

codex alimentarius commission



FOOD AND AGRICULTURE
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Agenda Item 17 (a)

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES AND CONTAMINANTS

Thirty-sixth Session

Rotterdam, The Netherlands, 22 -26 March 2004

PRIORITY LIST OF FOOD ADDITIVES, CONTAMINANTS AND NATURALLY OCCURRING TOXICANTS PROPOSED FOR EVALUATION BY JECFA

COMMENTS

The following comments have been received from: Japan, Switzerland, USA
and ISDI (International Special Dietary Food Industries)

in response to CL 2003/13-FAC and CL 2003/46-FAC

JAPAN

Background

1. The 26th Session of the Codex Alimentarius Commission recalled that the Proposed Draft Standard for Instant Noodles had been proposed by the Regional Coordinating Committee for Asia, and that based on the decision of the 47th Session of the Executive Committee the completion of the Standard would be undertaken by the Committee on Cereals, Pulses and Legumes by correspondence. The Coordinating Committee for Asia decided to forward the Proposed Draft Standard for Instant Noodles to Step 5, however member countries could not achieve consensus, especially on the inclusion of "Peroxide Value" (PV) proposed by Japan.

2. The Delegation of Japan stressed the importance of the inclusion of PV for the purpose of quality control and protection of consumer health and **requested consideration of PV by the Committee on Food Additives and Contaminants and JECFA before the standard could be advanced to Step 8.** The Delegation also announced that Japan had started a new study of PV and the results would be publicized by the end of March 2004. The Delegation of Indonesia strongly supported the adoption at Step 5 and proposed additional technical comments including the list of food additives. The Delegation of France, while supporting the draft proposed standard, raised its concern over the issue raised by Japan on PV.

3. The Commission adopted the Proposed Draft Standard for Instant Noodles at Step 5 and forwarded it to Committee on Cereals, Pulses and Legumes for further consideration by correspondence including technical comments submitted by Indonesia. **The Commission also asked the Committee on Food Additives and Contaminants to consider "Peroxide Value" (PV).**

Comments

1. Japan believes that the provisions on PV should be established to protect quality control and the health of consumers, because only the provision of Acid Value is not enough to catch the rancidity of oils and fats. PV holds the amount of peroxide caused by absorption of atmospheric oxygen in fats and shows the producing amount of peroxide as a toxic substance.

2. The toxicity of decomposed products from fats rapidly increases after the level of PV 30 meq/kg. The further deterioration is realized to produce carbonyl and aldehyde substance, which are certainly positive to the toxicity. At the stage that PV indicates over the level of 30 meq/kg, the decomposed substances are produced in large quantities and this stage of oxidation means that the food has been already obtained an outstanding low quality with high rancidity and not appropriate for food.

3. Therefore, the measuring of PV has scientific advantage to evaluate food rancidity for food safety and quality, and is necessary to be established in a Codex Standard for Instant Noodles. It is extremely important and essential, as long as the food is concerned, to realize the stage of initial oxidation by using PV measurement, which is namely the check of the starting point of toxic substances accumulation in food.

4. Japan submitted and distributed "Studies on Rancidity of Fats in Foods" regarding relationship between the Degree of Rancidity and the Toxicity of Fats in Pre-cooked Instant Noodles as CX/ASIA CRD2. Japan is performing the study on the Degree of PV and Toxicity of Fats with Rancidity of Fats in Instant Noodles, and also the study on actual condition of PV in Instant Noodles being distributed in the international markets. Japan will submit results of these studies mentioned above by the end of 2005. Therefore, these results will contribute to the consideration of PV.

5. Japan proposes that the provision of PV should be considered in the Codex Committee on Food Additives and Contaminants based on the evaluation by JECFA. (Information on PV to be evaluated by JECFA is attached below).

INFORMATION ON THE CONTAMINANT TO BE EVALUATED BY JECFA

1. Proposal for inclusion submitted by:

Japan

2. Name of compound; chemical name(s):

Peroxide Value

3. Identification of (additional) data (toxicology, metabolism) which could be provided to JECFA:

- (1) Crampton E.W., Common R.H., Farmer F.A., Berryhill F.M. and Wiseblatt L., "Studies to determine the nature of the damage to the nutritive value of some vegetable oils from heat treatment II. Investigation of the nutritiousness of the products of thermal polymerization of linseed oil." *J. Nutrition*, 44, 177-189 (1951)
- (2) Crampton E.W., Common R.H., Farmer F.A. and Berryhill F.M., "The effect of heat treatment on the nutritional value of some vegetable oils." *J. Nutrition*, 43, 431-440 (1951)
- (3) Kaneda T. and Ishii S., "Studies on the nutritive values of lipids VIII. Nutritive value or toxicity of highly unsaturated fatty acids (1)." *Bull. Jap. Soc. Sci. Fish.*, 19, 171-177 (1953)
- (4) Crampton E.W., Common R.H., Farmer F.A., Wells A.F. and Crawford D., "Studies to determine the nature of the damage to the nutritive value of some vegetable oils from heat treatment III. Segmentation of toxic and non-toxic material from the esters of heat-polymerized linseed oil by distillation and by urea adduct formation." *J. Nutrition*, 49, 333-346 (1953)
- (5) Matsuo N., "Studies on the toxicity of fish oil." *J. Biochem.*, 41, 481-487 (1954)
- (6) Raju N.V. and Rajagopalan R., "Nutritive value of heated vegetable oils." *Nature*, 176, 513-514 (1955)
- (7) Kaunitz H., Slanetz C.A. and Johnson R.E., "Antagonism of fresh fat to the toxicity of heated and aerated cottonseed oil." *J. Nutrition*, 55, 577-587 (1955)
- (8) Kaunitz H., Slanetz C.A. and Johnson R.E., "Biological effects of the polymeric residues isolated from autoxidized fats." *J. Am. Oil Chem. Soc.*, 33, 630-634 (1956)
- (9) Kaunitz H., Slanetz C.A., Johnson R.E. and Guilmain J., "Nutritional properties of the molecularly distilled fractions of autoxidized fats." *J. Nutrition*, 60, 237-244 (1956)
- (10) Crampton E.W., Common R.H., Farmer F.A. and DeFreitas A.S.W., "Studies to determine the nature of the damage to the nutritive value of menhaden oil from heat treatment." *J. Nutrition*, 62, 341-347 (1957)

- (11) Kaunitz H., Slanetz C.A., Johnson R.H., Knight H.B., Koos R.E. and Swern D., "Influence of feeding fractionated esters of autoxidized lard and cottonseed oil on growth, thirst, organ weights and liver lipids of rats." *J. Am. Oil Chem. Soc.*, 36, 611-615 (1959)
- (12) Perkins E.G., "Nutritional and chemical changes occurring in heated fats: A review" *Food Technol.*, 14, 508-514 (1960)
- (13) Andrews J.S., Griffith W.H. and Mead J.F., "Toxicity of air-oxidized soybean oil." *J. Nutrition*, 70, 199-210 (1960)
- (14) Kaunitz H., Johnson R.E. and Pegus L., "A long-term nutritional study with fresh and mildly oxidized vegetable and animal fats." *J. Am. Oil Chem. Soc.*, 42, 770-774 (1965)
- (15) Raju N.V., Narayana M., Rao and Rajagopalon R., "Nutritive value of heated vegetable oils." *J. Am. Oil Chem. Soc.*, 42, 774-776 (1965)
- (16) Miura T., Muto T., Matano K. and Miyaki K., "Studies on the poisonous products of edible oil and fat (I). Biological studies of the food poisoning caused by instant spaghetti." *Food Sanitation Research (Shokueisei-shi) (Japan)*, 7, 67-71 (1966)
- (17) Kaunitz H., "Nutritional aspects of thermally oxidized fats & oils." *Food Technol.*, 21, 278-280 (1967)
- (18) Miura T., Matano K. and Miyaki K., "Studies on the poisonous products of edible oil and fat. II. On the poisonous products and their toxicity of oil and fat of instant Chinese noodle." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 16, 503-505 (1967)
- (19) Miura T., Kudo M., Tsuchida M., Matano K. and Miyaki K., "Studies on the poisonous products of edible oil and fat. III. On the autoxidation products derived from oil contained in instant Chinese noodle and their toxicities." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 18, 726-729 (1969)
- (20) Yoshioka M. and Kaneda T., "Studies on the toxicity of autoxidized oils. I. The fractionation of the toxic compound and its identification (1)." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 21, 316-321 (1972)
- (21) Yoshioka M. and Kaneda T., "Studies on the toxicity of autoxidized oils. III. The toxicity of hydroperoxyalkenals." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 23, 321-326 (1974)
- (22) Yoshioka M., Tachibana K. and Kaneda T., "Studies on the toxicity of autoxidized oils. IV. Impairments of metabolic functions induced by autoxidized methyl linoleate." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 23, 327-331 (1974)
- (23) Tovar L.R. and Kaneda T., "Studies on the toxicity of the autoxidation oils. VI. Comparative toxicity of secondary oxidation products in autoxidized methyl linoleate." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 25, 169-172 (1977)
- (24) Nakatsugawa K. and Kaneda T., "Absorption of methyl linoleate hydroperoxides in rabbit." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 30, 74-77 (1980)
- (25) Nakatsugawa K. and Kaneda T., "Absorption and metabolism of methyl linoleate hydroperoxides in rats." *J. Jpn. Oil Chem. Soc. (Yukagaku)*, 32, 361-366 (1983)
- (26) Oarada M., Miyazawa T. and Kaneda T., "Distribution of ^{14}C after oral administration of (U- ^{14}C) labeled methyl linoleate hydroperoxides and their secondary oxidation products in rats." *Lipids*, 21, 150-154 (1986)
- (27) Esterbauer H., Zollner H., and Schaur R.J., "Aldehydes formed by lipid peroxidation: Mechanism of formation occurrence, and determination." *Membrane Lipid Oxidation Vol 1* (Edited by Vigo-Pelfrey, C.), Boca Raton, Florida, CRC Press. 2 (1990), 239-268
- (28) Pryor W.A. and Porter N.A., "Suggested mechanisms for the production of 4-hydroxy-2-nonenal from the autoxidation of polyunsaturated fatty acids." *Free Radic. Biol. Med.*, 8, 541-543 (1990)
- (29) Uchida K., "4-Hydroxy-2-nonenal: a product and mediator of oxidative stress." *Prog. Lipid Res.*, 42, 318-343 (2003)

- (30) Studies on Rancidity of Fats in Foods” regarding relationship between the Degree of Rancidity and the Toxicity of Fats in Pre-cooked Instant Noodles as CX/ASIA CRD2.
4. List of contact persons, including name and address, providing surveillance data with quality assurance information, preferably from three or more regions of the world:
- Codex Contact Point for Japan
5. Date on which data could be submitted to JECFA:
- Japan is performing the study on the Degree of PV and Toxicity of Fats with Rancidity of Fats in Instant Noodles, and also the study on actual condition of PV in Instant Noodles being distributed in the international markets. Japan will submit results of these studies by the end of 2005.

SWITZERLAND

BACKGROUND

1. The 35th Session of the Codex Committee on Food Additives and Contaminants agreed on the Priority List of Food Additives, Contaminants, and Naturally Occurring Toxicants Proposed for Evaluation by JECFA and also agreed to request additional comments for additions or amendments to its Priority List for consideration at its next Session (ALINORM 03/12A, paragraphs 190-191 and Appendix XV).
2. Switzerland is submitting comments for the inclusion of the additive pullulan on the Priority List of Food Additives, Contaminants and Naturally Occurring Toxicants Proposed for Evaluation by JECFA, which will be considered at the forthcoming 36th Session of the Codex Committee on Food Additives and Contaminants (Rotterdam, The Netherlands, March 2004).
3. Switzerland is convinced that the candidate food additive meets the criteria for the inclusion of food additives in the Priority List laid down in Annex I and thereby would like to give the information requested in Annex II, Part A as follows:

ANNEX II - Part A

INFORMATION ON THE ADDITIVE TO BE EVALUATED BY JECFA

1. Proposal for inclusion submitted by:

Switzerland
2. Name of compound; trade name(s); chemical name(s):

Pullulan, Pullulan PI-20
3. Names and addresses of basic producers:

Hayashibara Biochem. Inc.
2-3 Shimoishii 1-chome
Okayama 700, Japan
4. Has the manufacturer made a commitment to provide data?

Yes
5. Identification of the manufacturer that will be providing data (contact details):

Bioresco Ltd.
Food Scientific and Regulatory Services
Bundesstrasse 29
4054 Basel, Switzerland

6. Justification for use:

Pullulan is a naturally occurring, fungal polysaccharide. It is produced on an industrial scale by fermentation of liquefied starch under controlled conditions using a specific, not genetically modified strain of *Aureobasidium pullulans*, an ubiquitous, non-pathogenic and not toxigenic yeast-like fungus.

Pullulan is an essentially linear glucan consisting mainly of 1,6-linked maltotriose and some interspersed maltotetraose units. Its average molecular weight (at peak of a gel permeation chromatogram) is about 200,000 daltons. Pullulan yields viscous aqueous solutions which do not form gels but which form transparent, odour- and tasteless films on drying.

The commercially available pullulan (Pullulan PI-20) has a purity of $\geq 90\%$. The main impurities are mono-, di- and oligosaccharides which are carried over from the raw material (liquefied corn starch) into the final product. The specifications of Pullulan PI-20 include standard parameters of chemical and microbiological purity.

Considering that pullulan is produced from liquefied starch by an ubiquitous, nontoxigenic and non-pathogenic yeast-like fungus (*Aureobasidium pullulans*), that its chemical structure closely resembles that of traditional components of foods (glucans), that it is not digested and not absorbed to a significant extent but is fermented completely by the intestinal microflora like other fermentable dietary fibers, and that its estimated daily intake from all intended uses combined is 300-times below the NOAEL of the 62-week rat study and 10-times below levels that may be consumed by humans without untoward effects, it is concluded that pullulan may safely be used as firming/gelling- and glazing-agent in the manufacture of capsule shells (for dietary supplements), coated tablets (dietary supplements), and flavoured edible films (as a breath freshener).

Pullulan is a substitute for gelatine in capsules. This is a benefit for consumers who presently would like to avoid gelatine containing foodstuffs because of BSE concerns.

7. Food products and food categories within the GSFA in which the compound is used, including use level(s):

The film-forming properties of pullulan are the basis for its proposed use as:

- substitute for gelatine in the production of capsule shells (for food supplements; GSFA category number 13.6),
- ingredient of coated tablets (food supplements, GSFA category number 13.6), and
- ingredient of edible flavoured films (breath fresheners food supplements, GSFA category number 13.6).

The daily intake from these combined uses is estimated at not more than 1 g for the heavy (i.e., 90th percentile) consumer of pullulan containing products. In children, the intake is expected to not exceed 90 mg/day.

8. Has the compound been approved for use in 2 or more countries?

In Japan, pullulan is used as a food ingredient for a variety of applications since 1976. To date, more than three thousand metric tons of pullulan have entered the Japanese food chain. Adverse reactions or consumer complaints have not come to the attention of the petitioner.

In the US, the FDA has accepted the petitioner's GRAS notice without further questions. This notice covers a wide range of applications with an aggregated estimated daily intake (EDI) of 9.4 and 18.8 g for the mean and 90th percentile consumer, respectively.

9. List of data (toxicology, metabolism, specifications) available:

Ingested pullulan is not degraded by the enzymes of the digestive tract. In the distal parts of the gut, pullulan is completely fermented by the intestinal microbiota.

The safety of the source organism (*Aureobasidium pullulans*) and of pullulan has been examined in acute toxicity studies in mice and rats. The genotoxic potential of pullulan was examined in standard Ames tests, a DNA-repair test, an in-vivo micronucleus test and an in-vitro chromosome aberration test.

The subchronic toxicity of Pullulan PI-20 was tested in a standard 90-day toxicity study in rats. The chronic toxicity of pullulan was examined in a chronic toxicity study which, however, had to be terminated prematurely (after 62 weeks) due to intercurrent pneumonia in all groups. The results of all these studies demonstrate that pullulan has a very low toxicity. The LD₅₀ was >14 g/kg bw. Evidence of a genotoxic activity was not found. The NOAEL in the 62-week study, i.e., the study with the longest exposure time was 4.5 and 5.1 g/kg bw/d in male and female rats (corresponding to a dietary concentration of 10%, the highest dose level tested). Additional short-term feeding studies in rats with diets containing up to 40% pullulan also did not reveal any signs of toxicity.

The tolerance of pullulan was examined in humans as well. The ingestion of pullulan for 14 days at a dose of 10 g/day did not elicit unacceptable intestinal symptoms and was not associated with changes of standard clinical parameters.

10. Date on which data could be submitted to JECFA:

UNITED STATES OF AMERICA:

The US recommends the following list of flavor groups for consideration by the 36th CCFAC for inclusion in its priority list for JECFA. In the interest of saving space, we have not included a listing of all the substances we are proposing, but will be happy to provide this list to the 36th CCFAC and the JECFA Secretariat as appropriate.

Chemical Group Principal Name	# of substances
Supplement: Straight-chain primary aliphatic primary alcohols, aldehydes, acids, acetals, and esters	27
Supplement: Branched-chain primary aliphatic primary alcohols, aldehydes, acids, acetals, and esters	1
Supplement: alpha, beta-Unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids, acetals, and esters	4
Supplement: Non-conjugated and accumulated unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids, acetals, and esters	7
Supplement: Saturated and unsaturated aliphatic secondary alcohols, aldehydes, acids, acetals, and esters	10
Supplement: Aliphatic acyclic, alicyclic, and aromatic saturated and unsaturated tertiary alcohols and esters	13
Supplement: Primary alicyclic saturated and unsaturated alcohols, aldehydes, acids, acetals, and esters	2
Supplement: Secondary alicyclic saturated and unsaturated alcohols, aldehydes, acids, acetals, and esters	4
Supplement: Primary aliphatic saturated or unsaturated alcohols, aldehydes, acids, acetals, and esters	26
Supplement: Secondary aliphatic saturated or unsaturated alcohols, aldehydes, acids, acetals, and esters	8
Maltol Derivatives	7
Furyl Derivatives	27

Chemical Group Principal Name	# of substances
Supplement: Phenethyl alcohol, phenylacetic acid, related esters, phenoxyacetic acid and related esters.	1
Hydroxyallylbenzenes	4
Aliphatic & Aromatic Amines	17
Supplement: Aliphatic and aromatic mono- and di- thiols and mon-, di-, tri-, and poly-sulfides	18
Supplement: Aromatic ketones, secondary alcohols, and related esters, and ketals	2
Supplement: Benzyl alcohols, aldehydes, acids, acetals, and esters	4
Supplement: Pyrazine and quinoxaline derivatives	2
Supplement: Phenol derivatives	6
Anthranilates	12
Supplement: Thiazoles, thiophene, thiazoline and thienyl derivatives	3
Misc.	6
Misc. Nitrogen Substances	9
Supplement: Aliphatic and aromatic hydrocarbons	2
Epoxides	7
Supplement: Amino acids	1

Total number of substances

230

ISDI

Among the priority additives to be discussed at the next session of CCFAC (listed in CL 2002/44 Appendix II), ISDI brings herewith the justification for the use at certain levels of additives in Foods for Special Medical Purposes as described in category 13.3 of the Food Category System.

INS	Food cat No	Max level	ADI	Source	Step	Proposed numerical level / Justification
120 Carmines	13.3.1	50mg/kg	0-5 mg/kg bw	EU (6), ISDI (3)	6	The unusual ingredients in FSMPs often give an unpleasant colour to the product so the addition of colour improves visual aspect and taste perception and therefore dietary compliance. 50mg/kg as consumed equates to current level of use in FSMPs and the amount needed to achieve the required technological effect.
160a(ii) Carotenes vegetable	13.3.1	GMP 30mg/kg	Acceptable	EU(6), ISDI(3)	6	The unusual ingredients in FSMPs often give an unpleasant colour to the product. Addition of colour improves visual aspect and taste perception and therefore dietary compliance. Level : For young children over one year based on the Opinion of the EU Scientific Committee for Food, Dec.1996 on colours in FSMPs.
	13.3.2	30 mg/kg		ISDI (3)	3	The mixture of amino acids, vitamin, mineral complex, unusual fats or fatty acids etc. give an unpleasant colour to the FSMP product so the addition of colour improves visual aspect and taste perception and therefore dietary compliance Level: For young children over one year Opinion of the EU Scientific Committee for Food, Dec.1996
141i, 141ii Chlorophylls, copper complex	13.3	GMP 20mg/kg	141i not limited 141 ii 0-15 mg/kg bw	EU&SAfrica (6), ISDI (3)	6	The unusual ingredients in FSMPs often give an unpleasant colour to the product so the addition of colour improves visual aspect and taste perception and therefore dietary compliance. Level : For young children over one year based on the Opinion of the EU Scientific Committee for Food, Dec.1996 on colours in FSMPs
472e Diacetyltartaric and fatty acid esters of glycerol	13.3.1	GMP 400mg/kg	0-50 mg/kg bw	EU(6), ISDI(3)	6	<i>The unusual ingredients in FSMPs(eg amino acids, combination of oils) require a robust emulsifier such as E472e to provide stable emulsions to enhance product acceptability and hence patient compliance.</i> Level: 400mg/kg as consumed represents current level of use in FSMPs and the amount needed to achieve the required technological effect.
163ii Grape skin extract	13.3.1	GMP 20mg/kg	0-2.5 mg/kg bw	EU(6), ISDI(3)	6	The unusual ingredients in FSMPs often give an unpleasant colour to the product so the addition of colour improves visual aspect and taste perception and therefore dietary compliance. Level : based on Opinion of the EU Scientific Committee for Food, Dec.1996 .
	13.3.2	GMP 20mg/kg				The mixture of amino acids, vitamin, mineral complex, unusual fats or fatty acids etc. give an unpleasant colour to the product so the addition of colour improves visual aspect and taste perception and therefore dietary compliance. Level: For young children over one year based on the Opinion of the EU Scientific Committee for Food, Dec.1996.
955, Sucralose	13.3.	400 mg/kg	0-15 mg/kg bw	ISA(6), ISDI(3)	6	This intense sweetener, unlike aspartame, is stable to high temperature processing (such as that required for sterile FSMP products) and a wide pH range and has a nutritional composition which renders it suitable for for all disease applications including PKU.