

2008

Analytical expertise for seed, feed & food safety



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Inconspicuous chemicals that become
consumer concerns

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Content

Known and Emerging risks

Examples

- 3-MCPD esters
- furan
- benzene
- semicarbazide

Conclusion

Examples of known & emerging risks related to chemical contaminants

- Acrylamide
- Furan / alkylfurans
- 3-MCPD / 3-MCPD esters (« bound » 3-MCPD)
- Nitrosamines
- AGE's (CML, pentosidine,....)
- 5-HMF
- Semicarbazide
- Ethylcarbamate
- Lipid oxidation products (2-nonenal, 3-penten-2-one,...)
- PAH's
- Benzene / benzoic acid
- Packaging contaminants (e.g. BADGE, ITX)
-

and, more compounds are being added to the list.....

Database on potential toxicants found in heated foods: Heatox deliverable P3 & P8

- Lists 800 volatile products of the Maillard reaction and lipid oxidation together with predicted toxicological data
- Database will be accessible on the CSL website
- Updated, maintained by CSL as appropriate

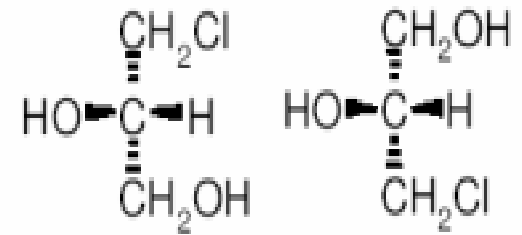
Compound Name CAS number (Chemical Class)	Predicted Toxicity (TOPKAT)	Predicted Toxicity (DEREK)	Other available toxicity information*
1,2-dimethyl-1H-pyrrole CAS No. 600-29-3 (Pyrrole)	Carcinogenicity = Positive Mutagenicity = Positive Rat oral LD ₅₀ = 106 mg/kg		Toxicity data not available
1-methylpyrrolo[1,2-a]- pyrazine CAS No. 64608-59-9 (Pyrazine)	Carcinogenicity = Positive Mutagenicity = Positive Rat oral LD ₅₀ = 135 mg/kg		Toxicity data not available
3-penten-2-one CAS No. 625-33-2, (Misc O)	Carcinogenicity = Positive Mutagenicity = Positive Rat oral LD ₅₀ = 246 mg/kg	Chromosome damage, Skin Sensitiser	No information available on carcinogenicity or mutagenicity. Rat oral LD ₅₀ = 3200 mg/kg
3-methyl-3-buten-2-one CAS No. 814-78-8, (Misc O)	Carcinogenicity = Positive Mutagenicity = Positive Rat oral LD ₅₀ = 149 mg/kg	Chromosome damage, Skin Sensitiser	Highly toxic by oral, percutaneous and respiratory routes. Irritant. Animal carcinogenicity studies are limited, but are generally negative. Agents in this group generally have little mutagenic activity (HSDB), Negative in AMES mutagenicity studies (CCRIS) Rat oral LD ₅₀ = 180 mg/kg

Furan and acrylamide are emerging risks with a high degree of attention because ...

- they are known industrial chemicals, used in high volumes
- known cases of occupational intoxication in humans
- known animal carcinogens
- heat induced formation in food is ***new*** (acrylamide)
- occurrence in sensitive foods / baby foods is ***new*** (furan)

3-MCPD

(3-monochloropropane-1,2-diol)



Background

- **Non-genotoxic carcinogen (JECFA, EU SCF) → threshold**
- **Kidney toxicity at chronic exposure**
- **Inhibits male fertility at high doses**

Occurrence

- **Hydrolyzed vegetable proteins (HVP)**
- **Low levels in foods (biscuits, bread, cooked/cured fish and meat)**
- **Migration (food contact materials)**

Human dietary exposure

- **2 μg/person/day from savory foods**

Safety

- **Food limits:**
HVP and soy sauce: 0.05 mg/kg dry product (EU)
different limits in other countries
- **Health based guidance values:**
Tolerable daily intake (TDI) 2 μg/kg bw/day (EU SCF and JECFA)

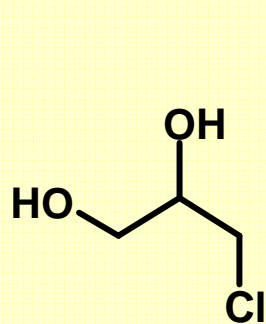
MCPD: summary of mitigation options

Ingredient/ food	Potential mitigation measure
HVP	Neutralization; enzyme hydrolysis
Savoury ingredients	Lipase inactivation; use of extracts
Bread	Bake or toast to « golden yellow »; ingredients (flour)
Roasted cereals	Roasting parameters (T/t)

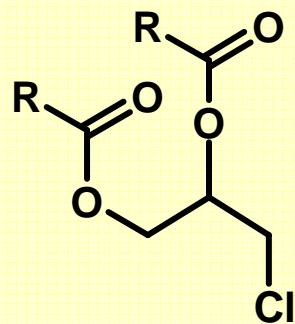
3-MCPD esters

Potential concern

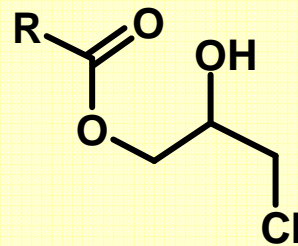
- Occurrence of 3-MCPD esters in a wide range of cooked foods (incl breast milk)
- Amounts of esters in foods is in most cases higher than free 3-MCPD
- 3-MCPD-esters in the diet may release some free 3-MCPD by action of gut lipases, potentially contributing to the overall dietary exposure to free 3-MCPD



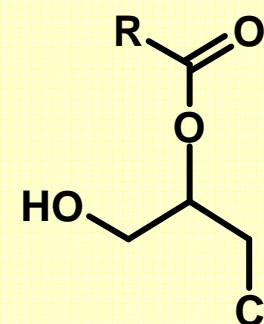
3-MCPD



3-MCPD diesters



3-MCPD monoesters



R = alkyl

3-MCPD esters: Occurrence

Product	Bound* 3-MCPD (mg/kg)
Bread	
- Crust	0.55
- Crumb	0.03
- Toasted	0.160
- Crisp bread	0.42
French fries	6.1
Dark malt	0.58
Coffee (soluble)	0.006
Doughnuts	1.21
Salty crackers	0.14
Almonds (roasted & salted)	0.5

* 3-MCPD as released from its esters during the analytical method, based on the molecular weight of free 3-MCPD, Irrespective if released from mono- or diesters

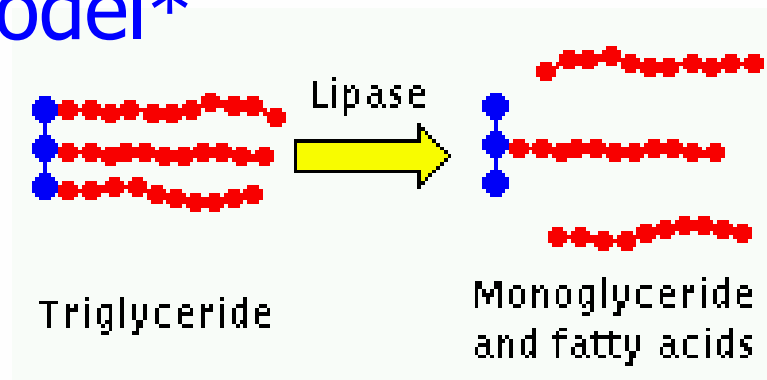
From: Svejowska et al., 2004; Dolezal et al., 2005; Hamlet & Sadd, 2004, 2005; Zelinkowa et al., 2006

3-MCPD esters : Research

– Analytical method improvement to quantify esters in food*

- separation of mono- and diesters
- ratio of chloro-monoesters to -diesters important with respect to the release of bound 3-MCPD (7-15% monoesters in vegetable oils)

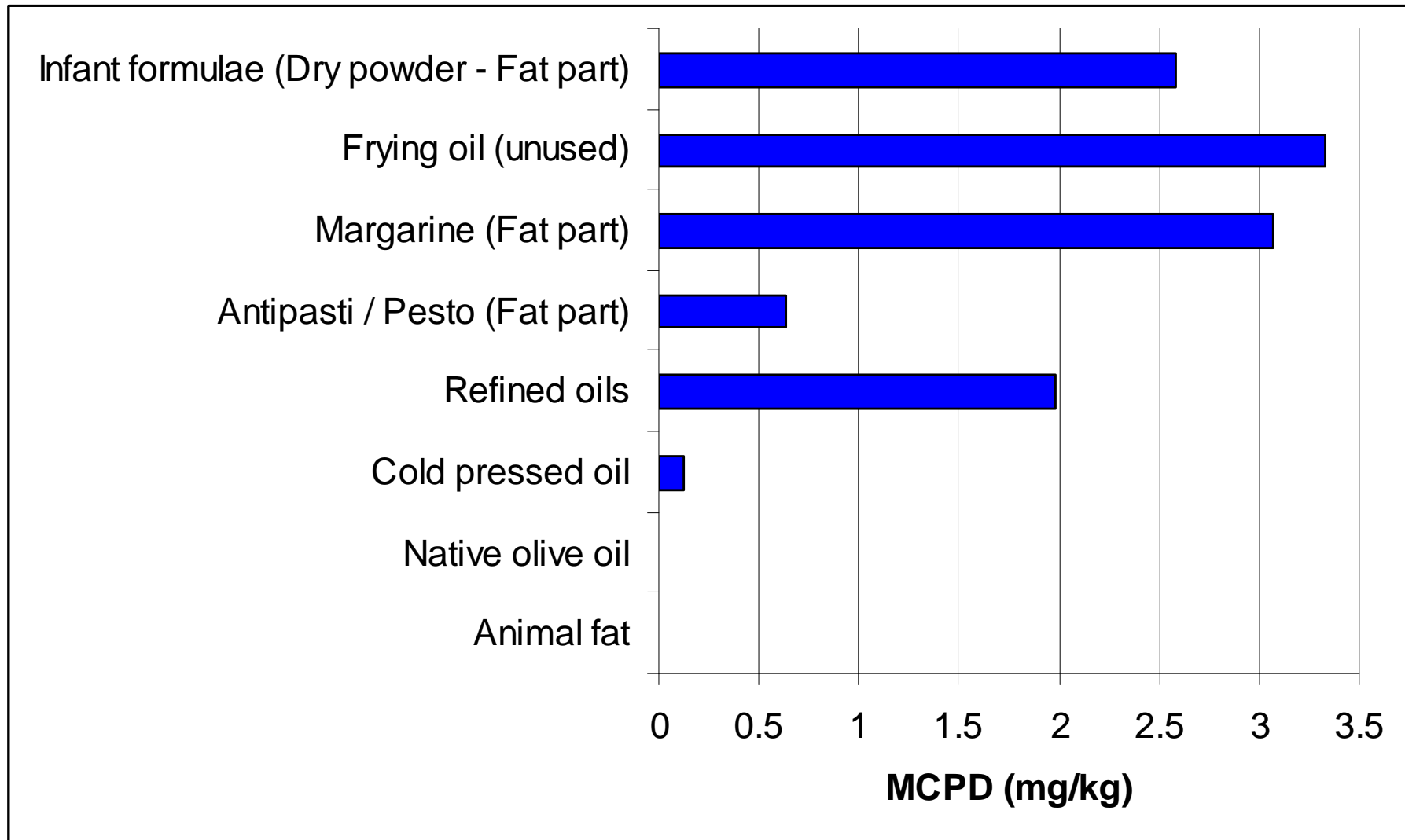
– Lipase gut model*



*Seefelder *et al.*, 2007, Food Additives & Contaminants

3-MCPD esters - Average values of product groups expressed as 3-MCPD

CVUA Stuttgart - November 2007



Säuglingsanfangs- und Folgenahrung kann gesundheitlich bedenkliche 3-MCPD-Fettsäureester enthalten

Stellungnahme Nr. 047/2007 des BfR vom 11. Dezember 2007

- Need for further research on the formation of 3-MCPD esters
- Efforts should be made to reduce the levels of 3-MCPD esters in edible oils, foods containing fats, and infant formulas
- Mothers that cannot breastfeed should continue feeding their babies with the commercial products currently available

Concern of all food manufacturers and not particular products or products of individual food companies.

3-MCPD esters : Evaluation & Management

- UK Food Standards Agency Stakeholder meeting September '06
- European Commission Working Party meeting
- JECFA call for data on esters (Jun '06, 67th meeting)

No toxicology data nor health-based guidance values for chloroesters are available

However, no evidence of adverse effects from dietary exposure to 3-MCPD esters

Furan

Potential concern

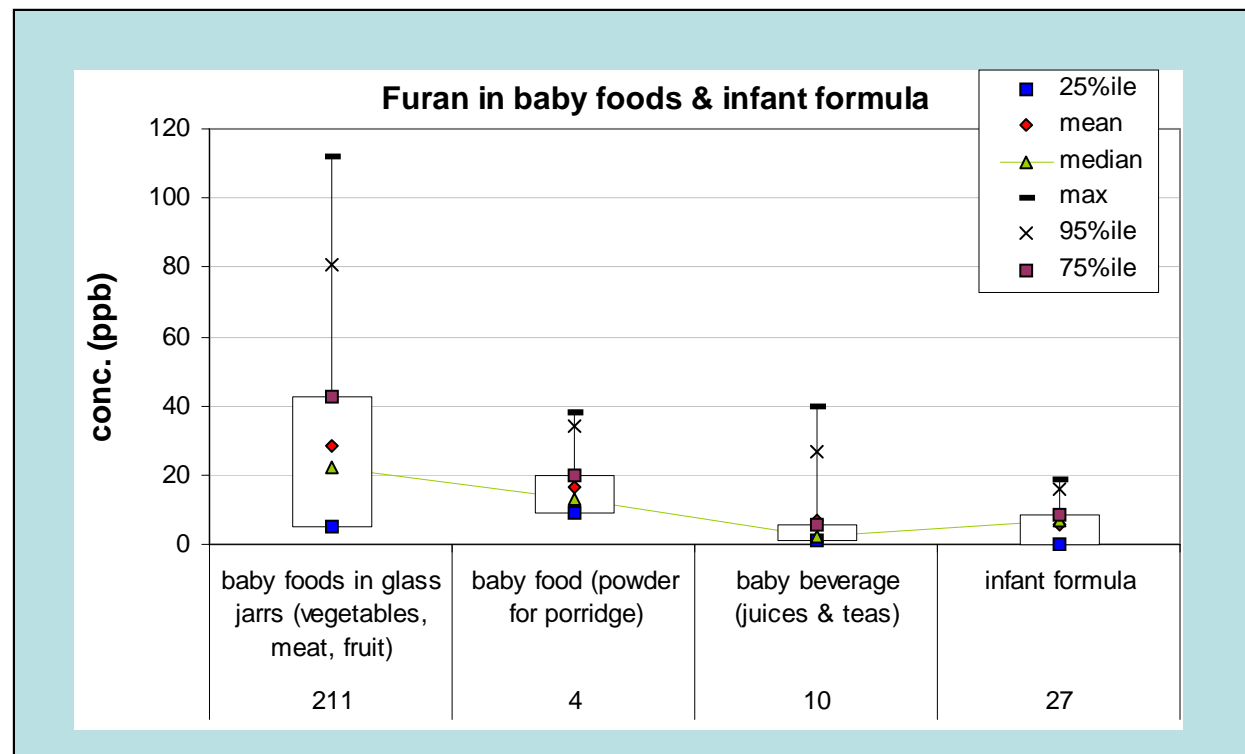
Foods, especially jarred and canned foods, subject to heat treatment can contain furan (in particular baby foods in jars)

- causes liver cancer in animal studies with high potency
- genotoxic carcinogen (IARC class 2B 'possibly carcinogenic to humans')
- no human epidemiological data on cancer

Exposure

No reliable exposure
Estimates

(~ 1 µg/kg bw/day)



Furan : Research

- Development and validation of a suitable analytical method (e.g. GC-SPME-MS)
- Analysis of concerned products and as prepared for consumption
- Sharing of data (CIAA)
- Mechanistic work: precursors, modelling
- Potential mitigation strategies
- Sharing research findings (DG Sanco, EFSA)
- Understanding constraints

Furan: possible mitigation concepts ?

(based on modelling work or lab/bench scale trials)

— PUFA

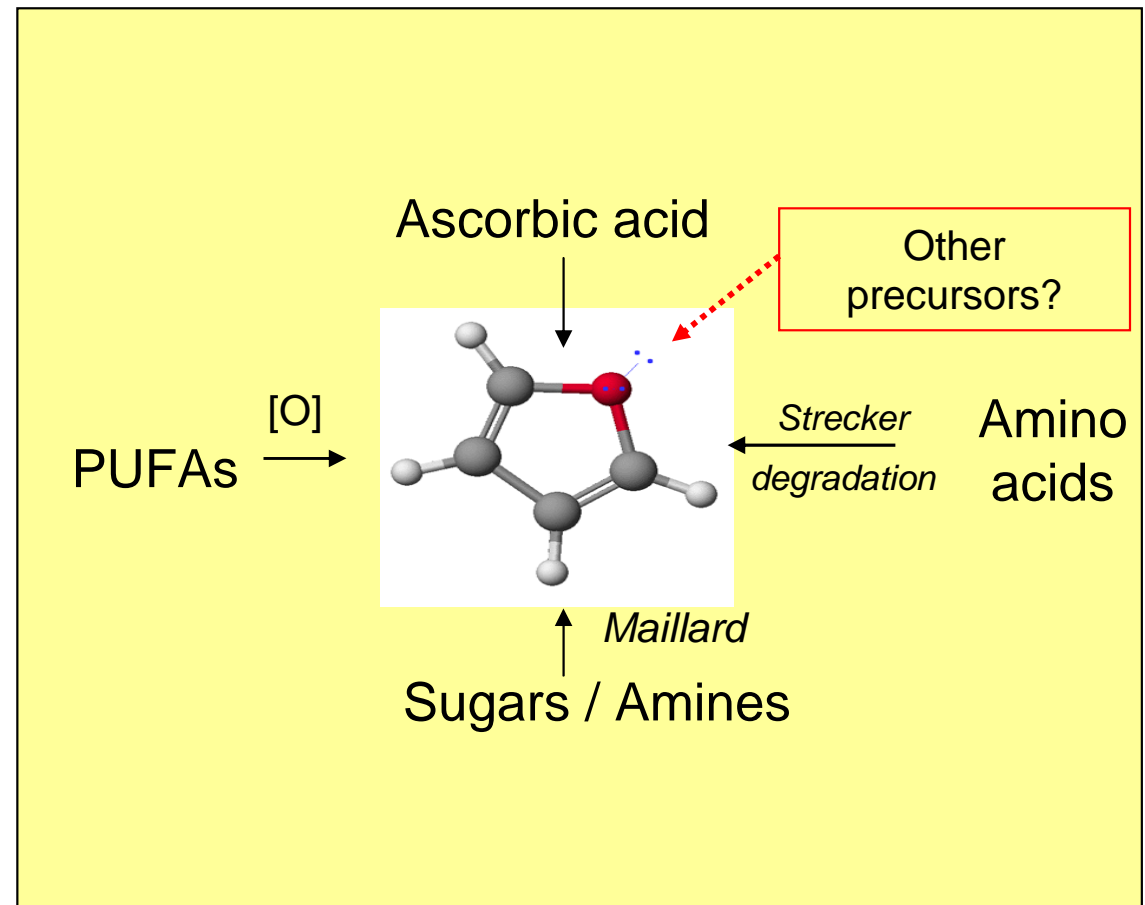
- Addition of “optimized” amounts of antioxidants in recipes
- reduction of oxygen prior to heat-treatment
- Addition of PUFA after heat-treatment

— Ascorbic acid

- Avoid heat-treatment in case of ascorbic acid fortification

— Reaction kinetics

- Heat-treatment at lower temperature for longer time



Risk/benefit and risk/risk considerations !

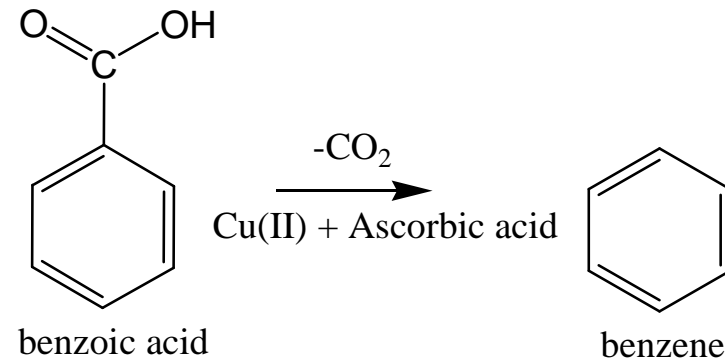
Furan: collective stakeholder efforts

- EU FP6 project “furan” (8 partners, focused on mech. tox. studies)
- EU Monitoring exercise (2007/196/EC)
 - Analysis of Commercial foodstuffs as purchased
 - Commercial foodstuffs as consumed after further preparation
- Coffee Industry Task Force
 - Impact of green coffee; roasting parameters; stability; consumer preparation practices
- Confederation of the Food and Drink Industries of the EU (CIAA) “Process Contaminant Expert Group”
- Joint DG SANCO/EFSA/DG JRC Workshop 2006 “Furan in Food”
 - Research update to be published in a Supplement of *Food Additives & Contaminants*, foreseen August 2007

Learnings from recent issues: Benzene

Background

- Widespread environmental contaminant
- Confirmed carcinogen
 - human occupational exposure (inhalation) causes leukaemia
 - carcinogenic in rodents (oral + inhalation)



The Potential Concern

- Traces found in drinking water and soft drinks since 1990's

Recently found again, linked to benzoate and ascorbic acid



FDA: Too Much Benzene In Some Drinks

High Levels Of Cancer-Causing Chemical Found In 5 Beverages On Market

- [Health Main Page](#) >
- [WebMD](#) >
- [Healthy Living](#) >
- [Early Show: Health News](#) >
- [Shape Up](#) >
- [Dr. Emily Senay](#) >
- [CBS Cares](#) >
- [HealthWatch Video](#) >

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RSS - ALL FEEDS

WASHINGTON, May 19, 2006



(AP)

(AP) A government analysis of more than 100 soft drinks and other beverages turned up five with levels of cancer-causing benzene that exceed federal drinking-water standards, the Food and Drug Administration said Friday.

The companies that make the drinks have been alerted and either have reformulated their products or plan to do so, the FDA said. Government health

Benzene: sources of intake

Source of exposure	Estimated exposure	Info Source
Air - inhalation - automobile related	220 µg/d 49 µg/d	EU Canada
Diet -food & drink products -food -water & food	0.2-3.1 µg/d 1.4 µg/d 1.4 µg/d	EU Canada ICPS*
Passive smoking	63 µg/d 50 µg/d	Canada IPCS*

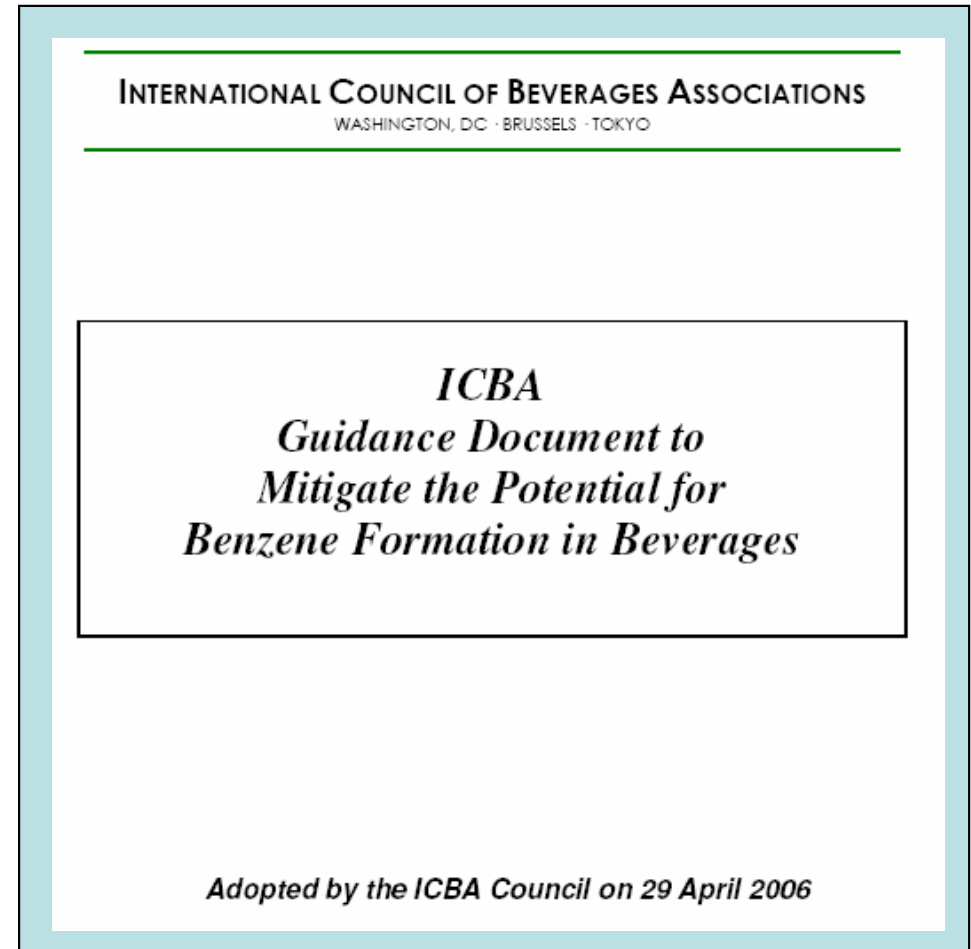
Source: http://www.nzfsa.govt.nz/consumers/food-safety-topics/chemicals-in-food/benzene/fact-sheet-benzene-in-flavoured-drinks-final.htm#P10_1521

*International Program on Chemical Safety

Benzene: a well known issue that can be kept under control in beverages

- **G**uidance on mitigation approaches available (ascorbic acid, benzoate)
 - *Review recipes*
 - *Test*
 - *Reformulate*
 - *Post-launch monitoring*
- **C**ompanies' internal data show that their actions have largely succeeded in keeping benzene levels under control
- **A**mounts are typically at limit of detection (1-5 µg/L) and mostly below 10 µg/L.

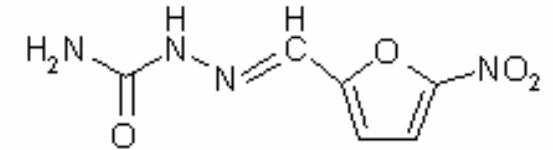
Human exposure: dietary intake is only small percentage of normal environmental exposure



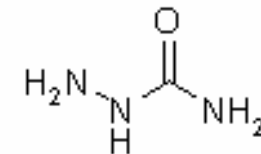
Semicarbazide (SEM) occurrence in lid gaskets

Background

- Shrimps and chicken contaminated with nitrofurazone residues (illegal drug usage)
- SEM is a marker for the usage of nitrofurazone (banned nitrofurazone antibiotic)
- SEM was detected in jarred foods that do not contain meat ! (baby food jars)



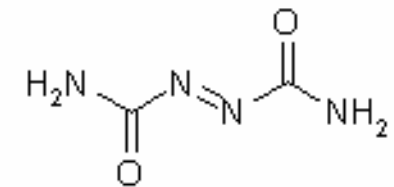
Nitrofurazone



Semicarbazide

The Concern

- Highly sensitive in relation to baby foods in jars
- Potentially carcinogenic
- Scientific uncertainty
- Substitution dangers (integrity of the closure)



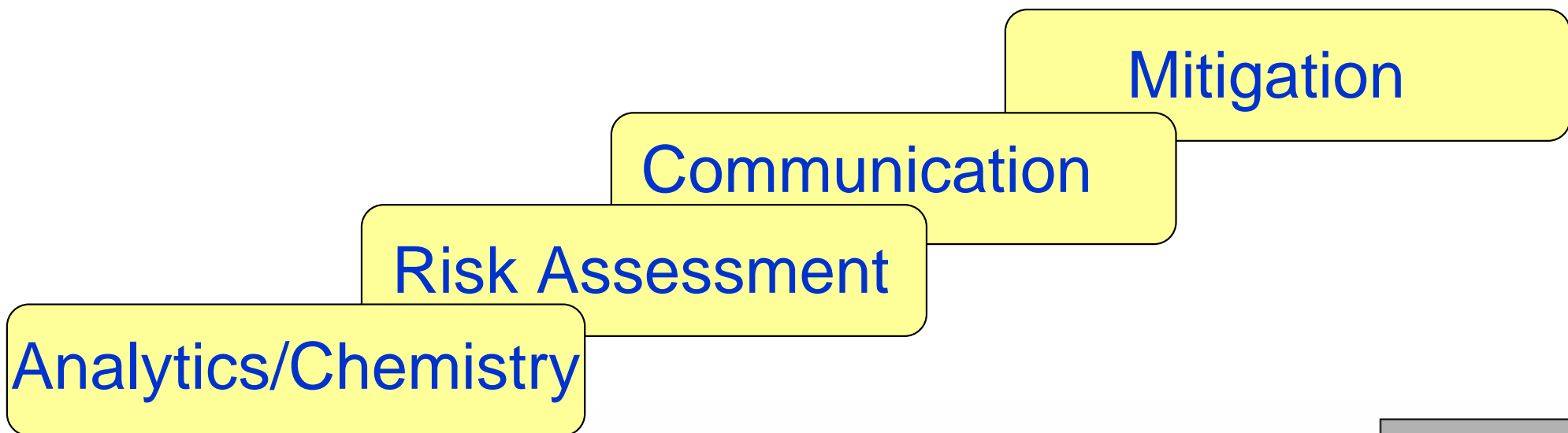
Azodicarbonamide

Semicarbazide : chronology of events

Early 2002	Nitrofurant detected in imported shrimp & chicken from SE Asian and S. American countries
Late 2002	Abberant results in chicken testing - meat negative but processed product positive
May 2003	Advice note issued by EU advising labs to test only the meat (not coating)
June 3rd	Problem detected by industry in bottled foods that do not contain meat. Source thought to be Azodicarbonamide (ADC)
End June/July	Authorities and EFSA informed by industry
July	European <i>Semicarbazide Joint Industry Group</i> (SEM JIG) was established and under the auspices of SEFEL (European metal lid manufacturers)
Oct 2003	EFSA press release : no change to current dietary habits: risk - if any – judged to be very small
2004	ADC removed from the positive list of plastic additives in EU



ACTION: Semicarbazide Joint Industry Group: Structure & Deliverables



- Method confirmation
- Thermal degradation of ADC
- Monitoring of food products (focus on baby foods in jars)
- Publication of the analytical method and chemistry of decomposition of ADC

Semicarbazide is a minor thermal decomposition product of azodicarbonamide used in the gaskets of certain food jars

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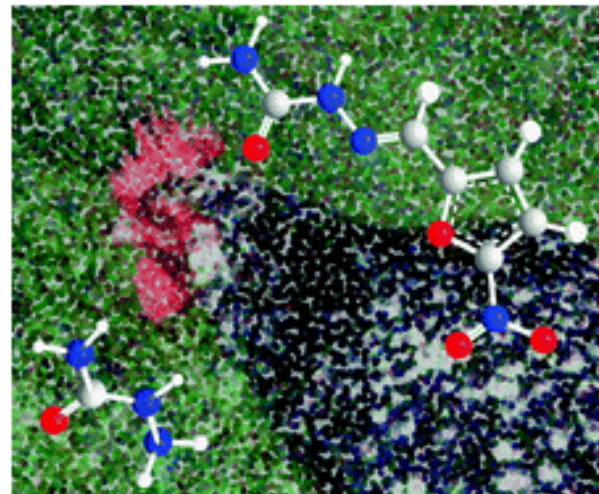
ARTICLE

THE
ANALYST
www.rsc.org/analyst

Semicarbazide: Learnings & Solutions

- Early commitment by industry (closures & food) to find solutions : SEM JIG
- Early involvement of authorities & co-ordination of activities
- Continuous open and transparent dialogue of all stakeholders

- Replacement of ADC by Na bicarbonate in lid gaskets
- Legislative action/ Directive 2004/1/EC of 13.1.2004
- Research to find alternative markers for nitrofurazone



Analyst, 2005, **130**, 824 - 827, DOI: 10.1039/b504327a

Nitrofurazone accumulates in avian eyes—a replacement for semicarbazide as a marker of abuse

Kevin M. Cooper, Robert J. McCracken and D. Glenn Kennedy

Conclusion (1)

- React timely to indications of an emerging risk (3-MCPD esters, furan)
- Devote adequate resources to address gaps
- Early safety evaluation of the hazard
Consider also the « emotional » climate (baby foods !)
- Where possible (i.e. non-competitive) share these through concerted and co-ordinated efforts
- Explain the rationale for prioritization
- Communicate with stakeholders, transparently and fair

Conclusion (2)

- Awareness that food contains a multitude of different compounds with many health beneficial and potentially hazardous effects
- Apply a holistic approach: evaluate the potential risks of individual compounds (e.g. acrylamide, furan) together with the health benefits of the food (e.g. whole grain, PUFA's)

..... risk-benefit modelling as a basis for defining priorities and to support management decisions



Thank you