General Hazard Profile of Pigments

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Data presented on the following slides

- has been gathered for the purposes of registration as an industrial chemical in the EU
- can be viewed online in form of robust study summaries at the European Chemicals Agency (ECHA)

BASF markets pigments for industrial uses (e.g., coating of cars, coloration of plastic articles, printing inks)

BASF does not support uses in tattoo inks
Dissiminated data via the European Chemicals Agency


Note
Copyright and legal notice
Key points of EC regulation 1907/2006 (REACH)

- Registrants share available company data
  - Study reports are reviewed for adequacy and reliability
  - Legal agreements (letter of access, etc)

- Hazard data from public databases is gathered
  - Literature data are reviewed for adequacy and reliability
  - Newly identified data holders are contacted for data sharing

Data gap filling with studies performed under GLP and following OECD testing guidelines

(deviations from standard procedure as in Annex XI)
Data base for industrial pigments

- Representative of pigments alone, not of pigment formulations (dispersing agents, fillers, etc)
- Thorough literature survey
- Experimental data from stakeholders interested in REACH
  - Companies with volumes of more than 1 tpa and active in the EU
  - Otherwise interested (data owners)
- No completeness claimed - possible existence of further experimental data for non-industrial uses or data held by stakeholders outside the EU
Data sources, examples Pigment Red 254, Pigment Red 101

### Impact of impurities on classification and labelling

exemple from ECHA dissimination view

#### General Information
- Identification
- Compositions
- Classification and Labelling
- GHS
  - Pigment Red 112 [not classified, < 1% (w/w)]
    - Naphthol AS-D, 3-hydroxy-2-methyl-2-naphthanilide
  - Pigment Red 112 [classified > 1% (w/w)]
    - Naphthol AS-D, 3-hydroxy-2-methyl-2-naphthanilide
- DSD - DPD
- Physical and chemical properties
- Environmental fate and pathways
- Ecotoxicological Information
- Toxicological information
- Guidance on safe use
- Reference substances

#### Identification

**Substance identification**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>3-hydroxy-N-(o-tolyl)-4-[[2,4,5-trichlorophenyl]azo]naphthalene-2-carboxamide</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EC Number</th>
<th>CAS Number</th>
<th>Molecular formula</th>
<th>IUPAC Name</th>
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<tbody>
<tr>
<td>229-440-3</td>
<td>6533-46-2</td>
<td>C24H16Cl3N3O2</td>
<td>3-hydroxy-N-(2-methylphenyl)-4-[[2,4,5-trichlorophenyl]diazenyl]-2-naphthamide</td>
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</tbody>
</table>

#### Type of substance

<table>
<thead>
<tr>
<th>Composition</th>
<th>mono constituent substance</th>
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<tbody>
<tr>
<td>Origin</td>
<td>organic</td>
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Pigment classes, examples

Metal-laked pigments

Copper-phthalo cyanines

Diarylides

Disazocondensations

Acetolones

Quinacridones

DPP

Inorganics (Iron oxides, TiO₂)
General physico-chemical properties, organic pigments

- Range of molecular weight: 350 (PR 254) - 1394 (PG 36) g/mol
- Water solubility (neutral pH) range ng – mg/L (methodical challenges)
  - some pigments soluble at extreme pH (eg PR 57:1)
- Octanol solubility range ng – mg/L (methodical challenges)
- Relative density > 1
- No melting point up to decomposition temperature (200 – 400 °C, actual temperature depending on the pigment)
Mandatory endpoints covered by REACH at maximum tonnage band

- Acute toxicity, relevant routes
- Skin irritation, eye irritation, skin sensitization
- Genotoxicity (bacteria, mammalian cells in vitro, in-vivo if in-vitro testing indicates a hazard)
- Repeated dose toxicity, relevant route
- Reproductive toxicity (Fertility by 2-generation study, developmental toxicity/teratogenicity study; 2 species), relevant route
- Carcinogenicity, two species, relevant route
Hazard data available for members of all mentioned chemical classes (I)

LD50 (oral) > 2000 mg/kg bw
LD50 (dermal) > 2000 mg/kg bw

virtually non-toxic by ingestion and skin contact

Skin irritation: non irritating

Eye irritation: non irritating

Skin sensitisation: non sensitising

Genotoxicity: not genotoxic (Ames with and without Prival-modification, Hprt/MLA, cytogenetic tests, in-vivo micronucleus, UDS)
Rats, 28-days or 42 days, oral dosing
More than 20 pigments: NOEL = 1000 mg/kg bw

Rats, 90-days, oral dosing
Pigment Yellow 74, Pigment Red 122; Pigment Green 15: NOEL = 1000 mg/kg bw

Metal laked pigments (dissociation in stomach acid):
Adverse effects on kidneys upon bolus dosing, NOEL ca 40 mg/kg bw; red discoloration of urine

18-months dermal toxicity study: PR 57:1 for use in lipstick (Carson 1984); dose 50 mg/kg bw, twice per week
Hazard data for members of all chemical classes (III) Carcinogenicity

- Na salt of Pigment Red 57:1 (feeding study, non carcinogenic)
- Skin painting «lipstick» studies (Carson 1984)
- Leuschner 1978 - Toxicology Letters 2: 253-260 (diarrulide pigments, feeding study, not carcinogenic)

- Copperphthalocyananine NTP decision on non-testing
  - CuPC: Haddow 1960: 8 weekly subcutaneous injections of 0.5 mg to 20 mice did not cause tumor formation in the 8-months observation period
Hazard data for members of all chemical classes (III) Reproductive toxicity, oral route

- **Teratogenicity**
  - Negative with PO 73
  - (negative with PR 57:1)

- **Screening studies**
  - (OECD 421/422)
  - No adverse effects found for more than 15 pigments

- **In-utero exposure/fertility study**
  - No effects with Na-salt of PR 57:1

- **Two-generation study**
  - ECHA testing proposal for PO 73
Literature publications on toxicokinetic properties

Lack of dermal and oral absorption of Pigment Yellow 12


Company data related to toxicokinetics

- Lack of accumulation of copper in kidney and liver upon subchronic feeding of a copper phthalocyanine pigment

- $^{14}$C-Pigment Red 254 with MW of 357 g/mol is not significantly absorbed upon single oral dosing (intestinal passage within 24h)

- No internal organ discoloration observed

- No urine discoloration observed

- Poor solubility in water/fat is unfavourable for transport across biological membranes

*No visual indication for absorption*
Summary

- Lack of systemic effects after ingestion observed in animal studies
- Systemic uptake upon skin contact not expected
- Relevant data for tattoo uses (intradermal application, decomposition products) not available
Thank you for your attention!