Chemical risk assessment
Implications for product safety

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The Author

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  - Member of the BfR Committee for Consumer Products
  - Member of the WG Textiles at BfR, now Panel Textiles & Leather of the BfR Committee for Consumer Products
Department Safety of Consumer Products

Administrative Task

- Health risk assessment of chemical constituents in products of daily use considering toxicology, dermatology, analytics, exposure, technology and hygiene

- *Products covered by LFGB (Food, Feed and Commodities Law)*
  - cosmetics
  - food packaging
  - toys, child articles
  - apparel
  - detergents
  - hygiene articles

- *Further consumer products*
  - tobacco, furniture, mattresses, carpets …
Regulation of consumer products

General requirements, horizontal regulation

- ‘product’ shall mean any product which is intended for consumers or likely, under reasonably foreseeable conditions, to be used by consumers even if not intended for them
- Producers shall be obliged to place only safe products on the market

Vertical Regulation
In certain areas specific regulations
→ big differences in intensity of regulation

Food contact > cosmetics > toys > clothing > other products
German ordinance
• Ban of azo dyes which may form carcinogenic amines
• Ban of certain flame retardants (TRIS, TEPA, PBB)
• Declaration > 0.15 % formaldehyde
• Ban of ChromVI release from leather

Commission Decision (2009/251/EC)
requiring Member States to ensure that products containing the biocide
**dimethylfumarate** are not placed or made available on the market

shall not be used in a concentration >0,1% in substances or preparations
placed on the market and in the impregnation of fibres and heavy-duty textiles
not intended in any case for clothing or for decorative furnishings

*Germany:* Chemikalienverbots-VO > 5 ppm Pentachlorophenol
Chromium (VI) in leather – assessment, communication, regulation

1. Identification of a problem:
   Chromium (III) salts are widely used for tanning leather, under certain conditions Cr (VI) is formed and consumers may be exposed, e.g. by shoes, leather garment, gloves

2. Discussion in expert groups
   1998 Working group Textiles of BfR: Cr (VI) is a potent contact allergen, leather gloves may be important

3. Data collection:
   2000 – 2009 Investigation by the federal states on leather goods with skin contact for chromium (VI) content,
   850 samples from the German market
   142/850 (17 %) contain levels of chromium (VI) > 10 mg/kg,
   Maximum values > 100 mg/kg (gloves, shoes)
Chromium (VI) in leather – assessment, communication, regulation

4. Risk assessment:
   2007 BfR risk assessment report to BMELV
   BfR recommends the regulation/limitation of Cr (VI)

5. Risk communication:
   2007 Risk assessment report posted to the BfR web site
   press release

6. Regulation:
   2010 Amendment of the German ordinance on commodities,
   Cr (VI) must not be detected
   (< 3 mg/kg, method § 64 Food and Feed Act)

7. REACH Annex XV
   2012 ECHA launches a six-month public consultation on the
   restriction of chromium VI in leather articles proposed by the
   Danish authorities
# Mutagenic and carcinogenic substances in textiles

**Ban on azo dyes which may form one the following amines**

**Germany:** BGVO, 1984

**EU:** 2002/61/EC

*Certain azo pigments are not covered!*

<table>
<thead>
<tr>
<th>Number</th>
<th>Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4-Aminobiphenyl</td>
</tr>
<tr>
<td>2</td>
<td>Benzidine</td>
</tr>
<tr>
<td>3</td>
<td>4-Chloro-o-toluidine</td>
</tr>
<tr>
<td>4</td>
<td>2-Naphthylamine</td>
</tr>
<tr>
<td>5</td>
<td>o-Aminoazotoluene</td>
</tr>
<tr>
<td>6</td>
<td>2-Amino-4-nitrotoluene</td>
</tr>
<tr>
<td>7</td>
<td>4-Chloroaniline</td>
</tr>
<tr>
<td>8</td>
<td>2,4-Diaminoanisol</td>
</tr>
<tr>
<td>9</td>
<td>4,4´-diaminodiphenylmethane</td>
</tr>
<tr>
<td>10</td>
<td>3,3'-Dichlorobenzidine</td>
</tr>
<tr>
<td>11</td>
<td>3,3'-Dimethoxybenzidine</td>
</tr>
<tr>
<td>12</td>
<td>3,3´-Dimethylbenzidine</td>
</tr>
<tr>
<td>13</td>
<td>3,3-Dimethyl-4,4'-diaminodiphenylmethan</td>
</tr>
<tr>
<td>14</td>
<td>p-Cresidine</td>
</tr>
<tr>
<td>15</td>
<td>4,4´-Methylen-bis-(2-chloroaniline)</td>
</tr>
<tr>
<td>16</td>
<td>4,4´-Oxydianiline</td>
</tr>
<tr>
<td>17</td>
<td>4,4´-Thiodianiline</td>
</tr>
<tr>
<td>18</td>
<td>o-Toluidine</td>
</tr>
<tr>
<td>19</td>
<td>2,4-Toluenediamine</td>
</tr>
<tr>
<td>20</td>
<td>2,4,5-Trimethylaniline</td>
</tr>
<tr>
<td>21</td>
<td>2-Methoxyaniline (o-Anisidine)</td>
</tr>
<tr>
<td>22</td>
<td>4-Aminoazobenzene</td>
</tr>
</tbody>
</table>
BfR Working Group Textiles, Results

Allergic reactions caused by textiles
• Mainly certain dyes are responsible for textile-induced contact allergies.
• The following 8 dyes should no longer be used in garments:

  - Disperse Blue 1
  - Disperse Blue 35
  - Disperse Blue 106
  - Disperse Blue 124
  - Disperse Orange 3
  - Disperse Yellow 3
  - Fisperse Orange 37/76
  - Disperse Red 1

Recent research project
• Sensitising potential of disperse dyes was investigated using a biphasic protocol of the local lymph node assay (LLNA).
• Strong sensitiser: Disperse Blue 124 and Disperse Blue 106.
• Lowest active test concentration was 0.003%, area dose of 0.75 µg/cm².
• This dose is lower than the no observable dose in humans of one of the strongest contact sensitisers ever tested in the LLNA assay, i.e. 2,4-dinitrochlorobenzene.

Risk assessment of textile dyes, exposure is the key

- No relevant amounts of dyestuff or auxiliaries should migrate to the skin of consumers under use-conditions.
  *Working Group Textiles, Bundesgesundheitsblatt 11/1996, 430*

- **ETAD 1983:** Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers

**Report on Extractability of dyestuffs from textiles**

500 cm² of dyed textile sample, release of dyestuff into a test solution (DIN 54020, 37 °C, 4 h):
- maximum migration factor 0.18 %
- 0.1 µg to 300 µg dye per 500 cm²

**Exposure calculation for simulated wearing event**
- < 1 µg to 0.4 mg per person or < 2 ng/cm² to 0.7 µg/cm²
Proposal for testing migration

- 0.5 g unwashed fabrics are shaken in 25 ml artificial sweat solution (liquor ratio 1:50) for 60 minutes at 40 °C with 90 rotations per minute.

- Elution is performed with acidic and alkaline sweat solution according to DIN 54020.

- The release of substances is measured with a suitable analytical method and quantified on the basis of released compound per g or per cm$^2$ textile.

- The highest value is used for the estimation of exposure.

- Measurements of this first migration are used for the estimation of the amount of a compound released from a clothing textile during the first wearing event of 16 hours.
Standard exposure

Assumptions:
- content is known
- textile mass per unit area 100 g/m²,
- exposed skin area 1 m²,
- body weight 60 kg

<table>
<thead>
<tr>
<th>Substance</th>
<th>Migration</th>
<th>Penetration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyes</td>
<td>0.5 %</td>
<td>1 % ¹, ²</td>
</tr>
<tr>
<td>Hydrophilic Auxiliaries</td>
<td>2 %</td>
<td>5 % ¹</td>
</tr>
<tr>
<td>Hydrophobic Auxiliaries</td>
<td>0.1 %</td>
<td>50 % ¹</td>
</tr>
</tbody>
</table>

¹ Exception: molecular weight >700 or logPow < -1 or >6
² for skin areas were sweat plays an important role, a penetration rate of 2 % may be used
Conclusion: risk of clothing textiles

Risk for the consumer identified:
- Textile based contact allergies (1.8 % of clinic patients)
- Allergies caused by sensitising disperse dyes, BfR recommends not to use 8 hazardous disperse dyes
- Azo dyes, which are split into carcinogenic amines
- Basis for safe clothing textiles is toxicological testing of dyes and auxiliaries, especially genotoxicity and sensitisation potential have to be excluded
- The decisive criterion of risk assessment is exposure: generally accepted models and data are missing.
Safety of cosmetic products

Article 2: …. a cosmetic product .. must not cause damage to human health .. under normal or reasonably foreseeable conditions of use

Elements of regulation

1. Positive lists
2. Negative lists
3. Product labelling
4. Product dossier
5. Inventory

The safety assessment of cosmetic products is based on the safety of the ingredients.
SCCS Scientific Committee on Consumer Safety

- 76/768/EWG Cosmetics Directive Article 8:
  SCC "Scientific Committee on Cosmetics",
  scientific advice to the EU-commission
- 1978 SCC established
- 1997 successor SCCNFP
- 2004 SCCP
- 2009 SCCS (Scientific Committee on Consumer Safety)

Evaluation of cosmetic ingredients,
Elements of risk assessment

1. Hazard assessment
2. Dose-response relationship
3. Exposure assessment
4. Risk characterization

Basis: Dossier of Industry
- Spezification (including contamination and stability)
- Toxicological data
- Human experience

Formal requirements:
- OECD-Guideline
- GLP
- SCCS Notes of Guidance
- SCCS Opinions
Risk assessment of cosmetic ingredients: Notes of Guidance SCCS/1416/12

1. Mutagenicity / carcinogenicity
   - Genotoxicity
   - (carcinogenicity)

2. Percutaneous absorption

3. Systemic toxicity
   - Acute toxicity
   - Subchronic toxicity
   - Reprotoxicity
     development (reproductive)
   - (chronic toxicity)

3. Dermatotoxicity
   - skin and eye irritation
   - skin sensitization
   - Phototoxicity UV-filter
     (irritation, mutagenicity, sensitization)

4. Toxicokinetics
   data not regularly provided
Memorandum SCCP/1111/07 & SCCS/1294/10: actual status of alternative methods

<table>
<thead>
<tr>
<th>Validated replacement alternatives available</th>
<th>Validated reduction / refinement alternatives available</th>
<th>No validated alternatives available</th>
</tr>
</thead>
<tbody>
<tr>
<td>• skin corrosivity / irritation</td>
<td>• acute toxicity</td>
<td>• eye irritation</td>
</tr>
<tr>
<td>• dermal absorption</td>
<td>• skin sensitisation</td>
<td>• repeated dose toxicity</td>
</tr>
<tr>
<td>• mutagenicity / genotoxicity</td>
<td></td>
<td>• carcinogenicity</td>
</tr>
<tr>
<td>• phototoxicity</td>
<td></td>
<td>• reproductive toxicity</td>
</tr>
</tbody>
</table>

*It is unlikely that the deadlines 2009 and 2013 can be met.*
Remaining and arising problems in cosmetics

- How to deal with extremely potent sensitizers in hair dyes?
- Evaluation of natural ingredients and cosmeceuticals
- Assessment of nanomaterials
- The future health evaluation without animal testing is a challenge. From the today’s point of view a concept is not feasible which covers both innovation and consumer protection at the present high level.
Conclusion: what is key for product safety assessment

The central deficits of chemical risk assessment of products are:

1. **Assessment of exposure:**
   methods and data are available for food contact materials and cosmetics, however scarce for toys, textiles and other consumer products

2. **Missing toxicological data:**
   for many chemicals used in products no sufficient toxicological data are available

3. **Good manufacturing practice:**
   The role of manufacturers for product safety is important, awareness in developing countries has to be improved
Thank you for your attention

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