Food and Agriculture Organization of the United Nations

World Health Organization

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES
Eighty-fourth meeting
Rome, 6–15 June 2017

SUMMARY AND CONCLUSIONS

Issued 22 June 2017

A meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) was held in Rome, Italy, from 6 to 15 June 2017. The purpose of the meeting was to evaluate certain food additives.

Dr R. Cantrill, American Oil Chemists' Society (AOCS), 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 Dr A. Tritscher, Department of Food Safety and Zoonoses, World Health Organization (WHO), served as Joint Secretariats.

The present meeting was the eighty-fourth 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; and (c) to review and prepare specifications for certain food additives.

The Committee evaluated the safety of nine food additives and revised the specifications for five other food additives.

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 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 on most of the substances that were considered will be published in WHO Food Additives Series No. 75. New and revised specifications for the identity and purity of the compounds will be published in FAO JECFA Monographs 20.

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/

Toxicological information, dietary exposures 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
Brilliant Blue FCF	R[a]	The Committee concluded that the available data support the revision of the ADI for Brilliant Blue FCF. In a long-term toxicity study in rats, a no-observed-adverse-effect level (NOAEL) of 631 mg/kg body weight (bw) per day was identified, based on a 15% decrease in mean terminal body weight and decreased survival of females at 1318 mg/kg bw per day. **The Committee established an ADI of 0–6 mg/kg bw** based on this NOAEL by applying an uncertainty factor of 100 for interspecies and intraspecies differences. The Committee noted that the conservative dietary exposure estimate of 5 mg/kg bw per day (95th percentile for children) is less than the upper limit of the ADI of 0–6 mg/kg bw established for Brilliant Blue FCF and **concluded that dietary exposure to Brilliant Blue FCF for children and all other age groups does not present a health concern**. **The previous ADI of 0–12.5 mg/kg bw was withdrawn.**
β-Carotene-rich extract from *Dunaliella salina*	N	The Committee noted that data have become available since the previous evaluation that show large differences in absorption of β-carotene between rodents and humans. The Committee considered that rodents are inappropriate animal models for establishing an ADI for β-carotene. The Committee noted that the toxicity of the other components of the β-carotene-rich d-limonene extract of *D. salina* (hereafter referred to as *D. salina* d-limonene extract) can be evaluated using the results of rodent studies. A short-term toxicity study in rats gave a NOAEL of 3180 mg/kg bw per day, the highest dose tested. No long-term toxicity or reproductive studies have been conducted. The *D. salina* d-limonene extract did not show genotoxicity or developmental toxicity. Correction of the NOAEL of 3180 mg/kg bw per day for the percentage of the algal component (20–35%) gives an adjusted NOAEL of 636–1113 mg/kg bw per day for the algal lipid component of the *D. salina* d-limonene extract. The margin of exposure for this algal lipid component is 2120–3710 using a dietary exposure of 18 mg/day (0.3 mg/kg bw per day). The Committee concluded that exposure to the algal component of the extract does not pose a health concern. The Committee noted that the total dietary exposure to β-carotene is not expected to increase when *D. salina* d-limonene extract is used as a food colour. **The Committee concluded that there was no health concern for the use of β-carotene-rich extract from *D. salina* when used as a food colour in accordance with the specifications established at this meeting.** The Committee emphasized that this conclusion applies to the use of this extract as a food colour, not as a food

Food additive	Specifications	Acceptable daily intakes (ADIs) and other toxicological and dietary exposure conclusions
		supplement.
Fast Green FCF	R[a]	The ADI of 0–25 mg/kg bw established previously by the Committee was based on a long-term rat dietary that identified a NOAEL of 5% Fast Green FCF (equivalent to 2500 mg/kg bw per day), the highest concentration tested. The Committee concluded that the new data that had become available since the previous evaluation gave no reason to revise the ADI and **confirmed the ADI of 0–25 mg/kg bw.** The Committee noted that the conservative dietary exposure estimate for Fast Green FCF of 12 mg/kg bw per day (95th percentile for adolescents) was below the upper bound of the ADI. **The Committee concluded that dietary exposures to Fast Green FCF for adolescents and all other age groups do not present a health concern.**
Gum ghatti	R[b]	The Committee took into account the lack of systemic exposure to gum ghatti because of its high molecular weight and polysaccharide structure, its lack of toxicity in short-term studies, the lack of concern for genotoxicity and the absence of treatment-related adverse effects in studies of gum arabic and other polysaccharide gums with a similar profile. The Committee concluded that gum ghatti is unlikely to be of health concern and **established an ADI "not specified"[c] for gum ghatti that complies with the specifications**. **The Committee concluded that the estimated dietary exposure to gum ghatti of 12 mg/kg bw per day does not present a health concern.**
Jagua (Genipin–Glycine) Blue	N,T	The Committee noted that the highest doses tested in two 90-day toxicity studies in rats and dogs were only 330 and 338 mg/kg bw per day (expressed on a "blue polymer" basis[d]), respectively. The Committee was concerned that the possible effects of the low molecular weight component of the "blue polymer" that could be absorbed were not adequately investigated. A comparison of the dietary exposure estimate (11 mg/kg bw per day) with the NOAEL from the 90-day studies of oral toxicity in rats and dogs (approximately 330 mg/kg bw per day) gives a margin of exposure of about 30. Because of the limited biochemical and toxicological database and the low margin of exposure, **the Committee was unable to complete the evaluation for Jagua (Genipin–Glycine) Blue**.
Metatartaric acid	T	As metatartaric acid undergoes enzymatic hydrolysis to tartaric acid prior to systemic absorption, the biochemical and toxicological data on tartaric acid considered at previous meetings are relevant to the safety assessment of metatartaric acid. Previously evaluated and new studies suggest no change to the group ADI previously established for L(+)-tartaric acid and its sodium, potassium and potassium–sodium salts, expressed as L(+)-tartaric acid. **The Committee concluded that metatartaric acid (when used in winemaking) should be included in the group**

Food additive	Specifications	Acceptable daily intakes (ADIs) and other toxicological and dietary exposure conclusions
		ADI of 0–30 mg/kg bw for L(+)-tartaric acid and its sodium, potassium, potassium–sodium salts, expressed as L(+)-tartaric acid. The Committee noted that the dietary exposure estimate for metatartaric acid for adult consumers of wine was 4% of the upper bound of the ADI and **concluded that dietary exposure to metatartaric acid in wine at the maximum use level of 100 mg/L does not present a health concern**.
Tamarind seed polysaccharide	N	The Committee noted the absence of toxicity in long-term rodent studies and lack of concern regarding genotoxicity, reproductive toxicity and developmental toxicity, and **established an ADI "not specified"[c] for tamarind seed polysaccharide**. **The Committee concluded that the estimated dietary exposure of 75 mg/kg bw per day based on proposed uses and use levels does not present a health concern.**
Tannins (oenological tannins)	–	The Committee noted that the available data do not provide clear information on which tannin sources and individual tannin compounds are present in commercially used oenological tannins and, thus, how the oenological tannins would compare to the tannins used in the submitted studies. Therefore, it is not possible to establish which studies are relevant and, consequently, the extent of the data gaps. The information on biochemical aspects is incomplete, with the implications of repeated dosing on absorption, tissue distribution and interindividual variation needing consideration. In general, there are also few data available on reproductive and developmental toxicity and/or long-term toxicity for some or all of the tannins. **In the absence of specifications and identification of the products in commerce, the Committee concluded that it was not possible to evaluate tannins used in winemaking.**
Yeast extracts containing mannoproteins	N,T	In addition to the natural presence of yeast mannoproteins in wine and the long history of consumption of yeast products in common foods, the Committee considered that the tentative product specifications for yeast extracts containing mannoproteins indicate that these do not contain chemical residues or microbiological contaminants of concern. In addition, the Committee estimated that dietary exposure to yeast mannoproteins due to the addition of yeast extracts containing mannoproteins to wine at the maximum level of 400 mg/L would result, on average, in a **20% increase in dietary exposure compared to the background exposure through the regular diet of 0.4–21 mg/kg bw per day**, primarily driven by bread and pastries. These conservative dietary exposure estimates are based on the assumption that 100% of the yeast extracts containing mannoproteins is mannoproteins. In considering the data and information regarding yeast and yeast-derived products, **the Committee concluded**

Food additive	Specifications	Acceptable daily intakes (ADIs) and other toxicological and dietary exposure conclusions
		that it is unlikely that there would be a health concern for the use of yeast extracts containing mannoproteins as a food additive for oenological uses at maximum use levels up to 400 mg/L for the stabilization of wine. The Committee noted that any change in the uses and/or use levels of yeast extracts containing mannoproteins as a food additive will require a new evaluation.

–: no specifications prepared; N: new specifications; R: existing specifications revised; T: tentative specifications

[a] A maximum limit for manganese was added. High-performance liquid chromatography (HPLC) methods were added for determining subsidiary colouring matters and organic compounds other than colouring matters. The method of assay was changed to visible spectrophotometry, and spectrophotometric data were provided for the colour dissolved in water or aqueous ammonium acetate.

[b] An HPLC method for the identification of the gum constituents was added to replace the thin-layer chromatography (TLC) method. One identification method, using a mercury-containing reagent, was removed. L-Rhamnose was added as one of the constituents of gum ghatti, based on current literature reports.

[c] 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.

[d] "Blue polymer" refers to the blue-coloured genipin–glycine polymer and dimer content of Jagua (Genipin–Glycine) Blue.

Food additives considered for specifications only

Food additive	Specifications
Microcrystalline cellulose	R[a]
Silicon dioxide, amorphous	R[b]
Sodium aluminium silicate	R[c]
Steviol glycosides	R[d]
Sucrose esters of fatty acids	R[e]

R: existing specifications revised

[a] The Committee assessed the information submitted on the solubility of microcrystalline cellulose and redesignated its solubility as "Insoluble in water and ethanol. Practically insoluble or insoluble in sodium hydroxide solution (50 g/L)".

[b] Silicon dioxide, amorphous was on the agenda at the present meeting for revisions related to pH, assay, loss on drying, loss on ignition and impurities. The Committee at its present meeting received the requested information. The tentative status was removed.

[c] At the current meeting, the Committee evaluated the data submitted for loss on ignition, impurities soluble in 0.5 mol/L hydrochloric acid and the suitability of the proposed assay method for the determination of aluminium, silicon and sodium. Information received on functional uses confirmed that the substance is used only as an anticaking agent. The tentative status was removed.

[d] The Committee received a validated HPLC–ultraviolet (UV) method for the assay of steviol glycosides, for which reference standards are commercially available. The presence of steviol glycosides in small quantities is confirmed using an HPLC–mass spectrometric method and quantified using HPLC–UV data. The Committee also received assay data for three batches of a commercial product using the proposed methods. The Committee, at its present meeting, assessed the information received and replaced the existing assay. Two additional saccharides (galactose and arabinose) have been identified in the extracts of *Stevia rebaudiana* Bertoni since the last evaluation of steviol glycosides. The Committee included the two saccharides in the definition of the specifications for steviol glycosides from *S. rebaudiana* Bertoni. The tentative status was removed.

The Committee received additional information pertaining to enzymatically modified steviol glycosides; however, the Committee noted that the data were outside the scope of the call for data for the current meeting and therefore did not consider them.

[e] The Committee assessed the information submitted on the solubility of sucrose esters of fatty acids and revised the solubility criterion. In addition, the Committee reviewed the information submitted on the chromatographic conditions for the separation of the compounds and revised the UV integration instructions.

Annex 1

Eighty-fourth meeting of the Joint FAO/WHO Expert Committee on Food Additives

Rome, 6–15 June 2017

Members

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Dr J. Bend, Department of Pathology and Laboratory Medicine, Schulich Medicine & Dentistry, Western University, London, Ontario, Canada
Dr D. Benford, Surbiton, London, England, United Kingdom
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Dr O.E. Orisakwe, University of Port Harcourt, Choba, Port Harcourt, Rivers State, Nigeria
Dr J. Schlatter, Zurich, Switzerland
Dr J. Smith, Bio|Food|Tech, Charlottetown, Prince Edward Island, Canada
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Ms L. Zhang, Joint FAO/WHO Food Standards Programme, Food and Agriculture Organization of the United Nations, Rome, Italy (*Codex Secretariat*)

[1] Unable to attend the meeting.

Annex 2

General considerations

An edited version of this section will appear in the report of the eighty-fourth 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.

Information requirements for submissions on products derived from natural sources

The Committee noted that, at the current meeting, a number of food additives were evaluated that were derived from natural sources. The Committee recalled that at previous meetings, the need for sponsors to provide sufficient data for chemical, technical, dietary exposure and toxicological evaluation was stressed. At its thirty-first meeting, the Committee emphasized that "A full understanding of the source and chemical nature of such products was considered essential for an evaluation of their safety-in-use". At the sixty-eighth meeting, the Committee provided considerations on "Extensions of an existing ADI to substances obtained from different sources and/or by different manufacturing processes".

The Committee recognized that a component of interest (e.g. carotenes) may be present in the product of commerce at a low percentage relative to other components either because it is extracted together with components of similar polarity or solubility or because of subsequent standardization in the final product formulation. The Committee also recognized that some substances (e.g. gums or tannins) are complex mixtures and their components are affected to varying degrees, depending on their source or through processing. It is important to fully characterize all components of the final product, taking care to also provide the detailed manufacturing process as well as information on the carryover of substances from the starting material to the final product.

The present Committee again stressed that a full characterization of the products in commerce and a relevant set of biochemical and toxicological data on such products are essential for the Committee to develop a specifications monograph and the related safety assessment. It is not possible to complete the evaluation of a food additive if its composition cannot be compared to the substances tested biochemically and toxicologically. This is particularly important where the submission relies on literature data.

The Committee encourages the Codex Committee on Food Additives (CCFA) to consider the above information requirements before accepting proposals for food additive evaluations to be included in the CCFA priority list.

Corrigenda for specifications monographs

The following requests for corrections in JECFA Food Additives Specifications Monographs were received by the JECFA Secretariat. The Committee at the current meeting evaluated the information provided and made the following corrections. These corrections will be published in the electronic versions and in the online database of JECFA Food Additives Specifications Monographs. The information is provided here to make interested parties aware of these changes.

Food additive	Original text	New text	Additional explanations
Carob bean gum (clarified) (JECFA 82, FAO JECFA Monographs	Heading: Carob bean gum	Heading: Carob bean gum (clarified)	In the original publication of FAO JECFA Monographs 19, the monograph heading

Food additive	Original text	New text	Additional explanations
19, 2016)			was omitted ("(clarified)"), while the specifications referred to the clarified carob bean gum
Carob bean gum (JECFA 82, FAO JECFA Monographs 19, 2016)	None Specifications have been prepared and adopted at JECFA 82 for carob bean gum but were not published in the FAO JECFA Monographs 19	Please refer to http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/detail/en/c/484/	
CITREM (JECFA 82, FAO JECFA Monographs 19, 2016)	Lead (Vol. 4) Not more than 2 mg/kg (Not more than 0.1 mg/kg for use in infant formula and formula for special medical purposes intended for infants)	Lead (Vol. 4) Not more than 2 mg/kg (Not more than **0.5**[a] mg/kg for use in infant formula and formula for special medical purposes intended for infants)	Transcription error
Diammonium hydrogen phosphate (JECFA 59, FAO JECFA Monographs 1, 2006)	CAS 7783-54-0	CAS 7783-28-0	
Dimethyl dicarbonate (JECFA 63, FAO JECFA Monographs 1, 2006)	CAS 004-525-33-1	CAS 4525-33-1	
Ferrous sulfate (JECFA 53, FAO JECFA Monographs 1, 2006)	CAS 7720-78-7	CAS 7782-63-0	
Ferrous sulfate, dried (JECFA 53, FAO JECFA Monographs 1, 2006)	No CAS number	CAS 7720-78-7	
Paprika extract (JECFA 79, FAO JECFA Monographs 16, 2014)	Preamble: An ADI of 0–1.5 mg/kg bw was allocated at the 79thJECFA (2014)	Preamble: An ADI of 0–1.5 mg/kg bw **(expressed as total carotenoids)**[a] was allocated at the 79th JECFA (2014)	
Paprika oleoresin (JECFA 59, FAO JECFA Monographs 1, 2006)	INS 160c	INS160c(i)	

Food additive	Original text	New text	Additional explanations
L-Malic acid (flavouring)	Optical rotation: −0.23 (25 °C)	Optical rotation: −2.3 (8.5 g/100 mL water at 20 °C)	The magnitude and direction of the optical rotation are dependent on solvent, temperature and concentration of L-malic acid

CAS: Chemical Abstracts Service; INS: International Numbering System for Food Additives
[a] Emphasis added for clarity only.

Annex 3

Future work and recommendations

β-Carotene-rich extract from *Dunaliella salina*

The Committee considered the basis for the ADI established for the group of carotenoids by the Committee at the eighteenth meeting. The group ADI (0–5 mg/kg bw) was derived using a four-generation study in rats with a NOAEL for β-carotene of 50 mg/kg bw per day with application of a safety factor of 10 because of the natural occurrence of carotenoids in the human diet and the low toxicity observed in animal studies. This ADI applies to the use of β-carotene as a colouring agent and not to its use as a food supplement.

Data that have become available since the previous evaluation show large differences in absorption of β-carotene between rodent species and humans. Specific β-carotene-15,15′-dioxygenase activity with β-carotene as substrate in the intestine of rodents is nearly 1 million–fold higher than that of humans. The Committee considered that rodents are inappropriate animal models for establishing an ADI for β-carotene because of the virtual absence of systemic absorption in rodents.

The Committee recommends that the group ADI for the sum of carotenoids, including β-carotene, β-apo-8′-carotenal and β-apo-8′-carotenoic acid methyl and ethyl esters, be re-evaluated in light of evidence that shows very low absorption of β-carotene in rodents and rabbits in contrast to humans.

Jagua (Genipin–Glycine) Blue

The Committee raised concern regarding the potential toxicity of a low molecular weight fraction of the total colouring matter in Jagua (Genipin–Glycine) Blue. The Committee recommends additional biochemical and toxicological information (e.g. absorption, distribution, metabolism and excretion studies and long-term toxicity, carcinogenicity, reproductive and developmental toxicity studies), including the use of higher doses of the "blue polymer" (which refers to the blue-coloured genipin–glycine content of Jagua (Genipin–Glycine) Blue), including the dimers, in order to complete an evaluation of the safety of Jagua (Genipin–Glycine) Blue.

To support the above, additional information is required on:

- characterization of the low molecular weight components of the "blue polymer";
- a validated method for the determination of dimers; and
- data on concentrations of dimers from five batches of the commercial product.

Metatartaric acid

The Committee received limited analytical data on metatartaric acid. In order to remove the tentative designation from the specifications, the following information on the products of commerce is requested:

- characterization of the products (optical rotation, content of free tartaric acid, degree of esterification and molecular weight distribution) and the corresponding analytical methods;
- infrared spectrum (in a suitable medium); and
- analytical results including the above parameters from a minimum of five batches of products currently available in commerce, along with quality control data.

The Committee requests that this information be submitted by **December 2018**.

Tannins

The Committee assessed the information received and concluded that there were insufficient data and information to prepare specifications for oenological tannins. The Committee requires data for the characterization of the products in commerce to be able to complete specifications for oenological tannins used as an antioxidant, colour retention agent and stabilizer in wine. The required information includes a detailed description of the manufacturing processes and thorough chemical characterization of the commercial products made from different botanical sources.

The following information is required:

- composition of tannins derived from the full range of raw materials as well as the processes used in their manufacture;
- validated analytical method(s) and relevant quality control data;
- analytical data from five batches of each commercial product including information related to impurities such as gums, resinous substances, residual solvents, sulfur dioxide content and metallic impurities (arsenic, lead, iron, cadmium and mercury);
- solubility of the products in commerce, according to JECFA terminology; and
- use levels, natural occurrence and food products in which tannins are used.

Submitters are encouraged to offer a rationale for a single specifications monograph for oenological tannins covering all products or individual monographs.

Yeast extracts containing mannoproteins

In order to complete specifications related to the use of yeast extracts containing mannoproteins in wine manufacture and remove their tentative designation, the Committee requires chemical characterization of the product in commerce along with supporting data. The following information is required:

- composition of yeast extracts containing mannoproteins as well as the processes used in their manufacture;
- analytical data from five batches of each commercial product, including information related to impurities; and
- data on concentrations of yeast mannoproteins in wine in which yeast extracts containing mannoproteins have been used.

The Committee requests that this information be submitted by **December 2018**.