Purpose of the Chemical Safety Assessment

Overview on information required for the CSR

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Webinar for registrants

CSA 1: Chemical Safety Assessment and Chesar

Overview

- Purpose of Chemical Safety Assessment
- Assessment workflow
- From study records to hazard assessment conclusions
- Conditions of use
- Exposure estimates
- Some challenges

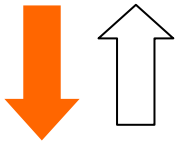
Purpose of CSA

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*

Registration under REACH

Technical Dossier including information as required according to Annexes VI-XI of REACH (*may include also exposure information*)



Chemical Safety Assessment

Hazard Assessment

Exposure Assessment

Risk Characterisation

Chemical Safety Report

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)

Purpose of the CSA process (1)

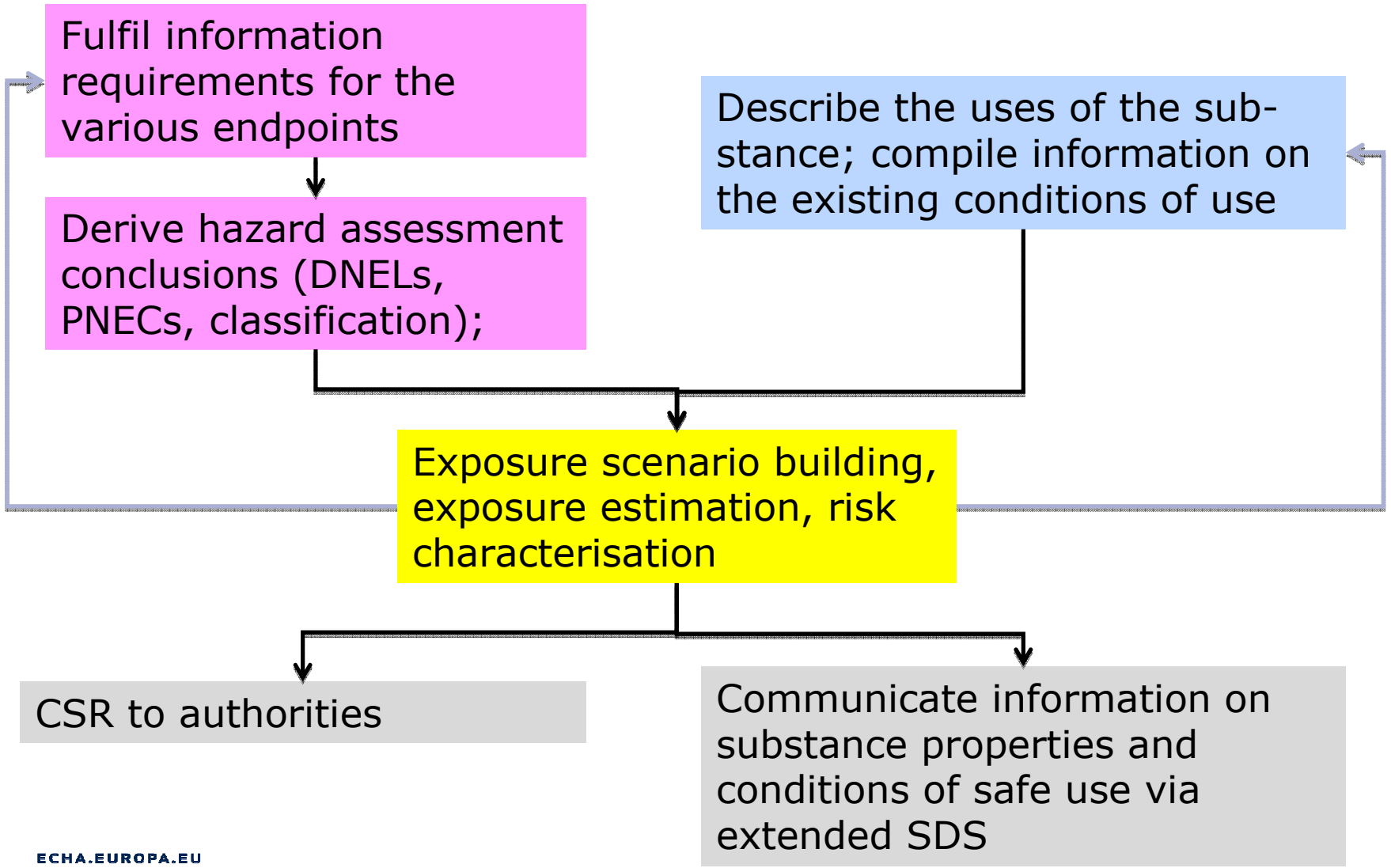
- Describe the conditions ensuring control of risks arising from the manufacture and use(s) of a substance
- Identify where further information is needed (exposure data or testing the substance).
- Inform users of the substance on the conditions of safe use (via exposure scenario attached to the SDS)
- Document the assessment in a CSR for the companies' own documentation.

Purpose of the CSA process (2)

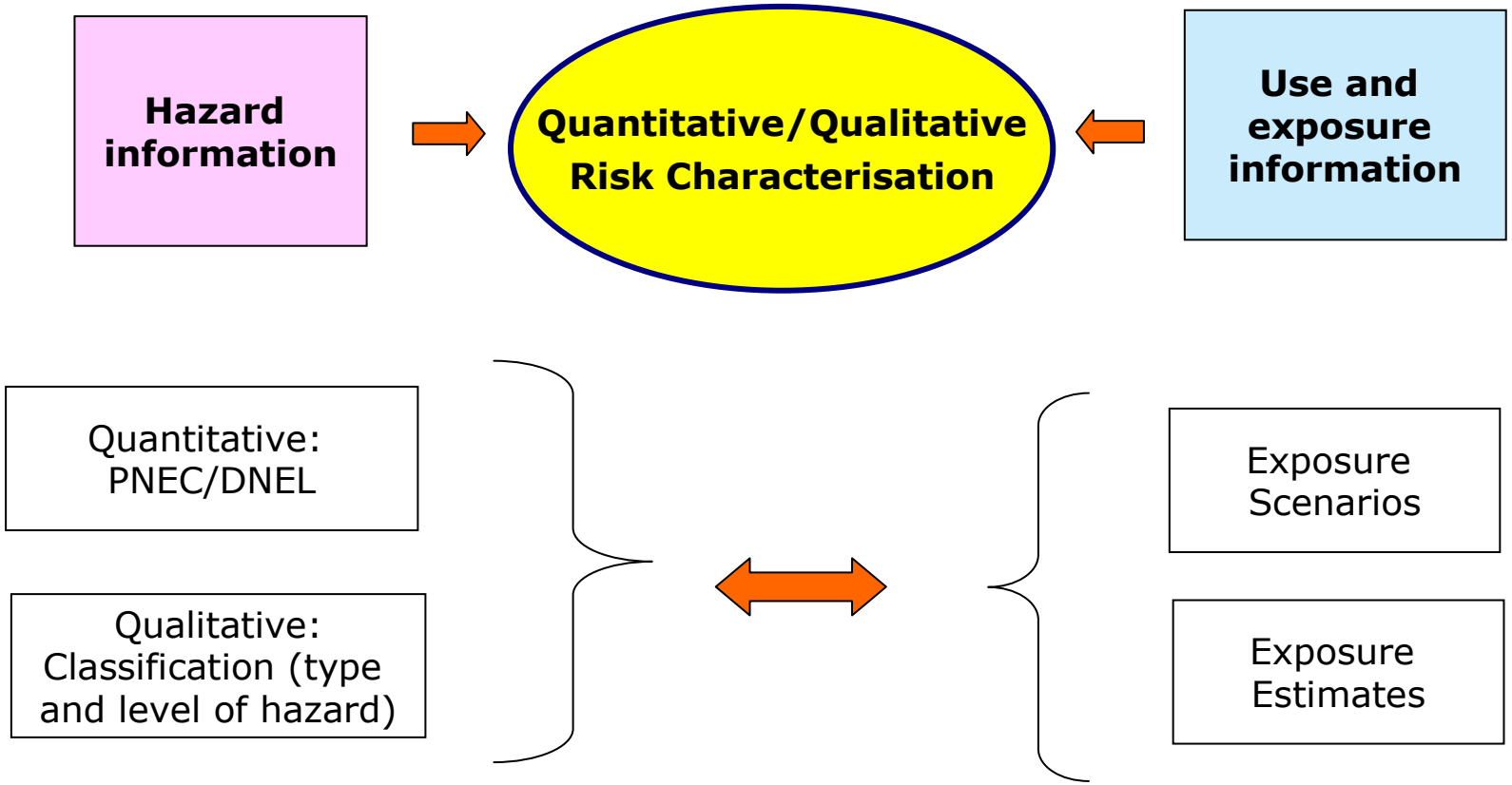
- Submit CSR to the authorities (ECHA and MS)
  - to justify i) additional testing of vertebrates or ii) the omission of information requirements
  - as the source of information for regulatory processes, e.g. selecting substances for substance evaluation or for candidate list authorisation
  - to enable spot checks on dossier compliance

Assessment work flow

Assessment Workflow



Risk Characterisation (RC)



Assessment types

Assessment Type	Exposure Scenario (conditions of use)	Exposure estimation	Risk characterisation
Quantitative	yes	yes	RCR < 1
Semi-quantitative	yes	yes	exposure < threshold + additional argument
Qualitative	yes	may be required to demonstrate minimisation	control strategy corresponds to hazard

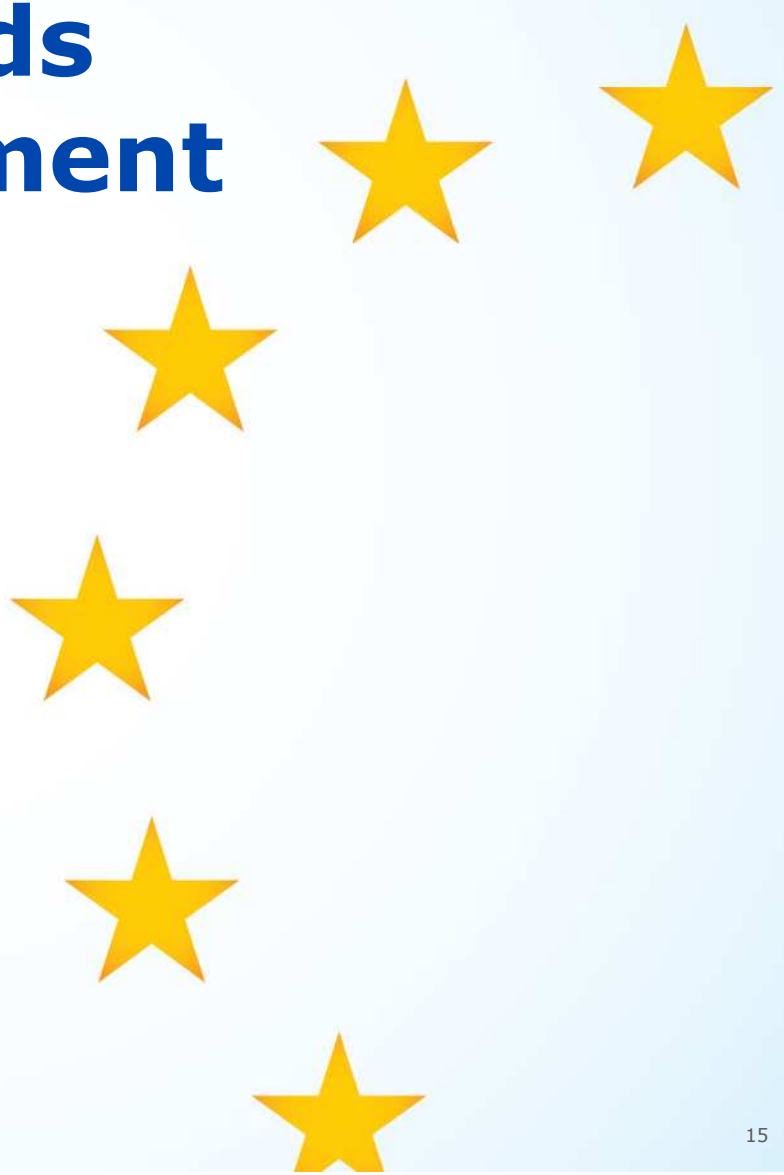
Mandatory elements of the CSA/CSR (1)

- Assessment of intrinsic properties/hazards
- physicochemical properties, “environmental fate” properties
- Human health hazard
  - 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 on predators (aquatic and terrestrial)

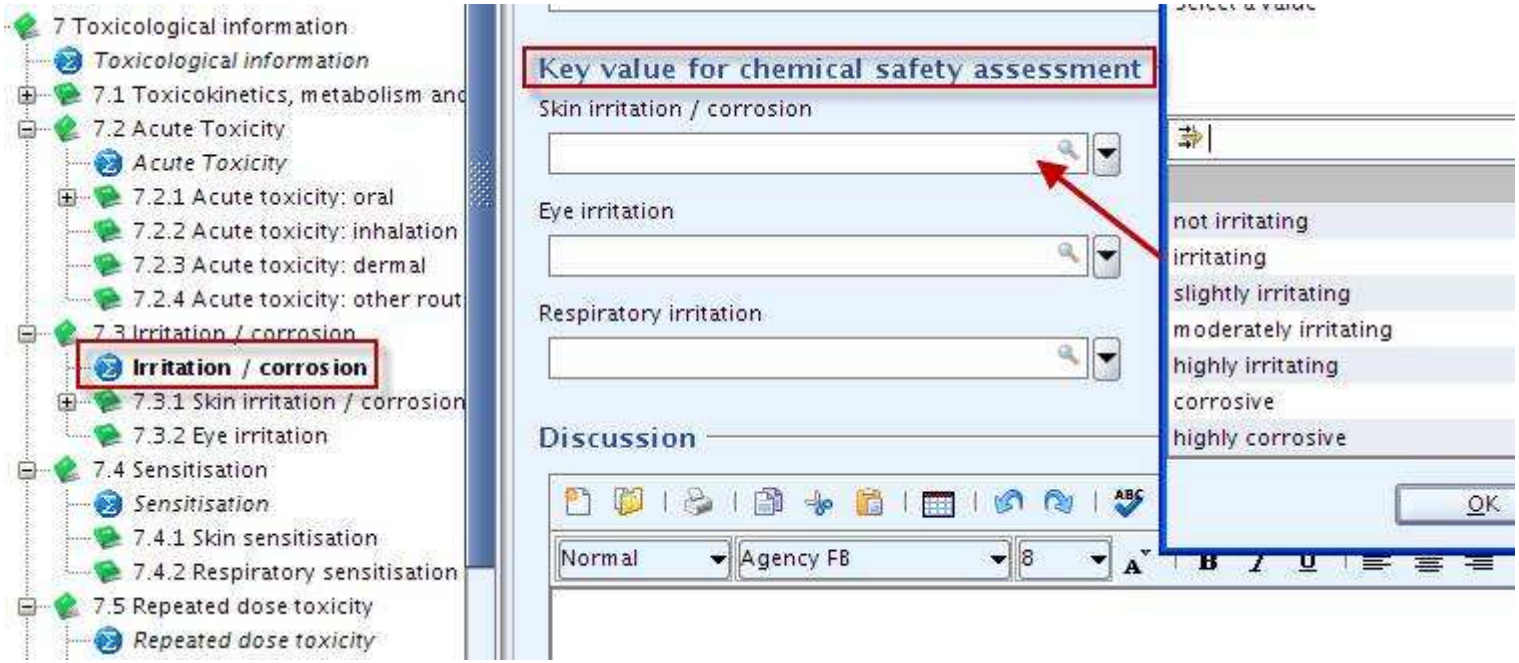
Mandatory elements of the CSA/CSR (2)

- 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.

From study records to hazard assessment conclusions
- Examples -



Hazard assessment information in IUCLID



Example (1): Overview on endpoint summaries in section 5.11 of the CSR

Source: IUCLID 5.4, section 7

Endpoint	Route	Dose descriptor or qualitative effect characterisation; test type;
Acute toxicity	Oral	No adverse effect observed
Acute toxicity	Dermal	No adverse effect observed
Acute toxicity	inhalation	No adverse effect observed
Irritation / Corrosivity	Skin	irritating
Irritation / Corrosivity	Eye	irritating
Irritation / Corrosivity	respiratory	No study available
Sensitisation	Skin	No adverse effect observed (not sensitising)
Repeated dose toxicity	Oral	NOAEL: 700 mg/kg bw/day (subacute; rat)
Repeated dose toxicity	Dermal	No study available
Repeated dose toxicity:	inhalation	No study available
Mutagenicity		No adverse effect observed (negative)
Reproductive toxicity: fertility impairment	Oral	No adverse effect observed

Example (2): Hazard conclusions in section 5.11 of the CSR

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

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

Remark: Table expected for workers and for general population

Example (3): Scope of exposure assessment for human health in section 9.02

Route	Type of effect	Type of risk characterisation	Hazard conclusion (see section 5.11)
Inhalation	Systemic effect - Long-term	Quantitative	DNEL = 24.7 mg/m3
	Systemic effects -Acute	Not required	No hazard identified
	Local effects - Long-term	Qualitative	Hazard unknown (no further information required)
	Local effects - Acute	Qualitative	Hazard unknown (no further information required))
Dermal	Systemic effect - Long-term	Quantitative	DNEL = 7 mg/kg bw /day
	Systemic effects -Acute -	Not required	No hazard identified
	Local effects - Long-term	Qualitative	Low hazard
	Local effects - Acute	Qualitative	Low hazard
Eyes	Local effects –Acute	Qualitative	Low hazard

Example (4): Explanation of DNEL derivation in section 5.11 of the CSR

		Assessment factors for DNEL derivation
Inhalation (Long-term - systemic effects)	**DNEL derivation method:** ECHA REACh guidance **Dose descriptor starting point** NOAEC = 617 mg/m3	AF for difference in duration of exposure: 2 (*DNEL is based on an oral 90 day study*) AF for interspecie differences: 1 (*AF not used for inhalation route*) AF for other interspecie differences: 2.5 AF for intra species differences:5 (workers) Overall Assessment Factor: 25
Dermal (Long-term - systemic effects)	**DNEL derivation method:** ECHA REACh guidance **Dose descriptor starting point** NOAEL = 700 mg/kg bw/day	AF for difference in duration of exposure: 2 (*based on an oral 90 day study*) AF for interspecie differences: 4 (*experimental animal was rat*) AF for other interspecie differences: 2.5 AF for intra species differences:5 (*this is for workers*) AF for remaining uncertainties: Overall Assessment Factor: 100

Explanation for route to route extrapolation: …….

Conditions of use Examples

Conditions of use (worker)

- frequency and duration of exposure
- physical state of product, e.g. dustiness, viscosity
- concentration of substance in a preparation
- amount used at a workplace
- type of process carried out with the substance
- level of containment or local exhaust ventilation
- general ventilation and room volume before inhalation
- personal respiratory protection
- skin contact area and personal skin protection

Conditions of use (environment)

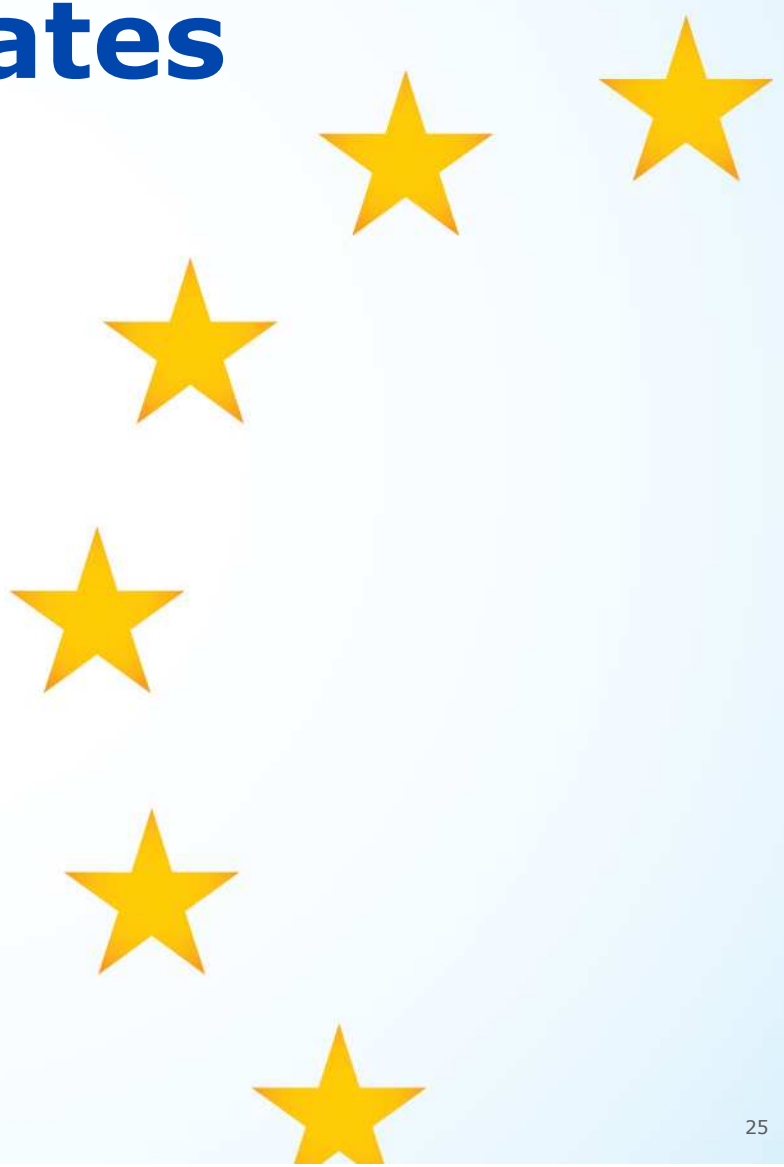
- Daily and annual tonnage used at generic sites
- Daily and annual tonnage in wide disperse use
- Process conditions driving the initial release
- Onsite risk management measures (with certain effectiveness)
- Flow rate of local sewage treatment plant and river flow rate.

Conditions of use (consumer)

- Type of product
- Concentration of substance in the product
- Number of events (product uses) per day
- Amount of product per event
- Duration of exposure
- Room size and ventilation conditions
- Skin surface exposed
- Relevance of oral contact

Conditions are often inherently related to the product type; based on habits and practices (if analysed) for many product types defaults are available

Exposure estimates

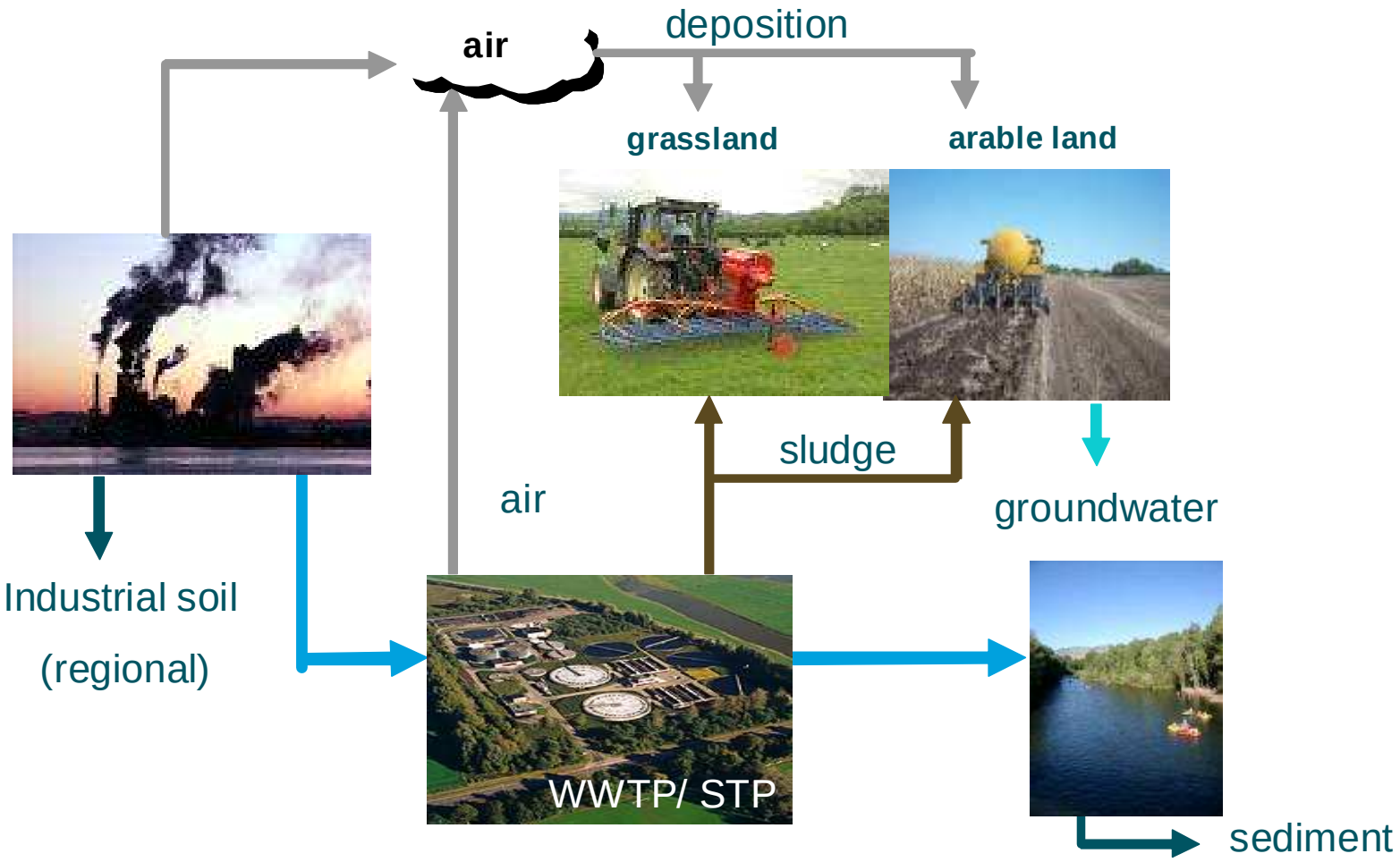


Human exposure

Exposure to be measured or modelled

Environmental release and exposure

Local releases from industrial settings



Exposure estimates can be derived from…

- Tier 1 tools
- Higher Tier tools
- Measured data

Challenges:

- Carry out measurements representing relevant conditions of use
- Express input parameters of existing Tier 1 tools as a condition of use that can be communicated as advice to downstream users
- Identify conditions of use corresponding to available measured data sets

Output: Exposure Scenarios

Initial Exposure Scenarios

- Short title
- Current operational conditions
- Current risk management measures

Assessment

Final Exposure Scenarios

- Short title
- Operational conditions (OC)
- Risk management measures (RMM)

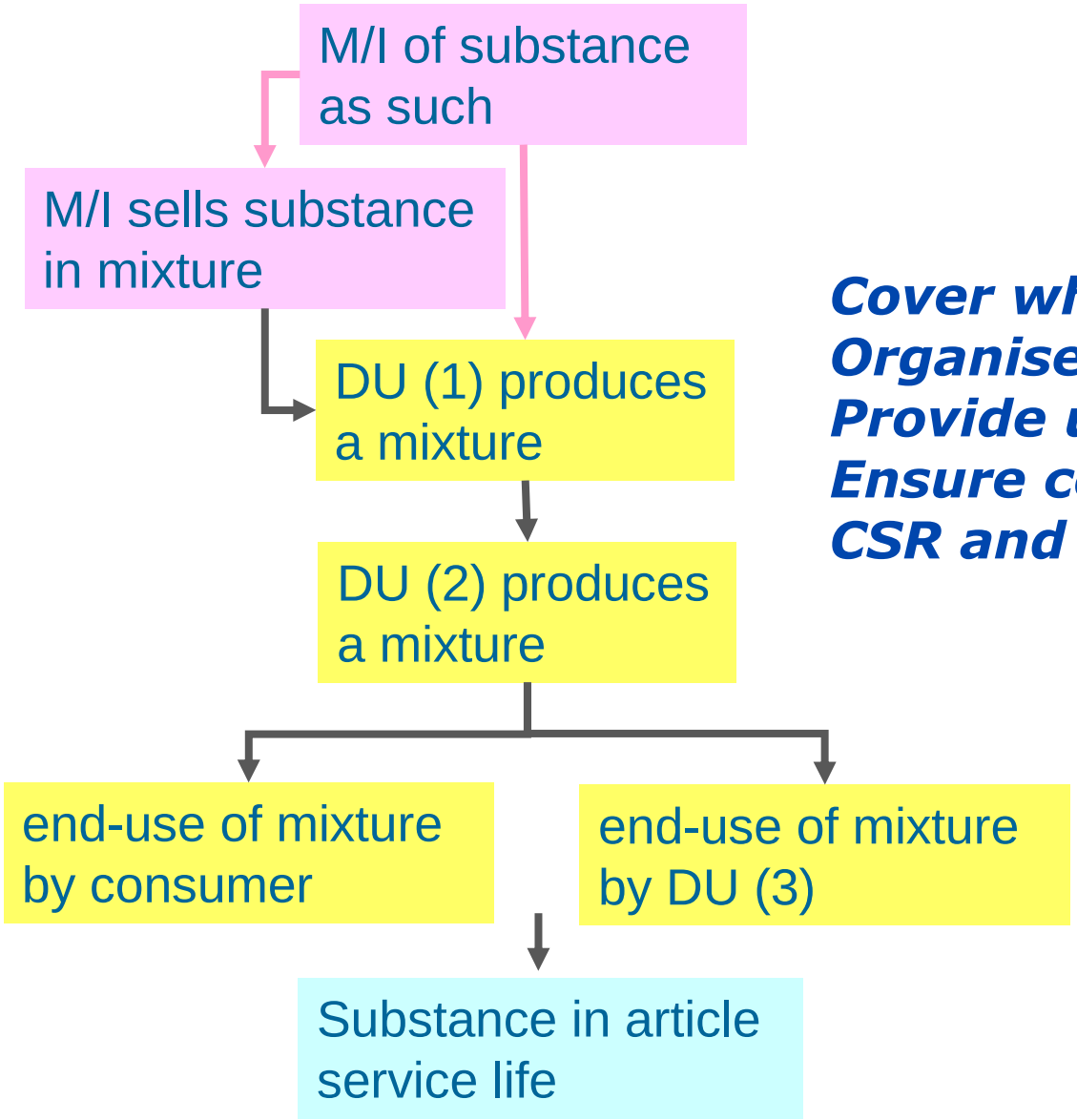
If risk not demonstrated to be controlled

Decisions by M/I

- Refine hazard assessment
- Refine exposure estimate
- More stringent RMM or OC
- Advise against use (if control of risk cant be demonstrated)

Challenges

Some Challenges



Cover whole life cycle!
Organise communication!
Provide useful advice!
Ensure consistency between CSR and SDSs!

Thank you.

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