codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 4(b) **CX/FA 07/39/4**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES

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ACTION REQUIRED AS A RESULT OF CHANGES IN ACCEPTABLE DAILY INTAKE (ADI) STATUS AND OTHER TOXICOLOGICAL RECOMMENDATIONS

1. This 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 67th Meeting (Rome, 20-29 June 2006).[1]

2. At its 67th 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.

[1] See the Summary and Conclusions of the 67th Meeting of the Joint FAO/WHO Expert Committee on Food Additives: on ftp://ftp.fao.org/ag/agn/jecfa/jecfa67_final.pdf for additional details.

Table 1. Food additives evaluated toxicologically at the 67th JECFA meeting

INS Number	Food additive	Acceptable daily intake (ADI) and other toxicological recommendations	Recommended action by CCFA
160 b	Annatto Extracts: Annatto B - solvent-extracted bixin (≥85 % bixin, ≤2.5% norbixin) Annatto E - aqueous processed bixin (≥25 % bixin, ≤7% norbixin) Annatto C - solvent extracted norbixin (≥85 % norbixin) Annatto F - alkali processed norbixin, acid precipitated (≥35% norbixin) Annatto G - alkali processed norbixin, not acid precipitated (≥15 % norbixin)	**ADI for bixin of 0-12 mg/kg bw** Applicable to the following Annatto extracts, provided they comply with the respective specifications: - solvent-extracted bixin (≥85 % bixin, ≤2.5% norbixin) - aqueous processed bixin (≥25 % bixin, ≤7% norbixin) **Group ADI for norbixin and its sodium and potassium salts of 0-0.6 mg/kg bw (expressed as norbixin)** Applicable to the following Annatto extracts, provided they comply with the respective specification: - solvent extracted norbixin (≥85 % norbixin) - alkali processed norbixin, acid precipitated (≥35% norbixin) and not acid precipitated (≥15 % norbixin) In re-evaluating the studies of toxicity with solvent-extracted bixin (92% bixin) and solvent-extracted norbixin (91.6% norbixin) and in light of the additional compositional data, the Committee considered that ADIs could be allocated to these pigments, based on the studies conducted on the extracts. The Committee established an ADI for bixin of 0–12 mg/kg bw on the basis of the NOEL of 1311 mg/kg bw per day from a 90-day study in male rats fed an extract containing 92% bixin, corrected for pigment content and applying a safety factor of 100. The Committee established a group ADI for norbixin and its sodium and potassium salts of 0–0.6 mg/kg bw (expressed as norbixin) on the basis of the NOEL of 69 mg/kg bw per day from a 90-day study in male rats fed an extract containing 91.6% norbixin, corrected for pigment content and applying a safety factor of 100. Based on compositional data and toxicological data on aqueous processed bixin and alkali-processed norbixin (acid precipitated), the Committee concluded that the use of these annatto extracts as sources of bixin or norbixin would not raise safety concerns, provided that they complied with the relevant specifications. Accordingly, the ADIs given above could be applied to bixin and norbixin derived from these annatto extracts.	Consider whether: - To revise the INS number to reflect the different types of annatto extracts; - To request proposals for inclusion in the GSFA with proposed acceptable maximum use levels based on bixin or norbixin.; - To ask the Codex Committee on Milk and Milk Products (CCMMP) to revise the ML for Annatto extracts in food category 02.2.1.1 (Butter and concentrated butter) in order to differentiate between annatto extracts containing primarily bixin and extracts containing norbixin. - To ask the following Codex committees to clarify the basis (bixin or norbixin) for the acceptable maximum use levels for annatto extracts in their standards: **CCMMP**: Unprocessed Cheese, Including Fresh Cheese (CODEX STAN 221-2001). Named Variety Process(ed) Cheese and Spreadable Process(ed) Cheese (CODEX STAN A-8(a)-1978), Process(ed) Cheese and Spreadable Process(ed) Cheese (CODEX STAN A-8(b)-1978), and Process(ed) Cheese Preparations (CODEX STAN A-8(c)-1978). **CCFO**: Edible Fats and Oils Not Covered by Individual Standards (CODEX STAN 19-1981), Named Animal Fats (CODEX STAN 211-1999). **CCFFP**: Quick-Frozen Fish Sticks (Fish Fingers), Fish Portions and Fish Fillets – Breaded or in Batter (CODEX STAN 166-1989).

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		The Committee noted that the pigment in alkali-processed norbixin (not acid-precipitated) consists of sodium or potassium salts of norbixin and that compositional data on this extract, complying with the specifications, did not raise safety concerns. Consequently, the Committee concluded that the group ADI for norbixin and its sodium and potassium salts is applicable to norbixin salts from this source. Assuming all annatto derived pigment were bixin, the estimated intake would amount to approximately 0.2% of the ADI (0–12 mg/kg bw). Assuming all annatto derived pigment were norbixin, the estimated intake would amount to approximately 4% of the ADI (0–0.6 mg/kg bw).	**CCPFV** Pickled Cucumber (CODEX STAN 115-1981).
160d	Lycopene (synthetic)	The Committee established an **ADI of 0–0.5 mg/kg bw for synthetic lycopene** based on the highest dose of 50 mg/kg bw per day tested in the 104-week study in rats (at which no adverse effects relevant to humans were induced), and a safety factor of 100. **This ADI was made into a group ADI to include lycopene from *Blakeslea trispora*,** which was also under consideration at the present meeting and was considered to be toxicologically equivalent to chemically synthesized lycopene. The estimate of high exposure (greater than 95th percentile) of 30 mg/person per day, equivalent to 0.5 mg/kg bw per day, which includes background exposure plus additional exposure from food additive uses, is compatible with the ADI.	Consider whether to: - Revise INS number to differentiate lycopene (synthetic) and lycopene from *Blakeslea trispora;* - Request information on technological need and maximum levels expressed as lycopene for inclusion in the GSFA.
	Lycopene from *Blakeslea trispora*	Lycopene from *Blakeslea trispora* is considered to be toxicologically equivalent to chemically synthesized lycopene, for which an ADI of 0–0.5 mg/kg bw was established. This was given further credence by the negative results obtained for lycopene from *B. trispora* in two tests for genotoxicity, and the absence of adverse effects in a short-term toxicity study considered at the present meeting. **The ADI for synthetic lycopene was therefore made into a group ADI of 0-0.5 mg/kg bw to include lycopene from *B. trispora*.** The exposure estimate is the same as for synthetic lycopene.	
235	Natamycin (aka pimaricin)	The data as a whole, including estimations based on GEMS/Food Consumption Cluster Diets and calculations for consumers with a high intake and children, confirm the results of the assessment made by the Committee at its fifty-seventh meeting and show that the **current ADI of 0–0.3 mg/kg bw is unlikely to be exceeded**.	Consider whether: - Inform the CCMMP

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216	Propyl paraben (aka propyl para-hydroybenzoate)	In view of the adverse effects in male rats, **propyl paraben (propyl phydroxybenzoate) should be excluded from the group ADI for the parabens used in food**. This conclusion was reached on the grounds that the group ADI was originally set on a NOEL of 1000 mg/kg bw per day for a different toxicological end-point—growth depression—taken from the range of studies then available for the methyl, ethyl and propyl parabens. Propyl paraben has shown adverse effects in tissues of reproductive organs in male rats at dietary doses of down to 10 mg/kg bw per day, which is within the range of the group ADI (0–10 mg/kg bw), with no NOEL yet identified. The specifications for propyl paraben were withdrawn. **The group ADI of 0–10 mg/kg bw for the sum of methyl and ethyl esters of p-hydroxybenzoic acid was maintained**.	Consider whether: - To discontinue work on all draft and proposed draft provisions for propyl paraben in the GSFA under the additive group "p-hydroxybenzoates," and recommend the Codex Alimentarius Commission (CAC) to revoke the existing provisions in relevant commodity standards (i.e., Jams (Fruit Preserves) and Jellies (CODEX STAN 79-1981) and Mango Chutney (CODEX STAN 160-1987)). - To withdraw Codex specification for propyl paraben.

Table 2. Food contaminants evaluated toxicologically at the 67th JECFA meeting

INS Number	Food additive	Tolerable intakes and other toxicological recommendations	Recommended action by CCFA
541i, 541ii 523 554 556 559	All food additives containing aluminium included in the GSFA (proposed draft, draft and adopted): - Sodium Aluminium Phosphates (acidic and basic) - Aluminium ammonium sulfate - Sodium aluminium silicate (Sodium Aluminosilicate) - Calcium aluminium silicate - Aluminium silicate (Table 5 of 67th JECFA report)	**PTWI : 1 mg/kg bw expressed as Al** JECFA concluded that aluminium compounds have the potential to affect the reproductive system and developing nervous system at doses lower than those used in establishing the previous PTWI and the PTWI was therefore revised. The available studies have many limitations and are not adequate for defining dose–response relationships. The Committee therefore based its evaluation on the combined evidence from several studies. The lowest LOELs for aluminium compounds in a range of different dietary studies in mice, rats and dogs were in the range of 50–75 mg/kg bw per day, expressed as Al. The Committee applied an uncertainty factor of 100 to the lower end of this range of LOELs (50 mg/kg bw per day expressed as Al) to allow for inter- and intraspecies differences. There are deficiencies in the database, notably the absence of NOELs in the majority of the studies evaluated and the absence of long-term studies on the relevant toxicological end-points. These deficiencies are counterbalanced by the probable lower bioavailability of the less soluble aluminium compounds present in food. Overall, it was considered appropriate to apply an additional uncertainty	Consider whether: - To remove sodium aluminosilcate (INS 554), calcium aluminium silicate (INS 556) and aluminium silicate (INS 559) from Table 3 of the GSFA - To request information on technological need and acceptable maximum levels, in particular for those food additives for which the use level is only limited by GMP with a view toward including the provisions for the aluminium-containing food additives in Tables 1 and 2 of the GSFA. - To consider the provisions in the GSFA for the aluminium-containing additives at the same time to ensure that safe acceptable maximum use levels are established.

INS Number	Food additive	Tolerable intakes and other toxicological recommendations	Recommended action by CCFA
		factor of three. The Committee confirmed that the resulting health-based guidance value should be expressed as a PTWI, because of the potential for bioaccumulation. The Committee noted that the PTWI is likely to be exceeded to a large extent by some population groups, particularly children, who regularly consume foods that include aluminium-containing additives. The Committee also noted that dietary exposure to Al is expected to be very high for infants fed on soya-based formula. The Committee recommended that the provisions for aluminium-containing food additives in the GFSA should be brought in line with the newly established PTWI of 1 mg/kg bodyweight expressed as aluminium. In particular, the Committee considered that provisions for aluminium-containing food additives in the GSFA which are used at levels consistent with GMP may lead to high exposure in the general population and in particular children The Committee requested additional information to be made available in order to be able to consider any revision of the PTWI as follows: • Further data on the bioavailability of different aluminium-containing food additives are required. • There is a need for an appropriate study of developmental toxicity and a multigeneration study incorporating neurobehavioural end-points, to be conducted on a relevant aluminium compound(s). • Studies to identify the forms of aluminium present in soya formulae, and their bioavailability, are needed before an evaluation of the potential risk for infants fed on soya formulae can be considered.	