Contaminants from food packaging

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Contaminants from food packaging
Outline of the talk

- What is chemical migration
- What may migrate
- Hazard assessment of packaging migrants in the EU
- Default assumptions for exposure assessment
- Case study – Bisphenol A diglycidyl ether (BADGE)
- Current status of risk assessment?
- Lessons learned from the case study
Packaging materials

are the most obvious, and important, example of:

“materials and articles intended to come into contact with foodstuffs”
Food packaging materials used

- Plastics
- Paper and board
- Varnishes and coatings on metals
- Glass
- Metals and alloys
- Ceramics
- Elastomers and rubbers
- Regenerated cellulose
- Paraffin waxes and micro-crystalline waxes
- Wood, including cork
- Textile products
Packaging

e.g.
glass
metals & alloys
ceramics

Food

x
y
z
<table>
<thead>
<tr>
<th>Packaging</th>
<th>Food</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g.</td>
<td></td>
</tr>
<tr>
<td>plastics</td>
<td></td>
</tr>
<tr>
<td>paper</td>
<td></td>
</tr>
<tr>
<td>rubber</td>
<td></td>
</tr>
</tbody>
</table>

- x
- y
- z
Consequences of chemical migration

Migration of chemicals from food contact materials

⇒ Impact on food quality

⇒ Impact on food safety
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Ingredients needed to make plastics

- Monomers & starting substances
- Catalysts
- Solvents & suspension media
- Additives
  - Antioxidants
  - Antistatics
  - Antifogging
  - Slip additives
  - Plasticisers
  - Heat Stabilisers
  - Nucleating agents
  - Dyes & pigments
Positive list of ingredients
Plastics & coatings

Acetic Acid

(2000+ Substances)

Xylene
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Hazard assessment of packaging migrants

- relatively few packaging migrants have a full TDI
‘The dose makes the poison’

The hazard assessment made in the EU is a tiered approach:

- the greater the extent of migration into food or food simulants, the more toxicological information is required
Classification of foods and the selection of food simulants

- aqueous - distilled water
- alcoholic - 10% (or greater) ethanol
- acidic - 3% acetic acid
- fatty - olive oil, sunflower oil, etc.
SCF (now EFSA) requirements for packaging migrants

Migration < 0.05 mg/kg

- Genotoxicity. In first instance, three *in vitro* mutagenicity assays
  - a test for gene mutations in bacteria
  - a test for chromosomal aberrations in cultured mammalian cells
  - a test for gene mutations in cultured mammalian cells
Requirements for packaging migrants

0.05 < Migration < 5 mg/kg

- subchronic (90-day) oral study
- peroxisome proliferation potential (alkyl esters)
- neurotoxicity (phosphoric and phosphorous acid esters)
- metabolism information
  ➞ data on the potential for accumulation
Requirements for packaging migrants

5 < Migration < 60 mg/kg

➢ ADME, adsorption, distribution, metabolism and excretion

▪ chronic (2 year) study for data on long-term toxicity/carcinogenicity

▪ reproduction data

▪ teratogenicity data

▪ effects on the immune system
Summary of toxicological information required

Migration < 0.05 mg/kg
- Genotoxicity. In first instance, three in vitro mutagenicity assays
  - a test for gene mutations in bacteria
  - a test for chromosomal aberrations in cultured mammalian cells
  - a test for gene mutations in cultured mammalian cells

0.05 < Migration < 5 mg/kg
- subchronic (90-day) oral study
- peroxisome proliferation potential (alkyl esters)
- neurotoxicity (phosphoric and phosphorous acid esters)
- metabolism information
  - data on the potential for accumulation in man

5 < Migration < 60 mg/kg
- ADME, adsorption, distribution, metabolism and excretion
- chronic (2 year) study for data on long-term toxicity/carcinogenicity
- reproduction data
- teratogenicity data
- effects on the immune system
Outcome of hazard assessment

Minimum dossier
   \( R = \text{nd (dl} = 0.01 \text{ mg/kg)} \)
   \( R = 0.05 \text{ mg/kg} \)

Intermediate dossier
   \( R = 5 \text{ mg/kg} \)

Full dossier
   TDI can be established
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Default assumptions for exposure assessment

“a closed positive list, but open too”

- Substances – not applications – get approval
  - Once on the positive list, any user can use that substance in any application, provided the migration limit is not exceeded.
“a closed positive list, but open too”

Default assumptions for exposure assessment

- 1 kg of packaged food eaten every day
- this food is in contact with up to 600 cm² of packaging
- this packaging always contains the substance (monomer, additive etc.)
- the substance always migrates at the highest level permitted (e.g. at the SML)
- no other significant sources of exposure
- a consumer has a body weight of 60 kg
Outcome of the default assumptions for exposure assessment

Specific migration limit (SML) = R
or

\[ SML = TDI \times 60 \]

mg / kg food or simulant mg / kg bw / day
Migration levels of interest

no threshold of toxicological concern or threshold of regulation
(US = 0.5 ppb, 1.5ug/day)

nd = 10 ppb (ug/kg)
to
OML = 60 ppm (mg/kg)
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Case study - BADGE
Bisphenol A diglycidyl ether
Case study – BADGE

- Starting substance of most epoxy resins currently used as internal can coatings.
- Plastics Directive 90/128/EEC set an SML of 20 ug/kg food for BADGE.

- Surveys conducted in several European countries (AU, CH, D, DE, I, NL, UK) found that BADGE migration was at unacceptable levels.
- In 1995-1996, more than 10 % of samples all over Europe, exceeded 1 mg/kg food.
Case study - BADGE

The types of cans responsible were:-
- deep drawn two-piece cans
- easy open lids
- cans for aggressive foodstuffs

The coatings were vinylic organosols (most frequent situation) or polyester-epoxy varnishes.

BADGE used as a starting substance (monomer) and as a stabiliser (additive).
<table>
<thead>
<tr>
<th>RESIN CLASS</th>
<th>NATURE</th>
<th>FLEXIBILITY &amp; PACK RESISTANCE</th>
<th>MAIN END-USES</th>
<th>TYPICAL FOOD PACKED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organosol</td>
<td>PVC dispersed in a suitable binder (epoxy)</td>
<td>Very good</td>
<td>- Drawn cans</td>
<td>- aggressive products</td>
</tr>
<tr>
<td>(often over epoxy-phenolic base coat)</td>
<td></td>
<td>Very good</td>
<td>- Easy Open Ends</td>
<td>- pickled food, some ready meals</td>
</tr>
</tbody>
</table>
Case study - BADGE

The types of cans responsible were:-
- deep drawn two-piece cans
- easy open lids
- cans for aggressive foodstuffs

The coatings were vinylic organosols (most frequent situation) or polyester-epoxy varnishes.

These materials have good mechanical properties and high chemical inertness.

BADGE used as a starting substance (monomer) and as a stabiliser (additive).
BADGE
BADGE.HCl
BADGE.H₂O.HCl
The problem of reaction products

- The chemicals that migrate may not be the starting substances

- Controls on the starting substances (‘positive list’ of ingredients, SMLs etc) may not give adequate control over the transformation products
SCF’s Opinion of 7 June 1996 on BADGE

- accordingly it was expected that the genotoxic activity of BADGE in vivo would be weak, or non-existent.

- Consequently, BADGE was provisionally re-classified with a temporary restriction of 1 mg/kg on the specific migration of:

  A: BADGE
  B: monoadduct, BADGE.H₂O
  C: diadduct, BADGE.2H₂O
  D: monoadduct, BADGE.HCl
  E: diadduct, BADGE.2HCl
BADGE in canned food (> 5% fat) from the Swiss market, before and after taking measures to reduce BADGE migration

<table>
<thead>
<tr>
<th>BADGE in food (mg/kg)</th>
<th>Jan-May 1996</th>
<th>Jun 1996-Mar 1997</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 10</td>
<td>2 %*</td>
<td>0 %</td>
</tr>
<tr>
<td>1-10</td>
<td>15 %</td>
<td>0.4 %</td>
</tr>
<tr>
<td>0.1 – 1</td>
<td>22 %</td>
<td>7 %</td>
</tr>
<tr>
<td>0.02 – 0.1</td>
<td>16 %</td>
<td>12 %</td>
</tr>
<tr>
<td>&lt; 0.02</td>
<td>45 %</td>
<td>80 %</td>
</tr>
</tbody>
</table>

* at 14, 16 & 23 mg/kg
Bisphenol F series (Novolacs)
2-ring NOGE (Novolac diglycidyl ether)
A 3-ring NOGE
p,o,o,p - isomer

o,o,o,p - isomer

o,o,o,o - isomer

p,o,o,o - isomer

p,p,o,o - isomer

p,p,p,o - isomer

p,p,p,p - isomer

\[ \text{Mw } 3 - \text{ ring NOGE, } C_{30}H_{26}C_6 = 474 \]
\[ \text{Mw } 4 - \text{ ring NOGE, } C_{30}H_{42}C_6 = 636 \]
\[ \text{Mw } 5 - \text{ ring NOGE, } C_{40}H_{56}C_{10} = 738 \]
\[ \text{Mw } 6 - \text{ ring NOGE, } C_{50}H_{72}C_{12} = 900 \]
Testing mixtures for toxicity

‘basic tenet of toxicology’

- Establish a dose-response relationship
  - But which one (or combination) of substances is the causative agent if a mixture is tested?
  - What substance (or combination of substances) needs subsequently to be controlled?
Estimate of consumer exposure to BADGE

- *per capita* consumption of canned food was 62 g/person/day.
- migration at 0.12 mg/kg
- ‘worst-case’ exposure of 0.007 mg/person/day for BADGE and its derivatives

Refined estimate of consumer exposure to BADGE

Requested of the SCF because the deadline for submission of the required toxicological data was missed:-

- assumed that canned fish in oil is the major source of exposure
- exposure from other canned foods was considered as minor and was not taken into consideration.
- took into consideration only the most recent survey data (all member states + CH) – i.e. excluding ‘old’ formulation can coatings

[Ref. Exposure assessment of BADGE and regulated derivatives released by canned food. CS/PM/4003 Rev.1]
Refined estimate of consumer exposure to BADGE

Concentration data
0.16 mg/kg as the mean total concentration
0.02 as the 50\textsuperscript{th} percentile
0.4 mg/kg as the 95\textsuperscript{th} percentile

Food intake date
In Europe, 140 g/day fish as the 95\textsuperscript{th} percentile.
In France, 11 g/day \textit{canned} fish (sardines + mackerel only) as the 97.5 percentile of consumption.
Refined estimate of consumer exposure to BADGE

- If a high consumer eating 140 gram of canned fish per day selects randomly from the market, the exposure would be at a maximum of 0.0028 mg of BADGE and its regulated derivatives per day (median value).
Refined estimate of consumer exposure to BADGE

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- if the same high consumer was buying (because of brand loyalty) always from the 5% of cans containing the highest migration levels, the exposure would be 20-times higher than the median value, at 0.056 mg/day.
Refined estimate of consumer exposure to BADGE

- if a high consumer eating 140 gram of canned fish per day selects randomly from the market, the exposure would be at a maximum of 0.0028 mg of BADGE and its regulated derivatives per day (median value).
- if the same high consumer was exposed (because of brand loyalty) to the 5% of cans containing the highest migration levels, the exposure would be 20-times higher than the median value, at 0.056 mg/day.
- if this high consumer of canned fish ate every day fish containing always the maximum permitted level of BADGE migration (1 mg/kg fish) then the exposure would be 0.14 mg per day.
Refined estimate of consumer exposure to BADGE

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CONCLUSIONS

Packaging migration:
- many & varied chemicals involved
- range of levels from <10 ppb to 60 ppm
- complex mixtures of migrants
⇒ An important source of potential food contamination
Current status of risk assessment?
Lessons learned from the case study - 1

The major uncertainties in the risk assessment process are:-

a) For starting substances:-
   - uncertainties in the extent of consumer exposure to packaging migrants

b) For reaction products etc:-
   - uncertainties in the identity and/or in the qualitative and quantitative biological properties of the substance(s)
Current status of risk assessment?
Lessons learned from the case study - 2

Information requirements - What is a ‘high’ consumer?

Diet
- consumers of large amounts of food wrt bodyweight
- consumers of large amounts of particular food groups
- sub-groups - vegetarians, ethnic groups

Packaging usage
- consumers of large amounts of e.g. convenience foods
- small pack sizes (high mass-contact area ratio)
- brand loyalty, link between brands, packaging type, & and migration levels
- low-income households and economy brands
Scope for harmonisation

- ToR – threshold of regulation
- FCF – food (type) consumption factors
- PUF – packaging usage factors
(end)