The Food and Environment Research Agency

Migration of chemicals from packaging materials into food

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Outline

1. Update on RA and RM of food contact materials in Europe.

2. Update on melamine.

3. The question of migration of the NIAS – non-intentionally added substances and the way forward for evaluation of substances generally.

4. Conclusions

Fera – Science with purpose

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Different roles of the Agency

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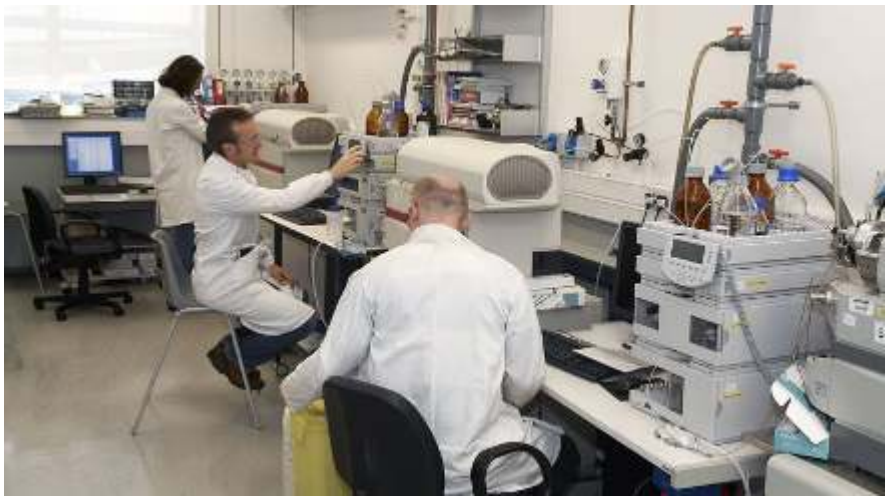
National Institute

Representation at national and international level



Contract Laboratory

Cost-efficient, timely delivery, customer focussed

R&D Institute

Applied R&D underpinning policy

Part 1. Developments in RA and RM
DG-SANCO

Background

- Currently only migrants from plastics are regulated harmonised EU wide rules - directive 2002/72/EC contains a positive list.
- Problems with ITX (2-isopropyl thioxanthone) in 2008 and 3-MBP (3-methylbenzophenone) in 2009.
- ITX and 3MBP (and BADGE before them) originated from non-plastic materials and caused considerable disruption to trade, dented consumer confidence, and took up a lot of time for EFSA and the EC and MSs.

note: BADGE - 2,2-Bis(4-hydroxyphenyl)propane bis(2,3-epoxypropyl) ether

Case study - 4-methylbenzophenone in breakfast cereals: risk assessment

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- German authorities RASFF - migration of 4-MBP, a volatile component of the inks on breakfast cereal cardboard boxes, into the cereal food.
- Concentrations in food - up to 3.7mg/kg.
- EFSA 'fast-track' procedure (Q-2009-410) was invoked and asked for statement on risk.
- No toxicological data for 4-MBP. However, tox data available for benzophenone and hydroxyl-benzophenone and a 1994 SCF TDI derived.
- 'Margin of exposure' (MOE) approach for the 'fast-track' statement rather than using the TDI. Conservative exposure scenario – 3350 for adults and 1,500 for children.

"Based on the limited exposure data available and applying knowledge on the toxicity of a similar substance, benzophenone, ***EFSA concludes that short term consumption of contaminated breakfast cereals should not pose a risk to most people.*** *However, if the use of 4-methylbenzophenone is to be continued, more data on occurrence ……. as well as appropriate toxicity data corresponding to the level of exposure for a full risk assessment."*

- Subsequently a new TDI for benzophenone of 0.03mg/kg bw/day

Case study: Interim risk management

- Standing Committee on the Food Chain and Animal Health endorsed EC statement (6 March 2009) that "*Food contact materials **printed with inks containing 4-MBP or Benzophenone should not be brought in contact with foods unless** it is demonstrated in the company's in-house documentation that the transfer into food of the sum of 4-MBP and Benzophenone **is below 0.6 mg per kg food**."*
- MSs were recommended to monitor the food packers using food contact material to ensure that they have are complying with GMP and have appropriate documentation in place.
- European Commission to raise the awareness of industry.

Risk Management by Regulation

February 2010 - Commission announced to Parliament its ambitious plans to regulate thousands of food contact materials in a new proposal.

What will this look like?

Part 1. Developments in RA and RM

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but .....

2000 + adhesive substances
3000 + ink substances

Most not evaluated at EU level to modern standards

ca. 800 plastic substances took 20+ years to for SCF and EFSA evaluate

Part 1. Developments in RA and RM
Council of Europe

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2009 - The CoE resumes its activities on evaluation of food contact materials after a dormant period.

- paper/board
- rubber/elastomers
- inks
- metals

The CoE staff visited EFSA in 2009 and stated they intend to follow similar risk assessment approaches as EFSA uses for the evaluation of substances used in plastics.

However....

Part 1. Developments in RA and RM
EFSA-Scientific Cooperation (ESCO) WG

In 2010 EFSA established ESCO working group on non-plastic food contact materials.

- summarise the state of knowledge and information gaps for the different (non-plastic) materials
- look at strengths and weaknesses in different approaches used nationally for risk assessment
- hold a workshop of interested parties in early 2011
- make recommendations on priorities - materials (non-plastics)

Part 1. Developments in RA and RM
EFSA activity on TTC

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Current approach used for plastics (tiered approach for data requirements based on migration level) is not sustainable for the 1000's of chemicals used in non-plastics. A streamlined approach may be needed.

- exposure estimates
- greater use of structural alerts

➢ EFSA is running a WG on the potential usefulness of the TTC (thresholds of toxicological concern) principle in each panel. Genotoxic carcinogens.

➢ The Cramer classification system is already used in the EFSA/JECFA evaluation of flavouring substances.

Part 2: Melamine

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- a high production volume chemical - used in FCMs
- gained notoriety following episodes of the adulteration of feed with melamine in 2007 and the adulteration of infant milk & other milk products in 2008
- rich in nitrogen (66%), had been added with a profit motive to give the appearance of increased protein levels (Kjeldahl method)
- In pet animals (100s - 1000s deaths) mainly from kidney damage caused by crystals or stones in the urinary tract.
- 5300 pet food products recalled.

Part 2. Melamine (and analogues)

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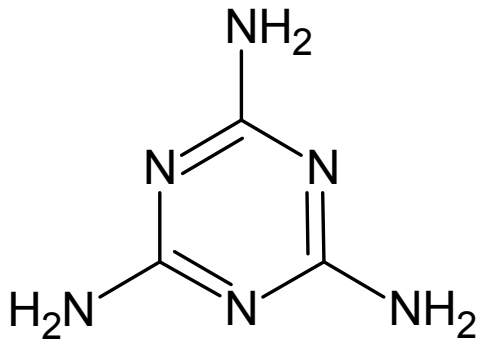
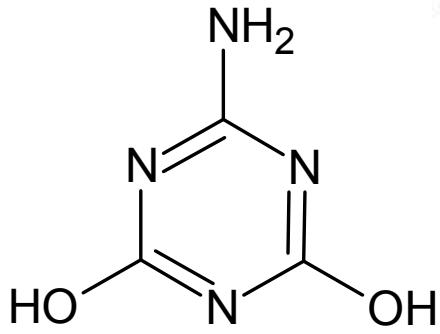
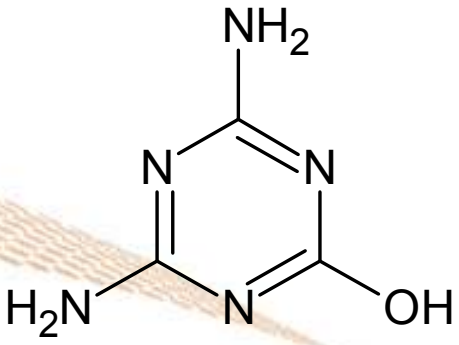
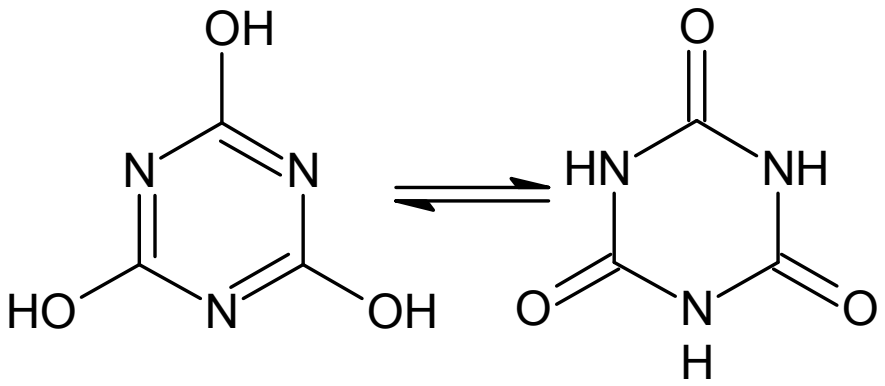
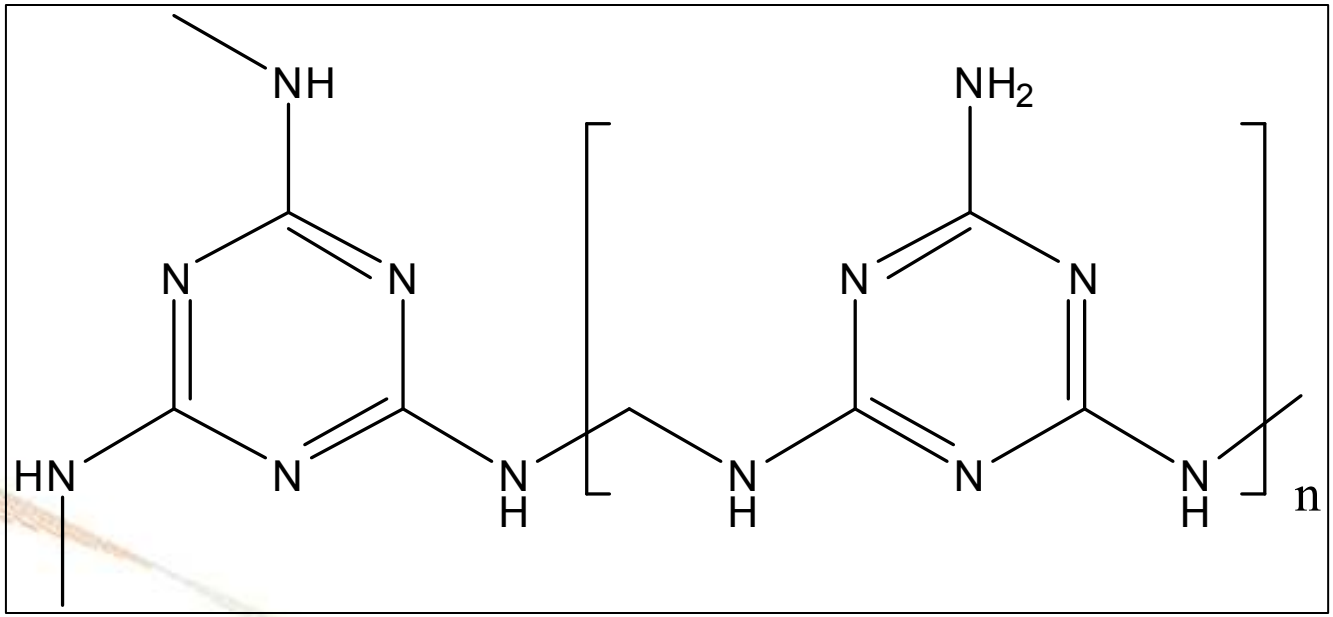
	
Melamine	Ammelide
	 *s*-triazine-2,4,6-triol *s*-triazine-2,4,6-trione
Ammeline	Cyanuric acid

Melamine

- monomer and additive for plastics
- monomer used to make can coatings, inks and adhesives

Melamine-Formaldehyde resins



Part 2. Melamine
Contaminated infant formula - 2008

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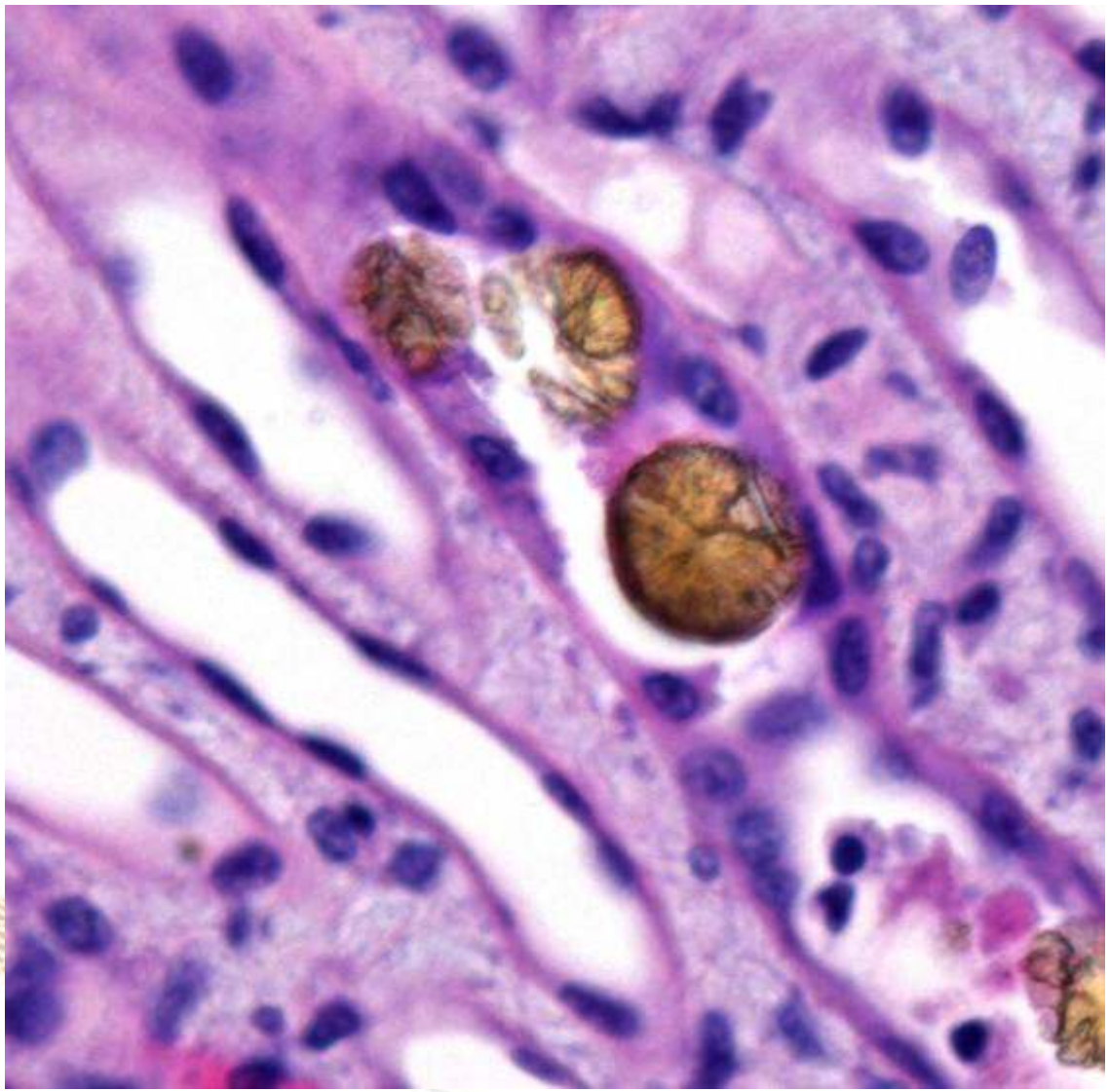
Melamine added to milk at the primary collection centres to disguise the dilution of milk with water

22 of 79 Chinese powdered infant formula producers affected.

Levels detected were up 4,700 mg/kg

Source: WHO presentation - 'The melamine story'



Stones are variable color, size, location.

- Images: melamine cyanurate in dog kidneys

Source: Reimschuessel, R, Hattan, D and Gu, Yan 2008

Part 2. Melamine

Infants affected in China

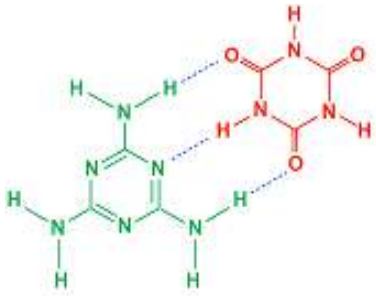
- 23 million Chinese infants (0-3years) had been screened for renal tube blockages and possible kidney stones
- 294,000 infants found to have some adverse effects, normally renal calculi (stones).
- 7 infants had died (to end-Jan 09)
- Some subsequent smaller scale ‘scares’ in Chinese provinces

Part 2. Melamine

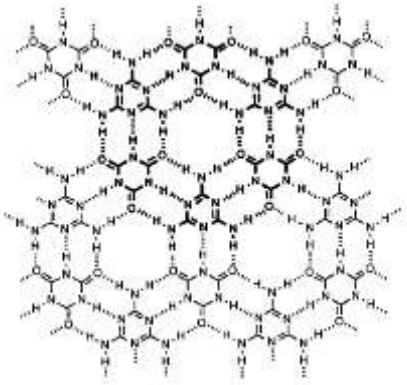
Toxicolology

- WHO, 2008 established TDI for melamine of 0.5mg/kg bw/day.
- EFSA 2010 revised the TDI for melamine 0.5 →0.2 mg/kg bw/day.
- Co-exposure to melamine and cyanuric show higher toxicity compared with melamine or cyanuric acid alone, due to the renal crystal formation.

Stones composed of MELAMINE: CYANURIC ACID



Melamine cyanurate complex formed



Part 2. Melamine

Sources of baseline levels in food

1. Migration from melamine-ware plastics
2. Migration from other food contact materials (FCMs) eg. (i) adhesive used in FCMs and (ii) melamine-formaldehyde resins (MFR) coating on tins
3. Residues of cyromazine → melamine is a metabolite in food & feed
4. Addition of cyanuric acid as a byproduct in feed grade biuret
5. Chlorine disinfectants in food production & processing
   - e.g. trichlormelamine → melamine
   - Sodium dichlorocyanurate → cyanuric acid
6. Ingestion of treated swimming pool water
7. Addition to fertilisers to control release?

Part 2. Melamine
Baseline levels – melamine dietary exposure

Product	Dietary exposure	Comments
Infant formula	0.54-1.6µg/kg body weight /day	Based on actual survey data
Foods other than infant formula	0.03 µg /kg bw/day to 0.12µg /kg bw/day	Based on actual survey data
Disinfectant use (ie. trichloromelamine)	7 µg /kg bw/day	Conservative estimate
Food contact materials	13 µg/kg bw/day	Conservative since migration under hot acidic conditions
Pesticide - cyromazine	0.04 -0.27 µg/kg bw/day (diet A - diets E, M).	Assumes maximum GAP
Animal feed	No data available	No data available

Part 2. Melamine

Melamine from coatings for cans and jar lids

- 8 commercial coatings tested using food simulants and LC-MS/MS
- the highest migration of melamine was 330 µg/kg
- commercial canning and retorting can be mimicked in laboratory tests with an autoclave or a simple pressure cooker
- strong influence of temperature of heat treatment applied in the experiments. Foods or simulants only a minor influence, particularly the food/simulant acidity
- hydrolytic degradation of the melamine-crossed-linked resins clearly takes place to release additional melamine

Part 2. Melamine

Melamine from melaware plastics

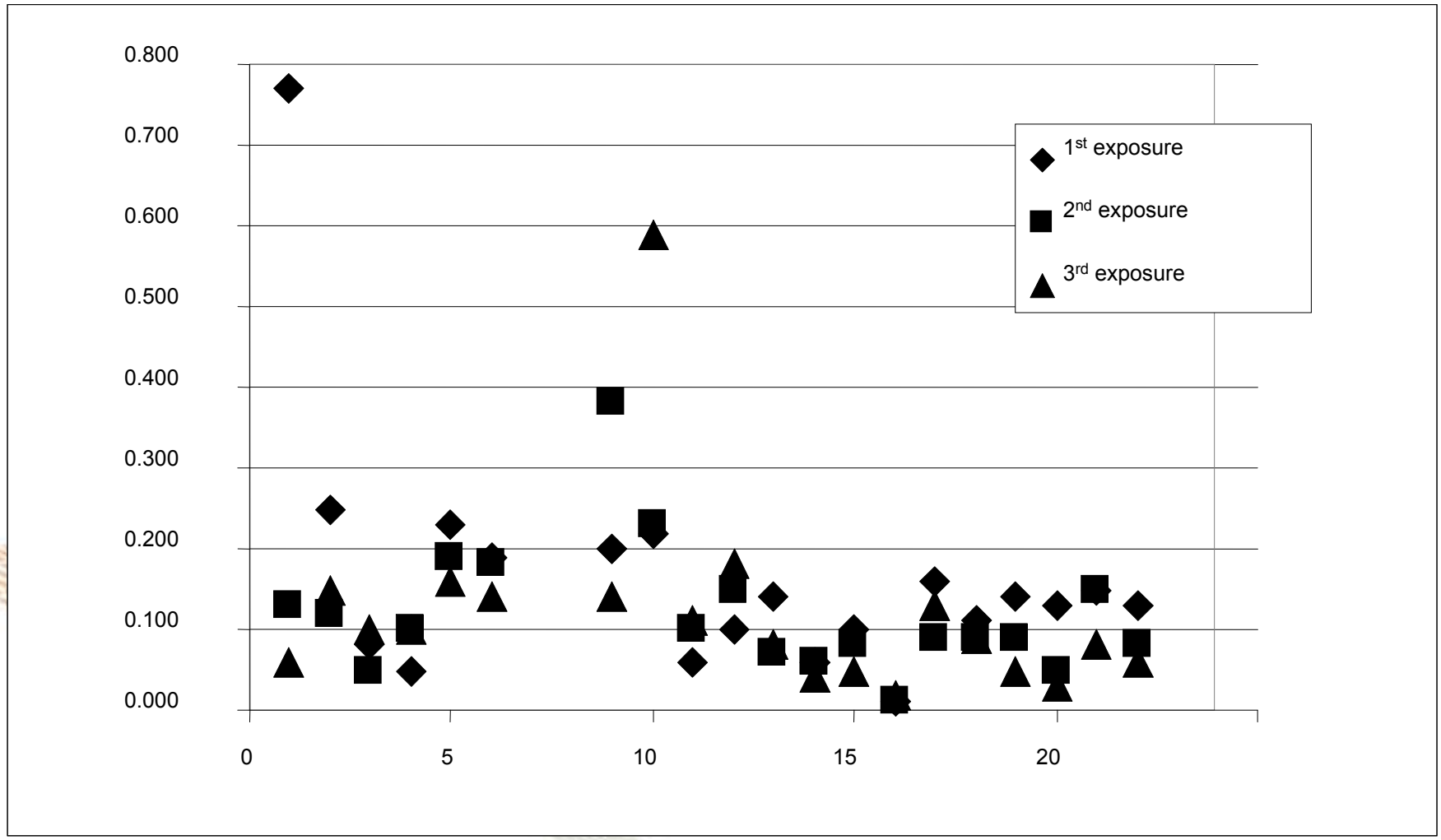
Large number of articles tested using foods and food simulants, by Fera (UK), BfR (DE) and TNO (NL)

- the simulant tea and black coffee) 3% acetic acid gave migration values about double those obtained using water under the same time and temperature test conditions

- migration into the fatty food simulant olive oil was not detectable and at least 20-fold lower than with aqueous food simulants

- migration levels into hot acidic beverages (apple juice, tomato juice, red-fruit) were rather similar to the acetic acid simulant when same time & temp test conditions used

Part 2. Melamine migration in mg/dm^2 from 22 melaware specimens – 3% acetic acid for 2 hours at 70ºC



Part 2.

Melamine from melaware plastics

Results:

- very strong influence of temperature with high migration in microwave heating or stove-top use.
- for stove-top use of spatulas, the boiling action of circulating food/simulant can have an additional effect in promoting surface erosion, increasing plastic decomposition and so elevating melamine release.
- erratic behaviour, migration sometime rising, sometimes falling, very difficult to set test conditions to indicate performance expected during a (long) service life.

Part 3: Non intentionally added substances (NIAS)

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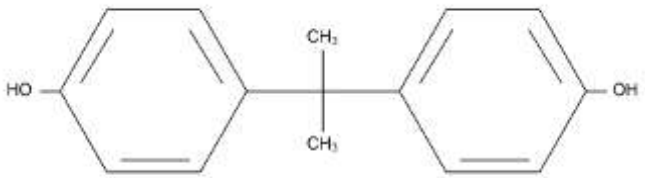
For melamine (and BPA) the migration comes not just from classical migration (diffusion) but from degradation of the plastic – to form known substances.
In most other cases new and or unknown substances can be released.

The NIAS – non intentionally added substances

- impurities in the starting substances
- degradation products
- reaction products
- oligomers



Biphenol-A

Part 3: Non intentionally added substances (NIAS)

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- The overall migrate can legally be up to 60 mg/kg from plastics we know the starting substances - monomers, additives etc - but relatively little detailed compositional information is known beyond this.

- The NIAS added to the non-evaluated starting substances means that different approaches to risk assessment and risk management must be considered.

Part 3: Non intentionally added substances (NIAS) - Next steps as proposed by authors

To evaluate the other (non-plastic) materials more efficiently and to deal with the NIAS it is suggested:

- revisit the 10 ppb (nd), 50 ppb, 5 ppm and 60 ppm migration thresholds used.
- align safety evaluation of FCS with elements of the approach used for flavouring substances eg. consider using Cramer classes
- more read-across
- invest in (Q)SAR for genotoxicity alert
- need the analytical methods and the exposure estimates to make it work

Conclusions

- Migrants can arise from classic migration or from degradation of the packaging material.
- Currently only plastics have EU-wide regulation.
- Potentially 10,000s of migrant chemicals may be found in food, incl. NIASs.
- Specific chemical-by-chemical regulation of all migrants in food not effective. Detailed scientific assessment of all would be enormous task.
- Need development of pragmatic science-based risk management tools.