



JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

Fifty-second Session

MATTERS OF INTEREST ARISING FROM FAO/WHO AND FROM THE 87TH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

Matters for information from FAO

1. The 163rd Session of the FAO Council (December 2019) has endorsed the allocation of an additional USD 1 million for the food safety scientific advice programme during the 2020-21 biennium. In addition, the FAO Director-General has approved a special 2019 allotment of USD 500,000 for the food safety scientific advice programme.

Matters for information from the 87th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

2. The results of the 87th meeting of JECFA (Rome, 4-13 June 2019) 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 78) will be accessible through the WHO JECFA publications website: <http://www.who.int/foodsafety/publications/jecfa/en/>. The specification monographs resulting from the 87th JECFA meeting will be published as FAO JECFA Monographs 23, FAO, Rome, 2019. The publication is available on the FAO JECFA website at: <http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-publications/en/>

Requests for scientific advice

3. 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

4. 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.

5. 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 Kim Petersen, Department of Nutrition and Food Safety, WHO (jecfa@who.int).

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

6. At its 87th meeting, JECFA evaluated the safety of 6 food additives (including one group of food additives). Toxicological recommendations or other scientific advice for these food additives are provided in the attached Table 1. CCFA52 is **invited** to consider the recommended actions (presented in Table 1) which might be required following the evaluations of these food additives

7. At its 87th meeting, JECFA also provided clarification to a request made by CCFA50¹. At CCFA50, the Codex Secretariat noted that some food additives – such as carotenoids (INS 160a(i), INS 160a(iii), INS 160e, INS 160f); chlorophylls and chlorophyllins, copper complexes (INS 141(i), INS 141(ii)); and polysorbates (INS 432, INS 433, INS 434, INS 435, INS 436) – were listed under the same food additive heading in the *Codex General Standard for Food Additives* (GSFA) (CXS192-1995), despite not being included in a group acceptable daily intake (ADI). The Codex Secretariat sought clarification from JECFA on the application of the term “group” ADIs.
8. In making recommendations on the safety of food additives, JECFA at its 87th meeting took 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]).
9. At its 87th meeting, JECFA 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 23rd meeting in 1980 and that JECFA did not explicitly use the term group ADI at those early meetings. For these food additives, JECFA was at its 87th meeting able to confirm that the chlorophylls and chlorophyllins, copper complexes, polysorbates, ascorbyl esters, ethylenediaminetetraacetates, thiodipropionates, ferrocyanides, tartrates, stearyl lactylates and iron oxides food additives should have been allocated group ADIs.
10. At its 87th meeting, JECFA also noted that 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. Regarding sodium aluminium phosphates, JECFA 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.
11. Regarding ortho-phenylphenols, an “unconditional” ADI of 0–0.2 mg/kg bw for 2-phenylphenol was first established by JECFA at its 8th meeting in 1964. According to FAO documents, 2-phenylphenol and sodium ophenylphenate 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 55th meeting of JECFA, JECFA 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, **JECFA is seeking advice from CCFA on their current usage as food additives** (i.e. ortho-Phenylphenol (INS 231) and sodium ortho-phenylphenol (INS 232)). At its 87th meeting JECFA noted that carotenoids (provitamin A) would be re-evaluated.
12. At its 87th meeting, JECFA also provided 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.
13. At its 87th meeting, JECFA 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.*
14. 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. At its 87th meeting, JECFA noted that Guideline 2 (Food Additives with an ADI of “Not Specified”) of the GSFA (CXS 192-1995) specifies:

¹ This matter was re-considered at CCFA51 (see REP19/FA, para. 10)

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 in mind that ADI not specified does not mean that unlimited intake is acceptable. The term is used by JECFA in case 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 higher intake.

15. At its 87th meeting, JECFA endorsed 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)

16. At its 87th meeting, JECFA 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.

17. At its 87th meeting, JECFA was informed that 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 have proposed changes to the relevant sections of EHC 240 and produced a checklist of information required in enzyme submissions for future JECFA evaluations. This work is ongoing and to be finalized before the next JECFA meeting on food additives in 2020.

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

18. At its 87th meeting, JECFA 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.

19. At its 87th meeting, JECFA was informed that 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 has also addressed recent developments and future directions. This work is ongoing and to be finalized before the next JECFA meeting on food additives in 2020.

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

20. At its 87th meeting, JECFA was informed about the progress made by an expert working group established in 2017 with the aim 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.

21. At its 87th meeting, JECFA was informed that 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 benchmark dose (BMD) approach. The draft revised chapter will include guidance on the use of the freely available BMD software. 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. This work is ongoing and to be finalized before the next JECFA meeting on food additives in 2020

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

22. At its 87th meeting, JECFA 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.

23. At its 87th meeting, JECFA was informed that 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. A draft chapter was reviewed by several dietary exposure experts at a consultation in September 2019. A final draft will be released for public comment in 2020.

Dietary exposure assessment reporting

24. At its 87th meeting, JECFA was informed that 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 [CIFOCOs], 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.

25. At its 87th meeting, JECFA determined that not all steps of the tiered approach are needed in every case to complete JECFA'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. JECFA 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

26. At its 87th meeting, JECFA noted that 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.

27. 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:

- Extraction: a process of hot water extraction from the leaves of *Stevia rebaudiana* Bertoni.
- Fermentation: a process in which a genetically modified microorganism is used to produce specific steviol glycosides.
- 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.
- 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.

28. 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 nonpathogenic sources. Residues from manufacturing processes do not pose any concerns with respect to toxicity or allergenicity.

29. 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.

30. At its 87th meeting, JECFA reviewed data on the methods of manufacture, identity and purity of steviol glycosides. JECFA 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.

31. 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 (INS 960a) prepared at the 84th JECFA).
- Annex 2: Steviol Glycosides from Fermentation (the specifications monograph for Rebaudioside A from multiple gene donors expressed in *Yarrowia lipolytica* (INS 960b(i)) prepared at the 82nd 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).

32. At its 87th meeting, JECFA 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. JECFA indicated that the ADI of 0–4 mg/kg bw established at the 69th 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. JECFA 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, JECFA 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.

Table 1. Food additives evaluated toxicologically and/or considered for specifications at the 87th JECFA meeting

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
INS 163(vi)	Black carrot extract	<p>The 87th JECFA concluded that due to the lack of toxicological data on black carrot extract, JECFA was not able to draw conclusions on its safety.</p> <p>The 87th JECFA 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 varied and often not fully described and/or the anthocyanin content of the test material is too low and variable.</p> <p>The 87th JECFA 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 87th JECFA noted that the dietary exposure to anthocyanins including from naturally occurring sources is as high as 25%.</p> <p>The 87th JECFA noted that the ADI for grape skin extract established by the previous JECFA meeting in 1982 was not reconsidered as part of this assessment and remains unchanged.</p> <p>New specifications and a Chemical and Technical Assessment were prepared. The specifications were made tentative pending the completion of the safety evaluation of black carrot extract and the submission of further information on the material of commerce. The 87th JECFA requested 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.</p>	<p>Note the JECFA conclusion that it was unable to complete the evaluation of black carrot extract.</p> <p>Note the JECFA conclusion that 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>Note that the ADI for grape skin extract previously established by JECFA was not reconsidered as part of this assessment and remains unchanged.</p> <p>Note the new tentative specifications for black carrot extract (see CX/FA 20/52/4).</p> <p>Note the JECFA request for further information on the material of commerce.</p>
151	Brilliant Black (Black PN)	<p>The 87th JECFA concluded that the new data that have become available since the previous evaluation of brilliant black (black PN) do not give reason to revise the ADI and confirmed the previous ADI of 0–1 mg/kg bw.</p> <p>The 87th JECFA noted that the range of estimated dietary exposures for brilliant black was below the upper end of the ADI and concluded that dietary exposure to brilliant black does not present a safety concern.</p> <p>The existing specifications for brilliant black were revised. A Chemical and Technical Assessment was prepared.</p>	<p>Note the JECFA conclusion that the new data that have become available since the previous evaluation of brilliant black do not give reason to revise the ADI and confirmed the previous ADI of 0–1 mg/kg bw.</p> <p>Note the new JECFA specifications for Brilliant Black PN (see CX/FA 20/52/4).</p>

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
160a(i) 160a(iii) 160a(iv) 160e 160f	Carotenoids (provitamin A)	<p>The 87th JECFA reaffirmed the conclusion from the 84th 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, JECFA withdrew the two group ADIs of 0–5 mg/kg bw for:</p> <p>(1) the sum of carotenoids including β-carotene, β-apo-8'-carotenal and β-apo-8'-carotenoic acid methyl and ethyl esters of β-apo-8'-carotenoic acid and</p> <p>(2) β-carotene (synthetic) and β-carotene derived from <i>Blakeslea trisporae</i>.</p> <p>The 87th JECFA 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>However, 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 87th JECFA noted that a generally accepted explanation for the cause of these effects has not been identified. The 87th JECFA 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 87th JECFA 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 β-carotene, synthetic (INS 160a(i)), β-carotene, <i>Blakeslea trispora</i> (INS 160a(iii)) and β-carotene-rich extract from <i>Dunaliella salina</i> (INS 160a(iv)).</p> <p>The 87th JECFA was unable to establish a group ADI for β-carotene (synthetic), β-carotene, <i>Blakeslea trispora</i>, β-carotene-rich extract from <i>Dunaliella 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.</p> <p>The 87th JECFA noted <u>that it is very unlikely that it will ever be possible to establish a group ADI</u> because further data from the population of heavy smokers cannot be gathered ethically. Because β-apo-8'-carotenoic acid methyl and ethyl esters were previously evaluated on the basis of β-</p>	<p>Note the JECFA conclusion that the group ADI of 0-5 mg/kg bw was withdrawn for (1) the sum of carotenoids including β-carotene, β-apo-8'-carotenal and β-apo-8'-carotenoic acid methyl and ethyl esters and (originally applicable to INS 160e, INS 160f)</p> <p>(2) β-carotene (synthetic) and β-carotene derived from <i>Blakeslea trisporae</i> (originally applicable to INS 160a(i) and INS 160a(iii)).</p> <p>JECFA reaffirmed that rodents are inappropriate animal models for establishing the safety of β-carotene.</p> <p>Note that JECFA was unable to establish a group ADI for INS 160a(i), INS160a(iii), INS 160a(iv), and INS 160f because a group ADI is applicable to the general population, which <u>includes heavy smokers</u>.</p> <p>Note <u>that it is very unlikely that JECFA will ever be possible to establish a group ADI</u> for INS 160a(i), INS160a(iii), INS 160a(iv), and INS 160f because further data from the population of heavy smokers cannot be gathered ethically.</p> <p>Note that no data was submitted for βapo-8'-carotenoic acid methyl and ethyl esters.</p> <p>Note that JECFA established an ADI of 0-0.3 mg/kg bw for INS 160e.</p>

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		<p>carotene and because no new data were submitted, the JECFA was unable to complete an evaluation on β-apo-8'-carotenoic acid methyl and ethyl esters.</p> <p>The 87th JECFA established an ADI of 0–0.3 mg/kg bw for carotenal, beta-apo-8'- (INS 160e) 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 JECFA (i.e. 0–0.3 mg/kg bw per day). The 87th JECFA noted that the estimated dietary exposure is overestimated and concluded that the current use of carotenal, beta-apo-8'- as a food additive will not pose a safety concern.</p> <p>The 87th JECFA noted that the use levels of β-carotene and carotenal, beta-apo-8'- provided by the sponsor were much lower than the corresponding maximum permitted levels as specified in the 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. JECFA 87th recommend that CCFA revises the current uses and permitted use levels.</p> <p>The existing specifications for carotenoids were revised. A Chemical and Technical Assessment was prepared.</p>	<p>Note that JECFA recommended that the CCFA should review current uses of INS 160a(i), INS160a(iii), INS 160a(iv), INS 160e and INS 160f in the GSFA, including the maximum permitted levels and the food categories in which these additives may be used.</p> <p>Note the existing specifications for carotenoids were revised (see CX/FA 20/52/4).</p>
418	Gellan gum	<p>The 87th JECFA retained the previously established ADI “not specified” for gellan gum based on the absence adverse effects in available studies.</p> <p>The 87th JECFA concluded on the basis of several considerations (e.g. the low toxicity of gellan gum, the NOAEL of of 100 mg/kg 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.</p>	<p>Note that JECFA retained the previously established ADI “<i>not specified</i>” for gellan gum.</p> <p>Note 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 is of no safety concern.</p>

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		<p>This conclusion applies only to the use of low-acyl clarified gellan gum. The 87th JECFA recognizes that there is variability in medical conditions among infants requiring these products and that these infants would normally be under medical supervision.</p> <p>Revised specifications and a Chemical and Technical Assessment were prepared. The 87th JECFA noted that 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:</p> <ul style="list-style-type: none"> • 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. 	<p>Note the new tentative specifications for gellan gum (see CX/FA 20/52/4).</p> <p>Note the JECFA request for further information on new methods for characterizing the three forms of gellan gum in commerce.</p>
456	Potassium polyaspartate	<p>The 87th JECFA 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> <p>The 87th JECFA noted that <i>in vitro</i> 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>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 polyaspartate in wine.</p> <p>The 87th JECFA noted that 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 87th JECFA 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. The estimated dietary exposure to D-aspartic acid from typical use of potassium polyaspartate in wine (up to 0.8</p>	<p>Note the JECFA conclusion on the use of potassium polyaspartate in wine - that the proposed maximum use level of 300 mg/L is not of safety concern.</p> <p>Note the new JECFA specifications for potassium polyaspartate (see CX/FA 20/52/4).</p>

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		<p>mg/kg bw per day) would be expected to be lower than the exposure from non-added sources in the diet. The 87th JECFA 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>New specifications and a Chemical and Technical Assessment were prepared.</p>	
392	Rosemary extract	<p>The 87th JECFA concluded that the new studies provided evidence for the absence of reproductive toxicity, but not for the absence of developmental toxicity. The 87th JECFA 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.</p> <p>The temporary ADI will be withdrawn if the requested studies are not submitted by the end of 2021.</p> <p>The 87th JECFA 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 87th JECFA 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.</p> <p>The 87th JECFA 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 JECFA did not consider the slight exceedance of the ADI to be a safety concern.</p> <p>The existing specifications for rosemary extract were revised. A Chemical and Technical Assessment was prepared.</p>	<p>Note that JECFA 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.</p> <p>Note that 2021 deadline for submitting the requested studies to JECFA otherwise the ADI will be withdrawn.</p> <p>Note the existing specifications for rosemary extract were revised (see CX/FA 20/52/4).</p>