

# **Chemical risk assessment**

## **Implications for product safety**

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# The Author

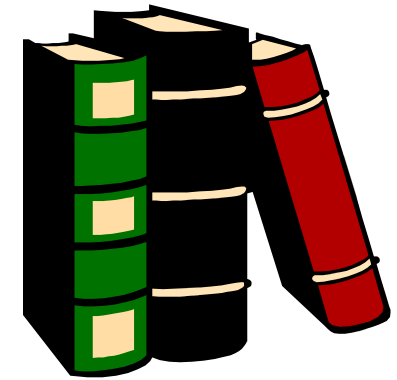
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# Department Safety of Consumer Products

## 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

Directive 2001/95/EC of 3 December 2001 on general product safety

- '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

# Regulatory background, textiles and leather clothing

## 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

## Pentachlorophenol Regulation (EC) No 1907/2006

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 !***

1	4-Aminobiphenyl	12	3,3'-Dimethylbenzidine
2	Benzidine	13	3,3-Dimethyl-4,4'-diaminodiphenylmethan
3	4-Chloro-o-toluidine	14	p-Cresidine
4	2-Naphthylamine	15	4,4'-Methylen-bis-(2-chloroaniline)
5	o-Aminoazotoluene	16	4,4'-Oxydianiline
6	2-Amino-4-nitrotoluene	17	4,4'-Thiodianiline
7	4-Chloroaniline	18	o-Toluidine
8	2,4-Diaminoanisol	19	2,4-Toluenediamine
9	4,4'-diaminodiphenylmethane	20	2,4,5-Trimethylaniline
10	3,3'-Dichlorobenzidine	21	2-Methoxyaniline (o-Anisidine)
11	3,3'-Dimethoxybenzidine	22	4-Aminoazobenzene



# 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/cm<sup>2</sup>.
- 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.

*Ahuja et al. Arch Toxicol (2010)*

# 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 cm<sup>2</sup> 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 cm<sup>2</sup>

## **Exposure calculation for simulated wearing event**

< 1 µg to 0.4 mg per person or < 2 ng/cm<sup>2</sup> to 0.7 µg/cm<sup>2</sup>

# Migration model

## 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<sup>2</sup> 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/m<sup>2</sup>,
- exposed skin area 1 m<sup>2</sup>,
- body weight 60 kg

<b>Substance</b>	<b>Migration</b>	<b>Penetration</b>
Dyes	0.5 %	1 % <sup>1, 2</sup>
Hydrophilic Auxiliaries	2 %	5 % <sup>1</sup>
Hydrophobic Auxiliaries	0.1 %	50 % <sup>1</sup>

<sup>1</sup> Exception: molecular weight >700 or logPow <-1 or >6

<sup>2</sup> for skin areas where 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.

# Cosmetics Regulation, Directive 76/768/EWG

## 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  
developmental  
(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

Validated replacement alternatives available	Validated reduction / refinement alternatives available	No validated alternatives available
<ul style="list-style-type: none"> <li>• skin corrosivity / irritation</li> <li>• dermal absorption</li> <li>• mutagenicity / genotoxicity</li> <li>• phototoxicity</li> </ul>	<ul style="list-style-type: none"> <li>• acute toxicity</li> <li>• skin sensitisation</li> </ul>	<ul style="list-style-type: none"> <li>• eye irritation</li> <li>• repeated dose toxicity</li> <li>• carcinogenicity</li> <li>• reproductive toxicity</li> <li>• toxicokinetics</li> </ul>

***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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