Risk Analysis in Emergency Situations and Response to Emergency Situations (Melamine case)

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The melamine-contaminated dairy products event first came to the attention of the international organizations on **11 September 2008.**

Over 54 000 children have sought medical treatment in China related to the consumption of melamine-contaminated infant formula. **Almost 12 900 are currently hospitalized.**

Both **WHO and FAO** have used **the International Food Safety Authorities Network (INFOSAN)** to inform and update national food safety authorities on this food safety crisis, one of the largest in recent years.

INFOSAN Emergency Alert
Melamine-contaminated powdered infant formula, China
16 September 2008

Prepared by the Department of Food Safety, Zoonoses and Foodborne Diseases
For the attention of the members of INFOSAN and INFOSAN EMERGENCY Network

INFOSAN recommendations to Member States in regard to the melamine-contaminated powdered infant formula event in China.

INFOSAN is alerting Member States to look for potential local distribution of melamine-contaminated milk, milk powder or powdered infant formula originated from China. Since the intentional addition of melamine to raw milk seems to have been on-going for several months, there is a potential for some of the contaminated milk or milk powder to have been distributed to other markets through informal channels.

INFOSAN is also alerting Member States to look out for symptoms involving kidney function complications in infants fed with powdered infant formula. Kidney stones in infants are rare and could be an indication that the contaminated products are on the local market.

Member States should be aware of the possible illegal distribution because of the large quantities involved, the intentional criminal nature of this contamination and the seriousness of the public health consequences of this event.

Current situation

The possible extent of the exposure

Action taken by the Government of China

Action taken by INFOSAN

Actions taken by Member States

Current situation

Report from Ministry of Health, China: 1253 cases of kidney stones in infants and 2 death across the country (as of 16 September). Kidney stones are extremely rare in infants and the outbreak has been shown to be due to the consumption of powdered infant formula contaminated with melamine. **(Outbreak Cases Report)**

The ingestion of melamine can lead to crystal formation in the kidneys. This can cause a complete inability to pass urine (anuria) and renal failure as the kidneys become damaged and, if not treated, can eventually lead to death. **(Cause of Outbreak)**

All the infants so far identified with kidney stones had consumed infant formula produced by Sanlu Co. Ltd. On 6 August authorities ordered a recall 8218 tons of Sanlu infant formula. The tainted milk was used in powder processed from March to 5 August. **(Source of the Problem)**

The possible extent of the exposure

Since **the contamination appears to have happened prior to processing**, the contaminated milk may also have been distributed elsewhere. Both **milk powder** and **powdered infant formula** have very long shelf lives. The health effect of contaminated infant formula which is often the sole element of their diet is very serious and life threatening.

Action taken by the Government of China

The Chinese government has established an emergency task force to tackle the situation. The Ministry of Health confirmed that melamine is the contaminant present in the milk powder. The Ministry of Health has been keeping WHO informed via INFOSAN responses and directly with WHO China office. The ministry also improve dissemination of health information to assure affected infants could receive treatment in time. **Specialists are visiting villages and other rural areas to conduct investigations, and transfer any affected babies to hospitals for treatment.** Training is being provided to paediatricians and radiologists in the affected areas of the country. The Ministry of Health also assures that affected patients will receive free treatment.

Action taken by INFOSAN

The Ministry of Health confirmed on the 12.09.08 that incriminated product had not been exported and provided WHO with a description of the development of the event. **Through further interaction between INFOSAN and the Ministry of Health the issue of potential other use of the contaminated milk powder** as well as parallel (illegal) distribution of contaminated milk powder was raised. Informal trade, illegal trade and smuggling of food products is an increasing problem worldwide as these products usually do not undergo the necessary controls for safety and quality. **The Ministry of Health, China has agreed for the issuance of this INFOSAN alert.**

Actions taken by Member States

The Ministry of Health, China, has confirmed that there has been **no export of contaminated powdered infant formula** from the Sanlu Company.

The United States Food and Drug Administration **(USFDA) has issued a warning to consumers** to avoid powdered infant formula originating from China. **Presently, no powdered infant formula from China** is legally imported into the USA but it could potentially be available in ethnic food shops.

New Zealand imports a very small amount of conventional dairy products such as milk, milk powder and cheese from China, and has begun testing powdered infant formula as a precautionary measure. **So far, none has been found to be contaminated.**

List of milk products that are reported to be positive for melamine

To update the list, please contact INFOSAN Emergency at emergencyinfosan@who.int

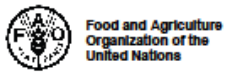
Updated on 02.10.2008 AM

This contaminated product list is a compilation of official test results obtained by INFOSAN via the relevant official sources. Since countries do not have an obligation to report such results to WHO this list might not be exhaustive. It should be noted that it will be continuously updated and changed based on the most current information available to INFOSAN. The purpose of this list is to alert authorities to potentially contaminated products.

NA: Non Available

BISCUITS, CAKES & CONFECTIONARY

N°	Product Name	Expiration date	Production date	Manufacturer	Country	Level of melamine found (ppm)	Level of cyanuric acid found (ppm)	Date tested	Source	Lot No.	Link
1	White Rabbit Creamy Candies	NA	NA	Shanghai Guang Sheng Yuan International Trade Co Ltd, 220 Cao Bao Road, Shanghai, China	New Zealand	180	1.4	24/09/2008	New Zealand Food Safety Authority	NA	http://www.nzfsa.govt.nz/publications/media-releases/2008/melamine-results-at-24-sep-2008.htm
		NA	NA	Shanghai Guang Sheng Yuan International Trade Co Ltd, 220 Cao Bao Road, Shanghai, China	Singapore	67-160	NA	21/09/2008	Agri-food & Veterinary Authority of Singapore	NA	http://www.ava.gov.sg/NR/rdonlyres/541AE049-0F81-4452-858D-B43237D4AA58/22029/CONSUMERADVISORYUPDATEONPRODUCTSDETECTEDTOCONTAINM.pdf
		20/01/2010	NA	Shanghai Guang Sheng Yuan International Trade Co Ltd, 220 Cao Bao Road, Shanghai, China	Belgium	11.25	NA	26/09/2008	Belgian Federal Food Safety Agency	NA	NA
		20/01/2010	NA	Shanghai Guang Sheng Yuan International Trade Co Ltd, 220 Cao Bao Road, Shanghai, China	Germany	152	NA	29/09/2008	The Federal Office of Consumer Protection and Food Safety (BVL)	NA	NA
		NA	NA	Shanghai Guang Sheng Yuan International Trade Co Ltd, 220 Cao Bao Road, Shanghai, China	Indonesia	456.04 - 945.86	NA	27/09/2008	The National Agency of Food and Drug, Indonesia	NA	http://118.97.48.164:8796/
2	Misarang Custard	21/04/2009	22/07/2008	NA	Republic of Korea	137	NA	24/09/2008	Korean Food and Drug Administration	NA	NA
3	Milk Rusk	02/01/2010	NA	NA	Republic of Korea	7	NA	24/09/2008	Korean Food and Drug Administration	NA	NA
4	Oreo Wafer Sticks	NA	NA	PT. Nabisco Food (Suzhou) Co. Ltd., China	Indonesia	361.69 - 366.08	NA	27/09/2008	The National Agency of Food and Drug, Indonesia	NA	http://118.97.48.164:8796/



Toxicological and Health Aspects of Melamine and Cyanuric Acid

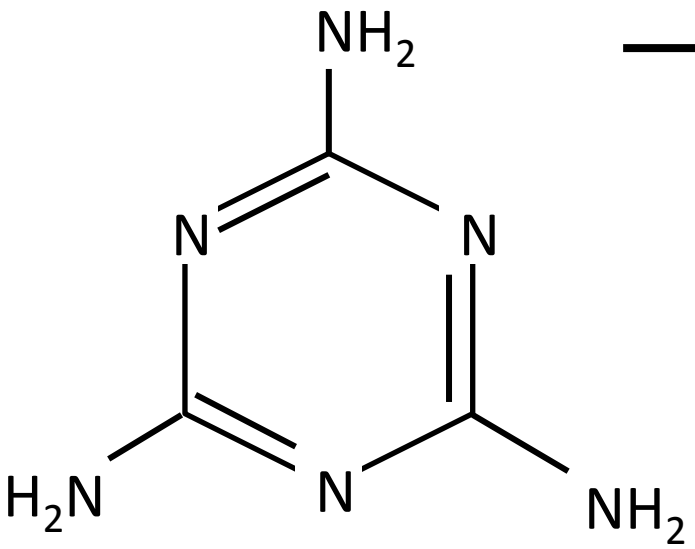
Report of a WHO Expert Meeting
In collaboration with FAO
Supported by Health Canada

Health Canada, Ottawa, Canada
1–4 December 2008

Geneva, 2009

Hazard Identification

Chemical Abstracts Service
[CAS] No. 108-78-1



Melamine

1g melamine per Kg of milk raise the apparent protein content from 2.7% to 3.1%

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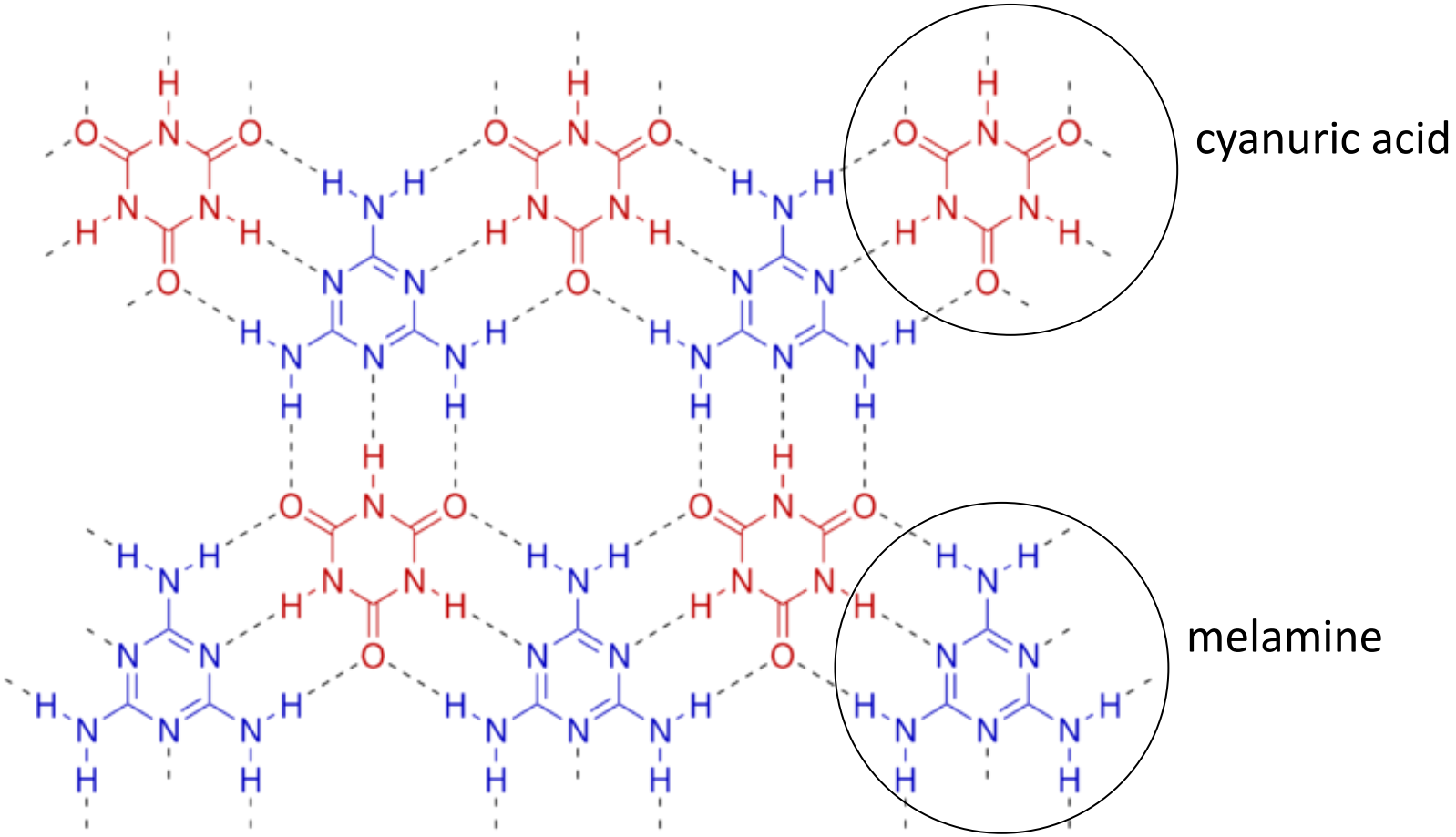
It is used primarily in the synthesis of melamine–formaldehyde resins for the manufacture of laminates, plastics, coatings, commercial filters, glues or adhesives, and moulding compounds for dishware and kitchenware



Melamine-Cyanurate Complex

Melamine and cyanuric acid are able to form self-assembling, high molecular weight complexes. ***Cyanuric acid*** **(CAS No. 108-80-5) is an oxytriazine melamine analogue that may be produced as a by-product in melamine synthesis.**

METHODS FOR THE ANALYSIS OF MELAMINE AND ITS ANALOGUES IN FOOD AND FEED

Review of methods of analysis

Existing methods for the analysis of melamine and its analogues (ammeline, ammelide, cyanuric acid, melamine–cyanurate) in foods and animal feeds were reviewed.

These methods include rapid screening and selective quantitative methods. Some are multiresidue methods and can be used to analyse for multiple compounds during one process.

- **Sample preparation**
- **Sample extraction**
- **Detection and quantification**
- **Validity of analytical data**

Development of an analytical strategy for measurement of melamine and its analogues

There are a number of factors that any organization or group that is planning to begin analysing melamine and its analogues should take into consideration.

These considerations deal with the choice of analytical method(s) to use and the steps required **to ensure that valid and accurate data are produced.**

- **Selection of analytical method**
- **Validation**
- **Quality control during analyses**
- **Sampling plans**

Table. Analytical techniques used for analysis of melamine and analogues in food and feed

Analytical technique	Selectivity	Sensitivity	Cost	Purpose	Remarks
ELISA	Low	Low	Low	Screening	Currently for detecting melamine only
HPLC-UV/ DAD	Low	Low	Medium	Screening and confirmation	Preferred for screening of melamine and analogues; however, validation is required for Confirmation
GC-MS	Medium	Medium	High	Screening and confirmation	Confirmatory method for melamine and analogues
GC-MS/MS	High	High	Very High	Screening and confirmation at traces level	Confirmatory method for melamine and analogues
LC-MS/MS	High	High	Very High	Screening and confirmation at traces level	Confirmatory method for melamine and analogues

Reported quantification limits for melamine and analogues range from 0.002 to 5 mg/kg and depend upon the matrix being analysed and the extraction method used.

OCCURRENCE OF MELAMINE AND ITS ANALOGUES IN FOOD AND FEED

The sources of melamine have been divided into "baseline" levels, which refer to levels in food that do not result from adulteration or misuse, and "adulteration" levels, including misuse, which refer to the intentional addition of melamine to food or unapproved use of melamine or substances that can degrade to form melamine.

Baseline **is defined as levels of melamine and related analogues in food from accepted uses that do not result from adulteration or misuse.**

This includes expected levels from the environment, food processing, packaging materials, residues from the legitimate use of triazine pesticides or veterinary drugs, and legitimate use of melamine in fertilizers or of cyanuric acid in feed additives.

Table. Melamine/cyanuric acid baseline sources and reported occurrence levels

Sources	MEL/ CYA	Reported level (mg/kg)	Additional notes	References
Migration from plastic tableware	MEL	**< 1**	Water, ethanol at 60 °C, 70 °C and 95 °C	Ishiwata, Inoue & Tanimura (1986); Bradley et al. (2005); Lund & Petersen (2006); Chinese Center for Disease Control and Prevention (unpublished data, 2008); Korea Food and Drug Administration (unpublished data, 2008)
		< 1	3% acetic acid at 60 °C and 70 °C	
		0.18 – 42.9	4% acetic acid at 95 °C	Ishiwata, Inoue & Tanimura (1986)
		0.5 – 2.2	Coffee, orange juice, lemon juice, fermented milk at 95 °C	Ishiwata et al. (1987)

Adulteration **is the intentional addition of melamine and/or analogues directly to food, food ingredients, animal feed, feed ingredients or pelletizing agents. It may also be present indirectly in foods of animal origin as a result of carry-over from the intentional addition to animal feed.**

Misuse **is defined as the inappropriate use of cyromazine (a pesticide that metabolizes to melamine) or biuret (a ruminant feed additive containing cyanuric acid) in animal feed or use of animal feed containing these additives in species for which it is not intended.**

Table. Melamine concentrations in Sanlu infant formula samples*
(the Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention)

	No. of samples	Mean (mg/kg)	Median (mg/kg)	90th percentile (mg/kg)	Maximum (mg/kg)	Range (mg/kg)
A	111	1212	1000	2600	4700	<0.05-4700
B	52	1674	1700	2880	4700	<0.05-4700

* A: all samples; B: samples collected from affected area in China. LOQ 0.05 mg/kg.

Table 4. Melamine concentrations in food and feed samples testing positive for melamine

Food item	Melamine concentration (mg/kg)
Biscuits, cakes and confectionery	0.6 – 945.86
Liquid milk and yoghurt products	0.5 – 648
Frozen desserts	39 – 60.8
Powdered milk and cereal products	0.38 – 1143
Processed foodstuff	0.6 – 41
Food processing ingredients	1.5 – 6694
Animal feed	116.2 – 410

EXPOSURE ESTIMATES FOR MELAMINE AND ITS ANALOGUES

Exposure to melamine and its analogues resulting from baseline levels

Category	Estimated daily exposure (µg/kg body weight)*	Comment
Infant formula	0.54 – 1.6	Mean exposure
Other foods	0.03 – 0.12	Adults, mean exposure
Disinfection of food processing	7	Adults, very conservative estimate
Migration from melamine-containing plastic	13	Adults, conservative estimate
Migration from melamine-containing adhesives	< 0.35	Adults, conservative estimate
Residues arising from cyromazine use	0.04 – 0.27	Adults, conservative estimate

* The Expert Meeting considered that it was not appropriate to sum the dietary exposure assessments from different sources, as the individual exposure assessments were generally very conservative. In addition, a consumer is very unlikely to be exposed simultaneously to the different sources of exposure.

Table. Estimated dietary exposure to melamine from Sanlu infant formula (111 samples)

Age (months)	Melamine dietary exposure estimates (mg/kg body weight per day			
	Mean concentration (1212 mg/kg)	Median concentration (1000 mg/kg)	90th-percentile concentration (2600 mg/kg)	Maximum concentration (4700 mg/kg)
3	28.4	23.4	61.0	110.2
6	26.0	21.4	55.7	100.7
12	18.2	15.0	39.0	70.5
24	10.4	8.6	22.3	40.3

EPIDEMIOLOGICAL AND TOXICOLOGICAL DATA

Age (months)	Number of examined infants (% of total)	Infants with stones (% of sameage infants examined)
<6	456 (54)	116 (25)
6–12	273 (32)	59 (22)
12–18	103 (12)	15 (15)
18–24	12 (1)	1 (8)
24–30	7 (1)	1 (14)
>30	0 (0)	0 (0)
Total	851 (100)	192 (23)

Risk Characterization

The dietary exposures based on the consumption of melamine-adulterated infant formula in China at the median levels of melamine reported in the most contaminated brand were estimated to range from 8.6 to 23.4 mg/kg body weight per day, based on data provided by the Chinese Center for Disease Control and Prevention.

This is about 40–120 times the TDI of 0.2 mg/kg body weight, explaining the dramatic renal toxicity observed in Chinese infants.

Conservative estimates of potential exposure of adults to melamine from foods containing adulterated milk products were 0.8–3.5 times the TDI.

Estimates of exposure to baseline levels of melamine from all sources (up to 13 µg/kg body weight per day) were well below the TDI.

In developing the TDI, the Expert Meeting specifically considered the sensitivity of infants. The TDI is derived from toxicological studies in weanling rats, and an additional uncertainty factor is applied to take into account some uncertainties

Risk Management

Many countries have introduced limits for melamine in infant formula and other foods. Limits for melamine in powdered infant formula (1 mg/kg) and in other foods (2.5 mg/kg) would provide a sufficient margin of safety for dietary exposure relative to the TDI.

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Thank You Very Much