Asia-Pacific
Economic Cooperation

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Risk Analysis in the International Setting - Examples

Submitted by: World Health Organization

APEC 2009 Singapore

Examination of Hot Issues in Risk Analysis Workshop
Singapore
1-2 August 2009

Risk Analysis in the International Setting

Examples

Dr. Angelika Tritscher
WHO Joint Secretary to JECFA and JMPR
Department of Food Safety and Zoonoses
World Health Organization
http://www.who.int/foodsafety/en/
http://www.who.int/ipcs/food/en/

Outline

- Melamine
- Acrylamide
- Aflatoxins
- *Cronobacter sakazakii* in Infant Formulae
- Risk Communication

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Example emerging issues: Melamine

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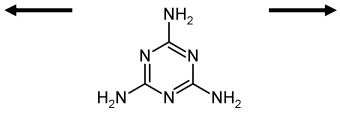
Melamine



- High production volume chemical (>1mill tons/yr, 2004)
- Major uses: resins, flame retardants, adhesive, (fertilizer)
- Slightly soluble in ethanol, in water appr 3g/L (20°C)

- Rich in nitrogen, intentionally added to food to disguise a low protein content (in diluted milk)

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Children affected in China

September 2008 China confirmed contamination incident with melamine in milk-based infant formula

- Patients screened 22.4 million
- Cases reported 294 000
- Cases hospitalized 51 900
- 6 deaths confirmed

(official numbers as of 1st Dec08)

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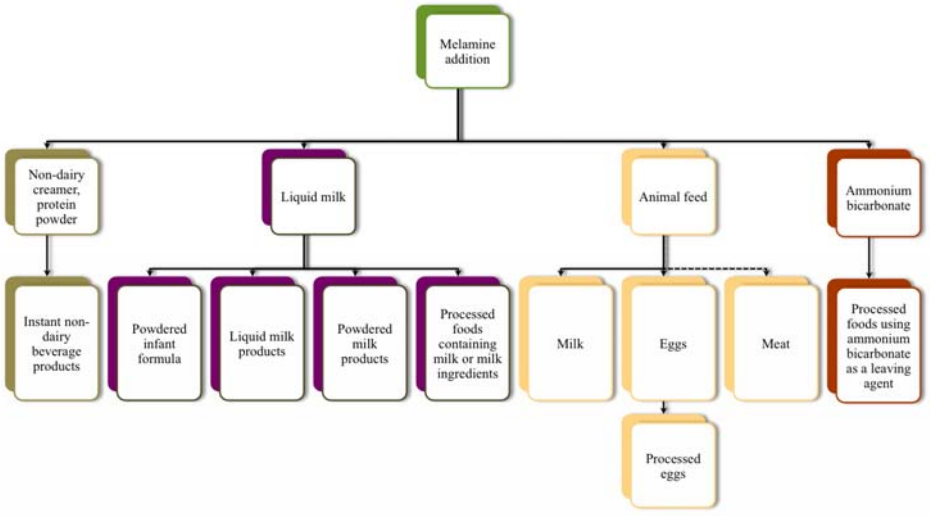
Contamination chain of events



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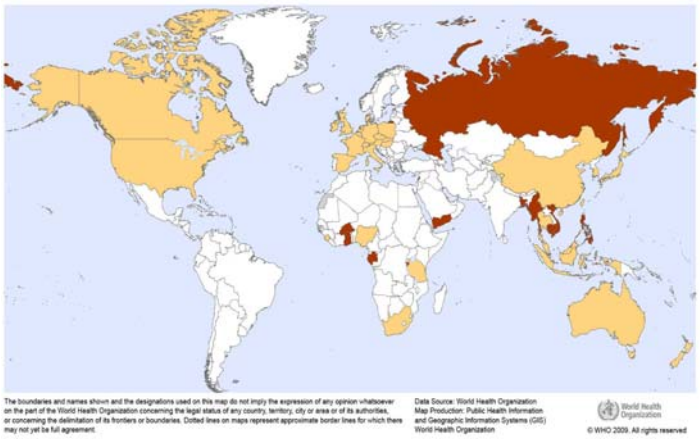
Global Implications

Analysis reported

Import of contaminated products reported



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Levels of Melamine

Product category	Melamine levels (mg/kg)
Infant formula	0.09 – 2 563
Liquid milk and yoghurt	0.6 - 648
Powdered milk and cereal products	<1 – 6 196
Biscuits, cakes & confectionary	0.6 - 945
Frozen desserts	4.4 - 60.8
Snackfood	0.5 - 54
Processed food	0.7 - 13.6
Non-dairy creamer	1.5 – 6 694
Ammonium bicarbonate	33.4 - 508
Dried egg powder	0.1 - 5.03
Eggs	2.9 - 4.7
Animal feed	116.2 - 410

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Clear Public Health Concern: Immediate Measures Taken

FAO and WHO actions

- **INFOSAN** **(International Food Safety Authorities Network)**
  - **INFOSAN Emergency network** (153 countries) regular updates of information shared (secured website)
  - **Close collaboration with Chinese MOH**
  - **Collaboration with affected countries** information verification and alerts
  - **Assistance to countries** Laboratory information, analytical methods, considerations for setting limits etc.
- **Public Websites** special websites, continuously updated;

Countries

- preliminary risk assessments (several different ADIs)
- limits in foods (mainly 1ppm infant formula, 2.5ppm other foods)
- import bans

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Need for scientific advice

- **To review current knowledge on:**
  - Chemistry of melamine alone and in combination with its analogues (cyanuric acid, ammeline, ammelide)
  - Analytical methods
  - Occurrence of melamine in foods (background and adulteration)
  - Toxicity of melamine alone and in combination with its analogues
  - Human health risk assessment, including species sensitivities and sensitive sub-populations, including exposure assessment
- **To identify knowledge gaps** to guide research efforts

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Rapid Scientific Advice

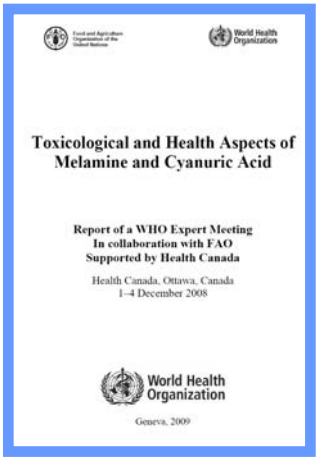
WHO Expert Meeting to review toxicological aspects of melamine and cyanuric acid

In collaboration with FAO

Ottawa, Canada, 1-4 December 2008

Supported by Health Canada

http://www.who.int/foodsafety/fs_management/infosan_events/en/index.html


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

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Geneva, 2009

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Outcome of expert meeting and impact for Member States and for Codex work

- TDI 0.2 mg/kg bw established, applicable to melamine only
- Background exposure below TDI, but estimated exposure of infants to adulterated formula 40-120 times the TDI
- Limits of 1ppm in powdered infant formula and 2.5 ppm in other foods provide sufficient margin of safety relative to TDI

- TDI as guidance for national risk assessments, interim measures for limits in food can be taken
- Discussed at CCCF – proposal for new work for adoption at 32nd CAC to establish MLs for melamine in food

Rapid reaction to new emerging issue with global impact

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Example genotoxic and carcinogenic compound with knowledge gaps: Acrylamide

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Contaminants: Acrylamide (AA)
Risk assessment activities

- 2002: new scientific concern raised by finding of AA in certain heat-treated foods. AA of know toxicity
- Rapid response via ad hoc expert consultation (2002):
  - Summary of available scientific knowledge and identification of gaps to direct research
- JECFA evaluation in 2004:
  - MOE approach, indication for health concern at current estimated exposure
  - Identification of major food categories contributing to exposure
  - Indication for mitigation measures
  - Recommendation for re-evaluation once more data are available
- JECFA re-evaluation :
  - Planned for February 2010 – call for data: http://www.who.int/ipcs/food/jecfa/jecfa72.pdf

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Contaminants: Acrylamide (AA)
Risk Management Activities

- CCFAC/CCCF:
  - Discussion on need for ML; however too much uncertainty, hence development of Code of Practice
- CCCF: Code of Practice developed……based largely on information provided through the JECFA assessment
- **Code of Practice for the Reduction of Acrylamide in Foods, adopted at 32nd CAC, July 2009**
- *Re-consideration of need for ML after JECFA re-evaluation*

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Example:
Risk Assessment and Management of Aflatoxins

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Aflatoxins

Quantitative risk assessment

Background

- B1, B2, G1, G2
  - metabolic products of molds
  - temporal contamination
    - humidity, heat, drought (stress), storage
  - corn, peanuts, treenuts, figs, wheat
- M1, M2
  - hydroxylated metabolites of B1
  - milk and milk products

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Aflatoxins: Risk Factors

- Aflatoxins associated with primary liver cancer (PLC)
- Competing or cooperative risk factors
  - alcohol consumption (cirrhosis)
  - parasitic infections
  - poverty
  - oral contraceptive use
  - other environmental factors
  - chronic infection with hepatitis B virus (HBV)
- Evidence from various epidemiological and clinical studies

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Data for Aflatoxin Risk Assessment

Epidemiology Data
- HBV status unknown
- HBV status known
- exposure assessment
  - food samples
  - urinary metabolites

Rodent Toxicology Data
- 18 studies with dose-response data
  - mostly hepatocarcinogenesis
  - other cancers
    - colon, kidney, lung, lymphoreticular
- mostly aflatoxin B1
  - one with M1, one with B1, G1 and B2 and one with aflatoxicol (aflatoxin metabolite

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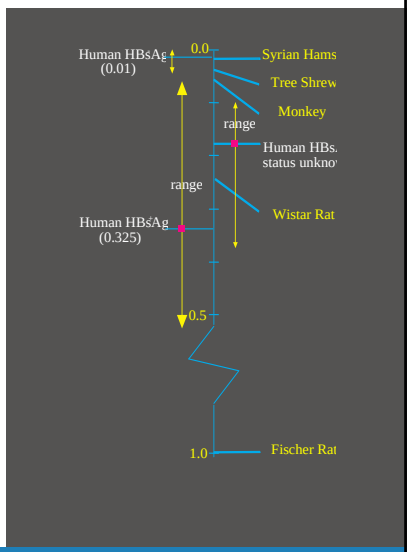
JECFA assessment of liver cancer risk

based on epidemiological and toxicological studies

Potency estimates for human liver cancer resulting from exposure to AfB1(cases per year/100,000 people per ng AfB1 /kg/day :

- Humans, HBsAg-
  - 0.01 cancers per 100,000
  - range [0.002,0.03]
- Humans, HBsAg+
  - 0.325 cancers per 100,000
  - range [0.05,0.5]



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Sample Risks

countries with different HBV status

Country	Standard	HBV Prevalence	Avg. Dietary Intake (ng/kg/day)	Avg. Risk (per 100k/yr)
US	20 ppb	1%	15	0.0033
	10 ppb	1%	14.3	0.0032
China	None	25%	1064.0	1.57
	20 ppb	25%	215.6	0.32
	10 ppb	25%	176.1	0.26

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Aflatoxin Risk Assessment: Conclusions

- Appr. one order of magnitude difference in cancer risk between population with high and low HBV prevalence
- 20 ppb vs. 10 ppb could be very important in countries with high HBsAg+ prevalence
- 20ppb vs 10 ppb unlikely to make large changes in population with low HBsAg prevalence
- Vaccinate!

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Further scientific advice:
Impact of different MLs on cancer risk:

Scenarios:

- Samples > 10 ug/kg excluded
- Samples > 15 ug/kg excluded
- Samples > 20 ug/kg excluded
- No samples excluded

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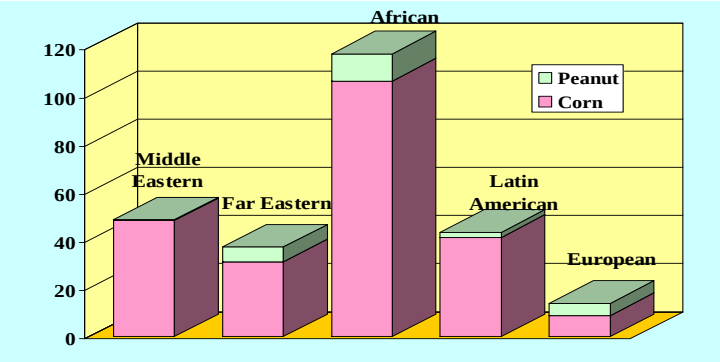
Corn and Peanut Consumption by GEMS/Food Regions (g/person/day)



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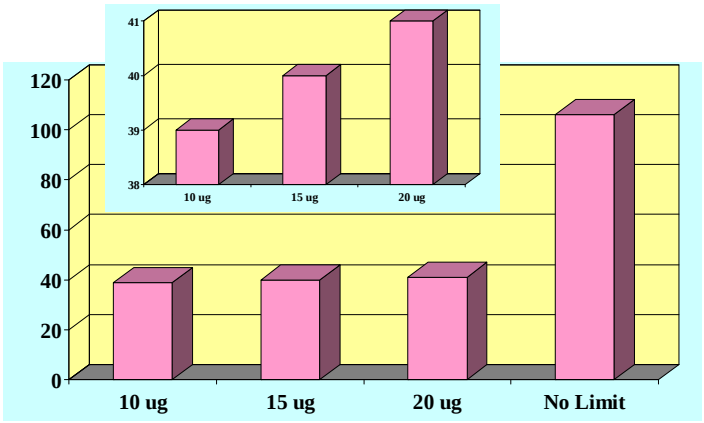
Risk of Cancer for the GEMS/Food European-type Diet for AflatoxinB$_1$
(cases/year/10^9 people)



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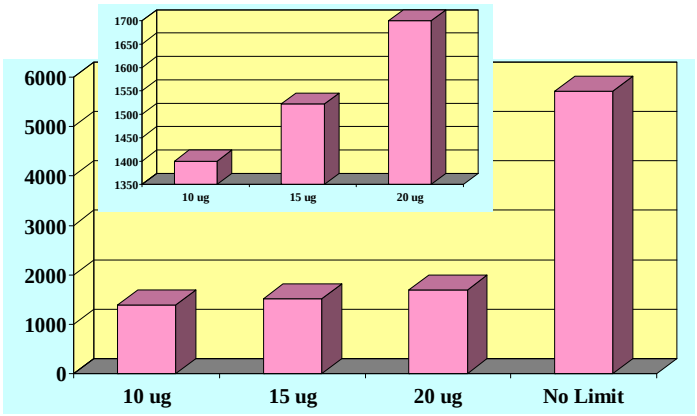
Risk of Cancer for the GEMS/Food Far East-type Diet for
Aflatoxin B$_1$(cases/year/10^9 people)



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Codex General Standard on Contaminants and Toxins in Food

CODEX STAN 193-1995

Limits for total aflatoxins

- Tree nuts (almonds, hazelnuts, pistachios) ready-to-eat:
  - 10 ug/kg
- Peanuts and Tree nuts intended for further processing:
  - 15 ug/kg

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What is the practical relevance? Example: EU

- EU aflatoxin limits for total aflatoxins:
  - Groundnuts, nuts and processed products thereof for direct human consumption: 4 µg/kg
- EU Rapid Alert System for Food and Feed
  - Border rejections

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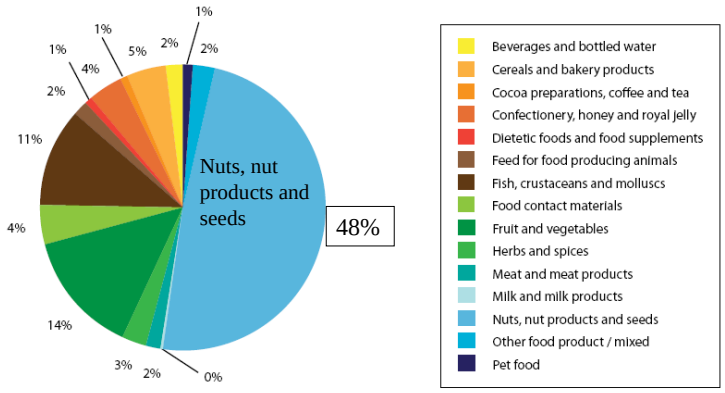
EU - RASFF

2008 – BORDER REJECTIONS BY PRODUCT CATEGORY



The Rapid Alert System for Food and Feed (RASFF), Annual Report 2008; © European Communities, 2009

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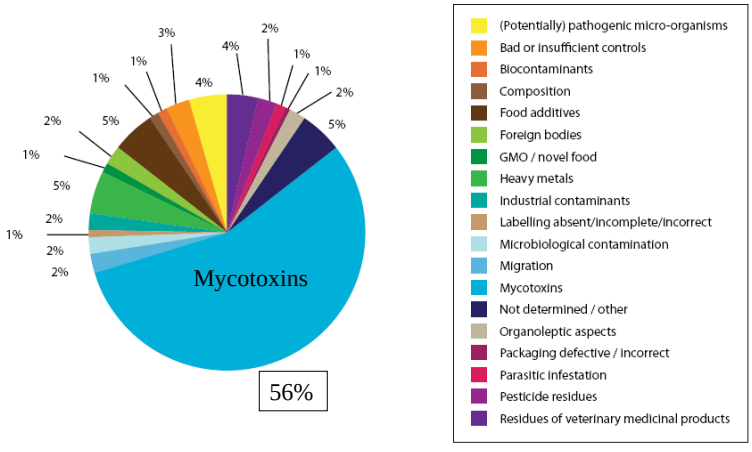
EU - RASFF

2008 – BORDER REJECTIONS BY IDENTIFIED RISK



The Rapid Alert System for Food and Feed (RASFF), Annual Report 2008; © European Communities, 2009

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What is the practical relevance? Example: EU

- EU in process of harmonization with Codex standards
- EFSA opinions

  CONTAM Panel concluded that public health would not be adversely affected by increasing the levels for total aflatoxins from 4 µg/kg to 10 µg/kg for all tree nuts

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Example microbiological risk: Cronobacter sakazakii in infant formula

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Cronobacter sakazakii: Introduction

Previously called *Enterobacter sakazakii*
Associated with powdered infant formula (PIF)

2004 Scientific assessment of *E.sakazakii and other pathogens in PIF*
2006 FAO/WHO Risk Assessment on *E.sakazakii in PIF*
2007 FAO/WHO guidelines on safe preparation, handling & storage of PIF
FAO/WHO web based user friendly risk management tool
2008 Codex adopts revised Code of Practice and Microbiological Criteria
2008 FAO/WHO Expert meeting on follow up formula
2009 Codex adopts micro criteria for *E.sakazakii* in follow up formula

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What was different to other food pathogens?

- Urgency
  - High mortality in infants
  - World Health Assembly requested rapid action (2005)
  - Request from risk manager was better defined
- Very specific product
- Product in international trade – Centralised production goes often to many different countries

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Cronobacer sakazakii: risk assessment

- **MRA basis for guidelines for the safe preparation, Codex Code of Practice, National regulatory changes**
- **Web-based model for public access since November 2007**
  - **Users do not require specialist software access or skills**
  - **This is a novel approach to the dissemination of QMRA models**

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Model: New user friendly focus

- Numerous inputs left to the decision of the user with real time response to risk managers questions (within reason / capability of model)
- Focus is on relative risk - comparison of intervention measures and associated risk reductions
- Model estimates the dose of *C. sakazakii* in prepared PIF at consumption

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Risk Communication: the 'step-child' in Risk Analysis

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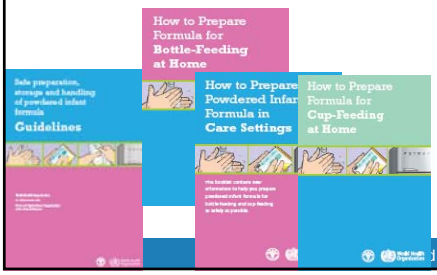
Cronobacter sakazakii in infant formula: Communication to Care Takers

- For at-risk groups
- Interventions available for risk reduction
- Translation into national guidance
- New languages for wider dissemination
- Validation of current guidance for follow-up formula



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