



Safe use information for mixtures: solutions are almost there!

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On behalf of the Cefic/VCI mixtures task force





Background



Safe use of (substances in) mixtures



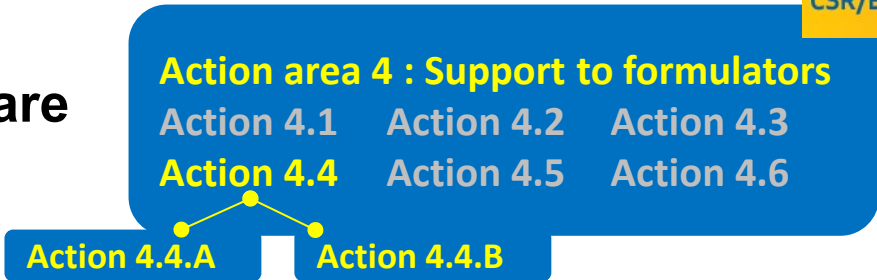
How to use ES information for the safe use of mixtures?



Lot of challenges!

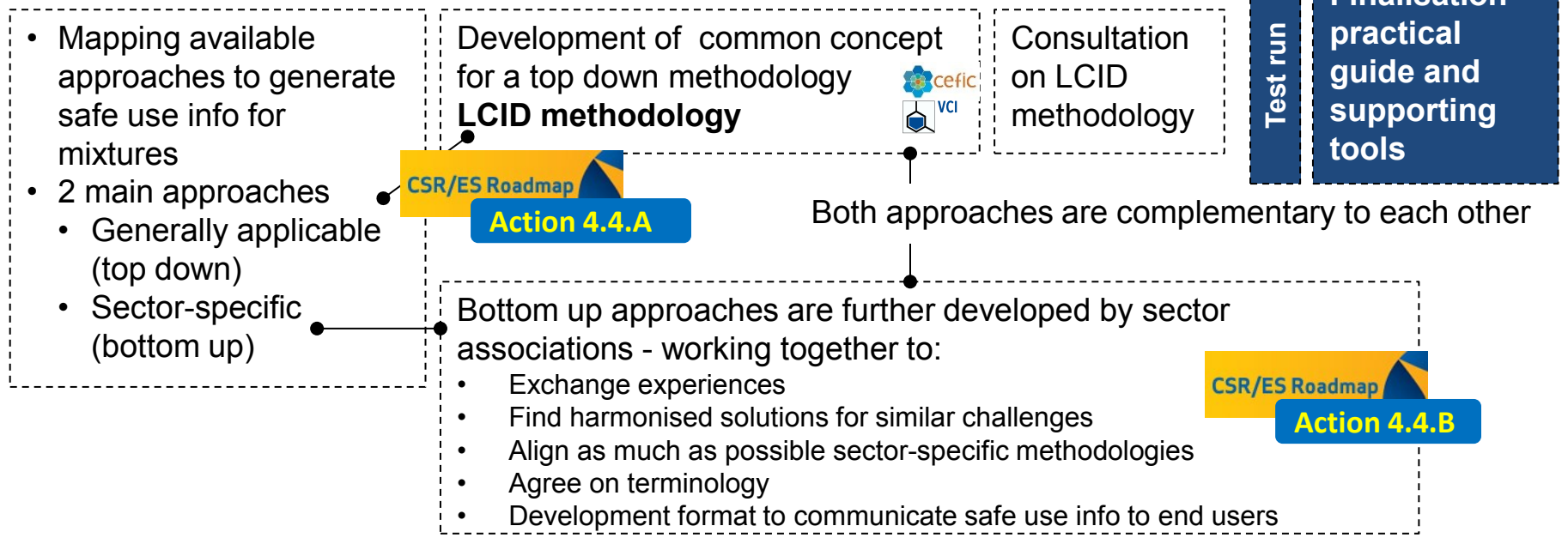
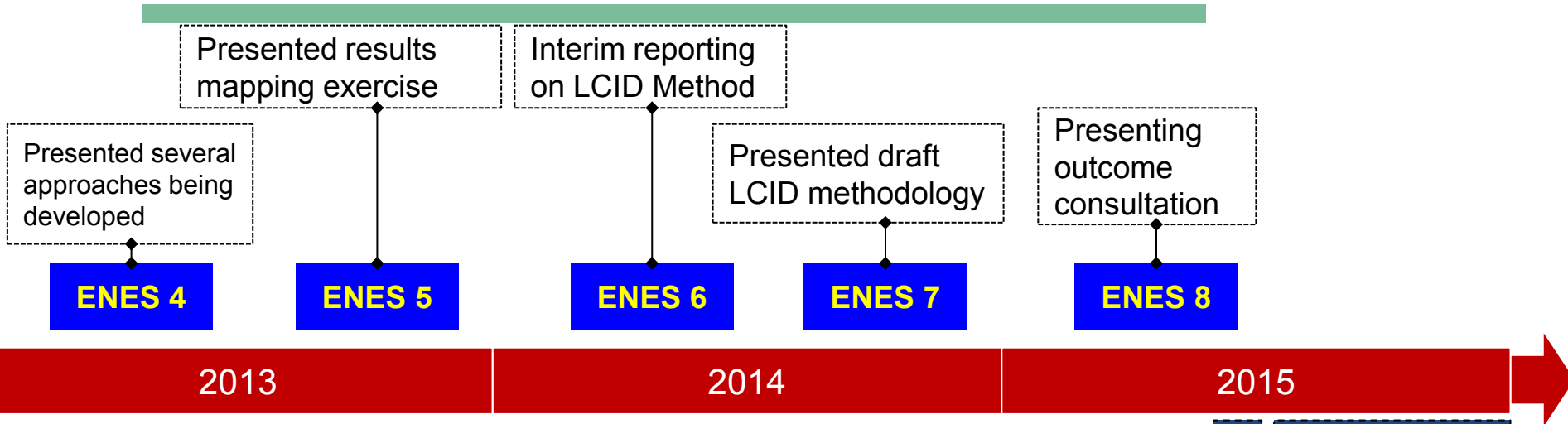


Practical solutions are being developed





Timeframe



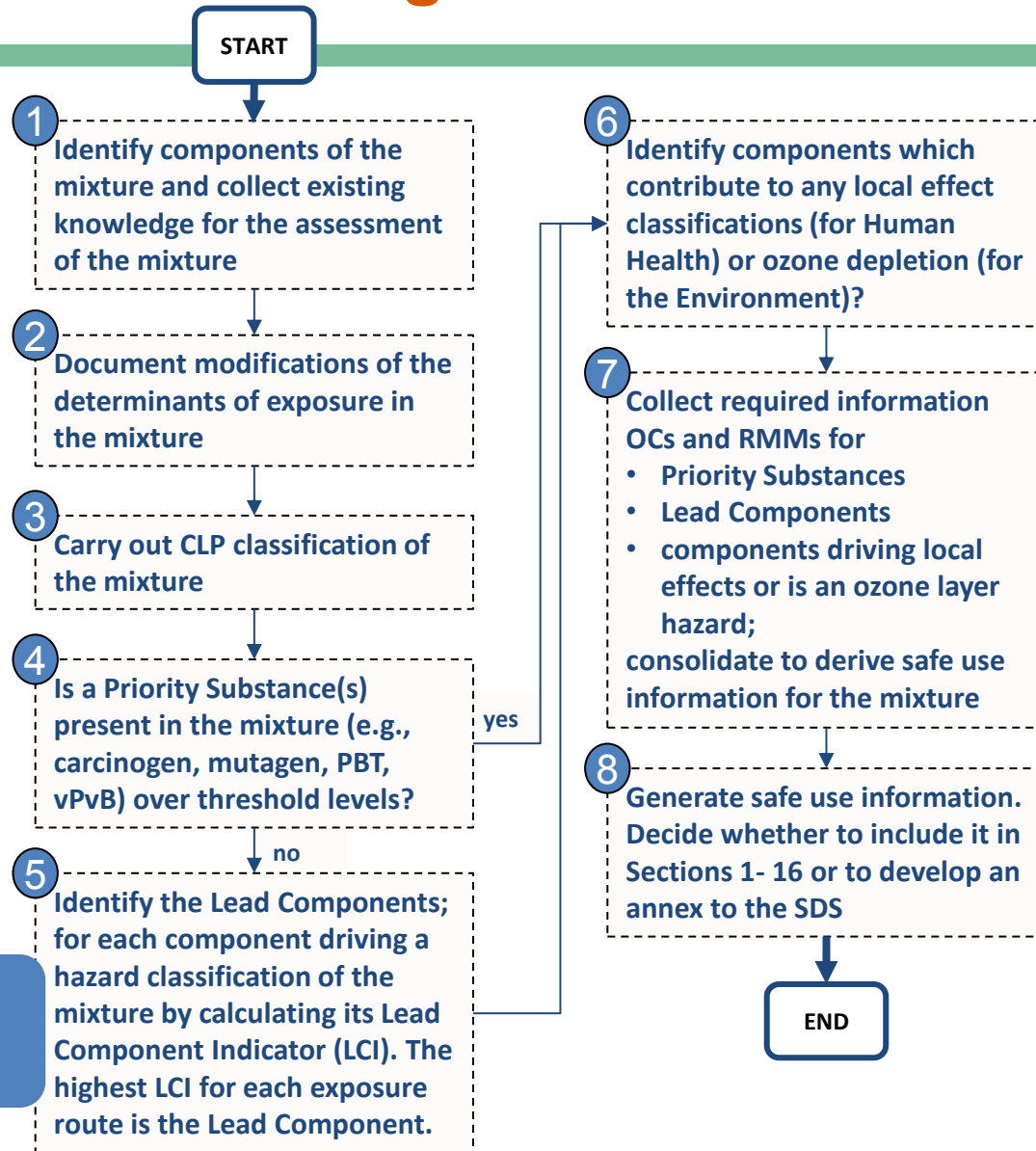


LCID method

- **Developed by a joint Cefic/VCI mixtures TF**
- **Based on:**
 - **available information / methods**
 - **scientific rationale**
 - **Input from practical examples / testing**
- **Aimed to be user friendly**
 - **Step by step workflows**
 - **Allowing maximum degree of automation**
- **Documented in a practical guide**



LCID method: high level workflow

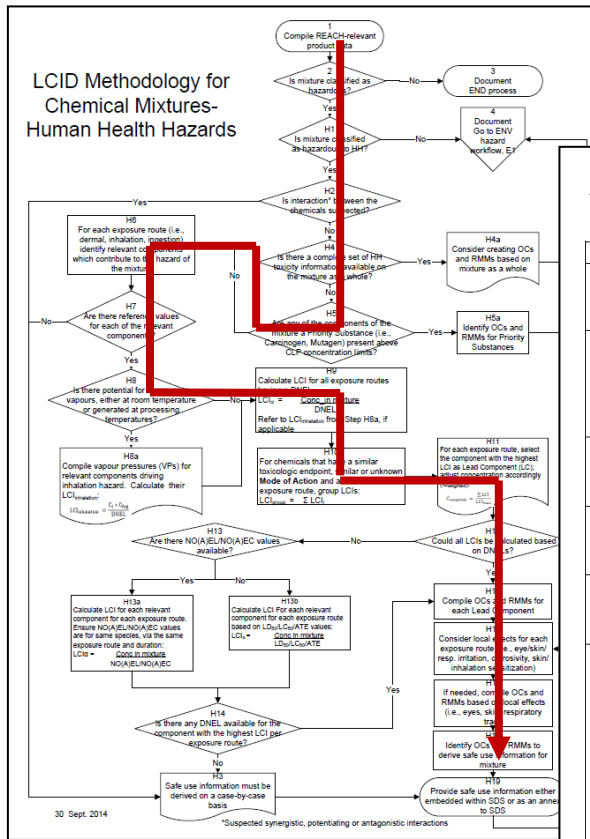


LCI: DNEL/PNEC based, backup approaches if no DNELs/PNECs are available !



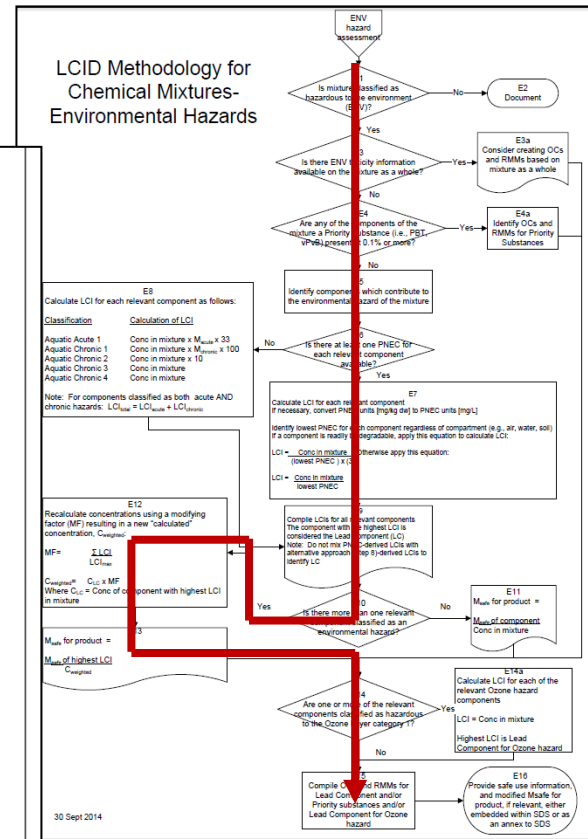
LCID method: detailed workflows

Different steps worked out in detail in a practical guide



28 Oct. 2014 DRAFT REACH Practical Guide / Part III: Mixtures under REACH

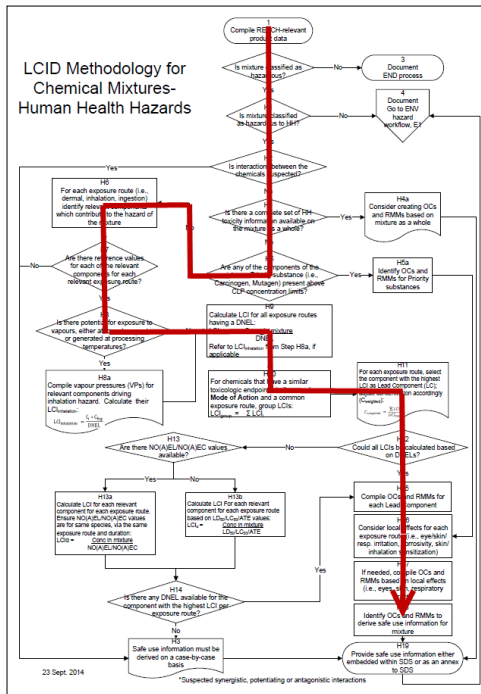
Step	Task	Comments
2	Is the mixture classified as hazardous?	Note: The primary source of information should be the supplier's (e)SDS. If other data sources are used, ensure that the obtained data is relevant for the components used in the formulation of the mixture. Go to Step 2. Refer to the CLP hazard classification of the mixture. Non-classified mixtures are considered non-hazardous as it applies to human health and the environment and, therefore, any use of the mixture is considered safe. Yes/No decision. If yes, go to Step H1. If no, go to Step 3.
3	Document	The mixture is not classified as hazardous, either as a human health (HH) or environmental (ENV) hazard. Document this assessment and allow for easy access to enforcement authorities, if required. Records should include date of review. END LCID methodology workflow.
H1	Is the mixture classified as a hazard to human health?	Refer to CLP hazard classification of the mixture. Yes/No decision. If yes, go to Step H2. If no, go to Step 4.
4	Document	Document the assessment that the mixture is not classified as a human health hazard and allow for easy access to enforcement authorities, if required. Records should include date of review. The mixture has, however, been classified as hazardous to the environment (ENV), therefore, go to Step E1.
H2	Is interaction between the chemicals expected?	Consider the potential for interactions between the components. Interaction is described as the combined effect of two or more chemicals as either stronger (synergistic, potentiating, supra-additive) or weaker (antagonistic, inhibitive, sub-additive, infra-additive) than would be expected on the basis of dose-concentration addition or response addition. Interactions may vary according to the relative dose levels, the route(s), timing and duration of exposure (including the biological persistence of the mixture components), and the biological target(s). Interaction considerations include: <ul style="list-style-type: none">Toxicokinetic interactions: a common cause of deviations from additivity. Examples are chemicals modifying the absorption of others (e.g. skin penetration enhancing substances in cosmetics) or chemicals competing for active transport mechanisms (uptake, clearance)Metabolic interactions: chemicals modifying the metabolism of other mixture componentsToxicodynamic interactions: interactions between the biological responses resulting from exposure to the individual





LCID method: examples

Several examples included to illustrate the method



Test Example 3	Test Example 3			Comments
Name of Product	Ac. Tox. 3 (oral, derm.), STOT RE 2, Skin corr. 1B, Eye dam. 1			
Classification	Component 1			Component 2
Relevant components	Component 1			Component 2
Relevant CAS Nos. (if available)	Component 1			Component 2
Concentration of relevant component	Component 1			Component 2
Health Hazard CLP classification of relevant component	Ac. Tox. 3 (oral)	STOT RE 2	Ac. Tox. 2 (dermal)	Skin corr. 1B Eye dam. 1
Priority Substance (yes/no)	No	No	No	
DNEL inh (mg/m³)	100	30	45	
DNEL derm (mg/kg bw day)	10	4	2	
LCI (DNEL) - oral (if applicable, e.g., consumer)	N/A	N/A	N/A	
Vapour Pressures @ 25°C (hPa)	N/A, mixture of solids			
LCI (DNEL) - inh	45 / 100 = 0.45	25 / 30 = 0.8	10 / 45 = 0.2	LCI = Conc / DNEL
LCI (DNEL) - derm	45 / 10 = 4.5	25 / 4 = 6.3	10 / 2 = 5.0	LCI = Conc / DNEL
LCI (DNEL) - oral	N/A	N/A	N/A	
Lead Component for relevant exposure routes		Lead Component for inhalation and dermal routes of exposure		Highest LCI-inhalation is Component 2 (0.8); Highest LCI-dermal is Component 2 (6.3)
Relevant local effects	None	None	Skin corr. 1B Eye dam. 1	Local effects come from Component 3 (Skin Corr. and eye damage)
Exposure Scenario				
Contributing Scenario				
Operating Conditions (OCs)	> 4h, 5 days a week	> 4h, 5 days a week	> 1h, 5 days a week	Exposure duration for Component 3 is not relevant for assessment of local effects, so the OCs were taken from the Lead Component (Component 2).
Risk Management Measures (RMMs)	Enhanced general ventilation Gloves tested to EN 374	Local exhaust ventilation Good general ventilation Gloves tested to EN 374	Gloves tested to EN 374 Goggles	
Modified OCs for the Mixture	> 4h, 5 days a week			From Component 2 as Lead Component-inhalation
Modified RMMs for the Mixture	Local exhaust ventilation Good general ventilation Gloves tested to EN 374 Goggles			From Component 2 as Lead Component-inhalation, -dermal and Component 3 - local effects on skin and eyes



LCID method: supporting tool

Cefic Lead Component Identification (LCID) Template (v.09)											
Results part - Priority Components											
Priority Component HH:											
Priority substance ENV:											
Results part - Lead Components (LC)											
	LC 1	LC 2	LC 3	Group concentration [%]	WARNING - check substance w/o DNEL (NO(A)EL/NO(A)ECL/LC50/LD50/AATE based):		Test implementation for prototype:	LC inhalation with TRA fugacity factor (for comparison)	LC inhalation w/o VP (for comparison)	LC inhalation with TRA C _{fug} (for comparison)	LC inhalation with correlation-based fugacity factor (for comparison)
LC Inhalation (w VP)				#NUM!			compare:				
LC Dermal				#NUM!			compare:				
LC Ingestion				#NUM!							
LC Eye (via classification)											
LC environment	- (acute), (chronic)				MF environment:	#NUM!	compare:				
LC Ozone depletion:					C _{weighted}	#NUM!	=> use in STEP E12				
LCID input part											
Is mixture classified for Human Health Hazards(s)?		yes	=> Goto cell D16 and columns A-I				User instructions: mandatory inputs optional inputs conditional inputs				
Is mixture classified for Environmental hazard(s)?		yes	=> Goto columns A-C and O								
Use CLP concentration limits for HH Priority substances?		yes	(default is "yes")								
Consider vapour pressure in LCID calculation?		yes	(default is "yes")								
Relevant Components in Mixture					Human health classification - per substance						
Substance ID (optional)	Component NAME (only classified components)	CAS No. (optional)	HH class.1	HH class.2	HH class.3	HH class.4	HH class.5	HH class.6	HH class.7	HH class.8	HH class.9
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LCID: test run

- **Is outcome of the LCID reproducible, independent from user?**
 - **Different people apply the LCID methodology independent from each other for the same cases**
- **July – august 2015**
- **Involving formulators and authorities**
- **Interested to participate?**
 - **Send an email to sva@cefic.be before 30 June**



Questions

