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 19/51/3**

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**JOINT FAO/WHO FOOD STANDARDS PROGRAMME**

**CODEX COMMITTEE ON FOOD ADDITIVES**

**Fifty-First Session**

# MATTERS OF INTEREST ARISING FROM FAO/WHO AND FROM THE 86TH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

***Matters for information from the 86th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)***

1. The results of the 86th meeting of JECFA (Geneva, 12-21 June 2018) 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 77) will be accessible through the WHO JECFA publications website: http://www.who.int/foodsafety/publications/jecfa/en/. The specification monographs resulting from the 86th JECFA meeting will be published as FAO JECFA Monographs 22, FAO, Rome, 2018. 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**

2. 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

3. 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.

4. 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***

5. At its 86th meeting, JECFA evaluated the safety of 8 food additives. Toxicological recommendations or other scientific advice for these food additives are provided in the attached Table 1. CCFA51 **is invited** to consider the recommended actions (presented in Table 1) which might be required following the evaluations of these food additives

6. At its 86th meeting, JECFA also evaluated 69 flavouring agents using the revised Procedure for the Safety Evaluation of Flavouring Agents. The results of the evaluations are summarized in the attached Table 2.

**Table 1. Food additives evaluated toxicologically and/or considered for specifications at the 86th JECFA meeting**

| INS Number | Food additive | Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information | Recommended action by CCFA |
|---|---|---|---|
| 1207 | Anionic methacrylate copolymer (AMC) | The 86th JECFA was unable to complete the evaluation of AMC. The 86th JECFA concluded that there were no concerns for the toxicity of AMC itself. However, the presence in AMC of the residual monomer methyl acrylate, for which it is not possible to conclude on genotoxic potential, and the insufficient carcinogenicity data for methyl acrylate preclude establishing an ADI for AMC.<br>The available toxicology data for AMC indicate that it's poorly absorbed and is excreted in the faeces. In short-term and developmental toxicity studies, the NOAELs for AMC range from 400 to 1500 mg/kg bw per day, the highest doses tested. Estimated exposures to AMC based on intended use levels range from 2.9 to 43 mg/kg bw per day.<br>The 86th JECFA was unable to conclude on the safety of methyl acrylate as a residual monomer in AMC. Estimated exposures to methyl acrylate range from 0.2 to 2.8 µg/kg bw per day.<br>New specifications and a Chemical and Technical Assessment were prepared. The specifications were made tentative pending the completion of the safety evaluation of AMC. | Note the 86th JECFA was unable to complete the evaluation of AMC.<br>Note the conclusion that to clarify the *in vivo* carcinogenic potential of the residual monomer methyl acrylate more data are required. |
| 1205 | Basic methacrylate copolymer (BMC) | The 86th JECFA established an ADI "not specified" for BMC<br>The 86th JECFA concluded that the use of BMC that complies with the specifications established at the 86th meeting is not a safety concern when the food additive is used as a coating or glazing agent for solid food supplements; for foods for special medical purposes; micronutrient encapsulation for food fortification and at the intended use levels.<br>The available toxicology data for BMC do not give rise to concerns for toxicity. The substance is poorly absorbed and is excreted in the faeces. In short-term and developmental toxicity studies, the NOAELs for BMC range from 750 to 2000 mg/kg bw per day, the highest doses tested.<br>The JECFA 86th evaluated the exposure to BMC for the copolymer and its monomers (n-butyl methacrylate, 2-(dimethylamino)ethyl methacrylate and methyl methacrylate). Estimated exposures to BMC range from 3.0 to 135 mg/kg bw per day. The total monomeric content of BMC is less than 0.3%.<br>The 86th JECFA concluded that the toxicological data on the residual monomers do not give rise to concerns when considering the low dietary exposures.<br>New specifications and a Chemical and Technical Assessment were prepared. | Note the JECFA conclusion on an ADI "not specified" was established for BMC.<br>Note the new JECFA specifications for BMC (see CX/FA 19/51/4).<br>Include BMC (INS 1205) in Table 3 of GSFA and circulate for comments at Step 3.<br>Request for comments/proposals on uses and use levels of BMC 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). |

| INS Number | Food additive | Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information | Recommended action by CCFA |
|---|---|---|---|
| 127 | Erythrosine | The 86th JECFA concluded that the new data had become available since the previous evaluation of erythrosine do not give reason to revise the ADI and confirmed the previous ADI of 0–0.1 mg/kg bw.<br>The 86th JECFA noted that the dietary exposure estimate for erythrosine of 0.09 mg/kg bw per day (95th percentile for children) was close to the upper bound of the ADI. Given that this estimate of exposure is for children and it is a high percentile for consumers only, such a level is unlikely to occur every day over a lifetime. Therefore, JECFA concluded that dietary exposures to erythrosine for all age groups do not present a health concern.<br>The existing specifications for erythrosine were revised. A Chemical and Technical Assessment was prepared. | Note the JECFA conclusion that the new data that have become available since the previous evaluation of erythrosine do not give reason to revise the ADI and confirmed the previous ADI of 0–0.1 mg/kg bw. |
| 132 | Indigotine | The 86th JECFA considered the new data that had become available since the previous evaluation as well as previously evaluated studies and concluded that there are no reasons to revise the ADI and confirmed the previous ADI of 0–5 mg/kg bw.<br>JECFA noted that the conservative dietary exposure estimate of 0.8 mg/kg bw per day (95th percentile for children and toddlers) is less than the upper limit of the ADI of 0–5 mg/kg bw established for indigotine. The 86th JECFA concluded that dietary exposure to indigotine for all age groups does not present a health concern.<br>The existing specifications for indigotine were revised.<br>The 86th JECFA prepared a Chemical and Technical Assessment. | Note the JECFA conclusion that the new data that have become available since the previous evaluation of indigotine do not give reason to revise the ADI and confirmed the previous ADI of 0–5 mg/kg bw. |
| | Lutein and lutein esters from *Tagetes erecta* and zeaxanthin (synthetic) | The 86th JECFA concluded that based on the absence of toxicity in a wide range of studies, a group ADI "not specified" for lutein from *Tagetes erecta* (INS 161b(i)), lutein esters from *Tagetes erecta* (INS 161b(iii)) and zeaxanthin (synthetic) (INS 161h(i)) was established.<br>The 86th JECFA noted that free lutein, lutein esters and free zeaxanthin including meso-zeaxanthin are biochemically and toxicologically equivalent.<br>The 86th JECFA concluded that there were sufficient toxicological data to complete a safety assessment of lutein and lutein esters from *Tagetes erecta*, synthetic zeaxanthin and *meso*-zeaxanthin. Free lutein, lutein esters and free zeaxanthin and *meso*-zeaxanthin are substances of low toxicity for which no adverse effects have been observed in a broad range of toxicological studies in laboratory animals and clinical studies in humans. | Note the JECFA conclusion on an ADI "not specified" for lutein from *Tagetes* erecta, lutein esters from *Tagetes* erecta and zeaxanthin (synthetic).<br>Note the JECFA conclusion that meso-zeaxanthin was not included in this group ADI, as specifications are not currently available. |

| INS Number | Food additive | Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information | Recommended action by CCFA |
|---|---|---|---|
| | | Meso-zeaxanthin was not included in this group ADI, as specifications are not currently available.<br>The group ADI of 0-2 mg/kg bw for lutein from *Tagetes erecta* and zeaxanthin (synthetic) was withdrawn.<br>The 86th JECFA concluded that the estimated dietary exposure from the use of free lutein, lutein esters and free zeaxanthin as colours or food supplements are in the same order of magnitude as the intakes from foods where these xanthophylls are naturally present.<br>The specifications for lutein from *Tagetes erecta* were revised, and the Chemical and Technical Assessment was updated. The specifications for lutein esters from *Tagetes erecta* and zeaxanthin (synthetic) were maintained. | Note the JECFA conclusion that the group ADI of 0-2 mg/kg bw for lutein from *Tagetes erecta* and zeaxanthin (synthetic) was withdrawn.<br>Note that the specifications for lutein from *Tagetes erecta* were revised and that. the specifications for lutein esters from *Tagetes erecta* and zeaxanthin (synthetic) were maintained.<br>Include lutein from *Tagetes* erecta (INS 161b(i)) and zeaxanthin (synthetic) (INS 161h(i)) in Table 3 of GSFA and circulate for comments at Step 3.<br>Request for comments/proposals on uses and use levels of the group food additives which includes lutein from *Tagetes* erecta (INS 161b(i)), lutein esters from *Tagetes* erecta (INS 161b(iii)) and zeaxanthin (synthetic) (INS 161h(i)) 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). |
| 1206 | Neutral methacrylate copolymer (NMC) | The 86th JECFA established an ADI “not specified” for NMC. The ADI “not specified” was made temporary because the specifications are tentative.<br>The 86th JECFA concluded that the use of NMC that complies with the specifications is not of safety concern when the food additive is used as a coating or glazing agent for solid food supplements and for foods for special medical purposes at the proposed use levels. The NOAELs for NMC ranged from 454–2000 mg/kg | Note the 86th JECFA conclusion on an ADI “not specified” for NMC. The ADI “not specified” was made temporary because the specifications are tentative. |

| INS Number | Food additive | Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information | Recommended action by CCFA |
|---|---|---|---|
| | | bw per day, and these were the highest doses tested.<br>The 86th JECFA evaluated exposure to NMC for the copolymer and its monomers (methyl methacrylate and ethyl acrylate). Estimated exposures to NMC range from 5.8 to 86 mg/kg bw per day. The total monomeric content of NMC is less than 0.01%. Toxicological data on the residual monomers do not give rise to concerns when considering the low dietary exposures.<br>The JECFA 86th prepared new specifications for NMC. The specifications were made tentative, requiring a suitable validated method for its assay. A Chemical and Technical Assessment was prepared. | Note the 86 the JECFA conclusion that there was no data submitted for a suitable method of assay. |
| 420(ii)) | Sorbitol syrup | Sorbitol syrup (INS 420(ii)) is currently included in the *General Standard for Food Additives* (CXS 192-1995) (GSFA) although it has not been assigned an ADI or determined, based on other criteria, to be safe.<br>The 86th JECFA was therefore requested to consider the previous evaluations of sorbitol, hydrogenated glucose syrups and other relevant substances, and advise on the need for a separate evaluation of sorbitol syrup or if the ADI "not specified" for sorbitol (INS 420(i)) is also applicable for sorbitol syrup.<br>The 86th JECFA noted that based on the similarity of the chemical constituents of sorbitol syrup to the previously evaluated sorbitol, maltitol syrup and polyglycitol syrup, JECFA concluded that there is no need for a separate evaluation of sorbitol syrup and established an ADI "not specified" for sorbitol syrup. | Note the 86th JECFA conclusion on an ADI "not specified" for sorbitol syrup. |
| 134 | Spirulina extract | The 86th JECFA established a temporary ADI "not specified" for spirulina extract.<br>The ADI was based on the absence of toxicity in repeated-dose animal studies with spirulina extract and dried spirulina. The ADI "not specified" was made temporary due to the tentative nature of the specifications.<br>Expressed as phycocyanins, estimated dietary exposure from the use of spirulina extract as a food colour based on the Budget method and exposure to spirulina extract and dried spirulina from other dietary sources, including food ingredients, dietary supplements, and coatings of food supplements was 190 mg/kg bw for adults (60 kg/person) and 650 mg/kg bw for a child (15 kg/person).<br>The 86th JECFA concluded that this dietary exposure does not present a health concern. | Note the 86th JECFA conclusion on an ADI "not specified" for spirulina extract. The ADI "not specified" was made temporary because the specifications are tentative.<br>Note the JECFA request for analytical data requested by December 2019. |

| INS Number | Food additive | Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information | Recommended action by CCFA |
|---|---|---|---|
| | | The 86th JECFA received limited analytical data on spirulina extract. To remove the tentative designation from the specifications, the following information on the products of commerce is requested by December 2019:<br>• Full compositional characterization of commercial products in both liquid and powder forms.<br>• Full compositional characterization of the aqueous extract before formulation/standardization.<br>• Validated analytical methods for identification of the substance with a suitable specificity (including validation data and representative batch data).<br>• Validated analytical methods for the determination of the purity of the substance with a suitable specificity (including validation data and representative batch data). | |

**Table 2. Flavouring agents evaluated at the 86th JECFA meeting**

The flavouring agents were evaluated by the revised Procedure for the Safety Evaluation of Flavouring Agents.

***A. Alicyclic primary alcohols, aldehydes, acids and related esters***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class I** | | | |
| Mixture of 1-Vinyl-3-cyclohexenecarbaldehyde and 4-Vinyl-1-cyclohexenecarbaldehyde | 2253 | N | No safety concern |
| *p*-Mentha-1,8-dien-7-ol | 974 | N | No safety concern |
| *p*-Mentha-1,8-dien-7-yl acetate | 975 | N | No safety concern |
| Formyl-6,6-dimethylbicyclo[3.1.1]hept-2-ene | 980 | N | No safety concern |
| Myrtenol | 981 | N | No safety concern |
| Myrtenyl acetate | 982 | M | No safety concern |
| **Structural class II** | | | |
| (1-Methyl-2-(1,2,2-trimethylbicyclo[3.1.0]hex-3-ylmethyl)cyclopropyl)methanol | 2254 | N | No safety concern |
| **Structural class III** | | | |
| (±)-Bicyclo[2.2.1]hept-5-ene-2-carboxylic acid, ethyl ester | 2255 | N | No safety concern |
| **Flavouring agent excluded at Step 1 of the revised Procedure** | | | |
| *p*-Mentha-1,8-dien-7-al (Perillaldehyde) | 973 | M | Genotoxicity data for *p*-mentha-1,8-dien-7-al raise concerns for potential genotoxicity |

N: new specifications

M: existing specifications maintained;

***B. Carvone and structurally related substances***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class I** | | | |
| Pinocarvyl isobutyrate | 2242 | N | No safety concern |
| Carvyl palmitate | 2243 | N | No safety concern |
| **Structural class III** | | | |
| 6-Hydroxycarvone | 2244 | N | No safety concern |
| **Flavouring agents not evaluated according to the revised Procedure** | | | |
| (+)-Carvone | 380.1 | M | The Committee did not re-evaluate (+)-carvone (No. 380.1) according to the revised Procedure given the lack of information on the oral exposure from all sources and the need to review the ADI.<br><br>A review of the ADI is recommended based on the evaluation of all biochemical and toxicological data. Also, data are needed for an exposure assessment for oral exposure to (+)-carvone from all sources to complete the evaluation for (+)-carvone. |
| (-)-Carvone | 380.2 | M | The Committee did not re-evaluate (-)-carvone (No. 380.2) according to the revised Procedure given the lack of information on the oral exposure from all sources and the lack of toxicological data. |

M: existing specifications maintained; N: new specifications

***C. Furan-substituted aliphatic hydrocarbons, alcohols, aldehydes, ketones, carboxylic acids and related esters, sulfides, disulfides and ethers***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class III** | | | |
| 2-Pentylfuran | 1491 | M[a] | No safety concern |
| 2-Heptylfuran | 1492 | M[a] | No safety concern |
| 2-Decylfuran | 1493 | M[a] | No safety concern |
| 3-Methyl-2-(3-methylbut-2-enyl)-furan | 1494 | M[a] | No safety concern |
| 2,3-Dimethylbenzofuran | 1495 | M[a] | No safety concern |
| 2,4-Difurfurylfuran | 1496 | M[a] | No safety concern |
| 3-(2-Furyl)acrolein | 1497 | M[a] | No safety concern |
| 2-Methyl-3(2-furyl)acrolein | 1498 | M[a] | No safety concern |
| 3-(5-Methyl-2-furyl)prop-2-enal | 1499 | M[a] | No safety concern |
| 3-(5-Methyl-2-furyl)butanal | 1500 | M[a] | No safety concern |

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| 2-Furfurylidene-butyraldehyde | 1501 | M[a] | No safety concern |
| 2-Phenyl-3-(2-furyl)prop-2-enal | 1502 | M[a] | No safety concern |
| 2-Furyl methyl ketone | 1503 | M[a] | No safety concern |
| 2-Acetyl-5-methylfuran | 1504 | M[a] | No safety concern |
| 2-Acetyl-3,5-dimethylfuran | 1505 | M[a] | No safety concern |
| 3-Acetyl-2,5-dimethylfuran | 1506 | M[a] | No safety concern |
| 2-Butyrylfuran | 1507 | M[a] | No safety concern |
| (2-Furyl)-2-propanone | 1508 | M[a] | No safety concern |
| 2-Pentanoylfuran | 1509 | M[a] | No safety concern |
| 1-(2-Furyl)butan-3-one | 1510 | M[a] | No safety concern |
| 4-(2-Furyl)-3-buten-2-one | 1511 | M[a] | No safety concern |
| Pentyl 2-furyl ketone | 1512 | M[a] | No safety concern |
| Ethyl 3-(2-furyl)propanoate | 1513 | M[a] | No safety concern |
| Isobutyl 3-(2-furan)propionate | 1514 | M[a] | No safety concern |
| Isoamyl 3-(2-furan)propionate | 1515 | M[a] | No safety concern |
| Isoamyl 3-(2-furan)butyrate | 1516 | M[a] | No safety concern |
| Phenethyl 2-furoate | 1517 | M[a] | No safety concern |
| Propyl 2-furanacrylate | 1518 | M[a] | No safety concern |
| 2,5-Dimethyl-3-oxo-(2*H*)-fur-4-yl butyrate | 1519 | M[a] | No safety concern |
| Furfuryl methyl ether | 1520 | M[a] | No safety concern |
| Ethyl furfuryl ether | 1521 | M[a] | No safety concern |
| Difurfuryl ether | 1522 | M[a] | No safety concern |
| 2,5-Dimethyl-3-furanthiol acetate | 1523 | M[a] | No safety concern |
| Furfuryl 2-methyl-3-furyl disulfide | 1524 | M[a] | No safety concern |
| 3-[(2-Methyl-3-furyl)thio]-2-butanone | 1525 | M[a] | No safety concern |
| O-Ethyl S-(2-furylmethyl)thiocarbonate | 1526 | M[a] | No safety concern |
| (E)-Ethyl 3-(2-furyl)acrylate | 2103 | M[a] | No safety concern |
| di-2-Furylmethane | 2104 | M[a] | No safety concern |
| 2-Methylbenzofuran | 2105 | M[a] | No safety concern |

M: existing specifications maintained

[a] The text indicating that the safety evaluation for these flavouring agents had not been completed was removed from the specifications and the specifications were maintained as full

***D. Linear and branched-chain aliphatic, unsaturated, unconjugated alcohols, aldehydes, acids and related esters***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class I** | | | |
| *trans*-6-Octenal | 2240 | N | No safety concern |

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| 2,6-Dimethyl-5-heptenol | 2241 | N | No safety concern |

N: new specifications

***E. Maltol and related substances***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class II** | | | |
| Maltol | 1480 | M | No safety concern[a] |
| **Structural class III** | | | |
| Ethyl maltol isobutyrate | 2252 | N | No safety concern |

M: existing specifications maintained

N: new specifications

[a] The previously established ADI for maltol was withdrawn by the Committee.

***F. Menthol and structurally related substances***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class I** | | | |
| Menthyl formate | 2246 | N | No safety concern |
| Menthyl propionate | 2247 | N | No safety concern |
| *l*-Menthyl butyrate | 2248 | N | No safety concern |
| *dl*-Isomenthol | 2249 | N | No safety concern |
| Dimenthyl glutarate | 2250 | N | No safety concern |
| Menthol | 427 | M | No safety concern[a] |
| **Structural class III** | | | |
| (±)-2-[(2-*p*-Menthoxy)ethoxy]ethanol | 2251 | N | No safety concern |

M: existing specifications maintained

N: new specifications

[a] The ADI of menthol of 0–4 mg/kg bw established at the fifty-first meeting was maintained.

***G. Miscellaneous nitrogen-containing substances***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class III** | | | |
| 2-(((3-(2,3-Dimethoxyphenyl)-1*H*-1,2,4-triazol-5-yl)thio)methyl)pyridine | 2235 | N | No safety concern |
| *S*)-1-(3-(((4-Amino-2,2-dioxido-1*H*-benzo[c][1,2,6]thiadiazin-5-yl)oxy)methyl)piperidin-1-yl)-3-methylbutan-1-one | 2236 | N | No safety concern |
| 2-(4-Methylphenoxy)-*N*-(1*H*-pyrazol-3-yl)-*N*-(thiophen-2-ylmethyl)acetamide | 2237 | N | No safety concern |

N: new specifications

***H. Saturated aliphatic acyclic branched-chain primary alcohols, aldehydes, and acids***

| Flavouring agent | No. | Specifications | Conclusion based on current estimated dietary exposure |
|---|---|---|---|
| **Structural class I** | | | |
| 8-Methyldecanal | 2238 | N | No safety concern |
| 8-Methylnonanal | 2239 | N | No safety concern |

N: new specifications