codex alimentarius commission E

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 3 **CX/FA 09/41/3**

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

Forty-first Session

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MATTERS OF INTEREST ARISING FROM FAO AND WHO AND FROM THE 69TH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

1. This document provides information on FAO and WHO activities in the area of provision of scientific advice to Codex and Member countries, as well as other activities which are of interest for CCFA.

Matters for information and action from the 69th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

2. The results of the 69th meeting of JECFA on food additives are available in the summary report[1]. The meeting report (WHO Technical Report Series, 2009) and the toxicological monographs (WHO FAS 60, 2009) will become available in due course and will be accessible through the WHO JECFA website: http://www.who.int/ipcs/publications/jecfa/en/index.html. The specifications monographs (FAO JECFA Monographs 5, 2008) are available at the FAO JECFA website at http://www.fao.org/docrep/011/i0345e/i0345e00.htm. In addition, all specifications monographs for food additives and flavouring agents are available in the updated on-line editions of the respective databases at the FAO JECFA website: http://www.fao.org/ag/agn/jecfa-additives/search.html and http://www.fao.org/ag/agn/jecfa-flav/search.html. See also paragraphs 17 - 22 and Tables 1 and 2 below.

Exposure assessment of flavouring agents

3. To respond to concerns that the maximized survey-derived intake (MSDI) estimation method may underestimate dietary exposure to some flavouring agent, JECFA discussed and evaluated an additional method of dietary exposure assessment for flavouring agents at its 68th and 69th meetings. This additional new method of dietary exposure assessment (since termed the Single Portion Exposure Technique, SPET) is based on actual use levels of flavours and the daily consumption of a single portion of food containing the specific flavour.

4. The JECFA noted that MSDI and SPET estimates of dietary exposure provide different and complementary information.

5. As it was not possible to elaborate criteria to identify the flavouring agents for which the MSDI underestimated dietary exposure and SPET estimates should be used, the Committee concluded it was necessary to incorporate SPET estimates into the Procedure for the Safety Evaluation of Flavouring Agents (the procedure) for all flavouring agents considered at future meetings of the Committee. The Committee agreed that it would not be necessary to re-evaluate flavouring agents that have already been assessed using the Procedure.

[1] See the Summary and Conclusions of the 69th Meeting of the Joint FAO/WHO Expert Committee on Food Additives for additional details: http://www.fao.org/ag/agn/agns/files/jecfa69_final.pdf and http://www.who.int/ipcs/food/jecfa/summaries/summary69.pdf

6. To enable a safety evaluation using the revised Procedure to be undertaken in the future, the Committee requested that added use-level data be provided for each flavouring agent in a timely fashion before the meeting, in addition to up-to-date data on production volumes, as part of the data package for the safety evaluation. The Committee will not perform a safety evaluation in the absence of such data.

Provision of Scientific Advice from FAO and WHO

Expert Consultation on the use of 'active chlorine' in the food industry

7. CCFAC and CCFH have requested FAO and WHO to address the safety of use of 'active chlorine' in the food industry. A core group of experts has been identified and met in November 2007 to clearly define the scope and outline of the project. Working papers were prepared as basis for discussion at and international expert consultation. The Joint FAO/WHO Expert meeting on the benefits and risks of the use of chlorine-containing disinfectants in food production and food processing was held 27-30 May 2008 in Ann Arbor, Michigan, United States of America. The expert meeting drew from the experience of 20 experts from 13 countries and was dedicated to assess the benefits of the reduction of foodborne disease risk by reduction and control of contamination of pathogenic micro-organisms by direct treatment of food with disinfectants in various steps of food production and processing and the potential health risks from ingestion of chlorine and non-chlorine chemical disinfectants and their reaction by-products. The predominating world-wide treatment scenarios for poultry, red meat, fish and fishery products, fresh produce (fresh fruit and vegetables, including sprouts and hydroponics) and food contact surfaces were used in the assessment of the benefits and risks in a step-wise qualitative approach and conclusions and recommendations were agreed. As further extensive drafting and editing of the report is necessary, a prepublication issue of the report is only foreseen 2009. Information on the project can be found at http://www.fao.org/ag/agn/agns/chemicals_chlorine_meeting_en.asp and http://www.who.int/ipcs/food/active_chlorine/en/index.html .

Principles and Methods for Risk Assessment of Chemicals in Food

8. FAO and WHO are in the process of finalising the project to update the principles and methods for risk assessment of chemical in food, including food additives, contaminants and natural toxins, residues of veterinary drugs and pesticides. The project has included several workshops on specific areas of risk assessment. The final draft document, intended to replace Environmental Health Criteria Documents 70 and 104, was posted on the websites of FAO and WHO for public comments in June 2008. A final expert consultation was held in Seoul, Republic of Korea, to consider the entire document and all comments received. Joint efforts are being made to finalize the guidance and publish it as a new Environmental Health Criteria document in 2009.

Expert consultation on melamine

9. An increased incidence of kidney 'stones' and renal failure in infants has been reported from September 2008 in China, associated with the ingestion of infant formula contaminated with melamine. Preliminary WHO risk assessments have provided many Member States with valuable information for action. An independent international scientific expert meeting has therefore been held as part of WHO's emergency measures in this area, in collaboration with FAO and supported by Health Canada. The meeting was held 1-4 December 2008 in Ottawa, Canada, and the executive summary, as well as the conclusions and recommendations have been published on the WHO and FAO websites: http://www.who.int/foodsafety/fs_management/infosan_events/en/index.html and http://www.fao.org/ag/agn/agns/chemicals_melamine_en.asp .

10. Besides assessments of the chemistry, analytical methods, occurrence and exposure, the meeting established a tolerable daily intake (TDI) level for melamine of 0.2 mg/kg body weight. Based on this TDI the meeting concluded that current limits in food as established by many authorities (1ppm infant formula, 2.5 ppm other foods) are health protective. The meeting also pointed out the importance of new findings of melamine in animal feed - melamine in feed can result in carry-over into human food (eggs, milk, meat etc.). The final report is in preparation on will be published on FAO and WHO websites.

Expert Consultation on the application of nanotechnology in the food industry

11. In response to concerns raised by member countries on the possible food safety implications of the application of nanotechnology to food and agriculture, FAO and WHO will implement an expert meeting to address this issue, to be held 1-5 June at FAO HQ in Rome. The aim of the meeting is three-fold (1) summarize actual and anticipated nanotechnology applications in the food and agriculture sectors, and develop a common view of their implications for food safety, (2) to review current risk assessment procedures and evaluate their adequacy for the assessment of nano-particles in relation to foods, (3) consider issues related to communication with all stakeholders, and overall agree on priority research to fill information gaps related to potential food safety issues and to develop guidance on the possible roles of FAO and WHO in addressing food safety issues linked to nanotechnology applications. FAO and WHO convened a meeting of a core group of experts from 14-15 May 2008 to further define the scope of the meeting and propose outlines for background papers to be prepared in advance of the meeting. A call for data and call for experts for the Joint FAO/WHO Expert Meeting on the Application of Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications have been issued and are available at: http://www.fao.org/ag/agn/agns/meetings_consultations_en.asp.and, http://www.who.int/foodsafety/fs_management/meetings/nano_june09/en/index.html

Follow-up of the FAO/WHO consultative process on provision of scientific advice to Codex and member countries

12. The "Consultative Process" which was initiated at the request of the 24th Session of the Codex Alimentarius Commission held in July 2001, and recommended that FAO and WHO carry out "a review of the status and procedures of the expert bodies in order to improve the quality, quantity and timeliness of scientific advice" began in earnest in 2003 and was concluded in 2007. The Framework document has now been published in English, French, Spanish, Chinese and Arabic. For details on how to obtain a copy please contact publications-sales@fao.org or proscad@fao.org.

13. Several initiatives are underway to facilitate and support the elaboration and dissemination of data from developing countries so that such data are more easily accessible to support the provision of scientific advice. More information is available in ALINORM 08/31/9G-Add 1.

Establishment of the Global Initiative for Food-related Scientific Advice (GIFSA)

14. In order to specifically address the issue of sustainability of the provision of scientific advice, FAO and WHO have established a Global Initiative for Food-related Scientific Advice (GIFSA). The specific objectives of the GIFSA are:

- To increase awareness of the FAO/WHO programme of work on the provision of scientific advice,
- To mobilise technical, financial and human resources to support the provision of scientific advice in food safety and nutrition, and
- To promote the timeliness of the provision of scientific advice by FAO and WHO, while ensuring the continuation of the highest level of integrity and quality.

The main focus of GIFSA is to establish a mechanism to facilitate the provision of extrabudgetary resources for scientific advice activities. Contributions are accepted from governments, organizations and foundations in accordance with WHO and FAO rules. Two separate accounts will be maintained, one at WHO and one at FAO. An FAO/WHO Committee manages the GIFSA, and procedures have been developed to ensure that all resources provided through GIFSA will be allocated to activities in an independent and transparent manner, taking into consideration the criteria for prioritization of activities already agreed by Codex, FAO and WHO and the specific needs of FAO and WHO member countries.

For additional information and advice on the procedure for making a donation/contribution please contact Sandra Avilés, Policy Assistance and Resources Mobilization Division (Sandra.Aviles@fao.org; Tel: + 39 06 57056733) at FAO; and Jorgen Schlundt, Department of Food Safety, Zoonoses and Foodborne Diseases, WHO (schlundtj@who.int; Tel: + 41 22 791 3445).

INFOSAN and its role in food incidents

15. The International Food Safety Authorities Network (INFOSAN) was initiated in 2004 by WHO in collaboration with FAO and currently has 170 countries involved. In order to efficiently support member states in case of food emergencies of international health concern, INFOSAN emergency regularly informs members on on-going events.

16. In the case of the melamine incident, INFOSAN provided 14 emergency alerts to the entire network and 4 alerts to specific member states to facilitate the identification, assessment and management of the incident. Each country is encouraged in the case of a food emergency to contact INFOSAN at WHO. More information on INFOSAN is available at the following web-links:

http://www.who.int/foodsafety/fs_management/infosan/en/index.html and

http://www.who.int/foodsafety/fs_management/No_04_IHR_May07_en.pdf

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

17. This section of the document summarizes actions required by the Codex Committee on Food Additives as a result of changes in the Acceptable Daily Intake (ADI) status of food additives or other toxicological recommendations concerning additives, as proposed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) at its 69th meeting in Rome, 17 -26 June 2008.

18. At its 69th meeting, JECFA recommended changes to existing ADIs and/or established new or temporary ADIs or gave other toxicological recommendations for food additives and ingredients as contained in the attached Table 1. The CCFA should decide and agree on any action which might be required concerning these changes.

19. At its 69th meeting, JECFA evaluated a large number of flavouring agents using the Procedure for the safety Evaluation of Flavouring Agents. On the majority of flavours JECFA concluded that these substances were of "no safety concern" based on current estimated intake, and these substances are not included in the attached Table 1.

20. The group of furan-substituted aliphatic hydrocarbons, alcohols, aldehydes, ketones, carboxylic acids and related esters, sulfides, disulfides and ethers were evaluated and concluded that the Procedure could not be applied to this group because of the unresolved toxicological concerns. JECFA requested studies of the influence of the nature and position of ring substitution on metabolism and on covalent binding to macromolecules. These flavours are attached in Table 2. No action is required by CCFA, but the committee is requested to take note of the data request.

21. Alkoxy-substituted allylbenzenes present in foods, essential oils, and used as flavouring agents were evaluated and JECFA concluded that the data provided evidence of toxicity and carcinogenicity to rodents given high doses for several of these substances. A mechanistic understanding of these effects and their implications for human risk have yet to be fully explored, and will have a significant impact on the assessment of health risks from alkoxy-substituted allylbenzenes at the concentrations at which they occur in food. These flavours are attached in Table 2. No action is required by CCFA, but the committee is requested to take note of the data request.

22. A number of flavouring agents were previously evaluated based on only anticipated poundage data and assessed as of 'no safety concern' on a conditional basis. Actual poundage data (volumes of production) were subsequently submitted for all 143 requested flavouring agents and were evaluated by the Committee, and only two flavours required a re-evaluation, these were No. 1414, l-monomenthyl glutarate and No. 1595, 2-isopropyl-N,2,3-trimethylbutyramide. The Committee concluded that the Procedure could not be applied to 2-isopropyl-N,2,3-trimethylbutyramide, because of some evidence of genotoxicity This flavouring agent is attached in Table 2. No action is required by CCFA, but the committee is requested to take note of the data request.

Table 1. Food additives evaluated toxicologically at the 69th JECFA meeting

INS Number	Food additive	Acceptable daily intake (ADI) and other toxicological recommendations	Recommended action by CCFA
	Asparaginase from *Aspergillus niger* expressed in *A. niger*	Asparaginase is manufactured by pure culture fermentation of a genetically modified strain of *A. niger* that contains multiple copies of the asparaginase gene derived from *A. niger*. Asparaginase is used in food processing to reduce the formation of acrylamide from asparagine and reducing sugars during baking or frying. There was no indication of the formation of toxic secondary metabolites under the fermentation conditions used in the production of asparaginase. An **ADI "not specified"** was established for use in the applications specified (manufacture of bread and other cereal-based products and baked and fried potato-based products, where the enzyme is added before heat treatment of these products with the intention of reducing the formation of acrylamide) and in according with good manufacturing practices.	Consider whether to: - Add to the inventory of processing aids (IPA)
	Calcium lignosulfonate (40-65) The suffix (40-65) reflects the weight-average molecular weight range (40 000–65 000) to distinguish it from other calcium lignosulfonates in commerce	Calcium lignosulfonate (40–65) is obtained from the sulfite pulping of soft wood; it is derived from lignin, the second largest component of wood. Calcium lignosulfonate (40–65) may serve as a protective colloid for formulations of fat-soluble vitamins, carotenoids and food colours. The **ADI of 0–20 mg/kg bw** is based on a NOEL of 2000 mg/kg bw per day from a 90-day toxicity study and a safety factor of 100. The maximum potential dietary exposure to calcium lignosulfonate (40–65) was low and not expected to exceed 7 mg/kg bw per day from use as a carrier of fat-soluble vitamins and carotenoids in food and supplements.	Consider whether to: - Request comments/proposals on uses and use levels of calcium lignosulfonate (40-65) - Request proposal to allocate INS number
243	**Ethyl lauroyl arginate**	Ethyl lauroyl arginate is synthesized by first esterifying L-arginine with ethanol to obtain ethyl arginate HCl, which is then reacted with lauroyl chloride to form the active ingredient ethyl-N^{α}-lauroyl-L-arginate HCl. The intended use of ethyl lauroyl arginate is as a food preservative to prevent microbial growth and spoilage, used at concentrations of up to 225 mg/kg. The **ADI of 0–4 mg/kg bw is** based on a NOAEL of 442 mg/kg bw per day in two reproductive toxicity studies and a safety factor of 100. Some of the estimates of high exposure (greater than 95th percentile) exceeded the ADI, but it is recognized that these estimates were highly conservative and that actual intakes were likely to be within the ADI.	Consider whether to: - Request comments/proposals on uses and use levels of ethyl lauroyl arginate

INS Number	Food additive	Acceptable daily intake (ADI) and other toxicological recommendations	Recommended action by CCFA
	Paprika extract (for use as food colour)	Since the source material and the manufacturing process differ for paprika preparations used as a spice and as a food colour, the name "paprika extract" was adopted for use as a food colour, leaving the term "paprika oleoresin" for use as a spice. **No. ADI was established.** Concern was expressed as to whether the material tested in the 90-day and long-term studies was representative of all commercial production of paprika extract used as food colour.	No action, No ADI allocated
	Phospholipase C expressed in *Pichia pastoris*	Phospholipase C is produced by pure culture fermentation of a genetically modified strain of *P. pastoris*, which expresses the phospholipase C gene derived from DNA purified from a soil sample. The phospholipase C gene was sequenced and shown to be devoid of DNA sequences associated with haemolytic activity characteristic of certain microbial phospholipases. Phospholipase C is to be used in refining vegetable oils intended for human consumption, specifically to hydrolyse phospholipids present in the crude oil. An **ADI "not specified"** was established for use in the applications specified and in accordance with good manufacturing practice.	Consider whether to: - Add to the inventory of processing aids (IPA)
	Phytosterols, phytostanols and their esters	Phytosterols and phytostanols are substances that are similar in structure to cholesterol and are formed exclusively in plants. They are added to food for their blood cholesterol-lowering properties. **A group ADI of 0–40 mg/kg bw** was established for phytosterols, phytostanols and their esters, expressed as the sum of phytosterols and phytostanols in their free form, based on an overall NOAEL of 4200 mg/kg bw per day to which a safety factor of 100 was applied.	No action, as phytosterols, phytostanols and their esters are added to food for other purposes than technological purposes.
900a	**Polydimethylsiloxane (PDMS)**	The **previously established ADI of 0–1.5 mg/kg bw was withdrawn**. Using an additional safety factor of 2, a **temporary ADI of 0–0.8 mg/kg bw** for PDMS was established, pending the results of studies to elucidate the mechanism and relevance of the ocular toxicity and provision of data on actual use levels in foods. The temporary ADI applies to PDMS that meets the revised specifications prepared at the 69th JECFA (see agenda item 8).	Consider whether to: - Review any draft provisions concerning PDMS in the GSFA - Encourage submission of the requested data on toxicity and actual use levels in foods

INS Number	Food additive	Acceptable daily intake (ADI) and other toxicological recommendations	Recommended action by CCFA
960	**Steviol glycosides**	Steviol glycosides are natural constituents of the plant *Stevia rebaudiana* Bertoni. Stevioside and rebaudioside A are the component glycosides of principal interest for their sweetening properties. An **ADI of 0–4 mg/kg bw expressed as steviol** was established based on a NOEL of 970 mg/kg bw per day from a long-term experimental study with stevioside (383 mg/kg bw per day expressed as steviol) and a safety factor of 100. The results of the new studies presented to the Committee showed no adverse effects of steviol glycosides when taken at doses of about 4 mg/kg bw per day, expressed as steviol, for up to 16 weeks by individuals with type 2 diabetes mellitus and individuals with normal or low-normal blood pressure for 4 weeks. Some estimates of high-percentile dietary exposure to steviol glycosides exceeded the ADI, particularly when assuming complete replacement of caloric sweeteners with steviol glycosides, although it was recognized that these estimates were highly conservative and that actual intakes were likely to be within the ADI.	Consider whether to: - Request comments/proposals on uses and use levels of steviol glycosides

INS Number	Food additive	Acceptable daily intake (ADI) and other toxicological recommendations	Recommended action by CCFA
220 221 222 223 224 225 227 228 539	**Sulfites** (Dietary exposure assessment) Sulfur dioxide Sodium sulfite Sodium hydrogen sulfite Sodium metabisulfite Potassium metabisulfite Potassium sulfite Calcium hydrogen sulfite Potassium bisulfite sodium thiosulfate	The main contributors to total dietary exposure to sulfites differ between countries owing to differing patterns of use of sulfites in foods and of consumption of foods to which sulfites may be added. Thus dried fruit, sausages and nonalcoholic beverages were the main contributors of sulfites in some countries, while in other countries these foods are generally produced without the use of sulfites. In countries where wine is regularly consumed, it was one of the main contributors to dietary exposure in adults. Dietary exposure in high regular consumers of wine (97.5^{th} percentile) was shown to exceed the ADI for sulfites (0-0.7 mg/kg bw) based either on MLs in Codex GSFA, on MLs in national legislation or on the average concentration determined analytically (about 100 mg/l). In children and teenagers, a significant contribution to mean exposure to sulfites could come from fruit juices and soft drinks (including cordial), sausages, various forms of processed potatoes, dried fruit and nuts. Other significant contributions to dietary exposure in the adult population come from dried fruit, sausages and beer.	Consider to: - Review the existing and draft MLs of sulfites in the GSFA - Encourage members to consider collecting data on the current use of sulfites in food and beverages available on their markets and investigating whether dietary exposure in some subpopulations exceeds the ADI. On the basis of such investigation, individual countries and the food industry could consider the possibility of taking one or more of the following measures to reduce dietary exposure to sulfites so that the ADI is not exceeded in the population: (1) align national legislation with Codex MLs where these are lower; (2) take action to effectively enforce national MLs; (3) encourage research on alternative methods of preservation, particularly on applications in which the use of sulfites is responsible for a significant contribution; (4) take action so that the use of sulfites is reduced in foods where safe alternative solutions are available. - Requesting review of the Codex Codes of practices for certain groups of food commodities, such as fruit juice, dried fruit and processed meat, to include advice to countries and the food industry in the implementation of a reduction of the use of sulfites in food.

Table 2. Flavouring agents for which the Procedure could not be applied

	No.	Flavouring agent	Recommended action by CCFA
Furan-substituted aliphatic hydrocarbons, alcohols, aldehydes, ketones, carboxylic acids and related esters, sulfides, disulfides and ethers		***Structural Class II***	No action is required
	1487	2-Methylfuran	
	1488	2,5-Dimethylfuran	
	1489	2-Ethylfuran	
	1490	2-Butylfuran	
	1491	2-Pentylfuran	
	1492	2-Heptylfuran	
	1493	2-Decylfuran	
	1494	3-Methyl-2-(3-methylbut-2-enyl)-furan	
	1497	3-(2-Furyl)acrolein	
	1499	3-(5-Methyl-2-furyl)prop-2-enal	
	1503	2-Furyl methyl ketone	
	1504	2-Acetyl-5-methylfuran	
	1505	2-Acetyl-3,5-dimethylfuran	
	1507	2-Butyrylfuran	
	1508	(2-Furyl)-2-propanone	
	1509	2-Pentanoylfuran	
	1510	1-(2-Furyl)butan-3-one	
	1511	4-(2-Furyl)-3-buten-2-one	
	1513	Ethyl 3-(2-furyl)propanoate	
	1514	Isobutyl 3-(2-furan)propionate	
	1515	Isoamyl 3-(2-furan)propionate	
	1516	Isoamyl 4-(2-furan)butyrate	
	1517	Phenethyl 2-furoate	
	1520	Furfuryl methyl ether	
	1521	Ethyl furfuryl ether	
	1522	Difurfuryl ether	
	1523	2,5-Dimethyl-3-furanthiol acetate	
	1524	Furfuryl 2-methyl-3-furyl disulfide	
	1525	3-[(2-Methyl-3-furyl)thio]-2-butanone	
	1526	*O*-Ethyl S-(2-furylmethyl)thiocarbonate	
		Structural Class III	
	1495	2,3-Dimethylbenzofuran	
	1496	2,4-Difurfurylfuran	
	1498	2-Methyl-3(2-furyl)acrolein	
	1500	3-(5-Methyl-2-furyl)-butanal	
	1501	2-Furfurylidene-butyraldehyde	
	1502	2-Phenyl-3-(2-furyl)prop-2-enal	
	1506	3-Acetyl-2,5-dimethylfuran	
	1512	Pentyl 2-furyl ketone	
	1518	Propyl 2-furanacrylate	
	1519	2,5-Dimethyl-3-oxo-(2H)-fur-4-yl butyrate	

	No.	Flavouring agent	Recommended action by CCFA
Alkoxy-substituted allylbenzenes present in foods, essential oils, and used as flavouring agents	1787	Apiole	No action is required
	1788	Elemicin	
	1789	Estragole*	
	1790	Methyl eugenol*	
	1791	Myristicin	
	1792	Safrole*	
	1595	2-isopropyl-N,2,3-trimethylbutyramide	No action is required