicity that, on the basis of the available chemical, biochemical and toxicological data as well as the total dietary intake of the substance (from its use at the levels necessary to achieve the desired effect and from its acceptable background in food), does not, in

the opinion of the Joint FAO/WHO Expert Committee on Food Additives, represent a hazard to health. For that reason, and for reasons stated in 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: that is, it should be technologically efficacious and should be used at the lowest level necessary to achieve this effect, it should not conceal inferior food quality or adulteration, and it should not create a nutritional imbalance.

Thus, the definition is based upon information on both toxicity and dietary exposure. A conclusion that a substance is of very low toxicity could be based, for example, upon evidence that the substance did not show adverse effects at the highest doses tested in relevant toxicological studies, is poorly absorbed and does not bioaccumulate, and does not contain toxicologically relevant impurities. The estimate of total dietary exposure (intake) is based upon the uses proposed at the time of the evaluation.

The Committee noted that Guideline 2 (Food Additives with an ADI of "Not Specified") of the GSFA (CODEX STAN 192-1995) specifies:

When an additive has been allocated an ADI "not specified" it could in principle, be allowed for use in foods in general with no limitation other than in accordance with Good Manufacturing Practices (GMP). It should, however, be born [*sic*] in mind that ADI not specified does not mean that unlimited intake is acceptable. The term is used by JECFA in case [*sic*] where "on the basis of the available data (chemical, biochemical, toxicological, and other) the total daily intake of the substance arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food does not, in the opinion of the Committee, represent a hazard to health.

If, therefore, a substance is used in larger amounts and/or in a wider range of foods than originally envisaged by JECFA it may be necessary to consult JECFA to ensure that the new uses fall within the evaluation. For example a substance may have been evaluated as a humectant without including a later use as a bulk sweetener, which could give considerable [*sic*] higher intake.

The Committee endorses Guideline 2 of the GSFA and recommends that it be applied by addition of appropriate qualifications in Table 3 of the GSFA.

Update of guidance on evaluation of enzyme preparations (EHC 240)

The Committee was informed about activities of an expert working group established in 2018 to discuss available information on the safety of enzymes used in food and current practices of the food enzyme industry. This activity is being undertaken within the context of a joint FAO/WHO project to update various chapters of EHC 240.

The starting point of the discussion was a background document prepared from a review of the current literature and conversations with representatives of the food enzyme industry and their technical experts.

It was noted that the current JECFA guidance on the evaluation of enzyme preparations was designed to address the potential toxicity of secondary metabolites generated by some enzyme sources (e.g. *Aspergillus* species) under certain growth conditions. The guidance includes a requirement to conduct genotoxicity tests as well as 90-day oral toxicity tests in animals.

After nearly 15 years of using this guidance to assess the safety of enzyme preparations, JECFA has not identified any that were toxic. The expert working group has proposed that the safety of enzyme preparations could be assessed with methodologies using fewer animals (e.g. metabolic profiling of microbial fermentation products, genomic DNA sequencing identifying mycotoxin synthesis genes). The expert working group focused on enzymes from genetically modified microorganisms and the information requirements for their safety evaluation.

The expert working group will propose changes to the relevant sections of EHC 240 and produce a checklist of information required in enzyme submissions for future JECFA evaluations.

The Committee urges the expert working group to finalize its work and make the output available for public comment in time for the next JECFA meeting in 2020.

Update of guidance on evaluation of genotoxicity of chemical substances in food (section 4.5 of EHC 240)

The Committee was informed about activities of a joint FAO/WHO expert working group established in 2018 to update and extend the guidance on evaluation of genotoxicity of chemical substances in food. This activity is being undertaken within the context of a joint FAO/WHO project to update various

chapters of EHC 240. The aim of the expert working group is to provide guidance on interpretation of test results, in addition to general descriptions of genotoxicity tests, special considerations for data-poor substances, and considerations for chemically related substances and mixtures. The expert working group will also address recent developments and future directions.

This work is ongoing. A public consultation is intended before finalization.

Update of guidance on dose–response assessment and derivation of health-based guidance values (Chapter 5 of EHC 240)

At the eighty-third meeting of the Committee (in 2016), some general considerations regarding dose–response modelling were discussed. The Committee recommended that an expert working group be established to develop detailed guidance for the application of the methods most suitable to its work, in particular for the use of the benchmark dose (BMD) approach. The Committee asked that the expert working group address several aspects, including the use of constraints when fitting models, the use of model averaging, the use of non-parametric methods as alternatives for dose–response risk assessment, the use of biological information for selection of models and transparent presentation of modelling outcomes in JECFA publications.

The Committee was informed that the recommended expert working group was established in 2017 to update and extend the guidance on dose–response assessment and derivation of health-based guidance values. This activity is being undertaken within the context of a joint FAO/WHO project to update various chapters of EHC 240.

The work was undertaken electronically and culminated in a meeting of the expert working group in March 2019 in Geneva to revise and update Chapter 5 of EHC 240, including the preparation of more detailed advice on the BMD approach. The draft revised chapter will include guidance on the use of the freely available BMD software (both the United States Environmental Protection Agency Benchmark Dose Software suite of models and PROAST, which was developed by the Dutch National Institute for Public Health and the Environment, now available through the European Food Safety Authority as a web tool). The draft guidance will encourage the use of the BMD approach wherever possible and appropriate, but will acknowledge that in some situations, use of the no-observed-adverse-effect level (NOAEL)/lowest-observed-adverse-effect level (LOAEL) approach may still be appropriate. The draft guidance will include a decision-tree to aid decision-making about which approach should be followed.

It is anticipated that a revised draft of Chapter 5 of EHC 240 will be ready in June 2019, to be reviewed by the expert working group. The draft will then go out for public consultation, will be revised if necessary and will be published online as a standalone chapter.

Update of guidance on assessing dietary exposure to chemical substances in food (Chapter 6 of EHC 240)

The Committee was informed about activities of a joint FAO/WHO expert working group established in 2018 to update and extend the guidance on assessing dietary exposure to chemical substances in food. This activity is being undertaken within the context of a joint FAO/WHO project to update various chapters of EHC 240.

A revision of the chapter was required to incorporate technological and methodological changes in dietary exposure assessments, including progress in the use of exposure models and more recently available data and databases.

WHO undertook an initial scoping exercise that identified areas of the current chapter that needed to be reviewed and new areas of work to be included and prepared a first draft of an updated chapter. The draft chapter will be reviewed by a number of dietary exposure experts at a consultation in September 2019. A final draft will be prepared and then released for public comment.

Dietary exposure assessment reporting

In 1996, WHO held an expert consultation that introduced dietary exposure assessment in JECFA's risk assessments for food additives and contaminants. At a 2005 expert consultation to prepare a dietary exposure assessment chapter for what would become EHC 240, a tiered process for systematically preparing dietary exposure assessments was elucidated. This process includes 1) a

budget or other screening method, 2) international and national dietary exposure assessments based on summary food consumption data (e.g. Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme [GEMS/Food] cluster diets, FAO/WHO Chronic Individual Food Consumption database – Summary statistics [CIFOcOss], national/regional surveys, published exposure assessments) and 3) refined dietary exposure assessment using food consumption data derived from individual consumers. In this last step, deterministic and probabilistic assessments could be completed as needed and appropriate. Guidance to JECFA monographers was prepared from these consultations.

At the current meeting, the Committee determined that not all steps of the tiered approach are needed in every case to complete the Committee's evaluations. When preparing monographs, JECFA experts comment on each of the steps as appropriate, but in the report of the meeting, only those assessments where sufficient data were available to produce reliable estimates of dietary exposure are described and used in the safety assessment. The Committee noted that lack of discussion of any of the steps in report items does not reflect a lack of consideration during the overall evaluation.

Framework for developing specifications for steviol glycosides by method of production

Steviol glycosides are constituents of the leaves of the plant *Stevia rebaudiana* Bertoni and have a sweet taste. The functional use of steviol glycosides in food is as a sweetener. Steviol glycosides are approximately 100–300 times sweeter than sucrose.

The major glycosides present in the extract of the leaves from the *Stevia rebaudiana* Bertoni plant are stevioside and rebaudioside A. The minor glycosides include rebaudioside M and rebaudioside D and about 40 other steviol glycosides that have been identified to date. Several minor glycosides have more favourable sensory characteristics than the major glycosides, prompting development of technologies that enhance the proportion of minor glycosides to modify the sensory profile of the articles of commerce. These technologies include the following:

- a. Extraction: a process of hot water extraction from the leaves of *Stevia rebaudiana* Bertoni.
- b. Fermentation: a process in which a genetically modified microorganism is used to produce specific steviol glycosides.
- c. Enzymatic modification: a process in which steviol glycosides that have been extracted from the leaves of *Stevia rebaudiana* Bertoni undergo enzymatic conversion of major steviol glycosides to minor ones.
- d. Enzymatic glucosylation: a process in which steviol glycosides that have been extracted from the leaves of *Stevia rebaudiana* Bertoni undergo enzyme-catalysed reactions to add glucose units to the steviol glycosides via α -(1-4) linkages.

The microorganisms used in the fermentation or in the production of enzymes used to modify steviol glycosides are of safe lineage. The inserted genes are isolated from non-toxicogenic and non-pathogenic sources. Residues from manufacturing processes do not pose any concerns with respect to toxicity or allergenicity.

Steviol glycosides consist of a mixture of compounds containing a steviol backbone conjugated to any number or combination of the principal sugar moieties (e.g. glucose, rhamnose, xylose, fructose, arabinose, galactose, deoxyglucose). Existing specifications for steviol glycosides require that the product consists of $\geq 95\%$ steviol glycosides on the dried basis.

At the present meeting, the Committee reviewed data on the methods of manufacture, identity and purity of steviol glycosides. The Committee noted that the reviewed products consist of $\geq 95\%$ steviol glycosides on the dried basis; the remaining 5% or less consists of residues of starting material and food-grade processing aids, depending on the method of production.

A framework was adopted for developing specifications for steviol glycosides by four different methods of production. Specifications for steviol glycosides produced by different production methods were included as annexes, as below:

- Annex 1: Steviol Glycosides from *Stevia rebaudiana* Bertoni (revised from the specifications monograph for Steviol glycosides from *Stevia rebaudiana* Bertoni prepared at the eighty-fourth JECFA (INS 960a)).
- Annex 2: Steviol Glycosides from Fermentation (specifications for Rebaudioside A from multiple gene donors expressed in *Yarrowia lipolytica* (INS 960b(i)) prepared at the eighty-second JECFA were revised to include other steviol glycosides from *Saccharomyces cerevisiae* and *Yarrowia lipolytica*).
- Annex 3: Enzyme Modified Steviol Glycosides (new specifications).

- Annex 4: Enzyme Modified Glucosylated Steviol Glycosides (new specifications, tentative pending further information concerning the analytical methods).

At the present meeting, the Committee determined that no safety issues exist for steviol glycosides produced by any one of these methods resulting in products with $\geq 95\%$ steviol glycosides as per existing specifications. The Committee indicated that the ADI of 0–4 mg/kg bw established at the sixty-ninth meeting of JECFA for steviol glycosides (expressed as steviol) applies to steviol glycosides produced by the four methods indicated in the annexes of the specifications monograph produced at the current meeting.

The Committee recognized that steviol glycosides could be produced via a new method or the modification or combination of the methods currently described in the annexes of the specifications monograph. If the final product meets the current specification of $\geq 95\%$ steviol glycosides, the Committee will evaluate possible impurities from the method of manufacture. When appropriate, the modifications will be introduced into the relevant annex; alternatively, a new annex would be added.

Corrigenda

The following requests for corrections, reported to the Joint JECFA Secretariat, were evaluated by the eighty-seventh meeting of JECFA and found to be necessary.

- The following corrections will be made only in the online database for specifications:*

Food additive	Original text	New text	Additional information
Copper sulfate (INS 519)	CAS: 7758-98-7	CAS: 7758-99-8	Original CAS number is for anhydrous form; however, the specifications are for the pentahydrate
Magnesium dihydrogen diphosphate (INS 450(ix))	METHOD OF ASSAY The determination of phosphorus contains the following formula: $P_2O_5, \%w/w = P\% \times 4.983$	METHOD OF ASSAY The determination of phosphorus contains the following formula: $P_2O_5, \%w/w = P\% \times 2.2921$	Original formula did not account for the presence of two phosphorus atoms per molecule
Basic methacrylate copolymer (INS 1205) Will also be applied to anionic methacrylate copolymer (INS 1207) and neutral methacrylate copolymer (INS 1206)	In section Definition: “Basic methacrylate copolymer is used as a coating and glazing agent for food supplements and foods for special medical purposes.”	Sentence deleted.	Deletion requested by the Fifty-first Session of the Codex Committee on Food Additives ¹ ; sentence provided only marginal information.
2-Acetyl-1-pyrroline (JECFA No. 1604)	CAS: 99583-29-6	CAS: 85213-22-5	Correction to CAS number

- The following name was missing from the List of participants in the meeting report of the eighty-sixth meeting of JECFA (WHO Technical Report Series, No. 1014, 2019):*

Dr E. Dessipri, European Directorate for the Quality of Medicines & HealthCare, Council of Europe, Strasbourg, France (*Member*)

- The following participants were indicated as not attending the eighty-sixth meeting, but actually participated in the meeting by video conference:*

¹ http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-711-51%252FReport%252FREP19_FAe.pdf

Dr M. DiNovi, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, United States Food and Drug Administration, College Park, Maryland, USA (*WHO Temporary Adviser*)

Dr J.R. Srinivasan, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, United States Food and Drug Administration, College Park, Maryland, USA (*FAO Expert*)

Annex 3

Future work and recommendations

Unsulfonylated primary aromatic amines in food colours

The Committee requests analytical data on unsulfonylated primary aromatic amines in the following synthetic food colours – Allura Red AC, Amaranth, Azorubine, Brilliant Black PN, Brilliant Blue FCF, Brown HT, Fast Green FCF, Fast Red E, Green S, Indigotine, Lithol Rubine BK, Patent Blue V, Ponceau 4R, Quinoline Yellow, Sunset Yellow FCF and Tartrazine – along with the analytical methods used, in order to update specifications.

Black carrot extract

To proceed with the assessment of black carrot extract, at least a 90-day toxicological study on a well-characterized extract representative of the material of commerce would be required.

The specifications were made tentative pending the submission of further information on the material of commerce, including a full characterization of the proteins, carbohydrates, lipids, fibre, minerals and non-anthocyanin polyphenol components in five lots each of the liquid and powder forms of black carrot extract.

Carotenoids (provitamin A)

The Committee noted that the use levels of β -carotene and β -apo-8'-carotenal provided by the sponsor were much lower than the corresponding maximum permitted levels as specified in the Codex General Standard for Food Additives (GSFA), and that the sponsor indicated that the majority of the maximum permitted levels are not justifiable from a technological point of view. Also, use levels were not provided for all authorized food categories. The Committee recommended that the Codex Alimentarius Commission should review current uses of β -carotene (synthetic β -carotene, β -carotene from *Blakeslea trispora* and β -carotene-rich extract from *Dunaliella salina*) and β -apo-8'-carotenal in the GSFA, including the maximum permitted levels and the food categories in which these additives may be used.

Gellan gum

The specifications were made tentative pending submission of new methods for characterizing the three forms of gellan gum in commerce by 2021. Specific information required is as follows:

- A method to differentiate the three commercial forms of gellan gum – i.e. high-acyl, low-acyl and low-acyl clarified.
- A method to determine the degree of acylation.
- Validation data for the above methods, including detailed description of the sample preparation.
- Data from five non-consecutive commercial batches of material using the proposed validated methods for all three forms of gellan gum.

Rosemary extract

Studies on the developmental toxicity of rosemary extract and studies to elucidate whether the effects noted on pup thyroid hormone levels can be replicated were identified as research needs to complete the evaluation. The Committee requests that this information be provided by the end of 2021.