Exposure Scenario processing for Mixtures

Critical Component Approach (CCA)

Pre-read information

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1. Introduction

Exposure Scenario processing for mixtures

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)*

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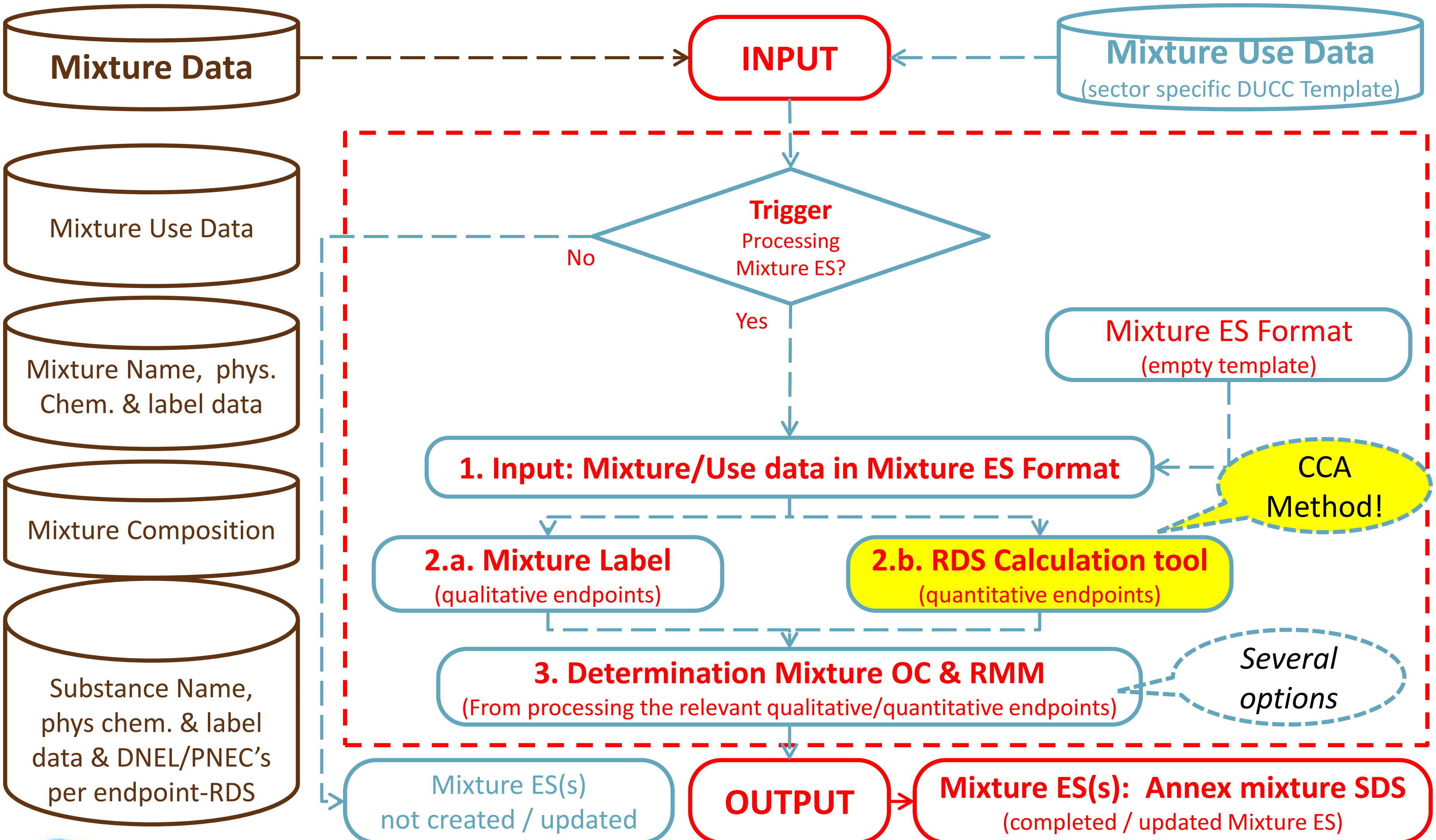
RISICOBEOORDELING VAN CHEMISCHE STOFFEN
CHEMICAL SUBSTANCES RISK ASSESSMENT

2. Outline exposure scenario processing for mixtures

Generic Mixture Exposure Scenario (GMES) Approach "top-down"



3. Critical Component Approach (CCA) method
Purpose and other methods

Determination of Risk Determining Substances (RDS) per quantitative endpoint is crucial to make the processing of ES for Mixtures practical

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:

- DPD - Dangerous Preparations Directive (1999/45/EC)
- CCA – Critical Component Approach (ECHA Guidance Part G & for downstream users)

3. Critical Component Approach (CCA) method
The main principles of the DPD+ method

- 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.

$$LSI_{inhalation} = Vp * C_i / C_L$$

$$LSI_{dermal,\ oral,\ eyes,\ or\ aquat.} = C_i / C_L$$

Vp = Vapour Pressure (hPa, at 25°C)

C_i = Concentration of substance (i) in mixture (%)

C_L = Concentration Limit for R-Phrase (%)

- Cefic Guidance (2009) & Cefic calculation tool available.

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.

$$\text{RDS-score}_{\textit{inhalation endpoints}} = Vp * C_i / DNEL_i$$

$$\text{RDS-score}_{\textit{other health endpoints}} = C_i / DNEL_i$$

$$\text{RDS-score}_{\textit{environmental endpoints}} = C_i / PNEC_i$$

CCA Calculation tool
(draft beta version;
see last slide for details)

Vp = 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)

3. Critical Component Approach (CCA) method

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

Mixture Composition

DPD+ Method (R-phrases)	**CCA Method (DNEL/PNEC's)**
1. Preparation breakdown	1. Preparation breakdown
2. Add information: Vapour Pressure & R-phases	2. Add information: Vapour pressure & DNEL/PNEC's
3. Calculation LSI Score (Cefic model)	3. Calculation RDS Score (CCA Method)
4. Determination RDS per end point:	4. Determination RDS per end point :
1) Inhalation 2) Dermal 3) Oral (only relevant for consumer) 4) Eyes 5) Environment (aquatic – fresh water)	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)

RDS per endpoint

Processing ES for Mixtures

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

DISCLAIMER: 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 whatsoever resulting from the use of of this excel sheet.

Background

This Critical Component Approach (CCA-method) enables the selection of the Risk Determing Substances (RDS) in mixtures.

This method follows the same steps as the DPD+ approach but the selection of risk determing substances is based on DNEL/PNEC instead of R or H-phrases of the components. In addition the CCA method is taking 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 & RMM 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 determing substances (RDS) determined by the critical component approach (CCA). The Mixture ES can be completed in a "top down process" or "bottom up process" alligned to the sector specific standardized uses. The completed Mixtue ES can be attached to the mixture SDS.

Steps		**Details**
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
3.1	Identify the relevant substances per end-point, taking into account the cut-off values from the classification & labelling process detailed in the CLP Regulation 1272/2008/EC (Annex 1)	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
3.2	Calculate the RDS-score per end-point for the substances with an DNEL/PNEC value for that end-point, but only if the substance is present in the mixture in a concentration above the cut-off value and it is hazardous (containing a H-phrase of R-phrase).	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
	Quantitative end-points Worker	***formula for calculation of RDS-score***
	1. INHALATION- Short term - Local effects	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL worker - inhalation short term-local
	2. INHALATION - Short term - Systemic effects	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL worker - inhalation short term -systemic
	3. INHALATION - Long term - Local effects	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL worker - inhalation long term-local
	4. INHALATION - Long term - Systemic	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL worker - inhalation long term -systemic
	5. DERMAL - Short term - Local effects	RDS = Percentage (%) / DNEL worker- dermal short term-local
	6. DERMAL - Short term - Systemic effects	RDS = Percentage (%) / DNEL worker - dermal short term-systemic
	7. DERMAL long term - Local effects	RDS = Percentage (%) / DNEL worker- dermal long term-local
	8. DERMAL- long term - Systemic	RDS = Percentage (%) / DNEL worker - dermal long term-systemic
	Quantitative end-points Consumer (general population)	***formula for calculation of RDS-score***
	a. INHALATION- Short term - Local effects	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL consumer - inhalation short term-local
	b. INHALATION - Short term - Systemic effects	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL consumer- inhalation short term -systemic
	c. INHALATION - Long term - Local effects	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL consumer- inhalation long term-local
	d. INHALATION - Long term - Systemic	RDS = Percentage (%) * Vapour pressure (hPa; 20°C) / DNEL consumer - inhalation long term -systemic
	e. DERMAL - Short term - Local effects	RDS = Percentage (%) / DNEL consumer- dermal short term-local
	f. DERMAL - Short term - Systemic effects	RDS = Percentage (%) / DNEL consumer- dermal short term-systemic
	g. DERMAL long term - Local effects	RDS = Percentage (%) / DNEL consumer- dermal long term-local
	h. DERMAL- long term - Systemic	RDS = Percentage (%) / DNEL consumer - dermal long term-systemic
	i. ORAL Short term - Systemic effects	RDS = Percentage (%) / DNEL consumer - oral short term-systemic
	j. ORAL Long term - Systemic effects	RDS = Percentage (%) / DNEL consumer - oral long term-systemic
	Quantitative end-points Environment	***formula for calculation of RDS-score***
	I. ENVIRONMENT - Aquatic - Fresh water	RDS = Percentage (%) / PNEC aquatic fresh
4.	**Identify for each end-point the substance with highest RDS-score: input for Mixture ES Template**	*see worksheet* :"CCA Result - Mixture ES format"

Remarks	**Solution of issue**
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.).	see worksheet: "Cut-off Limit values".
The oral end-point: only relevant for consumer exposure (oral exposure among workers is considered negligible)	n.r.
Not all quantitative end-points for the ENVIRONMENT are included (yet).	The other quantitative end-points for the ENVIRONMENT can be included in a similar approach (if needed).
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	n.r.
The identified RDS(s) in a mixture may differ between workers and consumers	n.r.
Substances in mixture with highest RDS-scores may differ between workers and consumers	n.r.
What if 2 substances have equal highest RDS-score for one end-point. Which substance to choose for the follow-up process?	proposal: Choose substance with highest DNEL for that end-point. If DNELs are equal, choose substance with highest %. If also % are equal choose substance with highest Vapour pressure.
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