Exposure Scenario processing for Mixtures

Critical Component Approach (CCA)

Pre-read information

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1. **Introduction**

*Exposure Scenario processing for mixtures*

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**OUR SOLUTION**

**Generic Mixture Exposure Scenario (GMES) approach**

1. **Ready to use, standardized “Mixture ES format” as base**
   - **Aligned to the sector specific use Information (DUCC Templates)**

2. **Stepwise process to complete the Mixture ES(s) for a specific mixture**
   - **Reliable determination of the mixture OC & RMM for the product uses, taking into consideration the Mixture Label & relevant Risk Determining Substances in the Mixture identified via the Critical Component Approach (CCA)**
   - **Can be organized “top-down” or “bottom-up” (sector specific GMES)**
2. Outline exposure scenario processing for mixtures

*Generic Mixture Exposure Scenario (GMES) Approach “top-down”*

- **Mixture Data**
- **Mixture Use Data**
- **Mixture Name, phys. Chem. & label data**
- **Mixture Composition**
- **Substance Name, phys chem. & label data & DNEL/PNEC’s per endpoint-RDS**

**INPUT**

- **Trigger**
  - Processing Mixture ES?
  - No
  - Yes

**OUTPUT**

- **Mixture ES(s): Annex mixture SDS**
  - (completed / updated Mixture ES)

1. **Input: Mixture/Use data in Mixture ES Format**

2. **Mixture ES Format**
   - (empty template)

   - **CCA Method!**

2.a. **Mixture Label**
   - (qualitative endpoints)

2.b. **RDS Calculation tool**
   - (quantitative endpoints)

3. **Determination Mixture OC & RMM**
   - (From processing the relevant qualitative/quantitative endpoints)

**Mixture Use Data**

- (sector specific DUCC Template)
3. Critical Component Approach (CCA) method

*Purpose and other methods*

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**1. DPD+ method** (Cefic)

*Identification of Lead substance based on R-phrases*

**2. CCA method** (ECHA)

*Assessment of Critical Components based on DNELs or PNECs*

**3. Hybrid methods** (Sectors & Companies)

Note:
- CCA – Critical Component Approach (ECHA Guidance Part G & for downstream users)
The DPD+ method determines the so-called lead substances.

Possible Lead substances are identified based on R-phrases for the following pathways:
- Inhalation
- Dermal
- Oral
- Eyes
- Aquatic environment

For each pathway a Lead Substance Indicator (LSI) is calculated. The highest LSI value determines the Lead substance per pathway.

\[
\begin{align*}
\text{LSI}_{\text{inhalation}} &= \frac{V_p \times C_i}{C_L} \\
\text{LSI}_{\text{dermal, oral, eyes, or aquat.}} &= \frac{C_i}{C_L}
\end{align*}
\]

- \(V_p\) = Vapour Pressure (hPa, at 25°C)
- \(C_i\) = Concentration of substance (i) in mixture (%)
- \(C_L\) = Concentration Limit for R-Phrase (%)

3. Critical Component Approach (CCA) method

The main principles of the CCA method

- The **CCA method**, as proposed by Jongerius Consult & Caesar Consult, determines the so-called critical components.

- Possible critical components are identified based on DNEL-/PNEC-values for the following endpoints:
  - Inhalation: short / long term & local / systemic
  - Dermal: short / long term & local / systemic
  - Oral: short / long term - systemic
  - Aquatic environment

- For each endpoint a Risk Determining Substance (RDS) score is calculated. The highest RDS score determines the critical component per endpoint.

  - **RDS-score**$_{\text{inhalation endpoints}}$ = $V_p \times C_i / \text{DNEL}_i$
  - **RDS-score**$_{\text{other health endpoints}}$ = $C_i / \text{DNEL}_i$
  - **RDS-score**$_{\text{environmental endpoints}}$ = $C_i / \text{PNEC}_i$

  - $V_p$ = Vapour Pressure (hPa, at 20/25°C)
  - $C_i$ = Concentration of substance (i) in mixture (%)
  - DNEL or PNEC$_i$ = relevant DNEL or PNEC of substance (i)

CCA Calculation tool
(draft beta version; see last slide for details)
3. Critical Component Approach (CCA) method

The practical steps of the CCA method (very similar as DPD+)

**DPD+ Method (R-phrases)**

1. Preparation breakdown
2. Add information: Vapour Pressure & R-phases
3. Calculation LSI Score (Cefic model)
4. Determination RDS per end point:
   1) Inhalation
   2) Dermal
   3) Oral (only relevant for consumer)
   4) Eyes
   5) Environment (aquatic – fresh water)

**CCA Method (DNEL/PNEC’s)**

1. Preparation breakdown
2. Add information: Vapour pressure & DNEL/PNEC’s
3. Calculation RDS Score (CCA Method)
4. Determination RDS per end point:
   1+2) Inhalation (short term - systemic & local)
   3+4) Inhalation (long term - systemic & local)
   5+6) Dermal (short term – systemic & local)
   7+8) Dermal (long term - systemic & local)
   [9+10] Oral (short & long term-syst.; only consumer)
   9/[11] Environment (aquatic – fresh water)

**Processing ES for Mixtures**
Identification of the Risk Determining Substances (RDS) in Mixtures: "CCA METHOD"

Disclaimers: The CCA method is developed by Caesar Consult & Jongerius Consult to the best of our current knowledge and expertise. It is provided in good faith. No representations or warranties are made with regards to the accuracy or completeness of this excel sheet. No liability will be accepted for damages of any nature resulting from the use of this excel sheet.

**Background**

This Critical Component Approach (CCA method) enables the selection of the Risk Determining Substances (RDS) in mixtures. This method follows the same steps as the DPD approach but the selection of risk determining substances is based on DNEL/PNEC instead of R or H phrases of the components. In addition the CCA method is taken into consideration the cut-off limit values from DPD / CLP.

The RDS(s) of a mixture as determined by the CCA Method (like any other RDS determination approach) are the input for the selection of the appropriate OC & RRM for the mixture. As such, the CCA method is an essential part of the Generic Mixture Exposure Scenario (GMES) approach developed by Jongerius Consult & Caesar Consult. The approach is based on a ready to use "Mixture ES Format" and stepwise processing of the qualitative endpoints of the mixture and quantitative endpoints of the Risk determining substances (RDS) determined by the critical component approach (CCA). The Mixture ES can be completed in a "top down process" or "bottom up process" aligned to the sector specific standardised uses. The completed Mixture ES can be attached to the mixture SDS.

**Steps**

1. **Mixture breakdown**
   - see worksheet: "CCA Calculation RDS-scores" - complete the columns A - F

2. **Add for each substance: Vapour pressure (at 25°C), the DNELs and PNECs**
   - see worksheet: "CCA Calculation RDS-scores" - complete the relevant substance details (marked yellow)

3. **Calculation of Risk Determining Substance-scores = RDS-score for each end-point**
   - see worksheet: "CCA Calculation RDS-scores" - the steps 3.1 and 3.2 are calculated automatically. The RDS column per end-point can result in:
     1) non-hazardous: if there are no H-statements filled in for the substance
     2) no DNEL / PNEC: if there is no DNEL/PNEC value for that end-point filled in for the substance
     3) below cut-off: if the concentration of the substance in the mixture is below the relevant cut-off value
     4) Value will represent calculated RDS-scores. The substance with the highest RDS-score will be the RDS for the specific end-point and will be marked yellow automatically

   - formula for calculation of RDS-score
     
     \[
     RDS = \frac{\text{Percentage} \times \text{Vapour pressure (hPa; 20°C)}}{\text{DNEL}}
     \]

4. **Identify for each end-point the substance with highest RDS-score: input for Mixture ES Template**
   - see worksheet: "CCA Result - Mixture ES Format"

**Quantitative end-points Worker**

- 1. INHALATION- Short term - Local effects
- 2. INHALATION- Short term - Systemic effects
- 3. INHALATION- Long term - Local effects
- 4. INHALATION- Long term - Systemic effects
- 5. DERMAL- Short term - Local effects
- 6. DERMAL- Short term - Systemic effects
- 7. DERMAL- Long term - Local effects
- 8. DERMAL- Long term - Systemic effects

**Quantitative end-points Consumer (general population)**

- a. INHALATION- Short term - Local effects
- b. INHALATION- Short term - Systemic effects
- c. INHALATION- Long term - Local effects
- d. INHALATION- Long term - Systemic effects
- e. DERMAL- Short term - Local effects
- f. DERMAL- Short term - Systemic effects
- g. DERMAL- Long term - Local effects
- h. DERMAL- Long term - Systemic effects
- i. ORAL Short term - Systemic effects
- j. ORAL Long term - Systemic effects

**Quantitative end-points Environment**

- 1. ENVIRONMENT - Aquatic - Fresh water
- 2. ENVIRONMENT - Aquatic - Saltwater

**Remarks**

For similar reasons as in the classification & labelling of Mixtures, the same cut-off limit value are introduced in the CCA method indicating when the presence of a substance needs to be taken into account (CLP Annex 1; 1.1.2.2.).

The oral end-point: only relevant for consumer exposure (oral exposure among workers is considered negligible)

Not all quantitative end-points for the ENVIRONMENT are included (yet).

CCA-method requires information on substance content in product (%), Vapour pressure of substance (at 25°C), cut-off values based on substance H-phrases), DNELs-worker, DNELs-consumer (if applicable) and PNEC aquatic.

The identified RDS(s) in a mixture may differ between workers and consumers.

Substances in mixture with highest RDS-scores may differ between workers and consumers.

What if 2 substances have equal highest RDS-score for one end-point. Which substance to choose for the follow-up process?

Not always Vapour Pressure (Vp) at 25°C:

- Calculate Vp (25°C) by using Clausius-Clapeyron relation (see worksheet: "Clausius Clapeyron"). Vapour pressure correction is not needed in the CCA calculation if the temperature of Vp determination is the same for all relevant substances in the Mixture.