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FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 5 **CX/CF 10/4/5 Add.1**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON CONTAMINANTS IN FOODS
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Izmir, Turkey, 26 – 30 April 2010

PROPOSED DRAFT MAXIMUM LEVELS FOR MELAMINE IN FOOD AND FEED (N13-2009)

Comments at Step 3 submitted by Egypt, European Union, Kenya, Libya, Mali, the Philippines, Thailand, CIAA and IDF

EGYPT

The maximum levels of melamine or one of its analogues alone not exceed than 1 mg/ kg in foodstuffs intended for children under 36 months of age and foodstuffs for special dietary uses 2.5 mg/ kg for all other foodstuffs and feeds.

EUROPEAN UNION

The European Union (EU) appreciates the very good work performed by the electronic Working group under the lead of Canada and provides following comments on the proposed maximum levels.

THE EFSA OPINION ON MELAMINE IN FOOD AND FEED[1]

The European Food Safety Authority (EFSA) adopted in March 2010 a scientific opinion related to the presence of melamine and the structural analogues (cyanuric acid, ammeline and ammelide) in food and feed which was published on Tuesday 13 April 2010.

EFSA identified the potential sources of melamine and cyanuric acid in food that were clearly not related to incidences of adulteration, including food contact materials, and estimated the associated dietary exposure.

Melamine does not exhibit systemic toxicity, but is able to complex with other substances such as endogenous uric acid or substances related to melamine to form crystals in the urine, which cause kidney damage. From the available toxicological data, a Tolerable Daily Intake (TDI) of 0.2 mg/kg body weight was established for melamine, which confirms the TDI derived by the WHO Expert Meeting held in collaboration with the FAO in December 2008.

[1] EFSA Panel on Contaminants in the Food Chain (CONTAM) and EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); Scientific Opinion on Melamine in Food and Feed. EFSA Journal 2010; 8(4):1573. [144 pp.]. doi:10.2903/j.efsa.2010.1573.
Available online: http://www.efsa.europa.eu/en/scdocs/doc/1573.pdf

SOURCES RESULTING IN SIGNIFICANT BACKGROUND PRESENCE OF MELAMINE IN FOOD AND FEED

There are potential approved sources of melamine in feed and food that are clearly not related to incidences of adulteration and which could result in levels of melamine in food and feed additives higher than 2.5 mg/kg. More details on these sources are provided hereafter.

a) Background melamine levels in food and feed from cyromazine use

(CX/CF 10/4/5, paragraph 40; EFSA opinion section 4.4.5 Background level from cyromazine use, p 45-46)

Cyromazine is used a plant protection product (insecticide) on a range of crops and as veterinary drug.

Maximum Residue Levels for cyromazine have been established at Codex level for a variety of crops from 0.1 to 10 mg/kg. Only cyromazine is included in the residue definition and not melamine. Data from the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) evaluation[2] indicate that in celery, tomatoes and lettuce, melamine may represent up to 11-44% of the total radioactive residue and cyromazine would represent 29-76%. The highest MRL for cyromazine in plants is 10 mg/kg plant material (cabbage, spinach and mustard green). Based on the medians of the range (22% = melamine and 50% = cyromazine), an amount of melamine of 4.4 mg/kg plant product can be estimated at this MRL.

In mushrooms, the Codex MRL for cyromazine is 7 mg/kg and melamine has been estimated to represent up to > 50% of the total residue.

The JMPR evaluation gives some indications that cyromazine could be used in forage plants (e.g. alfalfa, cotton (seed) and sudan grass hay) but it is not used in practice on such crops, so no melamine residue concentration have been estimated in animals from forages.

As regards the use of cyromazine as veterinary drug, at the Codex MRL of 300 µg/kg meat for cyromazine, the maximum levels of melamine found in animal tissues may be estimated from experimental data to be 4 µg/kg.

b) Background melamine levels in food from food contact materials

(CX/CF 10/4/5, paragraph 38; EFSA opinion section 4.4.4 Melamine levels in food and feed from food contact materials, p. 33-45)

In the EFSA opinion, typical and high melamine migration values were estimated for melaware for dry foods, aqueous foods, fatty foods and acidic foods. The typical melamine migration values ranged from 0.05 mg/kg for dry foods up to 1 mg/kg for acidic foods and the high melamine migration values ranged from 0.05 mg/kg for dry foods up to 5 mg/kg for acidic foods.

All migration results of melamine from commercial coatings on light metal packaging (cans, closures) were below 0.5 mg/kg.

Also some migration was observed into food from melamine gas barrier coatings (< 0.24 mg/kg)

c) Background melamine levels in feed from feed ingredients

(CX/CF 10/4/5, paragraph 48)

Melamine can be present at significant levels in certain feed additives/ingredients (such as guanidino acetic acid (GAA), urea and biuret) as an unavoidable impurity even when applying Good Manufacturing Practices (GMP). However the use of these feed additives/ingredients in compound feed will not result in a level of melamine in the compound feed exceeding the proposed ML of 2.5 mg/kg.

[2] JMPR (2008) Pesticide residues in food - 2006 evaluations. Part II - Toxicological. World Health Organization, 2008.

RISK FOR PUBLIC AND ANIMAL HEALTH FROM BACKGROUND PRESENCE OF MELAMINE IN FOOD AND FEED.

As regards animal health, EFSA concluded that the estimated exposures to melamine (and cyanuric acid) at the scenario of 2.5 mg/kg in feed are well below the doses causing toxicity and are therefore not expected to pose a risk to livestock and fish. Exposure to melamine or cyanuric acid individually at that level in feed is also not expected to pose a risk to pets (cats and dogs)

As regards public health, EFSA concluded that dietary exposure to melamine (and cyanuric acid individually) estimated from the available data relating to background approved sources (see above) is well below the respective TDIs and does not raise concerns for the health of consumers. This conclusion only applies if there is reasonable confidence that exposure is essentially to melamine or cyanuric acid alone. If there is a possibility of significant co-exposure to melamine, cyanurate, ammelide or ammeline health impact could arise at intakes of melamine well below the TDI.
When using conservative migration scenarios, dietary exposure of children to melamine from food contact materials such as melaware was estimated to be below or slightly above TDI for melamine. However, due to the conservative character of these estimates, a health concern was not identified.

EU POSITION ON PROPOSED MAXIMUM LEVELS

The maximum levels recommended to the CCCF for consideration are 1 mg/kg in infant formula (powdered) and 2.5 mg/kg in foods (other than infant formula) and animal feed. Furthermore consideration should be given to establish a lower maximum level for melamine at 0.5 mg/kg in ready-to-consume infant formula such as liquid milk or soy (paragraph 75)

The EU can agree with the proposed maximum level of 1 mg/kg in infant formula (powdered) but is of the opinion that as regards the proposed maximum level of 2.5 mg/kg in foods (other than infant formula) and animal feed, the CCCF should consider following **3 exemptions** and this in accordance with the conclusions from the WHO Expert Consultation and the EFSA:

1) Melamine present in feed and food as a result of cyromazine application

Melamine can be present in a range of food commodities where the use of cyromazine is authorised. In crops where an MRL for cyromazine of 4 mg/kg or more has been established, there is evidence that melamine, as metabolite of cyromazine, can be present in levels close to or exceeding the level of 2.5 mg/kg. It is therefore appropriate to exclude from the application of the proposed ML for melamine of 2.5 mg/kg, the foodstuffs containing significant levels of cyromazine as residue of an authorised use of cyromazine (foodstuff compliant with Codex MRL or other national MRL).

2) Melamine present in food from migration form food contact materials

Melamine is in many parts of the world, including in the EU, approved for use as a monomer and as an additive in plastics intended to come into contact with foodstuffs and has a specific migration limit higher than 2.5 mg/kg food. Melamine can also be used in non-plastics (e.g. paper and board, can coatings), coming into contact with food.

Therefore the EU is of the opinion that foods containing a melamine level exceeding the level of 2.5 mg/kg but below the specific migration limit (SML) applicable and for which it can be demonstrated that the melamine is present as the consequence of migration from food contact material, should not be considered as an adulterated product and should be allowed to be traded and be put/remain on the market.

3) Melamine in certain feed additives/ingredients

Melamine can be present in certain feed additives/ingredients (such as guanidino acetic cid (GAA), urea and biuret) as an unavoidable impurity even when applying Good Manufacturing Practices (GMP) (see paragraph 48). Therefore the EU is of the opinion that it is appropriate to restrict the application of the proposed ML of 2.5 mg/kg to feed materials and compound feed or to animal feed, excluding the feed additives/ingredients (i.e. GAA, urea and biuret) for which it has been demonstrated that the presence of melamine is unavoidable related to the normal production conditions.

The EU is of the opinion that the application of these exemptions in enforcement practice should be discussed within CCCF.

COMMENTS ON REFERENCES TO EU MEASURES AND LEGISLATION AS REGARDS FEED AND FOOD FROM CHINA

Reference is made in document CX/CF 10/4/5 to the EU measures taken following the melamine contamination incident (paragraph 58, References 18 and 19 and Appendix 1).

It is appropriate to update references 18 and 19 by the following "European Commission (2009). Commission Regulation (EC) No 1135/2009 of 25 November 2009 imposing special conditions governing the import of certain products originating in or consigned from China, and repealing Commission Decision 2008/798/EC. Official Journal of the European Union, L 311, 26.11.2009, p. 3 .

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:311:0003:0005:EN:PDF"

Given the significant decrease of Rapid Alert System for Food and Feed (RASFF) notifications since January 2009 as regards unacceptable presence of melamine in feed and food from China, the systematic checks on feed and food containing milk, milk products, soya or soya products and on ammonium carbonate were no longer appropriate and the Commission Regulation (EC) No 1135/2009 provided for a decrease of controls at import from 100 to 20 %.

In the Appendix I the measures from the EU should be completed by adding that 20 % of all consignments of ammonium bicarbonate and of feed and food containing milk, milk products, soya and soya products imported from China into the EU are controlled at import for the presence of melamine.

KENYA

Kenya has gone through the above mentioned document and would like to appreciate the effort of Codex Committee on Contaminants in Food who initiated this work at its third session. The appreciation also goes to the Electronic Working Group led by Canada together with WHO which thereafter did a good job to come up with the documents that provides information on the sources of melamine in food and feed.

Kenya Comment:

Concerning the proposed draft maximum levels for melamine in food and feed, Kenya supports WHO recommendations levels which are drawn from health based TDI considerations.

We suggest that sharing of melamine data on food and feeds in this issue will be important to all countries.

LIBYA

Since there are no scientific data available concerning background levels of melamine in the environment to be able to distinguish between sources of melamine in food (intentionally or unintentionally) therefore Libya has adapted a level of **0.5 mg/kg** melamine in all foods of animals origin. This level was based on daily consumption trend in Libya.

MALI

Mali supports the WHO proposal on the maximum levels for melamine in food:

- 1mg/kg for children;
- 2,5mg/kg for adults.

THE PHILIPPINES

The Philippines supports the work on the establishment of maximum limits of melamine in food and feed. In line with the WHO expert consultation, and as already adopted by several countries, the Philippines supports the proposed maximum levels below for consideration at the 4th Session of the CCCF:

1 ppm for melamine in powdered infant formulas

2.5 ppm for melamine in other foods and in animal feed

REASONS

The Philippines believes that the limits of 1 ppm in powdered infant formulas and 2.5 ppm in foods and animal feed are adequate for ensuring food safety. Based on an estimate of exposure, the limit of 1 ppm provides a 9-11 fold safety margin over the Tolerable Daily Intake (TDI) for infants less than 6 months old and 6-12 months old (see Table below). It also provides a 3-fold safety margin for the average Filipino weighing 59 kg assuming that half of the total dietary intake is contaminated with melamine.

The levels are adequate to distinguish the unavoidable presence of melamine from various sources which takes place in the ppb level (WHO) from that due to unacceptable adulteration to increase nitrogen content of some foods where melamine is added at much higher levels. The limits will also discourage such intentional adulteration which compromises the safety of products in the market.

The Philippines recognizes the possibility of melamine entering milk used in food production through veterinary drugs and feed additives and thus supports the application of above limits to animal feeds.

Exposure Scenarios of Filipino Infants and Average Adult

Calculations on exposure scenarios were made using the Tolerable Daily Intake (TDI) of 0.2 mg/kg body weight/day which is applicable to the whole population including infants as established by the WHO in Ottawa, Canada (December 2008).

For infant formulas, the table below shows the exposure scenario for two age groups of infants in the Philippines.

Stage	TDI	Body weight*	Maximum melamine intake	Daily formula consumption**	Maximum limit in formula
Infant <6 mos.	0.2 mg/kg bw /day	6 kg	1.2 mg/day	130 g	9.2 ppm (mg/kg)
Infant 6 -12 mos.	0.2 mg/kg bw/day	9 kg	1.8 mg/day	160 g	11.25 ppm (mg/kg)

* Source: Philippine Recommended Energy and Nutrient Intakes, 2002 Edition by Food and Nutrition Research Institute, Department of Health.

** Based on average recommended servings per day of Infant Formulas in the Philippine market.

Based on this exposure scenario, this limit of 1 ppm for melamine in powdered infant formulas provides a 9 to 11-fold safety margin over the TDI.

For other foods, the Philippines made an exposure scenario for an average 59-kg Filipino male, using the WHO's TDI of 0.2 mg/kg bw/day and a worst case exposure scenario assuming that half of a person's total daily dietary intake is contaminated with melamine (US FDA, October 2008). In the Philippine scenario, an average adult consumes 386g of solid food (based on total 1684 kcal per day, distributed at 73.6% from carbohydrates, 11.5% from protein and 14.9% from fat) and 2500 ml of liquid (Philippine RENI 2002 Edition), for a total of 2.89 kg food per day. Assuming that half of the food (1.44 kg) is contaminated with melamine, the maximum amount that can be present in the 1.44 kg food is 8 ppm (mg/kg). Based on this

worst-case exposure scenario, the limit 2.5 ppm for melamine in other foods provides a 3-fold safety margin over the TDI.

References

- **Health Canada, December 2008**. Survey and Health Risk Assessment of Background Levels of Melamine in Infant Formula Allowed for Sale in Canada. http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/pubs/melamine_errata-eng.pdf
- **EFSA, September 2008**. Statement of EFSA on risks for public health due to the presences of melamine in infant milk and other milk products in China. http://www.efsa.europa.eu/en/scdocs/doc/contam_ej_807_melamine_en,0.pdf
- **WHO, October 2008**. Melamine and Cyanuric acid: Toxicity, Preliminary Risk Assessment and Guidance on Levels in Food (25 September 2008 – Updated 30 October 2008). http://www.who.int/foodsafety/fs_management/Melamine.pdf
- **WHO, December 2008**. Expert Meeting to review toxicological aspects of melamine and cyanuric acid. http://www.who.int/foodsafety/fs_management/conclusions_recommendations.pdf
- **US FDA, October 2008**. Interim Safety and Risk Assessment of Melamine and its Analogues in Food for Humans. http://www.fda.gov/Food/FoodSafety/FoodContaminantsAdulteration/ChemicalContaminants/Melamine/ucm164522.htm
- **Food and Nutrition Research Institute (FNRI), Department of Health (DOH), 2002.** Recommended Energy and Nutrient Intakes Philippines, 2002 Edition.

THAILAND

Thailand would like to express our gratitude to Canada, the leader of the working group, for the effort of preparing the Discussion Paper on the Establishment of Maximum Levels for Melamine in Food and Feed. We are pleased to provide the following comments:

Proposed ML of 1 mg/kg for infant formula (powdered) and 2.5 mg/kg for food (other than infant formula)

We have estimated the dietary intakes of melamine using food consumption data of Thailand with WHO TDI of 0.2 mg/kg bw. The estimates were based on three age groups of infant and young children; (1) 0 to 6 months, (2) 6 to 12 months and (3) 12 to 36 months. The result shows that all age groups are at lower risk than TDI. Therefore, we agree with the proposed ML of melamine at 1 mg/kg for powdered infant formula. Moreover, we are of the opinion that the proposed ML at a level of 2.5 mg/kg for other food is also agreeable.

Proposed ML of 2.5 mg/kg for animal feed

We are of the opinion that if the ML of melamine for animal feed is set at 2.5 mg/kg, the exposure of melamine from food as a result of carryover from feed will be less than 2.5 mg/kg. However, if the melamine concentration in complete feed is set at 2.5 mg/kg, the melamine level in some feed ingredient may be higher than 2.5 mg/kg. Therefore, it is proposed that the description of animal feed should be clarified.

Issue on mixtures of melamine and melamine analogs

Background information in the discussion paper stated that the mixtures of melamine and melamine analogs such as melamine-cyanurate complex may present higher toxicity than melamine only. While the toxicological information for mixtures of melamine and melamine analogs is not available, the CCCF should considered requesting JECFA to evaluate promptly the toxicity for mixtures of melamine and melamine analogs. As there is no toxicological evaluation of mixtures of melamine and melamine analogs, we are of the view that, as a matter of adequate consumer protection, the ML should be established as a combination of melamine and analogs at the level of 1 mg/kg for powdered infant formula and 2.5 mg/kg for food (other than infant formula) and feed.

CIAA

In the document it is stated that the “ML for melamine in foods other than infant formula would be applied across all food items including raw materials, ingredients and finished foods. As such, melamine levels will even be lower in composite/finished foods where the maximum level has already been enforced on raw materials or ingredients” (page 15, No 67).

We would like to emphasize that the contrary is the case when considering dried ingredients/dried finished products. It is important to clarify therefore that the melamine ML of 2.5 mg/kg is valid for finished foods as consumed.

A similar problem are dried ingredients. A theoretical example: In fresh raw material, Melamine is detected below the limit of 2.5 mg/kg. After drying, the Melamine content is above the limit of 2.5 mg/kg. Here we face the problem that the raw material is in accordance with legislation, the ingredient prepared thereof is not. To overcome the problem, we propose to set an ML for melamine only for raw materials and finished products as consumed

We recommend to clarify this point in the paper.

IDF

General comments:

The IDF welcomes the document CX/CF 10/4/5 prepared by Canada.

However, we feel that verification of compliance of (any) limits is best done on the (raw) milk rather than on the various end products, as such approach is the most cost-effective approach. However we recognise that this is of course impractical for imported or transported products.

The paper rightly identifies adulteration of feed and food as the main source and the objective of the risk management action to establish an appropriate limit for use on different products. We consider that there is a case for a consistent limit for either powdered infant formula or reconstituted infant formula that is ready to consume.

Specific comments:

1. With regard to section "Methods of analysis" (p7), we suggest to modify the text as follows for more accurate information:

- Paragraph 33, lines 3-4: "... techniques to less sensitive immunoselective assays ..." should be replaced by "... techniques to less **selective** immunoselective assays ..."

- Paragraph 35: The two first sentences should be combined to read "**Techniques for melamine** analysis generally utilize either high performance liquid chromatography (HPLC) or gas chromatography (GC) **coupled with** either tandem mass spectrometry (MS/MS), single stage mass spectrometry (MS), diode array detection (DAD), and ultraviolet absorption (UV)".

The third sentence should read "The latter two detection systems used in combination with HPLC require **a careful optimization of the sample preparation due to the poor selectivity of the detection based on UV absorption of melamine**". In the fourth sentence, the quotation "(67)" should be modified into "(**14,** 67)".

2. In paragraph 12, it is mentioned that this paper is not intended to consider maximum levels for melamine related chemicals such as cyanuric acid. However, since analytical methods have been developed to detect both melamine and cyanuric acid, measurements indicating co-occurrence of these chemicals in the same products are being generated. Therefore, a provision on how to manage the co-occurrence of both components in food products would be valuable.

A suggestion could be that the maximum levels proposed in paragraph 75 apply to melamine singly or in combination with cyanuric acid, or its derivates as considered appropriate.

Recent toxicological information on melamine and cyanuric acid indicates that at environmental contamination levels of melamine (within the proposed limits), the concomitant presence of cyanuric acid is

unlikely to be of health concern (e.g. Dominguez et al., 2010, "*Using urinary solubility data to estimate the level of safety concern of low levels of melamine (MEL) and cyanuric acid (CYA) present simultaneously in infant formulas*", Regul. Toxicol. Pharm., doi:10.1016/j.yrtph.2010.03.002; Chen et al., 2009, Tox pathol., 37(7):959-968).

It would be appropriate that these new toxicological data on the mixture of melamine and cyanuric acid be considered and referenced. These new data suggest that the proposed limits for melamine in food are likely to cover the safety of the co-occurrence of both melamine and cyanuric acid.

A call for data on levels of melamine and cyanuric acid in food products should be recommended to further confirm the above mentioned statement.

3. IDF wishes to inform the CCCF delegates of the forthcoming publication of the **ISO Technical Specification/IDF Reviewed Method for Milk, milk products and infant formulae — Guideline for the quantitative determination of melamine and cyanuric acid by LC-MS/MS**, developed in the frame of the joint programme between ISO and IDF.