Exposure assessment and the Chemical Safety Report

Société Française de Toxicologie
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Overview

• Recap on REACH requirements
• Assessment workflow
• Scope of exposure assessment
• Few ECHA’s observations related to the exposure scenarios received so far
Recap on REACH requirements
CSA in a nutshell

- Determine the hazards based on the information required for registration of the substance
- Describe the conditions of safe use (operational conditions and risk management)
  - => set of exposure scenarios addressing all identified uses
- Estimate the expected exposure under these conditions
- Compare the expected exposure with the hazards
- Conclude whether control of risk is demonstrated; refine the assessment, if needed;
- Annex I of REACH sets out the general provisions for the assessment
When is a CSA required?

- Required if the substance is manufactured or imported at 10 tonnes or more per year.

- The CSA includes exposure assessment and risk characterisation for all the identified hazards
  - if one of the criteria is met to classify the substance as hazardous, or
  - if the substance is to be treated as PBT/vPvB, or
  - if information requirements are adapted based on exposure considerations according to Annex XI (3)

- Identified hazards = adverse effects observed based on guideline studies (or other adequate information)
Assessment
work flow
Assessment Workflow

Fulfil information requirements for the various endpoints

Derive hazard assessment conclusions (DNELs, PNECs, CnL);

Describe the uses of the substance; compile information on the existing conditions of use

Exposure scenario building, exposure estimation, risk characterisation

Communicate information on substance properties and conditions of safe use via extended SDS

CSR to authorities
Risk Characterization (RC)

- **Hazard information**
- **Quantitative/Qualitative Risk Characterisation**
- **Use and exposure information**

**Quantitative:** PNEC/DNEL

**Qualitative:** Classification (type and level of hazard)

**Exposure Scenarios**

**Exposure Estimates**
## Assessment types

<table>
<thead>
<tr>
<th>Assessment Type</th>
<th>Exposure Scenario (conditions of use)</th>
<th>Exposure estimation</th>
<th>Risk characterization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantitative</td>
<td>yes</td>
<td>yes</td>
<td>RCR &lt; 1</td>
</tr>
<tr>
<td>Semi-quantitative</td>
<td>yes</td>
<td>yes</td>
<td>exposure &lt; threshold + additional argument</td>
</tr>
<tr>
<td>Qualitative</td>
<td>yes</td>
<td>may be required to demonstrate control of risks</td>
<td>control strategy corresponds to hazard</td>
</tr>
</tbody>
</table>
Mandatory elements of the CSA/CSR (1)

Assessment of intrinsic properties/hazards:
- Physicochemical properties, “environmental fate” properties
- Human health hazards
  - Local effects (skin, eyes, or respiratory tract)
  - Systemic effects (intake via skin, inhalation or oral)
  - Effects after single event exposure (short term) or after repeated/long-term exposure
  - Effects due to flammability, explosivity, oxidising potential.
- Environmental hazards:
  - Adverse effects on organisms in water, sediments, soil or waste water treatment plant; adverse effects in the food-chain (aquatic and terrestrial)
Mandatory elements of the CSA/CSR (2)

- Use identification for the full life cycle
- Exposure assessment
  - Conditions of use (operational condition and risk management)
  - Corresponding release and exposure estimates
- Risk characterisation
  - Quantitative: Compare estimated exposure with PNEC or DNEL. RCR < 1 indicates control of risk
  - Qualitative: Compare estimated exposure and/or foreseen risk management with type and level of hazard.
Scope of exposure assessment

From study records to hazard assessment conclusions in IUCLID 5.4
Toxicological hazard conclusions

- The endpoint summary for section 7 of IUCLID 5.4 has been expended to better support
  - Transparency in the hazard conclusion (e.g. derivation of DNELs)
  - Identification of the scope of exposure assessment
Hazard assessment information in IUCLID
**Example (1): Overview on endpoint summaries in section 5.11 of the CSR**

*Source:* IUCLID 5.4, section 7

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Route</th>
<th>Dose descriptor or qualitative effect characterisation; test type;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute toxicity</td>
<td>Oral</td>
<td>No adverse effect observed</td>
</tr>
<tr>
<td>Acute toxicity</td>
<td>Dermal</td>
<td>No adverse effect observed</td>
</tr>
<tr>
<td>Acute toxicity</td>
<td>inhalation</td>
<td>No adverse effect observed</td>
</tr>
<tr>
<td>Irritation / Corrosivity</td>
<td>Skin</td>
<td>irritating</td>
</tr>
<tr>
<td>Irritation / Corrosivity</td>
<td>Eye</td>
<td>irritating</td>
</tr>
<tr>
<td>Irritation / Corrosivity</td>
<td>respiratory</td>
<td>No study available</td>
</tr>
<tr>
<td>Sensitisation</td>
<td>Skin</td>
<td>No adverse effect observed (not sensitising)</td>
</tr>
<tr>
<td>Repeated dose toxicity</td>
<td>Oral</td>
<td>NOAEL: 700 mg/kg bw/day (subacute; rat)</td>
</tr>
<tr>
<td>Repeated dose toxicity</td>
<td>Dermal</td>
<td>No study available</td>
</tr>
<tr>
<td>Repeated dose toxicity:</td>
<td>inhalation</td>
<td>No study available</td>
</tr>
<tr>
<td>Mutagenicity</td>
<td></td>
<td>No adverse effect observed (negative)</td>
</tr>
<tr>
<td>Reproductive toxicity: fertility impairment</td>
<td>Oral</td>
<td>No adverse effect observed</td>
</tr>
</tbody>
</table>
## Example (2): Hazard conclusions in section 5.11 of the CSR

**Source:** IUCLID 5.4, section 7 (overall toxicological summary)

<table>
<thead>
<tr>
<th>Route</th>
<th>Type of effect</th>
<th>Hazard conclusion</th>
<th>Most sensitive endpoint (referring to original study)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation</td>
<td>Systemic effect - Long-term</td>
<td>DNEL = 24.7 mg/m³</td>
<td>Repeated dose toxicity (oral)</td>
</tr>
<tr>
<td></td>
<td>Systemic effects - Acute</td>
<td>No hazard identified</td>
<td>Acute toxicity (Inhalation)</td>
</tr>
<tr>
<td></td>
<td>Local effects - Long-term</td>
<td>Hazard unknown (no further information necessary)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Local effects - Acute</td>
<td>Hazard unknown (no further information necessary)</td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>Systemic effect - Long-term</td>
<td>DNEL = 7 mg/kg bw /day</td>
<td>Repeated dose toxicity (oral)</td>
</tr>
<tr>
<td></td>
<td>Systemic effects - Acute</td>
<td>No hazard identified</td>
<td>Acute toxicity (dermal)</td>
</tr>
<tr>
<td></td>
<td>Local effects - Long-term</td>
<td>Low hazard</td>
<td>Skin irritation/corrosion</td>
</tr>
<tr>
<td></td>
<td>Local effects - Acute</td>
<td>Low hazard</td>
<td>Skin irritation/corrosion</td>
</tr>
<tr>
<td>Eyes</td>
<td>Local effects - Acute</td>
<td>Low hazard</td>
<td>Eye irritation</td>
</tr>
</tbody>
</table>

Remark: Table expected for workers and for general population
**Example (3): Scope of exposure assessment for human health in section 9.02**

<table>
<thead>
<tr>
<th>Route</th>
<th>Type of effect</th>
<th>Type of risk characterisation</th>
<th>Hazard conclusion (see section 5.11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation</td>
<td>Systemic effect - Long-term</td>
<td>Quantitative</td>
<td>DNEL = 24.7 mg/m3</td>
</tr>
<tr>
<td></td>
<td>Systemic effects - Acute</td>
<td>Not required</td>
<td>No hazard identified</td>
</tr>
<tr>
<td></td>
<td>Local effects - Long-term</td>
<td>Qualitative</td>
<td>Hazard unknown (no further information required)</td>
</tr>
<tr>
<td></td>
<td>Local effects - Acute</td>
<td>Qualitative</td>
<td>Hazard unknown (no further information required)</td>
</tr>
<tr>
<td>Dermal</td>
<td>Systemic effect - Long-term</td>
<td>Quantitative</td>
<td>DNEL = 7 mg/kg bw /day</td>
</tr>
<tr>
<td></td>
<td>Systemic effects - Acute -</td>
<td>Not required</td>
<td>No hazard identified</td>
</tr>
<tr>
<td></td>
<td>Local effects - Long-term</td>
<td>Qualitative</td>
<td>Low hazard</td>
</tr>
<tr>
<td></td>
<td>Local effects - Acute</td>
<td>Qualitative</td>
<td>Low hazard</td>
</tr>
<tr>
<td>Eyes</td>
<td>Local effects –Acute</td>
<td>Qualitative</td>
<td>Low hazard</td>
</tr>
</tbody>
</table>
Example (4): Explanation of DNEL derivation in section 5.11 of the CSR

<table>
<thead>
<tr>
<th>Route</th>
<th>DNEL derivation method:</th>
<th>Assessment factors for DNEL derivation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation (Long-term - systemic effects)</td>
<td>ECHA REACh guidance</td>
<td>AF for difference in duration of exposure: 2 (<em>DNEL is based on an oral 90 day study</em>)&lt;br&gt;AF for interspecies differences: 1 (<em>AF not used for inhalation route</em>)&lt;br&gt;AF for other interspecies differences: 2.5&lt;br&gt;AF for intra species differences: 5 (workers)&lt;br&gt;Overall Assessment Factor: 25</td>
</tr>
<tr>
<td></td>
<td>Dose descriptor starting point NOAEC = 617 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Dermal (Long-term - systemic effects)</td>
<td>ECHA REACh guidance</td>
<td>AF for difference in duration of exposure: 2 (<em>based on an oral 90 day study</em>)&lt;br&gt;AF for interspecies differences: 4 (<em>experimental animal was rat</em>)&lt;br&gt;AF for other interspecies differences: 2.5&lt;br&gt;AF for intra species differences: 5 (<em>this is for workers</em>)&lt;br&gt;AF for remaining uncertainties:&lt;br&gt;Overall Assessment Factor: 100</td>
</tr>
<tr>
<td></td>
<td>Dose descriptor starting point NOAEL = 700 mg/kg bw/day</td>
<td></td>
</tr>
</tbody>
</table>
Few observations on CSRs from first registration wave
What has been submitted to ECHA

- For about 1400 substances CSRs with exposure scenarios are principally available. That is a success.
- The CSR information is submitted in form of text documents attached to the Technical Dossier.
- The Technical Dossier is submitted in electronic format and usually contains
  - the brief description of identified uses in section 3.5 (required to be consistent with the titles of the exposure scenarios)
  - no information related to guidance on safe use
  - no information related to expected exposure or risk
- ECHA does not see the ES for communication.
Observations on the use description (1)

• Very generic, does not support understanding of what is practically done with the substance; no descriptive narratives (often just a bare list of descriptors)

• Includes often nearly all use descriptors (regardless of whether this is plausible or relevant for the substance)
  • Registrants try to cover everything i) just to be on the safe side or ii) to include everything they have received from downstream
  • Registrants have copied their use descriptions from lead registrant or even from a generic CSR generated at sector level
Observations on use description (2)

- The use descriptions lack consistency, e.g.
  - Article service life reported although the substance is described as a processing aid
  - Use descriptors indicating wide dispersive use are reported for industrial sites
Observations on scope of exposure assessment

- Environmental part of the ES missing
- Exposure men via environment missing
- RMM corresponding to qualitative hazards not addressed
- RMM related to physicochemical hazards not addressed
Support provided by ECHA

- All existing guidance and practical guide
- Chesar (Chemical Safety Assessment and Reporting tool): IT tool developed by ECHA to support registrants in carrying out their CSA and preparing their CSR
  
  http://chesar.echa.europa.eu/

- NEW: Practical guide 14: How to prepare toxicological summaries in IUCLID and how to derive DNELs
- NEW (to be published with IUCLID 5.4.1 in October): IUCLID Helptext for section 3.5 (life cycle description) and for endpoint summaries
Merci.

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