CODEX ALIMENTARIUS COMMISSION E

Food and Agriculture Organization of the United Nations

World Health Organization

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

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MATTERS OF INTEREST ARISING FROM FAO AND WHO AND FROM THE 80TH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

Matters for information from the 80th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

1. The results of the 80th meeting of JECFA (Rome, 16-25 June 2015) on certain food additives and contaminants will be available as follows: the meeting report (WHO Technical Report Series) and the toxicological monographs (WHO Food Additive Series No 71) will be accessible through the WHO JECFA publications website: http://www.who.int/foodsafety/publications/jecfa-reports/en/. The specification monographs will be available (in English only) on the JECFA Online Edition of: "Combined Compendium of Food Additive Specifications" www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/. The specification monographs resulting from the 80th JECFA meeting will be published as FAO JECFA Monographs 17, FAO, Rome, 2015. The publication will be 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 80th JECFA are summarized here:

Potential allergenicity of enzymes: change to the number of amino acids in segments used in allergen database searches

3. At its 80th meeting, JECFA considered as there is no conclusive test that will predict a likely human immunoglobulin E (IgE) response to a genetically modified enzyme following oral exposure, an important first step involves undertaking a comparison of the amino acid sequence with those of established allergens. This amino acid sequence comparison is intended to detect both global similarities and short contiguous amino acid sequences that may represent linear IgE epitopes. For the short amino acid sequences, it is recognized that the 2001 FAO/WHO Consultation on Allergenicity of Foods Derived from Biotechnology suggested moving from eight to six amino acid segments in searches. However, experience gained with a large number of enzymes at JECFA indicates that searches involving six amino acid segments result in positive matches that are of no biological relevance. The 80th JECFA recommends that such searches should consider only eight amino acid sequences.

Revised guidance for WHO JECFA monographers

4. At its 80th meeting, JECFA was provided with drafts of the two revised guidance documents for WHO monographers and reviewers evaluating i) food additives (excluding flavouring agents) and ii) contaminants in food and feed. These guidance documents are intended primarily for WHO Experts (monographers) who prepare monographs for JECFA and for Members (reviewers) who have been assigned to peer review them and propose evaluations. The guidance will also be useful to manufacturers who submit dossiers to WHO and other parties interested in understanding the process followed in the evaluation of food additives or contaminants in food and feed by JECFA. The 80th JECFA was asked to provide written comments to the Secretariat so that the documents can be finalized. The 80th JECFA requested that a separate guidance document on enzymes be prepared. The final documents will be published on the WHO website at http://www.who.int/foodsafety/chem/jecfa/guidelines/en/.

Update on FAO and WHO databases related to the work of JECFA

5. The JECFA Secretariat has started a project to modernize the FAO JECFA databases (one for food additives, one for flavouring agents and one for residues of veterinary drugs), starting with the one on flavouring agents. While the major features and output will not differ significantly from the current version, the project aims to develop an online platform that allows the JECFA Secretariat to manage the process from receiving data for proposed new or revised specifications to adding/updating records to the database and to publishing the adopted specifications.

6. The 80th JECFA was also updated on the latest developments on several WHO databases now available on a dedicated website[1]. The searchable JECFA summary database provides concise information and direct links to the JECFA reports and monographs for each compound evaluated by JECFA, including contaminants, providing details on critical studies and end-points and estimated dietary exposures. WHO's global platform for food safety data and information (FOSCOLLAB) combines information from several databases (e.g. JECFA, JMPR, GEMS/Food, Codex Alimentarius Commission) and provides the key information from each in one overview page (dashboard). Such dashboards have been developed for contaminants and for pesticides; another dashboard for veterinary drugs is under development. To further improve the data used for dietary exposure assessment, FAO and WHO initiated a project to collect national individual food consumption data, detailed by different age groups and consumers only. Summary statistics from (currently) 37 surveys (only those with a duration of 2 days or more) from 26 countries are published in the FAO/WHO Chronic Individual Food Consumption Database – Summary statistics (CIFOCOss).

Tentative specifications for food additives

7. At its 80th meeting, JECFA could not adopt specifications for two new additives (i.e. Mixed β-glucanase, cellulase and xylanase from *Rasamsonia emersonii* and Mixed β-glucanase and xylanase from *Disporotrichum dimorphosporum*) and could not revise the specifications of two other additives (Silicon dioxide, amorphous (INS 551) and Sodium aluminium silicate (INS 554)) as the information available was insufficient. The missing information and the suggested deadline for its submission are given in Table 1. It is recommended that such pending evaluations and the data needed are considered by the CCFA Working Group on priorities and by CCFA48 under Agenda Item 7(a) "Proposals for additions and changes to the Priority List of Substances proposed for evaluation by JECFA" with a view to have a clear commitment on whether and when data will be made available.

Requests for scientific advice

8. Both organizations continue to jointly prioritise 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.

9. 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.

10. 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

11. At its 80th meeting, JECFA evaluated the safety of six food additives and conducted an updated dietary exposure assessment for one food additives. Toxicological recommendations or other scientific advice for these food additives are provided in the attached Table 1.

12. CCFA48 **is invited** to consider the recommended actions (presented in Table 1) which might be required following the evaluations of these food additives.

[1] http://www.who.int/foodsafety/databases/en/

Table 1. Food additives evaluated toxicologically at the 79th JECFA meeting

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
	Benzoates: dietary exposure assessment	JECFA had previously established and ADI of 0-5 mg/kg bw for benzoates, and was asked now to update the exposure assessment based on actual use levels. Based on the available data set, the 80th JECFA noted that there is consistency in the average typical range of concentration levels for benzoates reported to be used or analysed in non-alcoholic ("soft") beverages (*General Standard for Food Additives* [GSFA] food category 14.1). For example, typical reported concentration levels from industries ranged from 83 to 209 mg/L, and analytically quantified measurements ranged from 63 to 259 mg/L in GSFA food category 14.1.4; these levels are lower than national maximum limits (150–400 mg/L) or limits for GSFA food category 14.1.4 (600 mg/L). The 80th JECFA also noted that most of the reported estimates for mean and high percentile benzoate exposure were below the ADI of 0–5 mg/kg body weight (bw), expressed as benzoic acid, despite different methodologies and assumptions applied in the preparation of the exposure estimates. None of the mean exposure estimates for consumers of non-alcoholic ("soft") beverages exceeded the upper bound of the ADI: 0.3–4.1 mg/kg bw per day for toddlers and young children, 0.2–2.7 mg/kg bw per day for other children including adolescents, and 0.1–1.7 mg/kg bw per day for adults. However, the 80th JECFA noted that the 95th percentile exposures for the consumers-only group exceeded the upper bound of the ADI in some cases: up to 10.9 mg/kg bw per day for toddlers and young children and up to 7.0 mg/kg bw per day for other children including adolescents. Additionally, the 80th JECFA noted that in some countries, the overall dietary exposure to benzoates for toddlers, young children and adolescents also exceeds the upper bound of the ADI at the high percentiles. Reduction of those exposures exceeding the upper bound of the ADI would require consideration of dietary patterns for both beverage and non-beverage foods containing benzoates and typical/allowed benzoate use levels in those countries.	Note the JECFA conclusion on the current estimated dietary exposures for benzoates. In light of JECFA conclusion on actual use levels, consider: - The feasibility to reduce the ML for benzoates in GSFA food category 14.1.4 Water-based flavoured drinks, including "sport," "energy," or "electrolyte" drinks and particulated drinks.
1104	Lipase from *Fusarium heterosporum* expressed in *Ogataea polymorpha*	No treatment-related adverse effects were seen at the highest dose tested (669 mg total organic solids [TOS]/kg bw per day) in a 13-week study of oral toxicity in rats. A comparison of the dietary exposure estimate of 0.5 mg TOS/kg bw per day (for a 60 kg individual) with the highest dose tested of 669 mg TOS/kg bw per day results in a margin of exposure (MOE) of at least 1300. The 80th JECFA established an ADI "not specified"[1]for lipase from *F. heterosporum* expressed in *O. polymorpha* when used in the applications specified and in accordance with good manufacturing practice.	Note the JECFA conclusion on an ADI "not specified" for lipase from *F. heterosporum* expressed in *O. polymorpha* when used in the applications specified and in accordance with GMP. Consider to: - Recommend inclusion in the

[1] 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

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			database on processing aids.
470(iii)	Magnesium stearate	The 80th JECFA estimated the potential total dietary exposure to magnesium stearate based on the proposed maximum use levels: 44 mg/kg bw per day for children and 83 mg/kg bw per day for adults, corresponding to 2 and 4 mg/kg bw per day, expressed as magnesium, respectively. These dietary exposures would contribute up to an additional 250 mg/day to the background exposure to magnesium from food of 180–480 mg/day. The 80th JECFA noted that the consumption of the food additive may lead to an additional dietary exposure to stearic and palmitic acids in the order of 5 g/day. An ADI "not specified" has previously been established for a number of magnesium salts used as food additives. JECFA concluded that there are no differences in the evaluation of the toxicity of magnesium stearate compared with other magnesium salts, and therefore confirmed the ADI "not specified" for magnesium salts of stearic and palmitic acids. However, the 80th JECFA was concerned that the use of magnesium salts in many food additives may result in combined exposure that could lead to a laxative effect. Therefore, the JECFA reiterated its previous recommendation to undertake an exposure assessment for magnesium from use of food additives.	Note the JECFA conclusion on the ADI "not specified" for magnesium salts of stearic and palmitic acids and consider to: - Include magnesium stearate (INS 470(iii)) in Table 3 of GSFA and circulate for comments at Step 3; and - Request comments/proposals on uses and use levels of magnesium stearate (INS 470(iii)) for the food categories listed in the Annex to Table 3. Note the JECFA recommendation on exposure assessment for magnesium from use of food additives and consider to: - Recommend countries to submit information to JECFA on actual use level for magnesium-containing food additives.
	Maltotetraohydrolase from *Pseudomonas stutzeri* expressed in *Bacillus licheniformis*	No treatment-related adverse effects were seen at the highest dose tested (93 mg TOS/kg bw per day) in a 13- week study of oral toxicity in rats. A comparison of the dietary exposure estimate of 0.1 mg TOS/kg bw per day (for a 60 kg individual) with the highest dose tested of 93 mg TOS/kg bw per day results in an MOE of at least 900. The 80th JECFA established an ADI "not specified" for maltotetraohydrolase from *P. stutzeri* expressed in *B. licheniformis* when used in the applications specified and in accordance with good manufacturing practice.	Note the JECFA conclusion on an ADI "not specified" for maltotetraohydrolase from *P. stutzeri* expressed in *B. licheniformis* when used in the applications specified and in accordance with GMP. Consider to: - Recommend inclusion in the database on processing aids.
	Mixed β-glucanase, cellulase and xylanase from *Rasamsonia emersonii*	No treatment-related adverse effects were seen at the highest dose tested (84.8 mg TOS/kg bw per day) in a 13- week study of oral toxicity in rats. A comparison of the dietary exposure estimate of 0.08 mg TOS/kg bw per day (for a 60 kg individual) with the highest dose tested of 84.8 mg TOS/kg bw per day results in an MOE of at least 1000.	Note the JECFA conclusion on an ADI "not specified" for the mixed β-glucanase, cellulase and xylanase enzyme preparation from *R. emersonii* when used in the

INS Number	Food additive	Acceptable daily intakes (ADIs) and other toxicological or safety recommendations and dietary exposure information	Recommended action by CCFA
		The 80th JECFA established an ADI "not specified" for the mixed β-glucanase, cellulase and xylanase enzyme preparation from *R. emersonii* when used in the applications specified and in accordance with good manufacturing practice. New tentative specifications were prepared, with a request for the following information: - a method to determine the identity for β-glucanase, including data from a minimum of five batches using the method described; - a method to determine the identity for cellulase, including data from a minimum of five batches using the method described; - a non-proprietary method to determine the identity and activity for xylanase that can be used by control laboratories, and data from a minimum of five batches using the method described. **The above-requested information should be submitted by December 2016** in order for the tentative specifications to be revised; failure to provide this information may lead to a withdrawal of the specifications, with a possible impact on the ADI.	applications specified and in accordance with GMP. No action required as the new specifications is tentative. Note the JECFA request for information to complete to revise the tentative specifications
	Mixed β-glucanase and xylanase from *Disporotrichum dimorphosporum*	No treatment-related adverse effects were seen at the highest dose tested (199 mg TOS/kg bw per day) in a 13- week study of oral toxicity in rats. A comparison of the dietary exposure estimate of 0.7 mg TOS/kg bw per day (for a 60 kg individual) with the highest dose tested of 199 mg TOS/kg bw per day gives an MOE of at least 280. The 80th JECFA established an ADI "not specified" for the mixed β-glucanase and xylanase enzyme preparation from *D. dimorphosporum* when used in the applications specified and in accordance with good manufacturing practice. New tentative specifications were prepared, with a request for the following information: - a method to determine the identity for β-glucanase, including data from a minimum of five batches using the method described; - a non-proprietary method to determine the identity and activity for xylanase that can be used by control laboratories, and data from a minimum of five batches using the method described. **The above-requested information should be submitted by December 2016** in order for the tentative specifications to be revised; failure to provide this information may lead to a withdrawal of the specifications, with a possible impact on the ADI.	Note the JECFA conclusion on an ADI "not specified" for the mixed β-glucanase and xylanase enzyme preparation from D. dimorphosporum when used in the applications specified and in accordance with GMP. No action required as the new specifications is tentative. Note the JECFA request for information to complete to revise the tentative specifications.
1209	Polyvinyl alcohol (PVA) – polyethylene glycol (PEG) graft copolymer	On the basis of the available studies, in which no treatment-related effects were seen at the highest doses tested, the 80th JECFA considered PVA-PEG graft copolymer to be a substance of low oral toxicity in rats, rabbits and dogs. The bioavailability of PVA-PEG graft copolymer in rats is negligible, and PVA-PEG graft copolymer is unlikely to be genotoxic and is not associated with reproductive or developmental toxicity. Therefore, the 80th JECFA concluded that calculation of an MOE for PVAPEG graft co-polymer would not be meaningful. Based on these data, the Committee would normally establish an ADI	Note the JECFA conclusion on the use of PVA-PEG graft co-polymer that complies with the specifications established at the current meeting is not of safety concern when the food additive is used as a glazing agent (aqueous film coating), stabilizer and binder for tablets in the preparation and

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		"not specified". However, the 80th JECFA decided not to establish an ADI "not specified" for PVAPEG graft co-polymer in view of the impurities present, some of which may also be impurities in other food additives. The 80th JECFA had concerns that establishing an ADI "not specified" could lead to additional uses beyond those considered at the current meeting and consequently could increase exposure to the impurities. The use of PVA-PEG graft co-polymer that complies with the proposed specifications could lead to a dietary exposure to ethylene glycol and diethylene glycol from both food supplements and pharmaceutical products up to 0.016 mg/kg bw per day for children (high consumers). This is 3% of the tolerable daily intake (TDI) of 0.5 mg/kg bw per day derived by the Scientific Committee on Food of the European Union, and therefore the exposure to ethylene glycol and diethylene glycol from the use of PVAPEG graft co-polymer that complies with the specifications established at the current meeting is not of safety concern when the food additive is used in the applications specified. The use of PVA-PEG graft co-polymer that complies with the proposed specifications could lead to a dietary exposure to vinyl acetate from both food supplements and pharmaceutical products up to 0.0008 mg/kg bw per day for children. This dietary exposure estimate is at least 62 500 times lower than the dose levels at which increases in tumour incidence are observed in oral studies of long term toxicity and carcinogenicity in rats and mice. Therefore, the dietary exposure to vinyl acetate from the use of PVA-PEG graft co-polymer that complies with the specifications established at the current meeting is not of safety concern when the food additive is used in the applications specified. The 80th JECFA concluded that the use of PVA-PEG graft co-polymer that complies with the specifications established at the current meeting is not of safety concern when the food additive is used as a glazing agent (aqueous film coating), stabilizer and binder for tablets in the preparation and formulation of food supplements and in accordance with good manufacturing practice.	formulation of food supplements and consider to: - Request comments/proposals the use level of Polyvinyl alcohol (PVA) – polyethylene glycol (PEG) graft copolymer s (INS 1209) for use as a glazing agent (aqueous film coating), stabilizer and binder only in food category for tablets in the preparation and formulation of food supplements and in accordance with good manufacturing practice. in food category 13.6 Food supplement of GSFA.
551	Silicon dioxide, amorphous	Prepared at the 80th JECFA and published in FAO JECFA Monographs 17 (2015), superseding tentative specifications prepared at the 77th JECFA (2013) and published in FAO JECFA Monographs 14 (2013). An ADI 'not specified' for silicon dioxide and certain silicates was established at the 29th JECFA (1985). Revised tentative specifications were prepared, with a request for the following information: - Raw materials used and methods of manufacture for different forms of silicon dioxide (pyrogenic silica, precipitated silica, hydrated silica, silica aerogel and colloidal silica) - Identification methods allowing the differentiation between the above forms of silicon dioxide - Functional uses of different forms, and information on the types of products in which it is used and the use levels in these products - Data on solubility using the procedure documented in "Compendium of Food Additives	No action required as the new specifications is tentative. Note the JECFA request for information to complete to revise the tentative specifications.

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		Specifications, Vol.4, Analytical methods" - Data on the impurities soluble in 0.5 M hydrochloric acid for all forms of silicon dioxide used as food additives, from a minimum of five batches. If a different extraction and determination method is used, provide data along with details of method and QC data. - Suitability of the analytical method for the determination of aluminium, silicon and sodium using the proposed "Method of assay" along with data, from a minimum of five batches. If a different method is used, provide data along with details of the method and QC data. - In addition to the above information, data on pH, loss on drying and loss on ignition for hydrated silica, silica aerogel and colloidal silica. **The above-requested information should be submitted by December 2016** in order for the tentative specifications to be revised; failure to provide this information may lead to a withdrawal of the specifications, with a possible impact on the ADI.	
554	Sodium Aluminium Silicate	Prepared at the 80th JECFA and published in FAO JECFA Monographs 17 (2015), superseding tentative specifications prepared at the 77th JECFA (2013) and published in FAO JECFA Monographs 14 (2013). An ADI 'not specified' for silicon dioxide and certain silicates was established at the 29th JECFA (1985). A PTWI of 2 mg/kg bw for total aluminium was established at the 74th JECFA (2011). The PTWI applies to all aluminium compounds in food, including food additives. Revised tentative specifications were prepared, with a request for the following information: - Functional uses other than anticaking agent, if any, and information on the types of products in which it is used and the use levels in these products - Data on solubility using the procedure documented in the "Compendium of Food Additives Specifications, Vol. 4, Analytical methods" - Data on the impurities soluble in 0.5 M hydrochloric acid, from a minimum of five batches. If a different extraction and determination method is used, provide data along with details of method and QC data. - Suitability of the analytical method for the determination of aluminium, silicon and sodium using the proposed "Method of assay" along with data, from a minimum of five batches, using the proposed method. If a different method is used, provide data along with details of the method and QC data. **The above-requested information should be submitted by December 2016** in order for the tentative specifications to be revised; failure to provide this information may lead to a withdrawal of the specifications, with a possible impact on the ADI.	No action required as the new specifications is tentative. Note the JECFA request for information to complete to revise the tentative specifications