CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 3(a) **CX/FA 18/50/3 Rev.1**
February 2018

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

Fifty Session

MATTERS OF INTEREST ARISING FROM FAO/WHO AND FROM THE 84TH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

Matters for information from the 84th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

1. The results of the 84th meeting of JECFA (Rome, 6-15 June 2017) on certain food additives will be available as follows: the meeting report (WHO Technical Report Series) and the toxicological and dietary exposure monographs (WHO Food Additive Series No 75) will be accessible through the WHO JECFA publications website: http://www.who.int/foodsafety/publications/jecfa/en/. The specification monographs resulting from the 84th JECFA meeting will be published as FAO JECFA Monographs 21, FAO, Rome, 2017. The publication is available on the FAO JECFA website at: http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-publications/en/

2. Some of the general considerations of the 84th JECFA are summarized here:

Information requirements for submissions on products derived from natural sources

3. At its 84th meeting, JECFA considered that a number of food additives were evaluated that were derived from natural sources. JECFA 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 31st meeting, JECFA 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 68th meeting, JECFA provided considerations on "*Extensions of an existing ADI to substances obtained from different sources and/or by different manufacturing processes*".

4. JECFA 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. JECFA 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.

5. At its 84th meeting JECFA 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 JECFA 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.

6. JECFA encourages CCFA to consider the above information requirements before accepting proposals for food additive evaluations to be included in the CCFA priority list.

Update on activities relevant to JECFA

7. At its 84th meeting JECFA was provided with an update of work in the WHO International Programme on Chemical Safety (IPCS). The chemical risk assessment network and its activities were described, including the work on a review of how chemical-specific adjustment factors are being used in regulatory and non-regulatory risk assessments.

8. JECFA was further informed about ongoing activities on risk assessment methodology and update of certain chapters of EHC240: *Principles and methods for the risk assessment of chemicals in food*. In particular, more detailed guidance on the interpretation and evaluation of genotoxicity studies will be developed; as well, the guidance on dose–response modelling and application of the benchmark dose approach will be updated. The chapter on exposure assessment will be updated, taking all recent developments into account. Further guidance will also be developed on the evaluation of enzyme preparations.

9. JECFA was also informed that the JECFA guidance for setting acute reference doses for veterinary drugs is now available online: http://www.who.int/foodsafety/chem/jecfa/guidelines/en/.

10. JECFA was informed that WHO recently has published a distance learning tool (DLT) on how to access and analyse the food contamination data submitted to the Global Environment Monitoring System - Food Contamination Monitoring and Assessment Programme (GEMS/Food) database. This tool was developed in collaboration with the Chulabhorn Research Institute (Bangkok, Thailand), a WHO Collaborating Centre. A password-protected access to the learning tool is available upon request from: vergerp@who.int.

Corrigenda for specifications monographs

11. JECFA at its 84th meeting evaluated information provided on requests for corrections in JECFA Food Additives Specifications Monographs 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 19, 2016)	Heading: Carob bean gum	Heading: Carob bean gum (clarified)	In the original publication of FAO JECFA Monographs 19, the monograph heading 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	

Food additive	Original text	New text	Additional explanations
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 79th JECFA (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)	INS160c	INS160c(i)	
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.

[a] Emphasis added for clarity only.

Requests for scientific advice

12. Both organizations continue to jointly prioritize the requests for scientific advice taking into consideration the criteria proposed by Codex as well as the requests for advice from Member Countries and the availability of resources. A list of all pending requests for scientific advice by JECFA will be posted on the respective FAO and WHO websites

13. In scheduling the JECFA meetings and developing the agenda, the Joint Secretaries have to take into account the priorities requested by CCFA, CCCF, and CCRVDF. Due to the increasing requests for scientific advice to JECFA, not all requests can be addressed in the subsequent meeting. In prioritizing the work the JECFA Secretariat takes into account existing criteria, on-going Codex work and available resources.

14. To facilitate provision of extra-budgetary resources for scientific advice activities, please contact Dr Markus Lipp, FAO Food Safety and Quality Unit (jecfa@fao.org) and Dr Angelika Tritscher, Department of Food Safety and Zoonoses, WHO (jecfa@who.int).

Actions required as a result of changes in acceptable daily intake (ADI) status and other toxicological recommendations from JECFA

15. At its 84th meeting, JECFA evaluated the safety of 9 food additives. Toxicological recommendations or other scientific advice for these food additives are provided in the attached Table 1.

16. CCFA50 **is invited** to consider the recommended actions (presented in Table 1) which might be required following the evaluations of these food additives.

Table 1. Food additives evaluated toxicologically and/or considered for specifications at the 84th JECFA meeting

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
133	Brilliant Blue FCF	The 84th JECFA concluded that the available data support the revision of the ADI for Brilliant Blue FCF and that the study on long-term toxicity in rats should be considered as the pivotal study. In this study, a NOAEL of 631 mg/kg 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. JECFA 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 previous ADI of 0–12.5 mg/kg bw was withdrawn. The 84th JECFA 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 existing specifications for Brilliant Blue FCF were revised at the 84th JECFA meeting, and 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.	Note the JECFA conclusion on an ADI of 0–6 mg/kg body weight (bw) for the Brilliant Blue FCF, which does not present a health concern for children and all other age groups. Note the existing specifications for Brilliant Blue FCF were revised. (see CX/FA 18/50/4). Request for comments/ proposals on uses and use levels of Brilliant Blue FCF in Table 1 and 2 of the GSFA (to be provided in response to the CL requesting proposals for new and/or revision of adopted food additives provisions in the GSFA).
	β-Carotene-rich extract from *Dunaliella salina*	The 84th JECFA noted that data have become available since the previous evaluation that shows large differences in absorption of β-carotene between rodents and humans. JECFA considered that rodents are inappropriate animal models for establishing an ADI for β-carotene. The 84th JECFA 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	Note the JECFA conclusion that there was no health concern for the use of β-carotene-rich extract from D. *salina* when used as a food colour at the proposed uses levels, and when the product is in accordance with the specifications. Note the JECFA recommendation 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.

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		exposure of 18 mg/day (0.3 mg/kg bw per day). JECFA concluded that exposure to the algal component of the extract does not pose a health concern. The 84th JECFA 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 84th JECFA 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. JECFA emphasized that this conclusion applies to the use of this extract as a food colour, not as a food supplement. The 84th JECFA 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.	Consider assigning an INS number to this food additive. Request proposals for use levels of β-Carotene-rich extract from *Dunaliella salina* (used a colour only) in Table 1 and 2 of the GSFA (to be provided in response to the CL requesting proposals for new and/or revision of adopted food additives provisions in the GSFA).
143	Fast Green FCF	The 84th JECFA 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. JECFA noted that the conservative dietary exposure estimate for Fast Green FCF of 12 mg/kg bw per day (95th percentile for adolescents - the age group with the highest exposure) was below the upper bound of the ADI. JECFA concluded that dietary exposures to Fast Green FCF for adolescents and all other age groups do not present a health concern. The existing specifications for Fast Green FCF were revised at the 84th JECFA meeting, and a maximum limit for manganese was added. HPLC methods were added to determine subsidiary colouring matters and organic compounds other than colouring matters. The assay method was changed to visible spectrophotometry, and spectrophotometric data were provided for the colour dissolved in water or aqueous ammonium acetate.	Note the JECFA conclusion on an ADI of 0–25 mg/kg body weight (bw) for the Fast Green FCF, which does not present a health concern for children and all other age groups. Note the existing specifications for Fast Green FCF, were revised (see CX/FA 18/50/4). Request for comments/ proposals on uses and use levels of Fast Green FCF in table 1 and 2 of the GSFA (to be provided in response to the CL requesting proposals for new and/or revision of adopted food additives provisions in the GSFA).
419	Gum ghatti	JECFA 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 (at doses up to 3044 mg/kg bw per day), the lack of concern for genotoxicity and the absence of treatment-related	Note the JECFA conclusion on an ADI "*not specified*" for gum ghatti. Include gum ghatti (INS 419) in Table 3 of

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		adverse effects in studies of gum arabic and other polysaccharide gums with a similar profile. JECFA concluded that gum ghatti is unlikely to be a health concern and established an ADI "*not specified"* for gum ghatti that complies with the specifications. JECFA also concluded that the estimated dietary exposure to gum ghatti of 12 mg/kg bw per day does not represent a health concern. The existing specifications for gum ghatti were revised at the 84th JECFA meeting; an HPLC method for the identification of the gum constituents was added to replace the thin-layer chromatography method. One identity 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.	GSFA and circulate for comments at Step 3. Request for comments/proposals on uses and use levels of gum ghatti for the food categories listed in the Annex to Table 3 (to be provided in response to the CL requesting proposals for new and/or revision of adopted food additives provisions in the GSFA). Note the existing specifications for gum ghatti, were revised (see CX/FA 18/50/4).
	Jagua (Genipin–Glycine) Blue	The 84th JECFA 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), 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 approximately 30. Because of the limited biochemical and toxicological database and the low margin of exposure, JECFA was unable to complete the evaluation for Jagua (Genipin–Glycine) Blue. JECFA raised concern regarding potential toxicity of low molecular weight fraction of the total colouring matter in Jagua (Genipin–Glycine) Blue. JECFA recommends additional biochemical and toxicological information (e.g. absorption, distribution, metabolism and excretion studies, long-term toxicity, carcinogenicity, reproductive and developmental toxicity studies), including the use of higher doses of the "*blue polymer*", 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	Note the JECFA conclusion that is was unable to complete the evaluation for Jagua (Genipin–Glycine) Blue. Note the request for additional information 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

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		batches of the commercial product. The 84th JECFA prepared new tentative specifications monograph and a Chemical and Technical Assessment.	
353	Metatartaric acid	The 84th JECFA noted that 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 the metatartaric acid. Additional information to support the safety assessment of metatartaric acid includes the absence of any effects in a bacterial reverse mutation test. JECFA evaluated a series of studies that had become available since L(+)-tartaric acid was last evaluated. The body of evidence suggests 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 84th JECFA concluded that metatartaric acid (when used in winemaking) should be included in the group ADI of 0–30 mg/kg bw for L(+)-tartaric acid and its sodium, potassium, potassium–sodium salts, expressed as L(+)-tartaric acid. JECFA 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. The 84th JECFA prepared new tentative specifications and a Chemical and Technical Assessment. JECFA 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.**	Note the JECFA conclusion on an ADI that metatartaric acid (when used in winemaking) should be included in the group ADI of 0–30 mg/kg bw for L(+)-tartaric acid and its sodium, potassium, potassium–sodium salts, expressed as L(+)-tartaric acid. Note the JECFA request for information to be submitted by **December 2018.**to complete the tentative specifications (see CX/FA 18/50/4).
	Tamarind seed polysaccharide	The 84th JECFA established an ADI "*not specified*" for tamarind seed polysaccharide. This conclusion was based on the absence of toxicity in repeated-dose animal studies of tamarind seed	Note the JECFA conclusion on an ADI "*not specified*" for tamarind seed

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		polysaccharide. In addition, there was no concern regarding genotoxicity. Reproductive toxicity and developmental toxicity were not considered a concern based on the lack of absorption of intact polysaccharide, the degradation and fermentation of tamarind seed polysaccharide into normal dietary constituents and the absence of reproductive and developmental effects in other polysaccharide gums. The estimated dietary exposure based on proposed uses and use levels was 75 mg/kg bw per day. JECFA concluded that this does not present a health concern. The 84th JECFA prepared new specifications monograph and a Chemical and Technical Assessment.	polysaccharide. Note the new JECFA specifications (see CX/FA 18/50/4). Consider assigning an INS number to this food additive. Include tamarind seed polysaccharide in Table 3 of GSFA for circulation for comments at Step 3. Request for comments/proposals on uses and use levels of tamarind seed polysaccharide for the food categories listed in the Annex to Table 3 (to be provided in response to the CL requesting proposals for new and/or revision of adopted food additives provisions in the GSFA).
	Tannins (oenological tannins)	The 84th JECFA 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. JECFA noted that 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. The 84th JECFA concluded that there were insufficient data and information to prepare specifications for oenological tannins. JECFA 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.	Note the JECFA conclusion on the lack of specifications and identification of the products in commerce; therefore it was not possible to evaluate tannins used in winemaking. Note the JECFA request for information on specifications and identification to complete to the evaluation. (see CX/FA 18/50/4) No action required as the new specifications is tentative.

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		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. JECFA noted that 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	The 84th JECFA noted that in addition to the natural presence of yeast mannoproteins in wine and the long history of consumption of yeast products in common foods, the tentative product specifications for yeast extracts containing mannoproteins indicate that these do not contain chemical residues or microbiological contaminants of concern. In addition, JECFA 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, JECFA concluded 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. JECFA 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. A new tentative specifications monograph and a Chemical and Technical Assessment were prepared. In order to remove the tentative designation of the	Note the JECFA conclusion 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. Note the JECFA request for information to complete to revise the tentative specifications. (see CX/FA 18/50/4) No action required as the new specifications is tentative.

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		specifications, the Committee requires chemical characterization of the product in commerce along with data to be able to complete specifications related to the use of yeast extracts containing mannoproteins in wine manufacture. 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.	