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# STATEMENT OF EFSA

## Statement of EFSA on risks for public health due to the presences of melamine in infant milk and other milk products in China

## (Question No. EFSA-Q-2008- 695)

## Issued on 24 September 2008

**Summary**

The European Food Safety Authority (EFSA) received a request on 19 September 2008 from the European Commission, Health and Consumers Directorate requesting urgent scientific advice on the risks to human health due to the possible presence of melamine in composite food products imported from China into the European Union (EU). Considering the urgency of this request for advice EFSA issued a statement following Art. 13 b of the "Decision concerning the establishment and operations of the scientific committee and panels" adopted by the Management Board of EFSA on 11 September 2007[1].

In 2008, high levels of melamine in infant milk and other milk products have led to very severe health effects in Chinese children. The import of milk and milk products originating from China is prohibited into the EU, however composite food products such as biscuits and chocolate, which could be made from contaminated milk powder, may have reached the EU. Therefore, the European Commission has requested EFSA to provide scientific advice on the risk for human health related to presence of melamine in such composite foods.

The primary target organ for melamine toxicity is the kidney. There is uncertainty with respect to the time scale for the development of kidney damage. Thus, EFSA

[1] Available at URL: http://www.efsa.europa.eu/cs/BlobServer/DocumentSet/mb_32ndmeet_annex_a_en_4.pdf?ssbinary=true

applied a tolerable daily intake (TDI) of 0.5 mg/kg body weight (b.w.) in considering possible health effects which might occur with repeated consumption of melamine contaminated products over a relatively short period.

EFSA was asked to consider health effects due to melamine exposure via the consumption of contaminated biscuits and confectionary. Based on available data, EFSA developed a number of theoretical exposure scenarios for biscuits and chocolate containing milk powder both for adults and children. In the absence of actual data for milk powder, EFSA used the highest value of melamine (approximately 2,500 mg/kg) reported in Chinese infant formula as a basis for worst case scenarios.

Based on these scenarios, estimated exposure does not raise concerns for the health of adults in Europe should they consume chocolates and biscuits containing contaminated milk powder. Children with a mean consumption of biscuits, milk toffee and chocolate made with such milk powder would also not exceed the TDI. However, in worst case scenarios with the highest level of contamination, children with high daily consumption of milk toffee, chocolate or biscuits containing high levels of milk powder would exceed the TDI. Children who consume both such biscuits and chocolate could potentially exceed the TDI by more than threefold. However, EFSA noted that it is presently unknown whether such high level exposure scenarios may occur in Europe.

**Keywords**

Melamine, composite food, exposure scenarios, Europe, health-based guidance value

**Acknowledgement**

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**Background to this request provided by the European Commission**

High levels of melamine are found in infant milk and other milk products in China. This has lead to very severe health effects in China.

The import into the EU of milk and milk products originating from China is prohibited by EU legislation. However, composite food products imported into the EU could contain or could be made from milk and milk products. From the import

statistics, it can be observed that significant amounts of biscuits and confectionary (chocolate) are imported from China. The competent authorities of the Member States and food business operators were asked to monitor the presence of melamine in imported composite food products.

It is referred to EFSA's provisional statement of 7 June 2007 related to melamine and structurally related compounds such as cyanuric acid in protein-rich ingredients used for feed and food (Question N° EFSA-Q-2007-093). The Commission received data on the presence of melamine in infant formula and other milk products in China.

Even if for the time being there is no evidence that food products containing melamine have been imported into the EU, it is appropriate to assess, based on the information provided as regards the presence of melamine in milk and milk products, the possible (worst case) exposure of the European consumer from the consumption of composite food products such as biscuits and confectionary (in particular chocolate) containing or made from milk and milk products containing melamine.

Therefore, in accordance with Article 31 of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority to provide before 24 September 2008 a scientific advice on the risks for human health related to the presence of melamine in composite foods. All information available to the Commission on this contamination incident will be provided to EFSA directly to the official responsible for this request.

## Evaluation

### *Introduction*

Melamine (2,4,6-triamino-1,3,5-triazine, CAS number 108-78-1) is a chemical intermediate used in the manufacture of amino resins and plastics. Its use has a long-standing history since it has been commercially available from the late 1930s onwards (IARC, 1999) in a range of products i.e. in combination with formaldehyde to produce melamine resin as durable thermosetting plastics, and melamine foam, a polymeric cleaning product. Other end products include countertops, fabrics, glues and flame retardants. It is also a major component of pigment yellow 150 (colorant for inks and plastics), fertilizers, and derivatives of arsenical drugs for the treatment of African sleeping sickness (trypanosomiasis). Melamine is also a minor metabolite of cyromazine, an approved insecticide used on a broad range of vegetable crops (FAO, 2006).

In June 2007 EFSA issued a provisional statement on a request from the European Commission related to an urgent scientific opinion on the risks to animal and human health related to the presence of melamine and structurally related compounds such as

cyanuric acid, ammeline and ammelide in protein rich ingredients used for feed and food (EFSA, 2007).

### *Health based guidance value*

The primary target organ for melamine toxicity is the kidney. The former Scientific Committee for Food (SCF) derived a tolerable daily intake (TDI) of 0.5 mg/kg body weight (b.w.) for melamine in the context of food contact materials but no details were given for its derivation (EC, 1986). Considering the data available on melamine toxicity EFSA recommended applying the TDI of 0.5 mg/kg b.w. also for the contamination case in pet food (EFSA, 2007). Because there is uncertainty with respect to the time scale for development of kidney damage, EFSA used this TDI, which is protective for exposure over a lifetime, in considering possible effects of exposure to melamine over a relatively short period, such as might occur with repeated consumption of melamine contaminated products.

The U.S. Food and Drug Administration (FDA) derived a TDI for melamine of 0.63 mg/kg b.w. (FDA, 2007).

### *Legislation*

Melamine is approved for use as a monomer and as an additive in plastics with a specific migration limit of 30 mg/kg food (Commission Directive 2002/72/EC related to materials and articles intended to come into contact with foodstuffs from 6 August 2002)[2].

### *Occurrence data on melamine*

*Previous data in food and feed*

Since melamine is a raw material in the production of some plastic products used for serving food, low-level migration of melamine into the food has been reported. Thus, melamine was detected using liquid chromatography in beverages at levels of 0.54, 0.72, 1.42 and 2.2 mg/kg in coffee, orange juice, fermented milk and lemon juice respectively, with a limit of detection of 0.05 mg/L. These levels originated from migration of melamine from the cup, made of melamine-formaldehyde resin, into the beverage under experimental hot and acidic conditions (95°C for 30 min) (Ishiwata *et al.*, 1987). Much higher levels of melamine have been detected in food, feed or raw materials following fraudulent practices: data reported in 2007 by the U.S. FDA (FDA 2007) showed melamine in wheat gluten and rice protein concentrate imported from China at levels in the range of 2 to 80 g/kg, with a limit of detection of 0.05-0.1 mg/kg. Analyses of actual food and feed products showed melamine in pet food,

[2] OJ, L39/2 of 13.2.2003, p.1-42

bakery meal, swine feed and fish feed samples ranging from 9.4 to 1,952 mg/kg, 10.6 to 59.6 mg/kg, 30 to 120 mg/kg and 53 to 400 mg/kg, respectively (FDA, 2007).

*Current available data on infant formula and milk products from China*

Following the current infant formula contamination incident, the Chinese State Administration of Quality Supervision, Inspection and Quarantine (AQSIQ) has announced the result of a wide investigation into the extent of the melamine contamination of dairy products (AQSIQ news release 16 September 2008[3]). Among the 175 manufacturers of domestic powdered infant formula, 66 had halted production while 109 had their products tested by the AQSIQ. A total of 491 batches of products from those companies were tested. Melamine at varying levels was detected in 69 batches produced by 22 companies. Products of the remaining 87 companies did not test positive for melamine. Among all the companies having products with a positive detection of melamine, a maximum of 2,563 mg/kg was measured from one company. Positive samples from other companies had maximum values ranging from 0.09 mg/kg to 619 mg/kg. The median for the reported maximum values was 29 mg/kg. Tests conducted on liquid milk showed that 24 of the 1,202 batches tested were contaminated. The highest melamine concentration found in liquid milk was 8.6 mg/kg.

***Manufacture of milk powder***

A major ingredient in infant formula is milk powder[4]. Whole (full cream) milk contains, typically, about 87% water and skim milk contains about 91% water. During milk powder manufacture this water is removed and approximately 13 kg of whole milk powder or 9 kg of skim milk powder can be made from 100 L of whole milk. There is thus a 10-fold concentration factor involved in producing milk powder from milk and equally melamine concentrations would be increased 10-fold in milk powder compared to liquid milk. The proportion of milk or milk powder in infant formula varies considerably between brands. There is no indication of the proportion of milk powder in samples reported positive for melamine. As an approximation it was thus assumed that the melamine concentration in the milk powder equated to the reported concentration in infant formula. In reality melamine concentration might be higher, but there could also be other sources of melamine in infant formulae present in which case the melamine concentration in milk powder might be lower.

As pointed out by the European Commission the importation of milk or milk products from China is prohibited by the EU legislation. However, milk powders of various types are used in a wide range of products other than infant formula such as baked

[3] http://www.aqsiq.gov.cn/zjxw/zjxw/zjftpxw/200809/t20080916_89958.htm
[4] Council Directive 2001/114/EC of 20 December 2001 - OJ L15 of 17.1.2002

goods, snacks and soups, chocolates and confectionary (e.g. milk chocolate), ice cream, infant formula, nutritional products for special use, reconstituted milks and other liquid beverages. According to the import statistics supplied to EFSA by the European Commission of products potentially containing milk or milk powder as an ingredient, biscuits and chocolate products are imported from China to the EU.

***Exposure scenarios***

*Hypothetical melamine dietary intake from biscuit consumption*

Biscuit is a collective description of a large range of different bakery wares of which only some contain milk as an ingredient. For milk-containing biscuits the bakery industry prefers to use non-fat milk solids in dried form as skim milk powder, but sometimes also dried whole milk powder, both for dough and fillings. In pastry or biscuit manufacturing the total amount of milk solids does not exceed 5%, and are typically between 1 and 3%. The situation is different for filled bakery ware. The mostly anhydrous creams may contain up to 20% milk powder (not more for taste reasons) but typically between 3 and 5%. Products like filled wafers and biscuits may have up to 75% filling cream resulting in a maximum of 16% of milk powder in filled bakery wares. In a likely scenario it is estimated that such biscuits would contain 2% of milk powder for plain biscuits and 3.5% of milk powder for filled biscuits.

It has been estimated that the average annual per capita consumption of biscuits and wafers varies from 0.5 kg in Ireland to 18.7 kg in the Netherlands with an EU mean of 8.0 kg (Caobisco website[5]). This is equivalent to an average EU daily per capita consumption of 0.022 kg. This is close to 10% of the overall cereal and cereal product consumption recorded in the Concise European Food Consumption database[6]. There is no indication of upper intake amounts in the Caobisco information, but referring to the Concise database high consumers at the 95$^{th}$ percentile level have a consumption close to double that of average consumers or, if applying this proportion to the Caobisco information, an estimated daily consumption of 0.044 kg.

Several scenarios for the dietary exposure to melamine from biscuit consumption are presented in Table 1. Two concentrations of melamine in milk powder were assumed (29 and 2,563 mg/kg – see page 5) as well as biscuits with three different concentrations of milk powder (2, 3.5 and 16%) consumed at mean or 95$^{th}$ percentile amounts (0.022 or 0.044 kg per day). Calculations are presented for adults at 60 kg b.w. and children at 20 kg b.w.

[5] http://www.caobisco.com/doc_uploads/Charts/consumption_biscuits.pdf

[6] http://www.efsa.eu.int/EFSA/ScientificPanels/DATEX/efsa_locale-1178620753812_ConciseEuropeanConsumptionDatabase.htm

**Table 1:** Scenarios for potential melamine dietary intake from consumption of contaminated biscuits imported from China.

| Melamine concentration | | Dietary exposure mg/kg b.w. per day | | | |
|---|---|---|---|---|---|
| | | 60 kg adult | | 20 kg child | |
| | | Mean[a)] | 95th percentile[b)] | Mean[a)] | 95th percentile[b)] |
| **Milk powder** | **Plain biscuit (2%)** | | | | |
| 29 mg/kg | 0.6 mg/kg | 0.0002 | 0.0004 | 0.0006 | 0.0013 |
| 2563 mg/kg | 51.3 mg/kg | 0.0188 | 0.0376 | 0.0564 | 0.1128 |
| | **Filled biscuit (3.5%)** | | | | |
| 29 mg/kg | 1.0 mg/kg | 0.0004 | 0.0007 | 0.0011 | 0.0022 |
| 2563 mg/kg | 89.7 mg/kg | 0.0329 | 0.0658 | 0.0987 | 0.1974 |
| | **Quality filled biscuit (16%)** | | | | |
| 29 mg/kg | 4.6 mg/kg | 0.0017 | 0.0034 | 0.0051 | 0.0102 |
| 2563 mg/kg | 410.1 mg/kg | 0.1504 | 0.3007 | 0.4511 | 0.9022 |

a) Mean daily consumption of 0.022 kg

b) 95$^{th}$ percentile daily consumption of 0.044 kg

Dietary exposure estimates vary between 0.0002 and 0.3007 mg/kg bodyweight per day for adults and between 0.0006 and 0.9022 mg/kg b.w. per day for children. The highest calculated exposure for children involving filled biscuits with a high level of milk powder exceeds the TDI. However, there is currently no information on whether such products are imported from China into Europe and how frequent such high level exposure may occur in Europe.

*Hypothetical melamine dietary intake from confectionary consumption*

Milk is used in milk toffees (also called fudge) or fillings for hard boiled candies. The normal percentage in toffees is about 10-12% of milk powder and even lower for filled candies.

Milk chocolate is formulated by substituting whole milk powder for a portion of the cacoa mass used in producing sweet chocolate. According to the EU legislation[7], milk chocolate must contain a minimum of 14% milk solid and family chocolate 20% of milk powder. However, manufacturers usually exceed this value, frequently going to 15–25 percent whole milk solid. In the exposure scenario for chocolate the upper end at 25% was used (see Table 2). Higher amounts of milk powder would negatively influence the taste of the product and are unlikely in practice.

It has been estimated that the average annual per capita consumption of chocolate confectionary varies from 0.8 kg in Poland to 10.0 kg in the United Kingdom with an EU mean of 5.2 kg (Caobisco website[8]). This is equivalent to an average EU daily per capita consumption of 0.014 kg. This is 36% of the overall sugar and sugar products

[7] Directive 2000/36/EC of the European Parliament and of the Council - OJ L197 of 3.8.2000

[8] http://www.caobisco.com/doc_uploads/Charts/consumption_choco.pdf

including chocolate consumption recorded in the Concise European Food Consumption database. There is no indication of upper intake amounts in the Caobisco information, but referring to the Concise database high consumers at the 95$^{th}$ percentile level have a consumption three times that of average consumers or, if applying this proportion to the Caobisco information, an estimated daily consumption of 0.042 kg.

Several scenarios for the dietary exposure to melamine from confectionary consumption are presented in Table 2. Two melamine concentration levels for milk powder are assumed (29 and 2,563 mg/kg) as well as confectionary with two concentrations of milk powder (10 and 25%) consumed at mean or 95$^{th}$ percentile amounts (0.014 or 0.042 kg per day). Calculations are presented for adults at 60 kg b.w. and children at 20 kg b.w.

**Table 2:** Scenarios for potential melamine dietary intake from consumption of contaminated confectionary imported from China.

| **Melamine concentration** | | **Dietary exposure mg/kg b.w. per day** | | | |
|---|---|---|---|---|---|
| | | **60 kg adult** | | **20 kg child** | |
| | | Mean[a)] | 95th percentile[b)] | Mean[a)] | 95th percentile[b)] |
| **Milk powder** | **Milk toffee (10%)** | | | | |
| 29 mg/kg | 2.9 mg/kg | 0.0007 | 0.0020 | 0.0020 | 0.0061 |
| 2563 mg/kg | 256.3 mg/kg | 0.0598 | 0.1794 | 0.1794 | 0.5382 |
| | **Chocolate (25%)** | | | | |
| 29 mg/kg | 7.3 mg/kg | 0.0017 | 0.0051 | 0.0051 | 0.0152 |
| 2563 mg/kg | 640.8 mg/kg | 0.1495 | 0.4485 | 0.4485 | 1.3456 |

a) Mean daily consumption of 0.014 kg

b) 95$^{th}$ percentile daily consumption of 0.042 kg

Dietary exposure to melamine from confectionary consumption varies between 0.0007 and 0.4485 mg/kg bodyweight per day for adults and between 0.0020 and 1.3456 mg/kg bodyweight per day for children. The highest calculated exposure for children involving chocolate with a high level of milk powder exceeds the TDI by more than two times. However, there is currently no information on whether such products are imported from China into Europe and how frequently such high level exposure may occur in Europe.

***Exposure estimates compared to the health based guidance value***

Results from the dietary exposure scenarios developed in Tables 1 and 2 were compared with the TDI (Table 3).

**Table 3:** A comparison of dietary exposure to melamine in relation to the TDI of 0.5 mg/kg.

| **Melamine concentration** | **Dietary exposure in proportion of TDI** | | | |
|---|---|---|---|---|
| | **60 kg adult** | | **20 kg child** | |
| | Mean | 95$^{th}$ percentile | Mean | 95$^{th}$ percentile |
| **Plain biscuit (2%)** | | | | |
| Median | 0.0% | 0.1% | 0.1% | 0.3% |
| High | 4% | 8% | 11% | 23% |
| **Filled biscuit (3.5%)** | | | | |
| Median | 0.1% | 0.1% | 0.2% | 0.4% |
| High | 7% | 13% | 20% | 40% |
| **Quality filled biscuit (16%)** | | | | |
| Median | 0.3% | 0.7% | 1% | 2% |
| High | 30% | 60% | 90% | 180% |
| **Milk toffee (10%)** | | | | |
| Median | 0.1% | 0.4% | 0.4% | 1.2% |
| High | 12% | 36% | 36% | 108% |
| **Chocolate (25%)** | | | | |
| Median | 0.3% | 1% | 1% | 3% |
| High | 30% | 90% | 90% | 269% |
| **Combined consumption** | | | | |
| Biscuit | 30% | | 90% | |
| Chocolate | | 90% | | 269% |
| Combined | | 120% | | 359% |
| Biscuit | | 60% | | 180% |
| Chocolate | 30% | | 90% | |
| Combined | | 90% | | 270% |

Based on these scenarios calculated exposure does not raise concerns for the health of adults in Europe should they consume chocolates and biscuits containing contaminated milk powder. In worst case scenarios, children eating products with the highest melamine contamination level reported at the 95$^{th}$ percentile level either as biscuits or confectionary could exceed the TDI of 0.5 mg/kg bodyweight on individual occasions. If consuming both chocolate and biscuits there is the potential for children to exceed the TDI by more than three times. It should be remembered that the dietary exposure calculation involving quality filled biscuits might be a gross overestimation of the actual situation since there is no indication that China exports such products to Europe, but it can not be completely excluded. The chocolate scenario is considered more realistic.

## Conclusions

In conclusion, EFSA was asked to consider health effects due to melamine exposure via the consumption of contaminated biscuits and confectionary. Based on these scenarios, estimated exposure does not raise concerns for the health of adults in Europe should they consume chocolates and biscuits containing contaminated milk powder. Children with a mean consumption of biscuits, milk toffee and chocolate made with such milk powder would not exceed the tolerable daily intake (TDI). However, in worst case scenarios with the highest level of contamination, children with high daily consumption of milk toffee, chocolate or biscuits containing high levels of milk powder would exceed the TDI. Children who consume both such biscuits and chocolate could potentially exceed the TDI by more than threefold. However, EFSA noted that it is presently unknown whether such high level exposure scenarios may occur in Europe.

## References


European Community (EC), 1986. Report of the Scientific Committee for Food on certain monomers of other starting substances to be used in the manufacture of plastic materials and articles intended to come into contact with foodstuffs. Seventeenth series. Opinion expressed on 14 December 1984. Available at URL http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_17.pdf.

EFSA (European Food Safety Authority), 2007. EFSA´s provisional statement on a request from the European Commission related to melamine and structurally related compounds such as cyanuric acid in protein-rich ingredients used for feed and food. Available at URL: http://www.efsa.europa.eu/cs/BlobServer/Statement/efsa_statement_melamine_en_rev1.pdf?ssbinary=true

FDA (U.S. Food and Drug Administration), 2007. Interim melamine and analogues safety/risk assessment. Available at URL: http://www.cfsan.fda.gov/~dms/melamra.html

FAO (Food and Agriculture Organization of the United Nations), 2006. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy, 3–12 October 2006; FAO Plant Production and Protection Paper, 187, 1-400.

IARC (International Agency for Research on Cancer), 1999. Some chemicals that cause tumours of the kidney, or urinary bladder in rodents and some other substances. IARC Monogr.Eval.Carcinogen.Risks.Hum. 73, 329-338.

Ishiwata,H., Inoue,T., Yamazaki,T., and Yoshihira,K. 1987. Liquid chromatographic determination of melamine in beverages. J.Assoc.Off Anal.Chem. 70, 457-460.