Complex inorganic UVCBs Chemical Safety Assessment

ECHA

22 January 2014

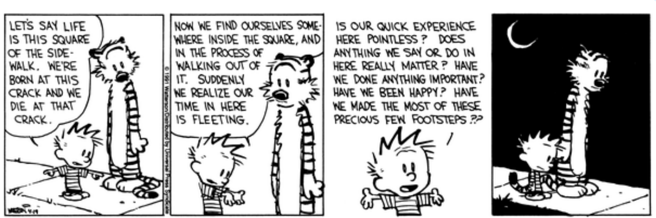
Outline

- Introduction: setting the scene for inorganic UVCBs CSA
- Substance composition, SID, Classification:
  - Main principles
  - Illustration pilot case
- Hazard assessment: environment, human health
  - Main principles
  - Illustration pilot case

Outline

- Exposure assessment: environment, human health
  - Main principles
  - Illustration pilot case
- Risk Characterisation: environment, human health
  - Main principles
  - Illustration pilot case
- Uncertainty analysis
- Combined toxicity

Introduction



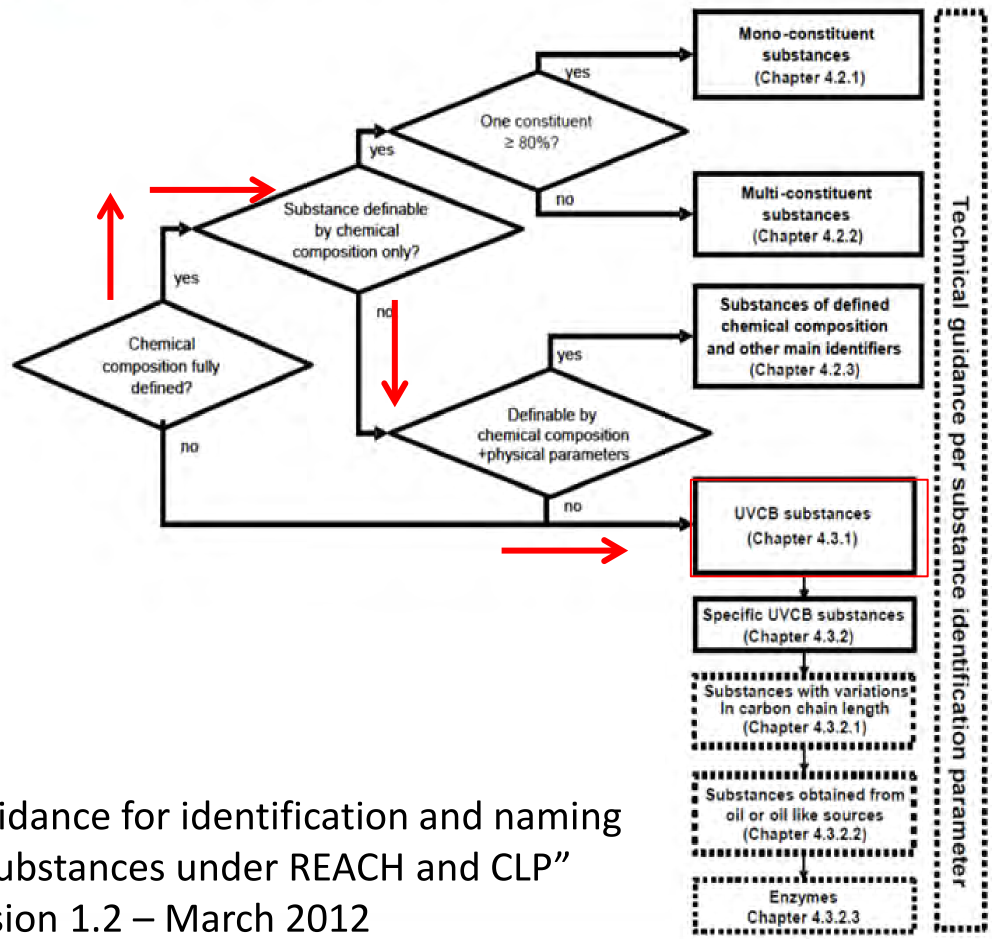
Setting the scene (1)

- Important aspects to consider in the inorganic UVCBs' CSA:
  - ➢ inorganic UVCBs are characterised by **varying** concentrations of a **number** of constituents (metals, metal compounds and/or minerals)
  - ➢ an inorganic UVCB may have different physical forms

Setting the scene (2)

- The current focus of our UVCBs assessment is on intermediates, as a number of substances were identified in 2010 - for <u>registration/data sharing</u> purposes- as:
  - Intermediates assessed compliant with definition and 2008 SCC guidance
  - UVCBs for reasons of variable composition

Figure 4.1:Key to guidance document chapters and appendices for appropriate guidance for various types of substances



"Guidance for identification and naming of substances under REACH and CLP"
Version 1.2 – March 2012

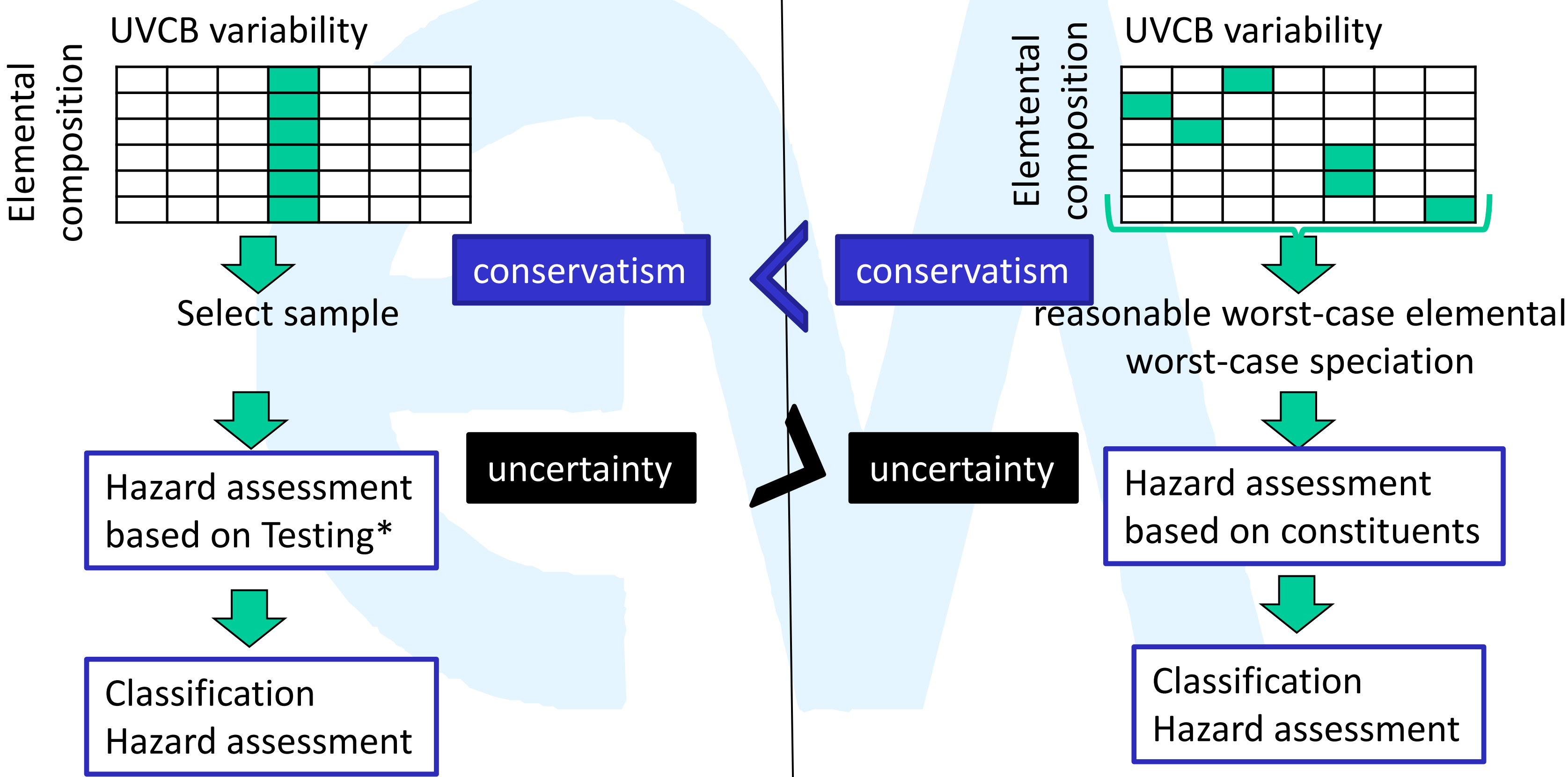
Setting the scene (3)

- The dossiers that will be submitted in 2014 are ‘upgraded’ (full article 10 dossiers) for intermediates

- Our objectives:
  - **Be compliant** with Registration requirements but also with Evaluation/Enforcement needs (quality, transparency)
  - **Methodology, assumptions, justifications, limitations made clear in the reporting**
    - Special focus on the use of information on UVCB constituents

Setting the scene (4)

- Standard substance approach
- Inorganic UVCB approach



* Existing data are generally not available

Setting the scene (5)

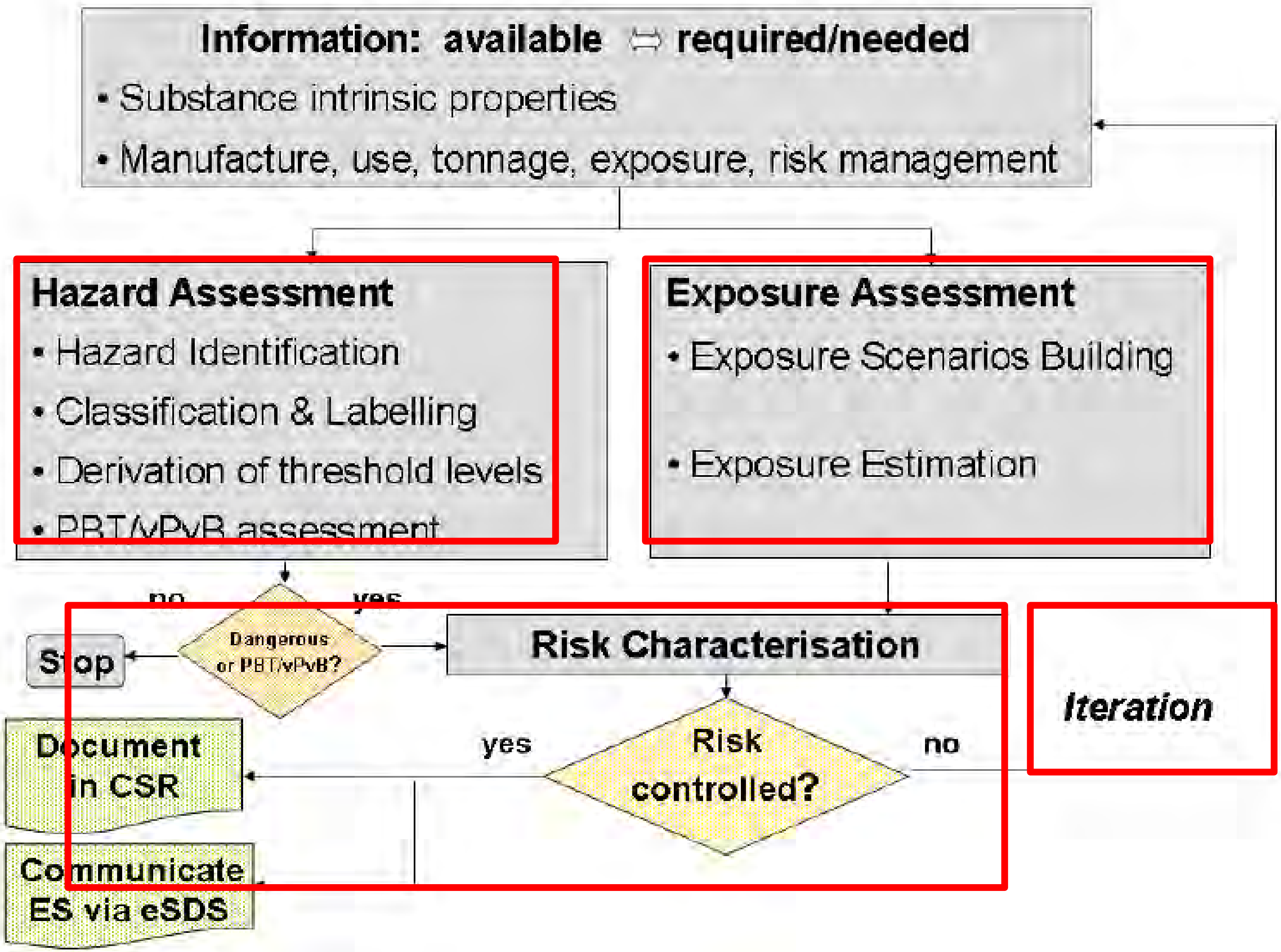
- For inorganic UVCBs, **toxicity testing** is usually **not possible**:
  - ➢ how to identify a representative sample for testing considering the "spatial and temporal variability" of the substance?
  - ➢ taking a worst-case for all constituents of the inorganic UVCB is not realistic and not in line with the industrial processes used (i.e. maximising the content of one component while simultaneously decrease the content of other components)

- An **alternative conservative strategy** is therefore supported:
  - ➢ UVCBs are assessed based on toxicological and ecotoxicological information of their constituents
  - ➢ Constituents' variability is taken into account and reasonable worst cases are selected for the assessment
  - ➢ To avoid animal testing

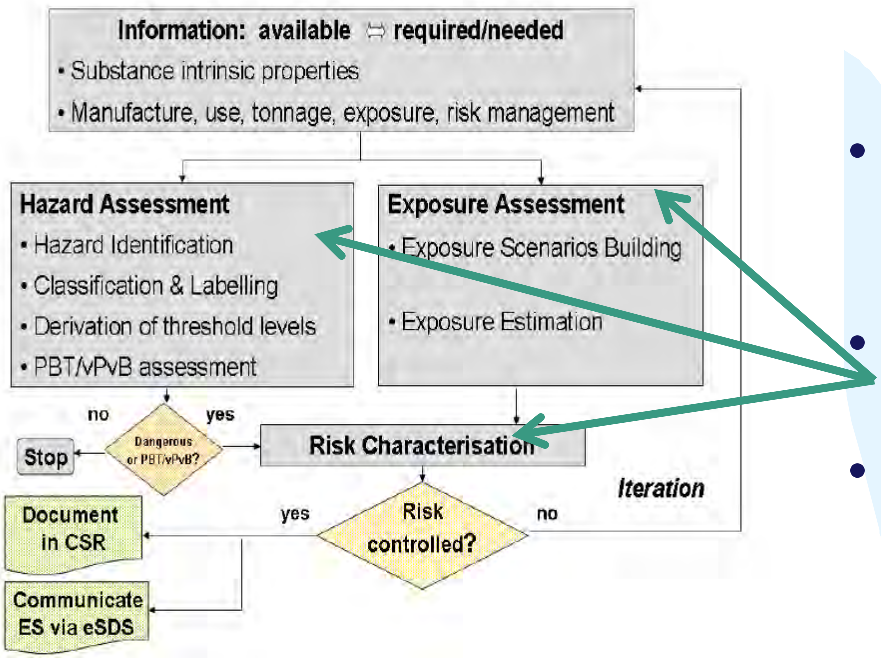
A last re-cap on the U and the V of the inorganic UVCB before going to the CSA

	UVCB: unknown	UVCB: variable	Analytical testing
Elemental composition	Known	Large variability	By each registrant
Speciation/ mineralogical composition	Largely known, some unknown	No to minor variability for enriched UVCBs and sometimes large variability for side-product UVCBs	By consortium

Standard Chemical Safety Assessment flow



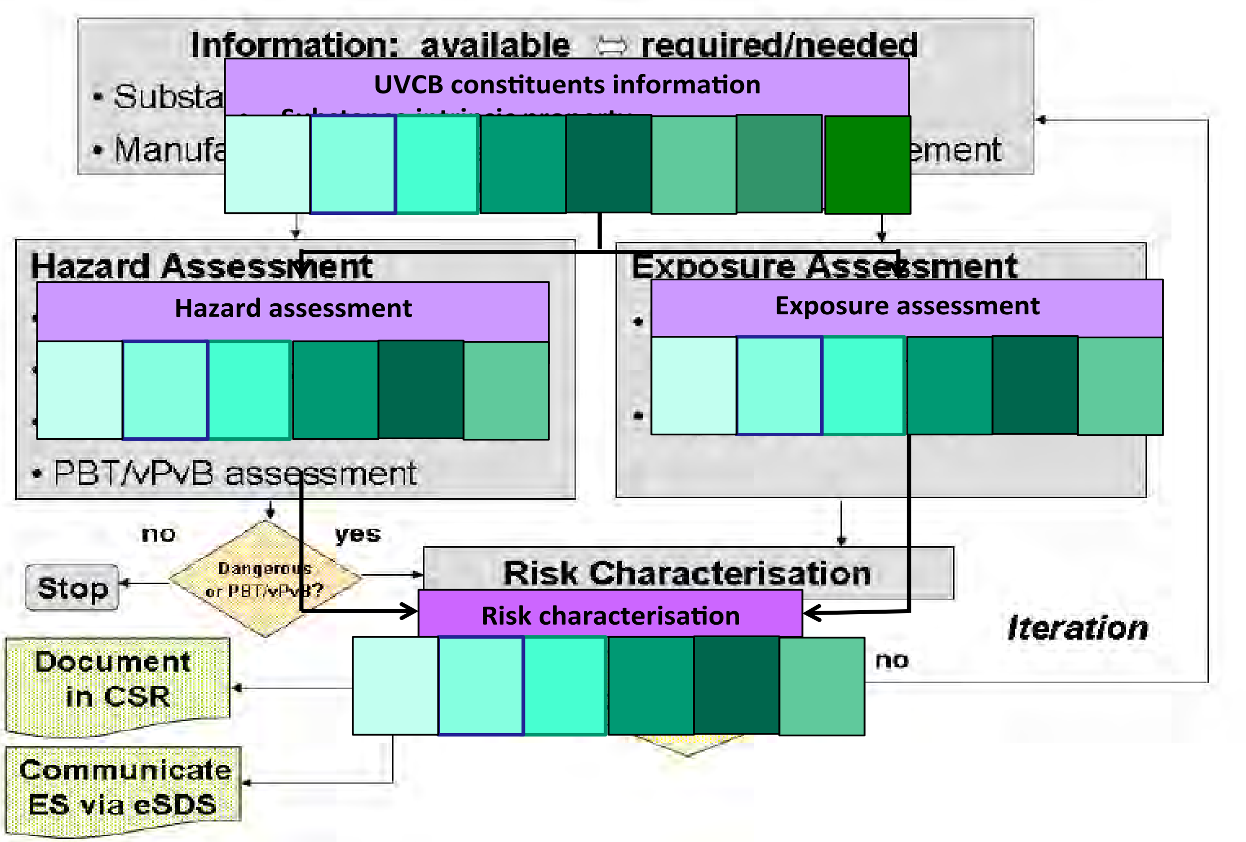
Chemical Safety Assessment flow: amendments for inorganic UVCBs



- Basic assumption: the **toxicity** of the inorganic UVCB is **driven by its constituents**
- **Number of constituents** that are relevant for hazard and/or exposure assessment
- **Varying concentrations** of constituents
- **Physical form/appearance** of the inorganic UVCB may vary during the conducted processes
- **Metal species *present* in the inorganic UVCB often differs from species *released/emitted***

Chemicals Safety Assessment flow

Multi-constituents CSA



To summarise

Since inorganic UVCBs are characterized by:

- **varying concentrations** of a number of constituents (i.e. chemical elements), with their corresponding species
- Often varying physical forms of the substance during manufacture/processing

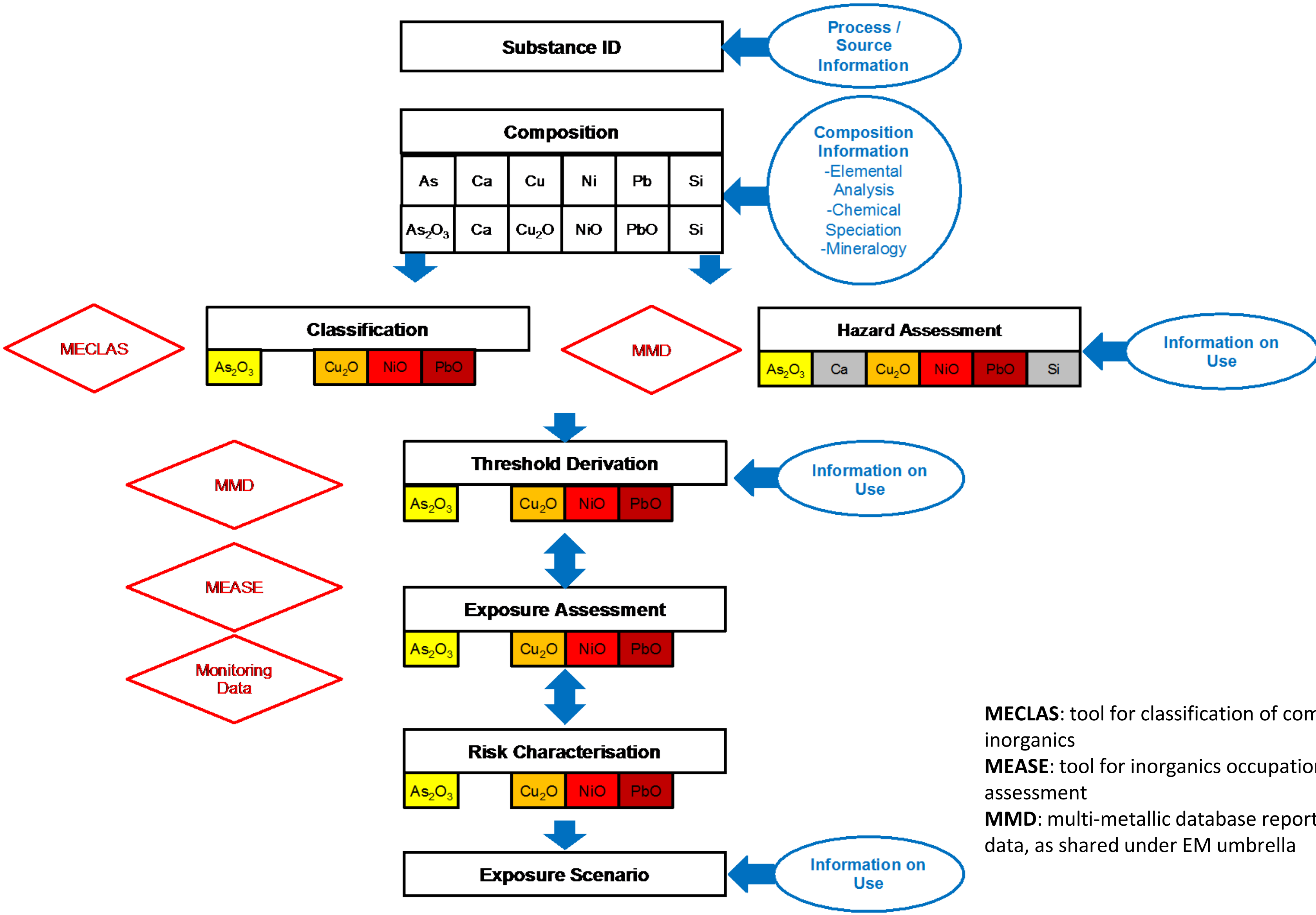
Assessing inorganic UVCBs shall:

- address **variability** in composition and (un)known **speciation**
- address inorganic UVCBs characteristics over the complete assessment (relevant lifecycle steps: if the UVCB is used as an intermediate exclusively in industrial settings, the assessment will focus on workers and the different environmental compartments where emissions occur)

⇩

Amended CSA flow

Amended CSA flow for inorganic UVCBs



MECLAS: tool for classification of complex inorganics
MEASE: tool for inorganics occupational assessment
MMD: multi-metallic database reporting hazard data, as shared under EM umbrella

Illustration with pilot case (1)

- **Pilot cases** are under development, based i.a. on the discussions with ECHA:
  - May 2012: generic discussion
  - January 2013: SID
  - October 2013: classification (MECLAS)

- The developed pilot cases may differ in their complexity due to e.g. the number of constituents of the UVCB but **the overall approach remains the same**

Illustration with pilot case (2)

- Pilot cases:
  - ➢ Cu slime
  - ➢ PM Refinable
  - ➢ Pb dross

- Today, the case of **copper slime** will be used to illustrate the CSA flow

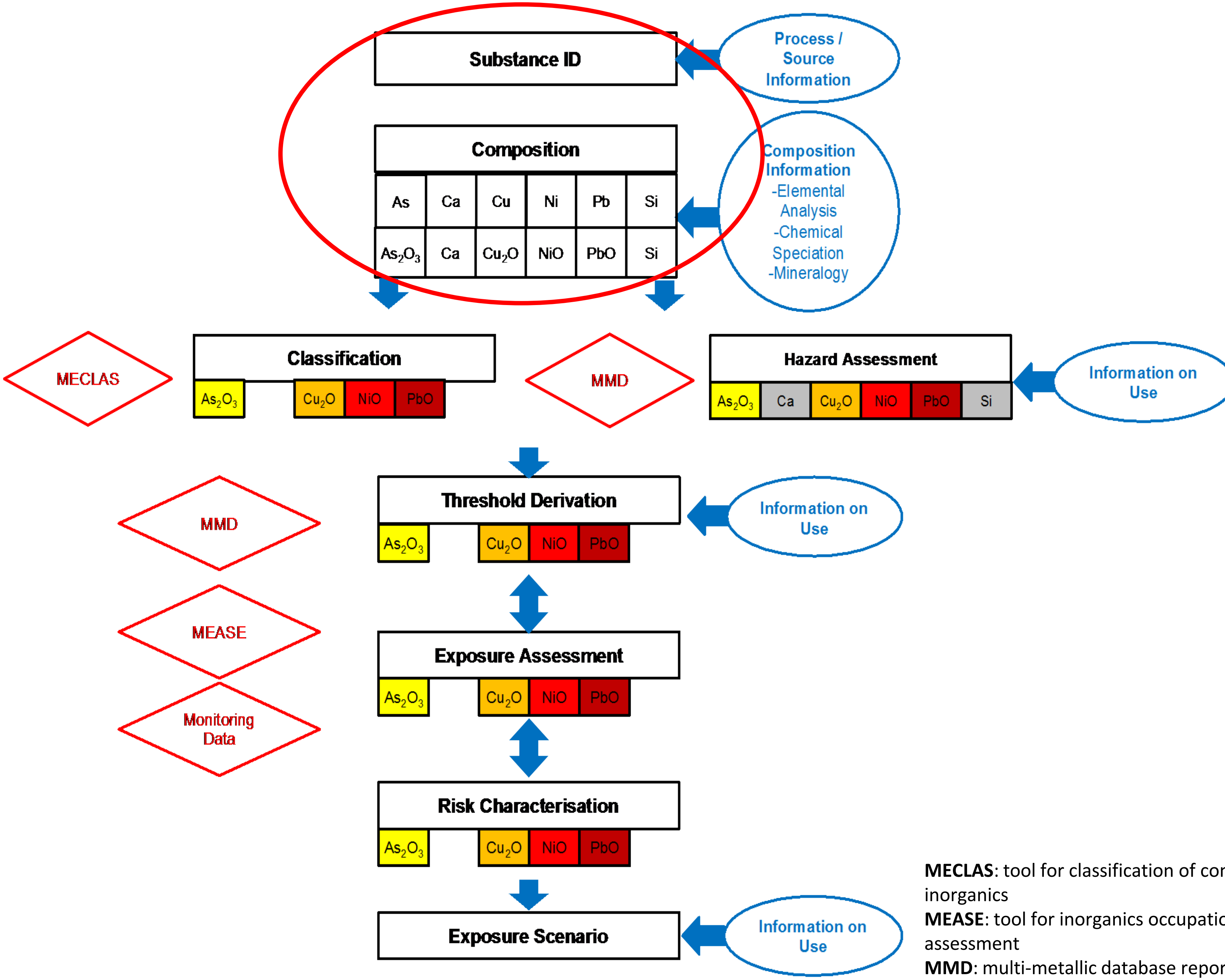
- The proposed CSA flow allows us to:
  - ➢ move from SID to risk characterisation consistently across inorganic UVCBs

  and

  - ➢ gives the possibility to bring in further refinements depending on data availability/needs/complexity

Substance ID

- Main principles
- Illustration Cu slime case



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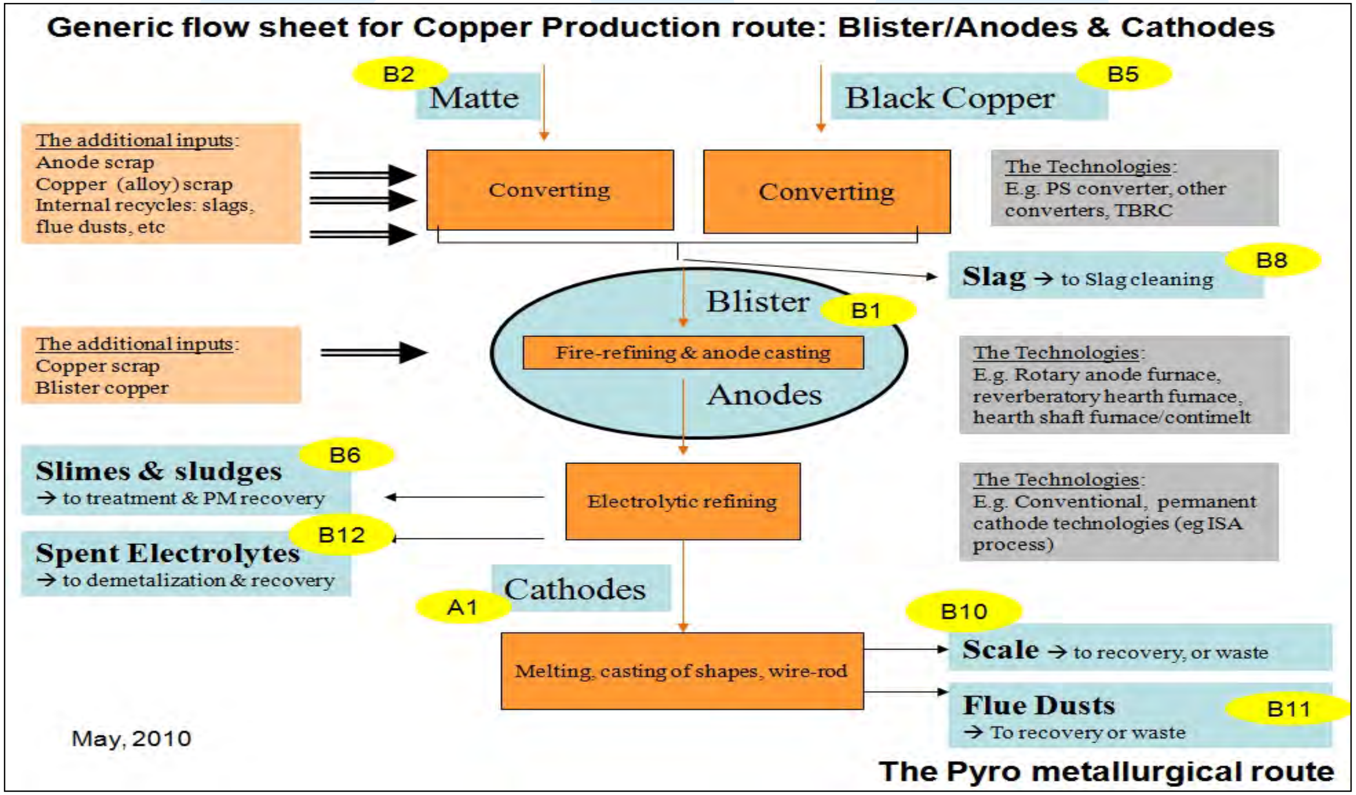
SID

- Main principles :
  - ➢ The (updated) EC description is the skeleton of the UVCB Identity
  - ➢ SID of the UVCB is based on
    - consideration across all manufacturers, over several years
    - chemical elemental composition, with additional information on mineralogy, source & process, etc
  - ➢ Information on process, on feedings/sources, etc is used to address the various levels of variability
  - ➢ Reporting: The information is reported in CSR chapter 1/IUCLID section 1.1, where both LE specific and Generic composition are reported

Illustration: Cu slime case

- Slimes & sludges come from copper electrolysis processes
- It is a complex combination of insoluble compounds produced by precipitation during the copper electrolytic refining or winning processes



How is the pilot case characterised in terms of U and V?

	UVCB: unknown	UVCB: variable	Analytical testing
Elemental composition	Known	Large variability	By each registrant
Speciation/ mineralogical composition	Largely known, some unknown	No to minor variability for enriched UVCBs and sometimes large variability for side-product UVCBs	By consortium

Illustration: Cu slime case

- Important to know:
  - It consists typically of **various metals** (such as e.g. precious metals, copper, antimony, tin, selenium, tellurium, arsenic, lead and nickel), as well as their oxides and/or sulfates.
  - Metal constituents are built in into **complex mineralogical structures** consisting mainly of (more noble) **metal sulphates/oxides** that settled down and precipitated during electro refining

Illustration: Cu slime case
Composition

- **Legal entity (LE) specific composition = across year(s)**, for each elemental constituent:
  - ➢ LE Typical concentration = +/- average concentration
  - ➢ LE Minimum concentration
  - ➢ LE Maximum concentration (without "outliers")

- **Generic composition = across industry** (used to derive verified classification), for each elemental constituent:
  - ➢ Typical concentration = average of LE typicals
  - ➢ Minimum concentration = minimum of LE typicals
  - ➢ Maximum concentration = maximum of LE typicals or (generic/specific) concentration limit

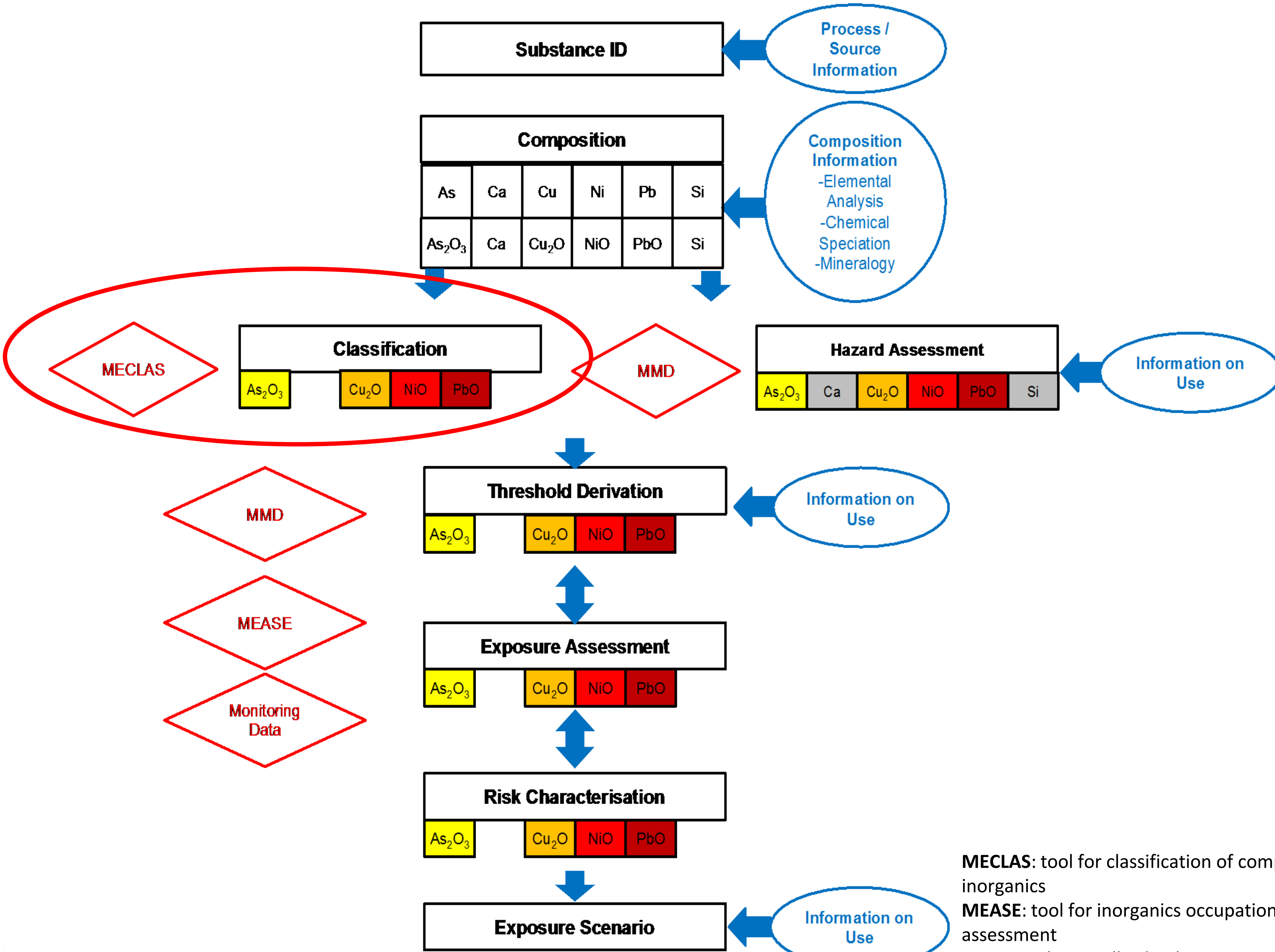
Illustration: Cu slime case

Grade 1: generic composition

Constituent	Typical concentration	Concentration range	Remarks
copper EC no.: 231-159-6	<= 8.0 % (w/w)	>= 0.0 — <= 73.0 % (w/w)	refers to % element. Cu is present as CuSOx (sulfates)
silver EC no.: 231-131-3	<= 16.5 % (w/w)	>= 0.003 — <= 40.4 % (w/w)	refers to % element. Ag is present as Ag metal (only minor % is in inclusions)
arsenic EC no.: 231-148-6	ca. 2.1 % (w/w)	>= 0.0 — <= 4.0 % (w/w)	refers to % element. As is present mainly as As2O3
nickel EC no.: 231-111-4	<= 1.0 % (w/w)	> 0.37 — <= 4.0 % (w/w)	refers to % element. Ni is present as (intermetallic) sulphates
lead EC no.: 231-100-4	<= 20.5 % (w/w)	>= 0.1 — <= 46.0 % (w/w)	refers to % element. Pb is present as sulphates
cobalt EC no.: 231-158-0	<= 0.003 % (w/w)	>= 0.0 — <= 0.02 % (w/w)	refers to % element. Co is typically present as (intermetallic) sulphates
zinc EC no.: 231-175-3	<= 0.7 % (w/w)	>= 0.0 — <= 3.7 % (w/w)	refers to % element. unknown mineralogy/species (WC ZnSO4 assumed)
etc			

Classification

- Main principles
- Illustration Cu slime case



MECLAS: tool for classification of complex inorganics
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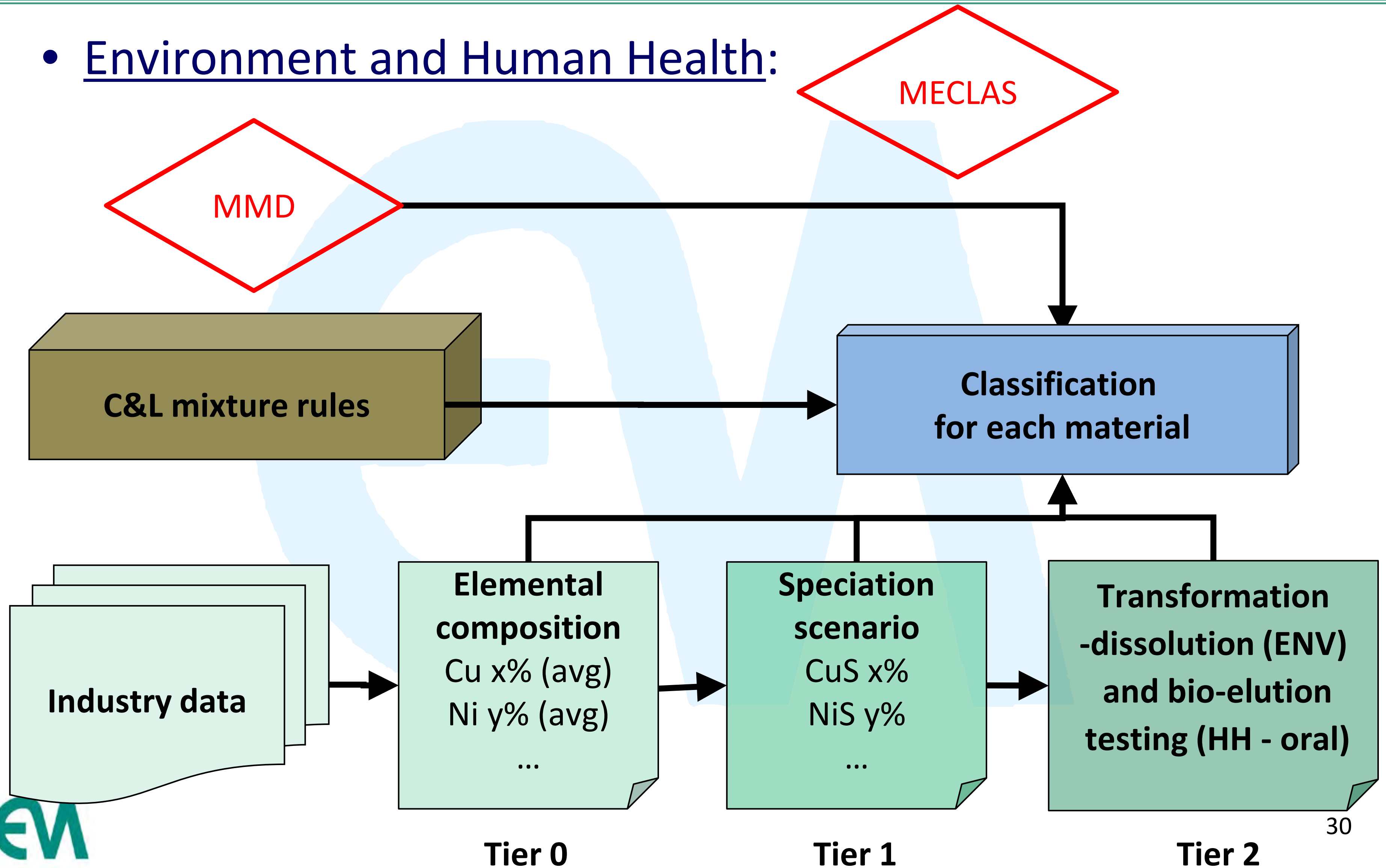
Classification: main principles

Classification for Physical, Environmental, Human Health hazards:

- Phys-chem properties: following standard information requirements:
  - Tests conducted on the UVCB
  - Tested several samples for physchem properties across industry
  - Column 2 waiving statements where relevant (not UVCB specific)
  - Reported in CSR chapter 1.3 and IUCLID section 4

Classification: main principles

- <u>Environment and Human Health</u>:



Classification: main principles

- Environment and Human Health:
  - ➢ Link to SID: input values used: **Generic composition = across industry**, for each elemental constituent:
    - Typical concentration = average of LE typicals
    - Minimum concentration = minimum of LE typicals
    - Maximum concentration = maximum of LE typicals or concentration limit → used for classification
    - Maximum of LE maxima → sensitivity analysis
  - ➢ Report in CSR chapter 3 and IUCLID section 2

How are U and V addressed in classification?

Elemental constituent	Speciation constituent	Variability
Known (close to 100%) but variable	Largely known, some unknown	Low to high variability on elemental concentrations No or little variability on speciation of enriched UVCB Medium variability on speciation of side-product UVCB

Solutions:

If unknown, species with worst-case classification is selected

Maximum of the typical of elemental concentrations (and worst-case species)

Illustration: Cu slime case

Grade 1: generic composition

Constituent	Typical concentration	Concentration range	Remarks
copper EC no.: 231-159-6	<= 8.0 % (w/w)	>= 0.0 — <= 73.0 % (w/w)	refers to % element. Cu is present as CuSOx (sulfates)
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etc			

Illustration: Cu slime case
Example on Pb constituent in Cu slime

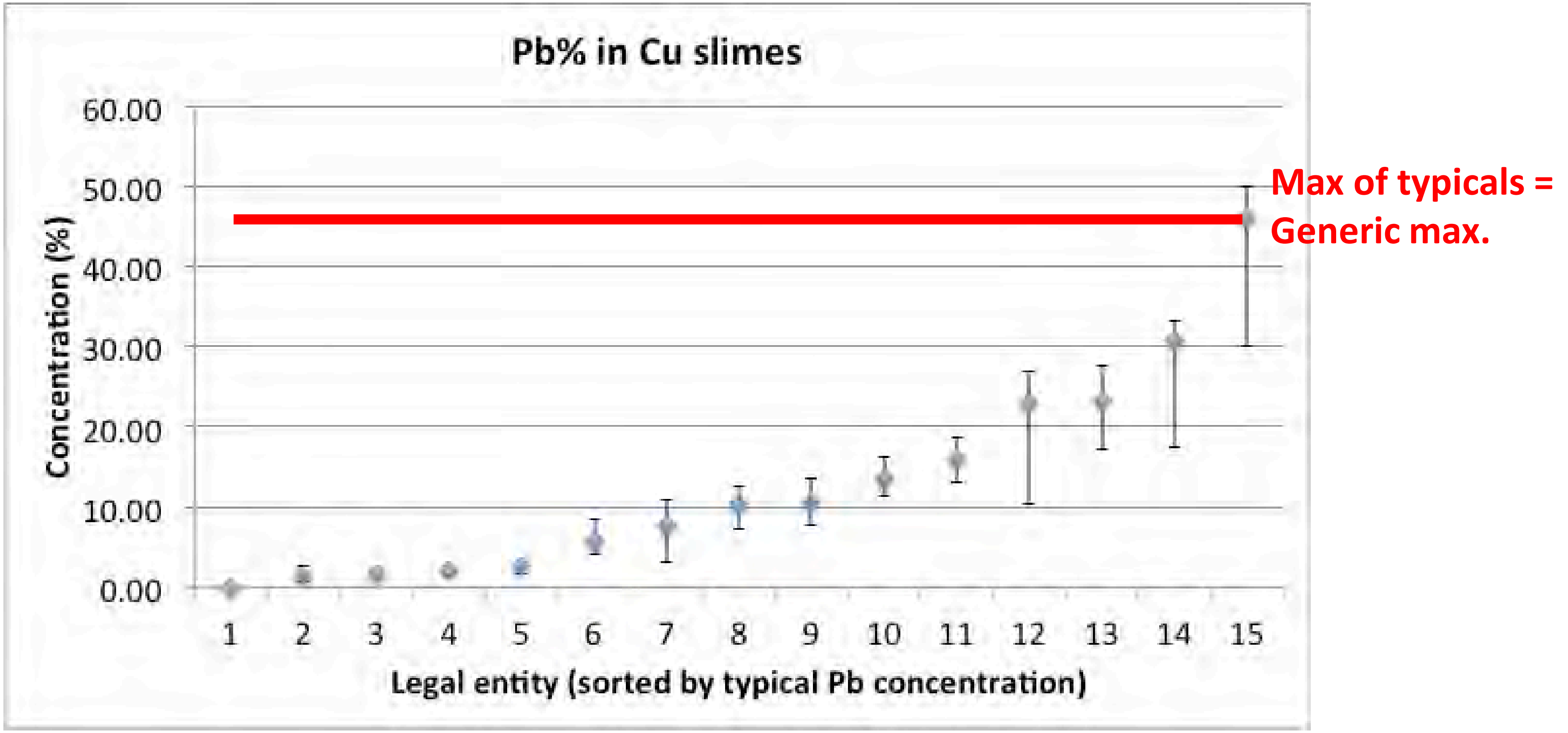


Illustration: Cu slime case
Example on As constituent in Cu slime

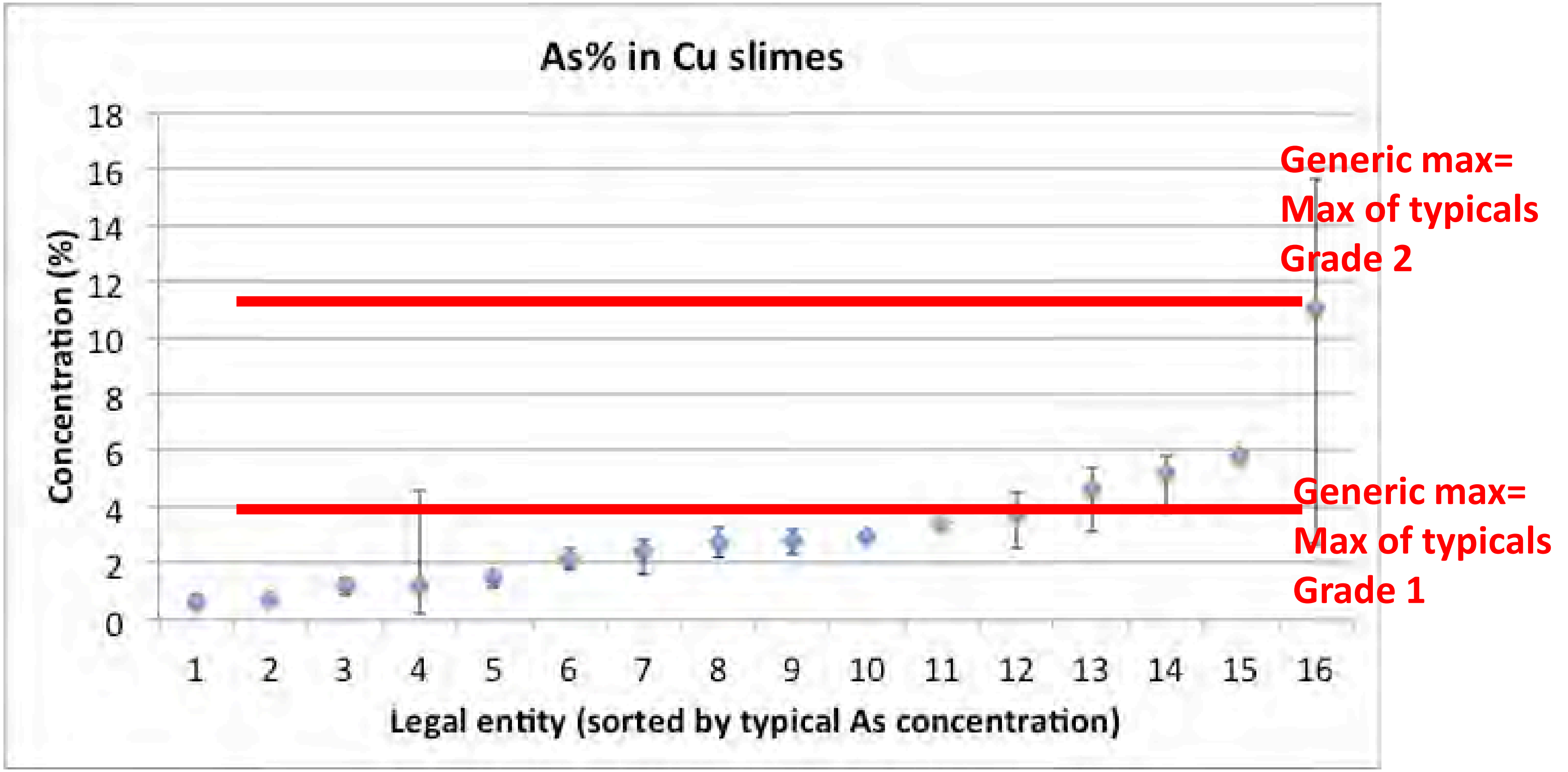


Illustration: Cu slime case
Constituent summary for classification

UVCB constituent		Variabiliy of elemental composition	Classification according each relevant endpoint
Element	Speciation		
Cu	$CuSO_4$, see IUCLID/CSR section 1.2 composition	Maximum of typicals	Harmonised and worse self-classification of the species, see MECLAS report in CSR Annex I
Ag	Ag (powder), see IUCLID/CSR section 1.2 composition	Maximum of typicals	Self-classification of the species, see MECLAS report in CSR Annex I
Ni	$NiSO_4$, see IUCLID/CSR section 1.2 composition	Maximum of typicals	Harmonised classification of the species, see MECLAS report in CSR Annex I
Pb	Pb compounds, see IUCLID/CSR section 1.2 composition	Maximum of typicals	Harmonised and worse self-classification of the species, see MECLAS report in CSR Annex I
Co	$CoSO_4$, see IUCLID/CSR section 1.2 composition	Maximum of typicals	Harmonised classification of the species, see MECLAS report in CSR Annex I
Zn	$ZnSO_4$, see IUCLID/CSR section 1.2 composition	Maximum of typicals	Harmonised classification of the species, see MECLAS report in CSR Annex I
Sn	Sn compounds, see IUCLID/CSR section 1.2 composition	Maximum of typicals	Self-classification of the species, see MECLAS report in CSR Annex I
Sb	Sb_2O_3, see IUCLID/CSR section 1.2 composition	Maximum of typicals	Harmonised classification of the species, see MECLAS report in CSR Annex I
etc			

Illustration: Cu slime case
MECLAS in-between calculations

Classification Entry	Concentration (%)	Classification Acute Toxicity - oral	Acute toxicity oral: Conc/ATEi
Mg/Mg compounds	0.009		
CoSO4	0.02		4E-005
ZnSO4	9.03753533191	Cat. 4; H302	0.0180750706638
Cl / Cl compounds	3.91		
Se	13.8	Cat. 3; H301	0.138
Sb2O3	12.9286448752		
NiSO4	10.546675072	Cat. 4; H302	0.021093350144
lead compounds with the exception of those specified elsewhere in Annex VI	46	Cat. 4; H302	0.092
MnSO4	0.0109941388474		
inorganic compounds of mercury with the exception of mercuric sulphide and those specified elsewhere in Annex VI	2E-005		4E-00
CuSO4	183.352390394	Cat. 4; H302	0.366704780789
CdSO4	0.000927279601459		9.27279601459E-006

etc for other endpoints

Improved MECLAS output sheet
Based on ECHA recommendation
Last classification meeting

etc for other speciations

Illustration: Cu slime case MECLAS output

CLP

Signal word: Danger

CLP classification of generic grades

Endpoint	Grade 1 Classification	Grade 2 Classification	Major driver
Acute toxicity-oral	Cat. 3; H301	Cat. 2; H300	$ZnSO_4$,Se,$NiSO_4$,lead compounds with the exception of those specified elsewhere in Annex VI,$CuSO_4$,As_2O_3 / AsO_3,Arsenic compounds, with the exception of those specified elsewhere in Annex VI,As,$FeSO_4$
Acute toxicity-dermal	Not classified	Not classified	/
Acute toxicity-inhalation	Cat. 4; H332	Cat. 4; H332	Se,$NiSO_4$,lead compounds with the exception of those specified elsewhere in Annex VI,Arsenic compounds, with the exception of those specified elsewhere in Annex VI,As
Skin corrosion/irritation	Cat. 2; H315	Cat. 1B; H314	As_2O_3 / AsO_3
Serious eye damage/eye irritation	Cat. 1; H318	Cat. 1; H318	$ZnSO_4$,CaO,As_2O_3 / AsO_3
Respiratory or skin sensitisation	Resp./Skin Sens. Cat. 1; H334/H317	Resp./Skin Sens. Cat. 1; H334/H317	$NiSO_4$
Germ cell mutagenicity	Cat. 2; H341	Cat. 2; H341	$NiSO_4$
Carcinogenicity	Cat. 1A; H350	Cat. 1A; H350	As_2O_3 / AsO_3
Reproductive toxicity	Cat. 1A; H360	Cat. 1A; H360	lead compounds with the exception of those specified elsewhere in Annex VI
Specific target organ toxicity - single exposure	Not classified	Not classified	/
Specific target organ toxicity - repeated exposure	Cat. 1; H372	Cat. 1; H372	lead compounds with the exception of those specified elsewhere in this Annex
Aspiration hazard	Not classified	Not classified	/
Hazardous to aquatic environment - ACUTE	Acute Cat. 1; H400	Acute Cat. 1; H400	$ZnSO_4$,$NiSO_4$,lead compounds with the exception of those specified elsewhere in Annex VI,$CuSO_4$,As_2O_3 / AsO_3,Arsenic compounds, with the exception of those specified elsewhere in Annex VI,Ag powder
Hazardous to aquatic environment - CHRONIC	Chronic Cat. 1; H410	Chronic Cat. 1; H410	$ZnSO_4$,$NiSO_4$,lead compounds with the exception of those specified elsewhere in Annex VI,$CuSO_4$,As_2O_3 / AsO_3,Arsenic compounds, with the exception of those specified elsewhere in Annex VI,Ag powder

Illustration: Cu slime case IUCLID reporting

E.g. Cu slime Grade 1

Health hazards

	Hazard category	Hazard statement	Reason for no classification
Acute toxicity - oral	Acute Tox. 3	H301: Toxic if swallowed.	
Acute toxicity - dermal			conclusive but not sufficient for classification
Acute toxicity - inhalation	Acute Tox. 4	H332: Harmful if inhaled.	
Skin corrosion/irritation	Skin Irrit. 2	H315: Causes skin irritation.	
Serious eye damage/ eye irritation	Eye Damage 1	H318: Causes serious eye damage.	
Respiratory sensitisation	Resp. Sens. 1	H334: May cause allergy or asthma symptoms or breathing difficulties if in	
Skin sensitisation	Skin Sens. 1	H317: May cause an allergic skin reaction.	
Aspiration hazard			conclusive but not sufficient for classification

Reproductive toxicity

Reproductive toxicity	Repr. 1A	H360: May damage fertility or the unborn child <state specific effect if kno	
Specific effect			
Route of exposure			
Effects on or via lactation			data lacking

Germ cell mutagenicity

Muta. 2

Carcinogenicity

Carc. 1A

Specific target organ toxicity - single

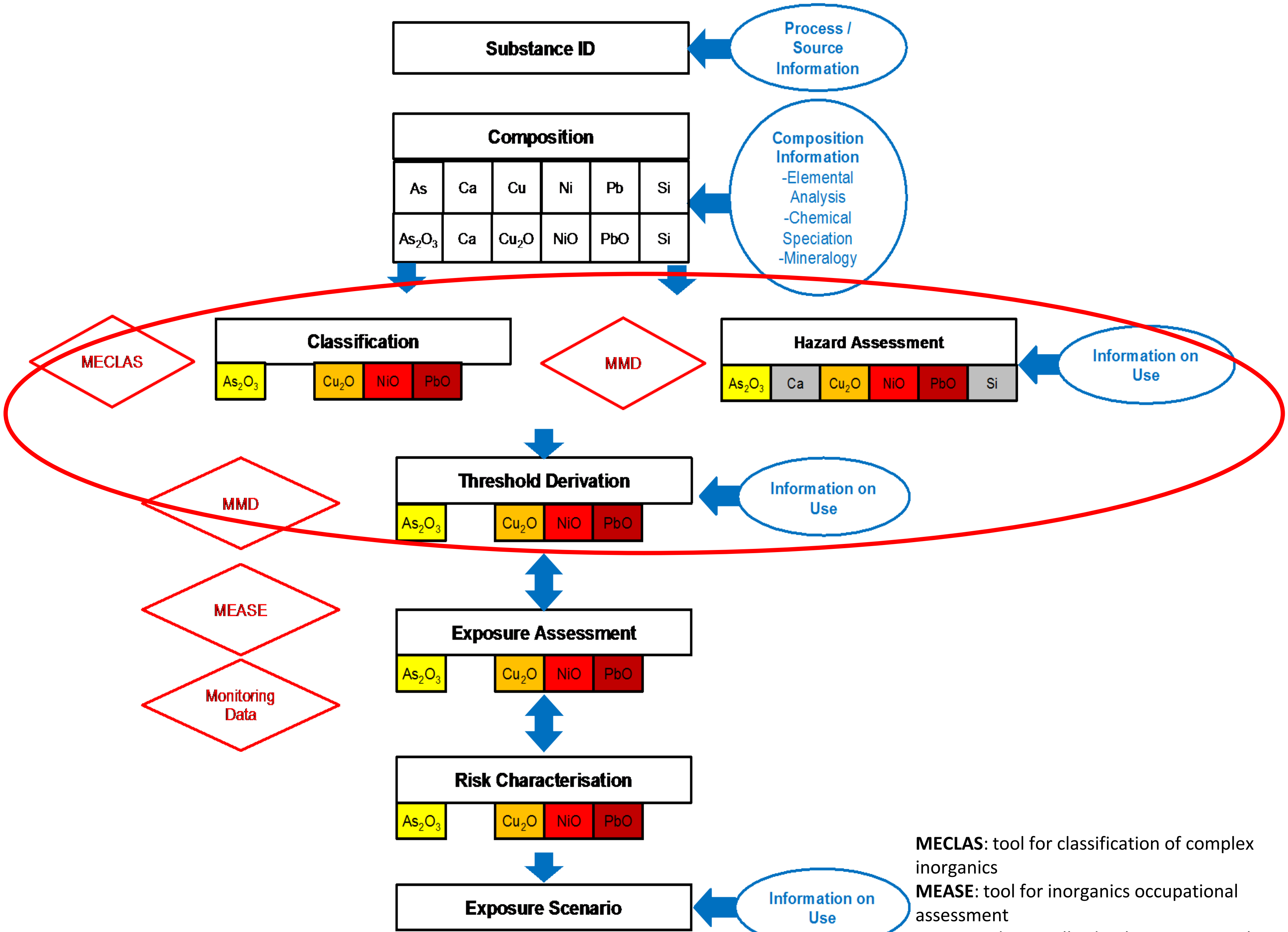
conclusive but not sufficient for classification

Specific target organ toxicity - repeated

STOT Rep. Exp. 1

Hazard Assessment

- Main principles
- Illustration Cu slime case



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Hazard assessment: main principles

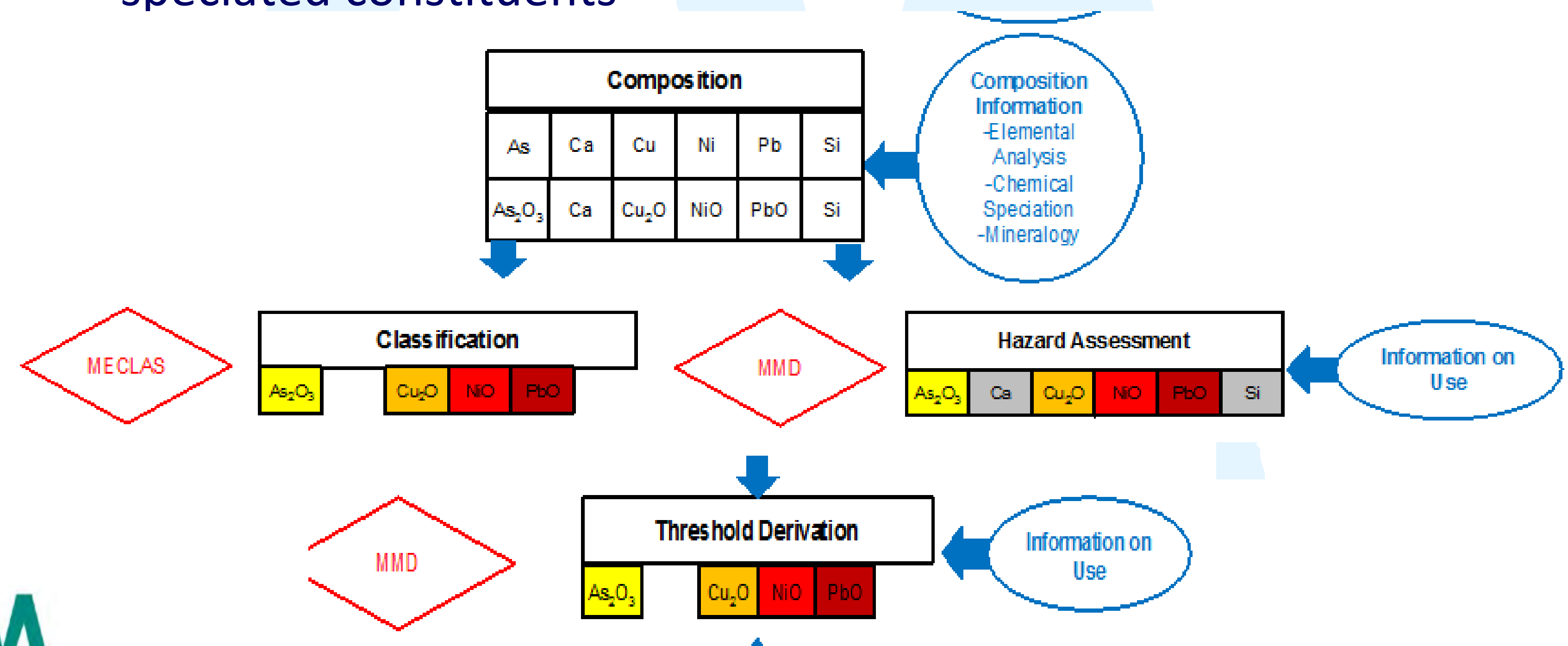
- Objectives of the hazard assessment
  - ➢ Fulfil the standard information requirements
  - ➢ Based on the hazard assessment of the **individual speciated constituents**
    - Identify hazards (links with classification)
    - Use derived thresholds/non-thresholds values

Hazard assessment: main principles
Sources of data

- Fate and (eco)toxicity of the UVCB substance itself
- Fate and (eco)toxicity data on UVCB constituents:
  - ➢ REACH dossiers (LoA)
  - ➢ Available via the Multi-metallic Database (MMD)
    - ➢ several metals consortia agreed to share REACH Registration dossiers information on substances
    - ➢ to ensure consistency in data used for further assessments (i.e. threshold values and reasoning leading to the numbers)
    - ➢ continuously updated
  - ➢ ECHA dissemination website
  - ➢ National/European acceptable limits, as OELs, EQS

Hazard assessment: main principles

- To ensure that the constituents approach is sufficiently protective:
  - ➢ use of information on constituents hazard profile
  - ➢ use of information on **all classified** (or expected to be classified) speciated constituents



HH hazard assessment: main principles

- Importance of speciation:
  - ➢ In some cases, human health toxicity is driven by the metal ion
  - ➢ In other cases, human health toxicity is different per species
  - ➢ By default, the constituent-driven hazard assessment is conducted by assuming the **most hazardous species** for each of the individual constituents:
    - For classification purpose: species with worst HH classification
    - For effect assessment purpose: species with lowest DNEL
  - ➢ This can be refined by bringing in data on speciation and/or plausibility considerations:
    - e.g. oxides may be assumed to be present/released in oxidic conditions

HH hazard assessment
Reporting

In order to fulfil information requirements:

- **For classification**: Robust study summaries on MECLAS or waiver for (each) HH endpoint
  - Reporting format: MECLAS is considered as “hazard prediction tool” fulfilling the 5 OECD criteria on QSARs (well defined endpoint, unambiguous algorithm, defined applicability domain, robust prediction, mechanistic interpretation)
  - Examples:
    - Acute Tox Cat. 2, inhalation => acute toxicity estimate ATE: > 5 — <= 50 mg/kg bw based on: dissolved (prediction)
    - Resp/Skin sens cat 1: driver NiSO4 => sensitizer
    - Muta cat 2: driver NiSO4 => mutagene

HH hazard assessment: Reporting

- **For effect assessment (threshold derivation):**
  - ➢ **Derivation of DNELs for the UVCB as such is meaningless**
  - ➢ Review of the hazard sections of all relevant constituents and assessment (data-sharing via the MMD):
    - On relevant endpoints and exposure routes:
      - Local –systemic, acute- chronic
      - Inhalation – dermal route (if intermediate, used exclusively at the workplace)
      - Hazard for the eye
    - Is there a DNEL or DMEL available?
  - ➢ DNEL summaries

How are the U and the V addressed in effect assessment?

Elemental constituent	**Speciation constituent**	**Variability**
Known (close to 100%) but variable	Largely known, some unknown	Low to high variability on elemental concentrations Medium variability on speciation concentrations

Solutions:

If unknown,
species with worst-case DNEL/PNEC is selected by default
(usually expressed as elemental ion)

Considered in exposure assessment

Illustration: Cu slime case HH
Constituent summary for effect assessment

UVCB constituent		Variability	DNELs for systemic and local effects, inhalation and dermal route, short term and long term.
Element	**Speciation used for occupational exposure assessment**		
Cu	Cu ion is toxic driver	RWC exposure level	See respective DNEL summary in IUCLID and table below
Ni	Ni ion is toxic driver except NiSO4 for systemic acute inhalation and NiS for local acute inhalation	RWC exposure level	See respective DNEL summary in IUCLID and table below
Pb	Pb ion is toxic driver	RWC exposure level	See respective DNEL summary in IUCLID and table below
As	As ion is toxic driver	RWC exposure level	See respective DNEL summary in IUCLID and table below
Zn	Soluble Zn compounds	RWC exposure level	See respective DNEL summary in IUCLID and table below
Ba	Species (BaSO4, BaCl, BaOH) with worst-case DNEL	RWC exposure level	See respective DNEL summary in IUCLID and table below
Co	Species (CoCl2, CoCO3, Co) with worst-case DNEL	RWC exposure level	See respective DNEL summary in IUCLID and table below
Sn	Sn ion is toxic driver	RWC exposure level	See respective DNEL summary in IUCLID and table below
Sb	Sb ion is toxic driver	RWC exposure level	See respective DNEL summary in IUCLID and table below
Te	Te compounds	RWC exposure level	See respective DNEL summary in IUCLID and table below
Se	Se compounds	RWC exposure level	See respective DNEL summary in IUCLID and table below
Ag	Ag compounds	RWC exposure level	See respective DNEL summary in IUCLID and table below
Additional relevant at site			

Illustration: Cu slime case HH Threshold overview

Route	Type of effect	Cu	Pb	As	Ni	Cd	H_2SO_4		
Assessment rationale for different species		Conservative read-across from Cu2+	Lead cation is the primary mediator of lead toxicity	Arsenic ion is the driver for toxicity	Difference between Ni metal and Ni sulphate, Ni sulphide, Ni oxide	Cd and Cd compounds effect assessment based on Cd			…s: …nces … and
Inhala-tion	Systemic Long Term	See internal DNEL	See internal DNEL	1.9 µg As/m^3 (based on As_2O_3: 5 µg/m^3)	0.05 mg/m^3 (inhalable) (same for all)	0.00…			
	Systemic Acute	20 mg/m^3	No hazard identified	No DNEL avail…					…threshold effect and/or no dose-response information available
	Local Long Term	OEL 1 mg/m^3	DNEL not re…				…05 mg/m^3	/	No threshold effect and/or no dose-response information available
	Local Acute					…effect …dose-response …formation available	0.1 mg/m^3	/	No threshold effect and/or no dose-response information available
	OE…				… mg/m^3 (Inhalable)	0.01 – 0.15 mg/m^3 (inhalable) 0.002-0.01 mg/m^3 (respirable)	0.1-1 mg/m^3	0.05-0.2 mg/m^3	ZnO fume: 4-5 mg/m^3 ZnO dust: 3-15 mg/m^3 ZnCl: 0.5-5 mg/m^3
Derma…				…112 µg/kg bw/day As acid: 85 µg/kg bw/d	Not applicable	Exposure based waiving	No threshold effect and/or no dose-response information available	/	83.3 mg/kg bw/day
	…ay		No hazard identified	No DNEL available	Not relevant (negligible absorption)	Exposure based waiving	No threshold effect and/or no dose-response information available	/	No threshold effect and/or no dose-response information available

Table based on best science available, subject to updates

ENV Fate assessment: main principles

- Assessing transport and distribution, bioaccumulation and secondary poisoning has no meaning for the inorganic UVCB as such
- However, the assessment of constituents that can be emitted is relevant:
  - Classification: removal from water column, e.g. Al, Fe
  - Risk assessment: adsorption, bioaccumulation, removal in STP
- Environmental fate reported in CSR Chapter 4 / IUCLID Section 5

ENV Hazard assessment: main principles

- Hazard assessment:
  - For the environment, most often, it is the metal ion that is the toxic driver. Different speciation is therefore typically not considered/relevant
  - Consolidated metal-specific PNECs (Predicted No Effect Concentration) are to be collected for each environmental compartment from the MMD
- Environmental hazard conclusions reported in CSR Chapter 7 / IUCLID Section 6

ENV hazard assessment
Reporting

<u>In order to fulfil information requirements,</u>

- **For classification:** Robust study summaries on MECLAS or waiver for each ENV endpoint
  - ➢ Reporting format: MECLAS is considered as "hazard prediction tool" fulfilling the 5 OECD criteria on QSARs (well defined endpoint, unambiguous algorithm, defined applicability domain, robust prediction, mechanistic interpretation)
  - ➢ Examples:
    - Aquatic Acute Cat. 1 => EC50 < 1 mg/L
    - Aquatic Chronic Cat. 1 => NOEC < 0.1 mg/L

ENV hazard assessment: Reporting

- **For effect assessment (threshold derivation)**:
  - ➢ **Derivation of PNECs for the UVCB as such is meaningless**
  - ➢ Review of the hazard sections of all relevant constituents and assessment (data-sharing via the MMD):
    - On relevant compartments
    - Is there a PNEC available?
  - ➢ PNEC summaries

Illustration: Cu slime case ENV Constituents for effect assessment

UVCB constituent		Variability	PNECs
Element	**Speciation used for environmental risk assessment**		
Cu	Metal ion	RWC exposure level	See respective PNEC summary in IUCLID and table below
Ni	Metal ion	RWC exposure level	See respective PNEC summary in IUCLID and table below
Pb	Metal ion	RWC exposure level	See respective PNEC summary in IUCLID and table below
As	Metal ion	RWC exposure level	See respective PNEC summary in IUCLID and table below
Zn	Metal ion	RWC exposure level	See respective PNEC summary in IUCLID and table below
Ba, Co, Sn, Sb, Te, Se, Ag	Metal ion	Not relevant	Qualitative assessment conducted

Illustration: Cu slime case ENV
Threshold overview

PNECs

Protection target	Unit	Cu	Pb	As	Ni	[illegible]	[illegible]	[illegible]	[illegible]
Freshwater	µg/L	7.8	6.5	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	34
Marine water	µg/L	5.2	3.4	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	3.4
Freshwater sediment	mg/kg_{dw}	87	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	235.6	3.3
Marine sediment	mg/kg_{dw}	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0.64	113	0.34
Soil	[illegible]	[illegible]	[illegible]	[illegible]	29.9	0.9	107	3.4	
STP	[illegible]	[illegible]	[illegible]	[illegible]	330	20	52	100,000	
[illegible]	[illegible]	[illegible]	[illegible]	0.5	12.3	0.16	Quali-tative	Quali-tative	

Table based on best science available, subject to updates

[illegible]ental constituents

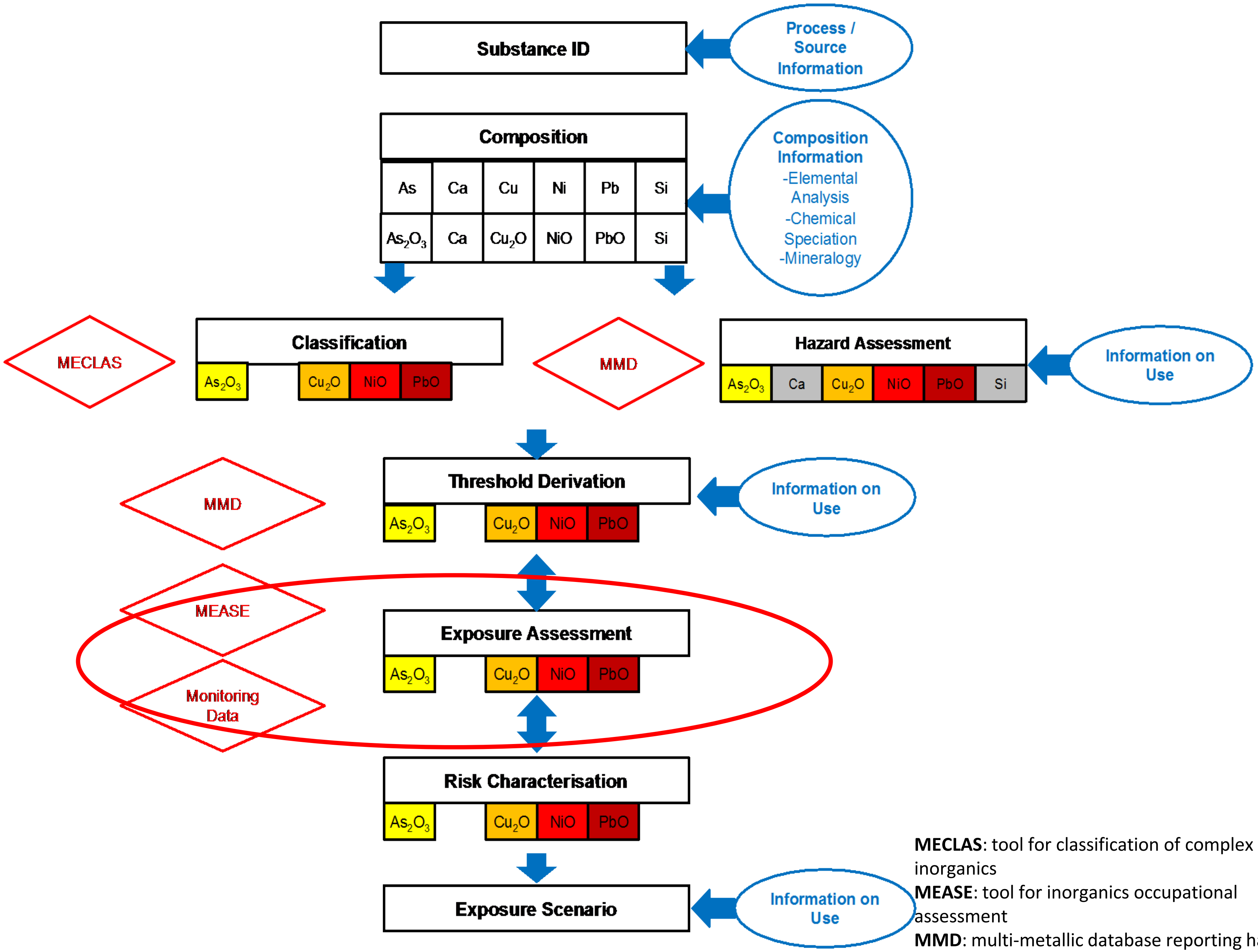
Illustration: Cu slime case ENV
Fate assessment overview

	Unit	Cu	Pb	As	Ni
Suspended matter (freshwater)	L/Kg	30,246	295,121	10,000	26,303
Suspended matter (marine)	L/Kg	131,826	1,518,099	10,000	15,848
Sediment (freshwater)	L/Kg	24,409	154,882	6,607	7,079
Soil	L/Kg	2,120	6,400	191	724
BCF/BAF (aquatic)	L/kg	NR	1,553	270 (fresh) 5,866 (marine)	270
BCF/BAF (terrestrial)	kg/kg dw	NR	0.39	NA	
Removal rate STP to sludge	%	80	84	26*	40

etc for other elemental constituents

Exposure Assessment

- Main principles
- Illustration Cu slime case



MECLAS: tool for classification of complex inorganics
MEASE: tool for inorganics occupational assessment
MMD: multi-metallic database reporting hazard data, as shared under EM umbrella

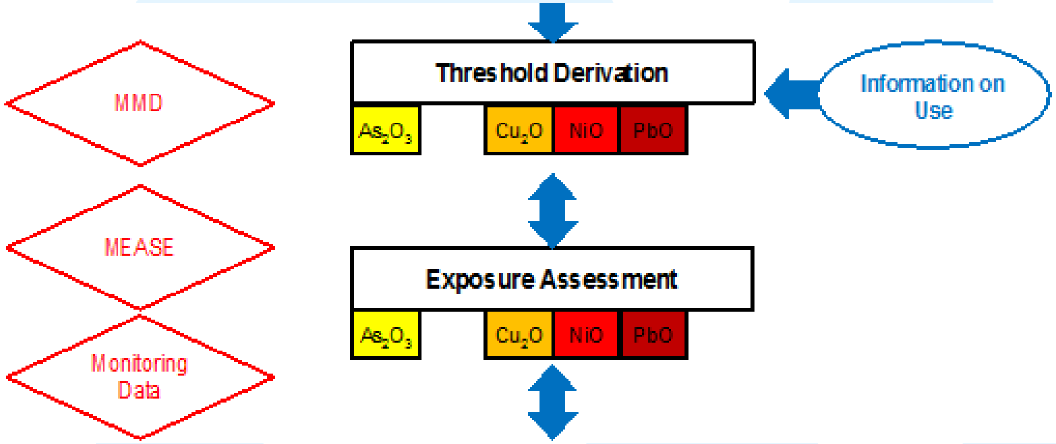
Exposure assessment: main principles

- ES have to describe the operational conditions (OC) and risk management measures (RMM) ensuring safe use of the substance

- Necessary to assess
  - all environmental/workplace relevant releases (liquids, solids, fumes)
  - all relevant environmental compartments (water, sediment, sewage treatment plants, soil)
  - all relevant exposure routes

Exposure assessment: main principles

- As a consequence of the hazard assessment, the exposure assessment has to consider all relevant constituents as identified in the hazard assessment



Exposure assessment HH: sources of information

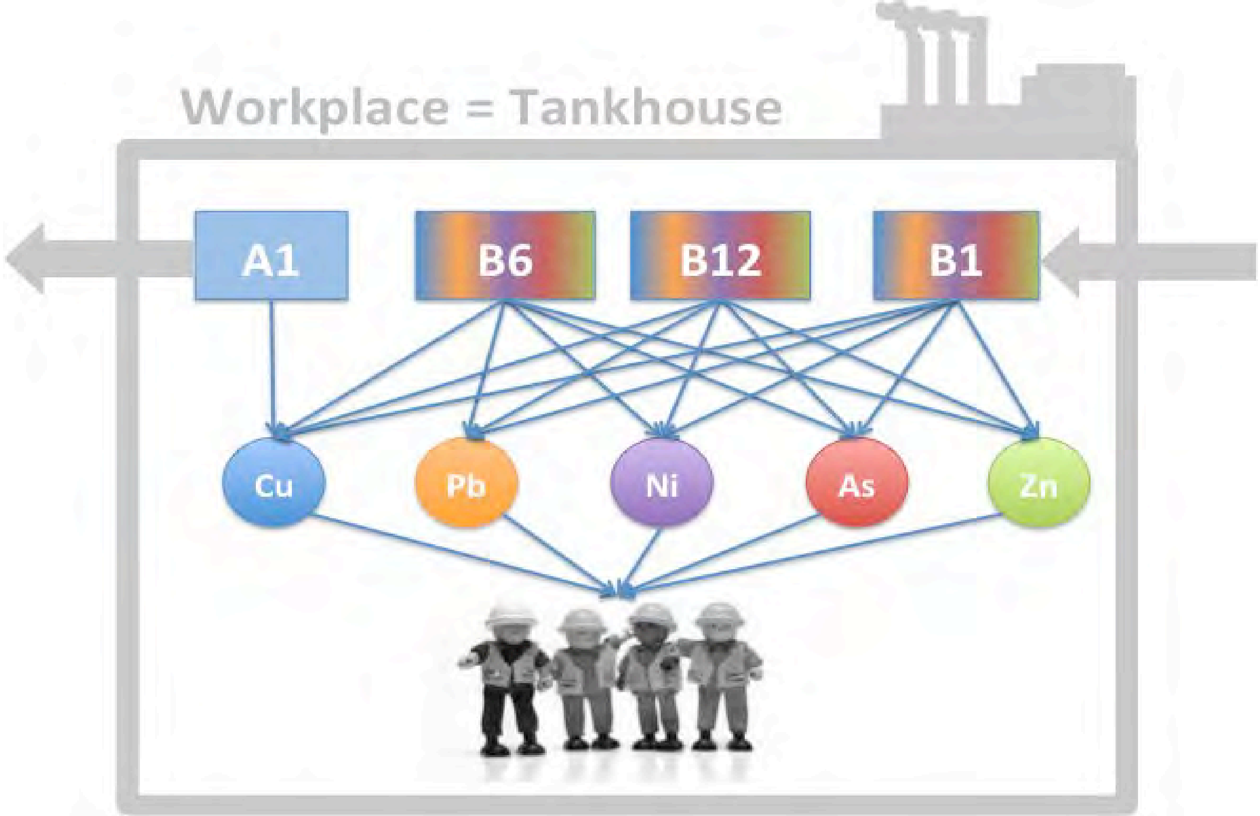
- The exposure assessment can be based on monitoring data, exposure models, analogous data

➢ **Monitoring data:**

- Contextual information required (OC, implemented RMMs, details on sampling methodology)
- Dermal exposure data representing actual workplace measurements are rarely available
- Oral exposure data: for workers, oral exposure is assumed to be sufficiently controlled by strict occupational hygiene practices and is therefore currently not considered in the assessment of workplace exposure

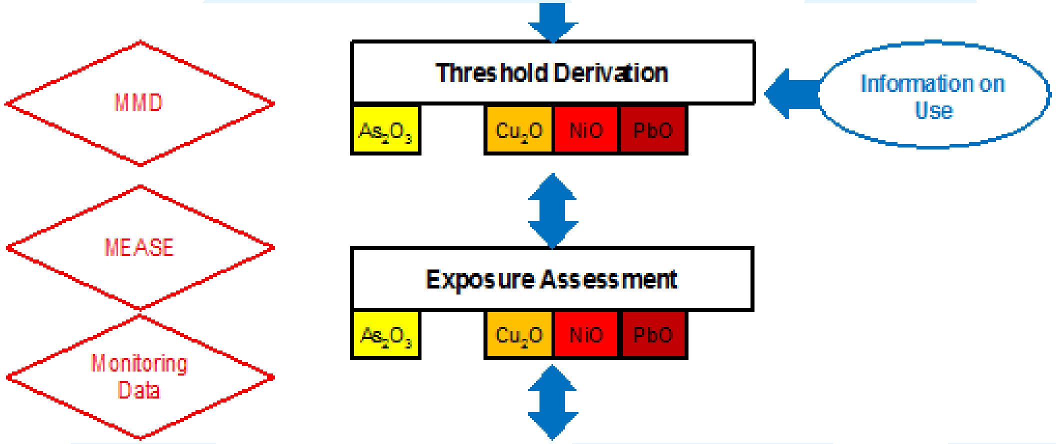
Exposure assessment HH: sources of information

- Exposure monitoring data are commonly available in the metals sector. For inhalation however these data are not (or not easily) attributable to individual substances and do not always include information on each of the constituents.



Exposure assessment: main principles extension

- The exposure assessment has to consider all relevant constituents as identified in the hazard assessment



Add constituents from other (UVCB) substances simultaneously produced/used (emissions from those can not be separated during monitoring at site)

How are the U and the V addressed in exposure assessment?

Elemental constituent	Speciation constituent	Variability
Known (close to 100%) but variable	Largely known, some unknown	Low to high variability on elemental concentrations Medium variability on speciation concentrations

+ additional known metals in workplace/ environmental releases not part of the UVCB

Solutions:

If unknown, species with worst-case DNEL/PNEC is selected by default	Considered in selection of RWC percentile of representative elemental monitoring data

Exposure assessment HH: sources of information

- At the workplace, the use of **inhalation monitoring data** presents the following advantages:
  - The **impact of varying content** of any constituent in the substance on exposure to that constituent is **intrinsically reflected**. The impact of process conditions and risk management measures are also directly reflected in any sample.
  - Generic dust is analysed for individual elements. Further chemical speciation is normally not done and in most cases even not possible (**use of worst-case chemical species**)
- Other substances (including UVCBs) handled in parallel having the same constituent(s) as the substances are contributing to overall exposure and are thus automatically included in the sample.

Exposure assessment HH: sources of information

- The assessment for the substance is therefore intrinsically conservative (i.e. precautionary) with respect to legal REACH requirements
  - **Modelling tools:** MEASE
  - **Analogous data:** need to include a justification for the extrapolation

Tools

- Use of bio-monitoring data for e.g. Pb: bio-monitoring data already reflect uptake through all routes of exposure

Illustration: Cu slime case
Conditions of use for each site

Site code*	1	2	3	4	5
Processes covered	Electrolyte preparation, charging of anodes into cells, electrolysis, slimes removal and refining/ leaching	Electrolyte preparation, charging of anodes into cells, electrolysis, slimes removal and refining/ leaching	Electrolyte preparation, charging of anodes into cells, cleaning of cells, electrolysis, slimes removal and refining / leaching	Electrolyte preparation, charging of anodes into cells, electrolysis, slimes removal and refining/ leaching	Electrolyte preparation, charging of anodes into cells, electrolysis, slimes and spent electrolyte removal
Conditions and measures related to personal protection, hygiene and health evaluation					
Dermal protection	M (body + hand)	M (gloves)	M (acid proof cloth + gloves)	M	M (body + hand)
Respiratory protection	V (ABE +P3)	No	No	M (P3)	No
Other conditions affection workers exposure					
Place of use	Indoor				
Process temp during electrolysis °C	63-70	63	65	65	60
Skin surface potentially exposed	1980 cm²				
Amount used (or contained in articles), frequency and duration of use/exposure					
Frequency (days/year)	365	355-365	365	365	365
Duration of activity (h/shift)	8	8	8-12	8	4-6
Technical and organisational conditions and measures					
General ventilation	Yes	Yes	Yes	Yes	Yes
Containment during electrolysis	Open (covered for electrolyte preparation)	Open, covered (with textile)	Closed tanks, open cells	Open, covered (with screen)	Open, covered
Local exhaust ventilation	No (fans in whole tank house)	No	Control room ventilation	95% closed cover and hood with filter + second plastic layer	No
Manual or automatic tasks	Manual/semi automated	Manual	Automated/ manual/ partly automated	Semi automated/ manual	Automated/ manual

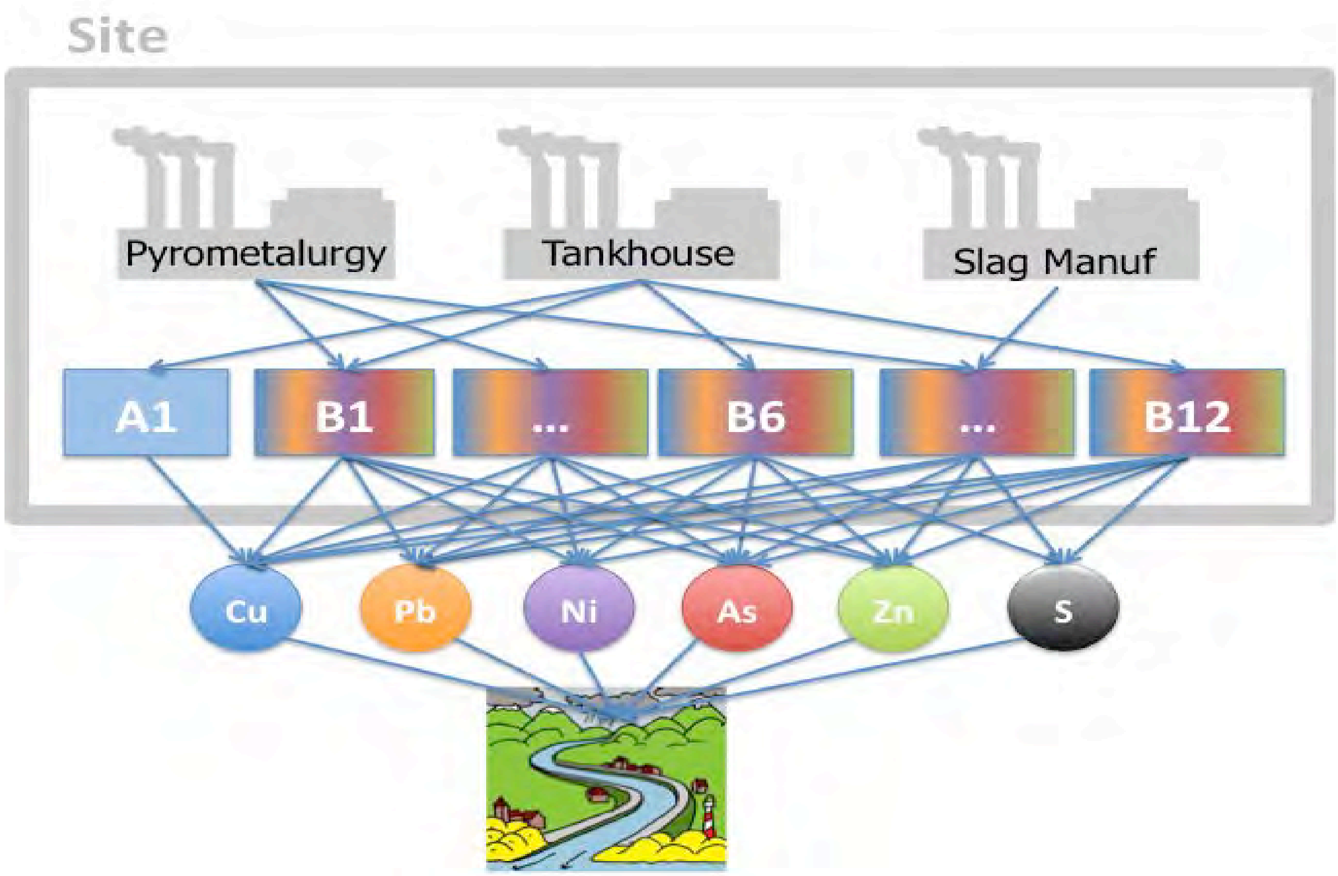
Illustration: Cu slime case

- Personal inhalation exposure concentrations
  - Cu: 0.012 – 0.043 mg/m^3 (N = 7 – 33 per site, total 130)
  - Pb: 0.0014 – 0.0258 mg/m^3 (N = 6 – 33 per site, total 129)
  - As: 0.0006 – 0.0053 mg/m^3 (N = 7 – 33 per site, total 128)
  - Sb: 0.0007 – 0.0028 mg/m^3 (N = 7 – 14 per site, total 26)
  - etc…

- Biomonitoring (internal exposure concentrations)
  - Pb: 7.89 - 29 ug/L
  - etc…

Exposure assessment ENV: main principles

- Assessing each UVCB intermediate separately is not feasible because available monitoring data do not allow determining relative contribution of each UVCB present at the workplace/site



Exposure assessment ENV: main principles

Releases to water:

- Hydrometallurgical processes (leaching or electrolysis) are source of process water, solutions arise at different stages but they are typically collected together and re-circulated or re-used in various ways for metal recovery.
- Effluent discharge is typically kept at small volumes to prevent losses of metals.
- On-site water treatment plant collects all effluents from the site including effluents from other metal production streams

Exposure assessment ENV: main principles

Releases to air:

- Furnace operations are associated with emissions of dust and metals to air from several intermediates collected together and directed to the abatement technique (e.g. dust filter or scrubber)

- Furthermore during hot processes, some metals (As, Pb, Hg) can become volatile and presence /relative contribution of the emitted trace metals is different compared to composition of certain intermediate in solid state, intrinsically covered in emission data

Exposure assessment ENV: main principles

- Use of **effluent monitoring data** presents following advantages:
  - ➢ Intrinsically reflects on exposure:
    - Variability of any constituent content in the UVCB substance
    - Variability in conditions of use
  - ➢ Automatically includes (worst-case):
    - Other substances (including UVCBs) handled in parallel having the same constituent(s) as the substance and contributing to overall exposure
  - ➢ It is more realistic (less uncertain) than modelled estimates

Tools

- Use of **SPERCs**: it is demonstrated that solid-water partitioning is a dominating explanatory variability for release to wastewater (rather than conditions of use)

Illustration: Cu slime case
Conditions of Use for each site

Site code	1	2	3	4	5	6	7	8	9	10	11
Amount used, frequency and duration of use											
Emission days											
Daily/annual use at a site (tonnes)											
Percentage of tonnage used at regional scale											
Conditions and measures related to sewage treatment plant											
On-site STP											
Municipal STP: yes/no											
Discharge rate of STP (m3/d)											
Application of the STP sludge on agricultural soil:											
Other conditions affecting environmental exposure											
Receiving surface water flow rate											
Dilution factor											

Illustration: Cu slime case
Local releases from each site

Site code		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Release **Release factor estimation method**	**Metal**	**Local release rate** (kg/day)										
Water **Local release rate** (kg/day) based on measured effluent concentrations (after site-specific STP if relevant) or calculated emissions (kg/year)	Copper											
	Lead											
	Nickel											
	Arsenic											
	Zinc											
	Cadmium											
	Manganese											
	Chromium											
Air **Local release rate** (kg/day) based on calculated emissions (kg/year)	Copper											
	Lead											
	Nickel											
	Arsenic											
	Zinc											
	Cadmium											
	Manganese											
	Chromium											
Soil **Final release factor (%):**	All metals											

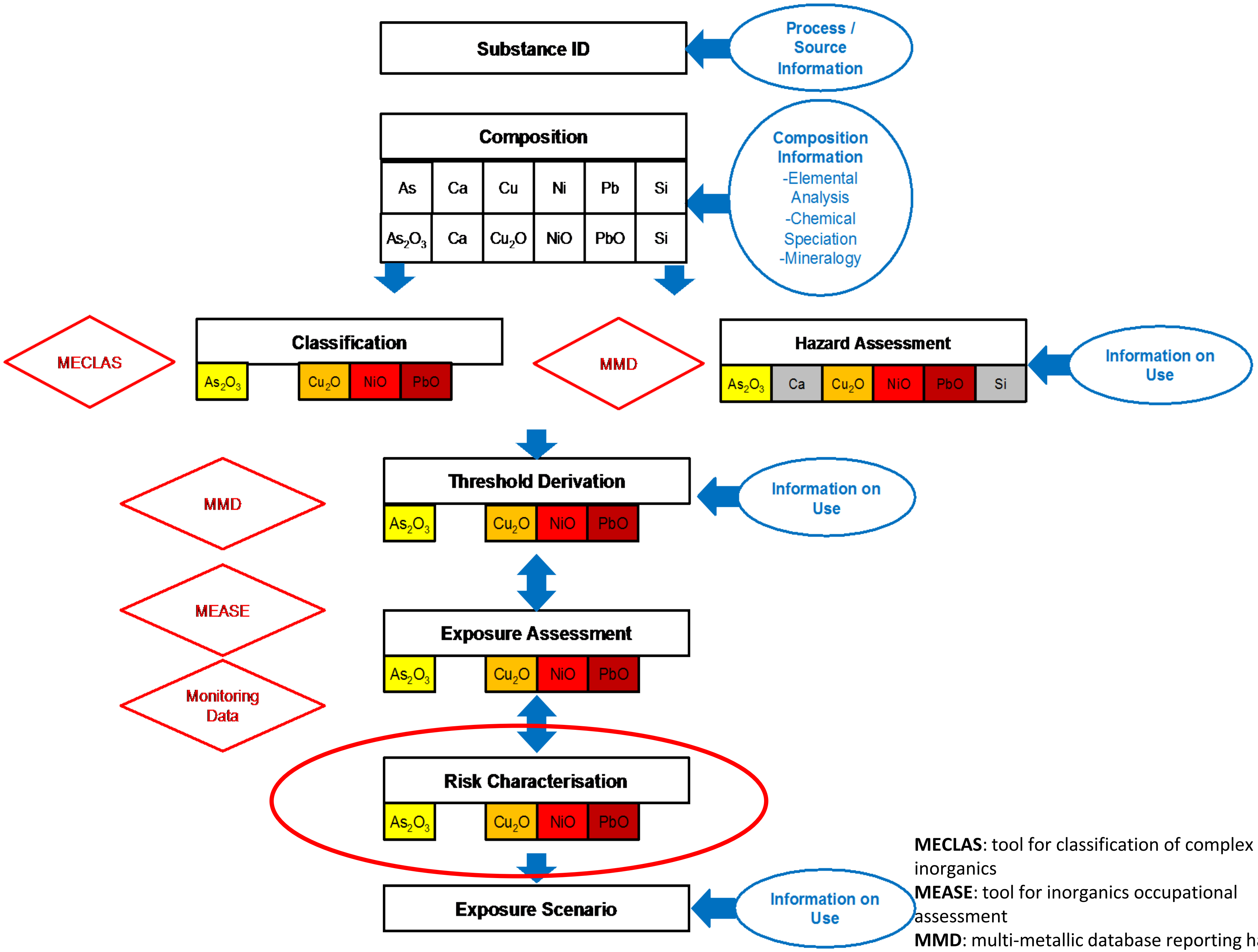
Illustration: Cu slime case
Quantitative Predicted Enviromental Concentrations (PEC)

Site code		1	2	3	4	5	6	7	8	9	10	11
Protection target	**Metal**	**Exposure concentration (local PEC)**										
Freshwater (µg/l) for companies 3-11) Marine water (µg/l) for companies 1-2)	Copper											
	Lead											
	Nickel											
	Arsenic											
	Zinc											
	Cadmium											
	Manganese											
	Chromium											
Sediment* (freshwater) (mg/kg dw) (for companies 3-11) Sediment (marine water) (mg/kg dw) for companies 1-2)	Copper											
	Lead											
	Nickel											
	Arsenic											
	Zinc											
	Cadmium											
	Manganese											
	Chromium											

etc

Risk Characterisation

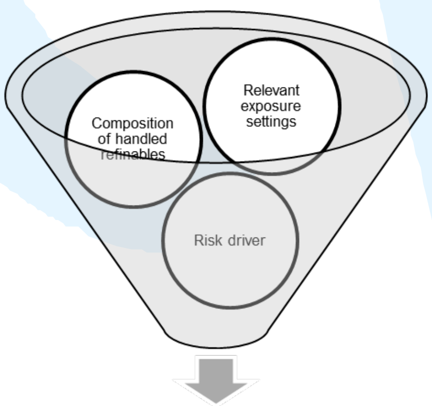
- Main principles
- Illustration Cu slime case



MECLAS: tool for classification of complex inorganics
MEASE: tool for inorganics occupational assessment
MMD: multi-metallic database reporting hazard data, as shared under EM umbrella

Risk characterisation: main principles

- Based on the comparison between exposure and effect levels
- Quantitative/qualitative approaches
- Communication: site-specific scenarios



Site-specific exposure scenario

Risk characterisation

ECHA
EUROPEAN CHEMICALS AGENCY

Assessment types

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

ECHA.EUROPA.EU

Risk characterisation HH: main principles

Hazard Conclusion	Explanation	Subsequent Exposure assessment and risk characterisation
DNEL	When DNEL is available (and data sharing agreement) and relevant exposure is present	Quantitative
	When DNEL is available, e.g.: - at ECHA dissemination website but no data access - and/or no or low exposure, hazard and risk expected	Qualitative assessment of emission and hazard potential
Other threshold (OEL,…)	When no DNEL is available but hazard is identified, relevant exposure is present and alternative threshold is available (e.g. OEL)	Semi-quantitative
Qualitative (no threshold)	When no DNEL is available but hazard is identified (low – medium –high)	Qualitative
No hazard identified	When no hazard	Not needed

Illustration: Cu slime case
Scope of assessment

Route	Type of effect	Cu	Pb	As	Ni	Cd	Sb	H_2SO_4	Se	Sn	Mn	Zn	Te
Inhalation	Systemic Long Term	Not relevant due to internal DNEL	Not relevant due to biomonitoring	SemiQuantitative	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Quantitative	Quantitative	Quantitative	Qualita
	Systemic Short term	Quantitative	Qualitative	Qualitative	Quantitative	Qualitative	Qualitative	Qualitative	Qualitative	Quantitative	Qualitative	Qualitative	Qualita
	Local Long Term	SemiQuantitative	Qualitative	Qualitative	Quantitative	Qualitative	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualita
	Local Short term	Qualitative	Qualitative	Qualitative	Quantitative	Qualitative	Qualitative	Quantitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualita
Dermal	Systemic Long Term	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualita
	Systemic Short term	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualita
	Local Long Term	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualita
	Local Short term	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualita
Internal (biomonitoring)	Systemic Long Term	Quantitative	Quantitative	Semiquantitative	Semiqualitative	Semiquantitative	Not available	Not available	Not available	Not available	Not available	Not available	Not ava
Eye	Qualitative												

Risk characterisation ENV: main principles

Hazard Conclusion	Explanation	Subsequent Exposure assessment and risk characterisation
PNEC	When PNEC is available (and data sharing agreement) and relevant exposure is present	Quantitative
	When PNEC is available, e.g.: - at ECHA dissemination website but no data access - and/or no or low exposure, hazard and risk expected	Qualitative assessment of emission and hazard potential
Other threshold (EQS,…)	When no PNEC is available but hazard is identified, relevant exposure is present and alternative threshold is available (e.g. EQS, …)	Semi-quantitative
Qualitative (no threshold)	When no PNEC is available but hazard is identified (low – medium – high)	Qualitative
No hazard identified	When no PNEC and no hazard	Not needed

Illustration: Cu slime case

- The environmental assessment is based on all classified constituents of all relevant UVCBs on the site:

  Cu, Zn, Sb, Se, Ni, Cr, Cd, Pb, Mn, Hg, Co, Ba, As and Ag.

Protection target	Type of risk characterization											
	Cu	Pb	Ni	As	Zn	Cd	Mn	Cr	Co	Sb	Se	Hg
Freshwater	Quantitative	Quantitative	Quantitative	Semi-Quantita	Quantitative	Quantitative	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Qua ve
Sediment (freshwater)	Quantitative	Quantitative	Quantitative	Semi-Quantita	Quantitative	Quantitative	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Qua ve
Marine water	Quantitative	Quantitative	Quantitative	Semi-Quantita	Quantitative	Quantitative	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Qua ve
Sediment (marine water)	Quantitative	Quantitative	Quantitative	Semi-Quantita	Quantitative	Quantitative	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Qua ve
Sewage treatment plant	Quantitative	Quantitative	Quantitative	Semi-Quantita	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qua ve
Air	Not needed	Not needed	Not needed	Not needed	Not needed	Not needed	Not needed	Not needed	Not needed	Not needed	Not needed	Not nee
Agricultural soil	Quantitative	Quantitative	Quantitative	Semi-Quantit	Quantitative	Quantitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qua ve
Predator (aquatic)	Qualitative	Quantitative	Quantitative	Semi-quantitat	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Quantitative	Qua ve
Top predator (aquatic)	Qualitative	Quantitative	Quantitative	Semi-quantitat	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Quantitative	Qua ve
Predator (terrestrial)	Qualitative	Quantitative	Quantitative	Semi-quantitat	Qualitative	Quantitative	Qualitative	Qualitative	Qualitative	Qualitative	Qualitative	Qua ve

Illustration: Cu slime case ENV

All classified constituents of the UVCB

+ all classified constituents of other UVCBs on the site (if any)

→ Cu, Zn, Sb, Se, Ni, Cr, Cd, Pb, Mn, Hg, Co, Ba, As and Ag.

- Quantitative risk characterisation
- Qualitative risk characterisation (example):

  Effluent discharge from Tank house is expected to contain metals that are soluble in the electrolyte such as Ni, As. The process is designed to retain Ag, Se in the slime, it settles in the cells and is not soluble in the electrolyte therefore these elements are not expected in the effluent.

Uncertainty analysis

Uncertainty analysis: main principles

Aims:

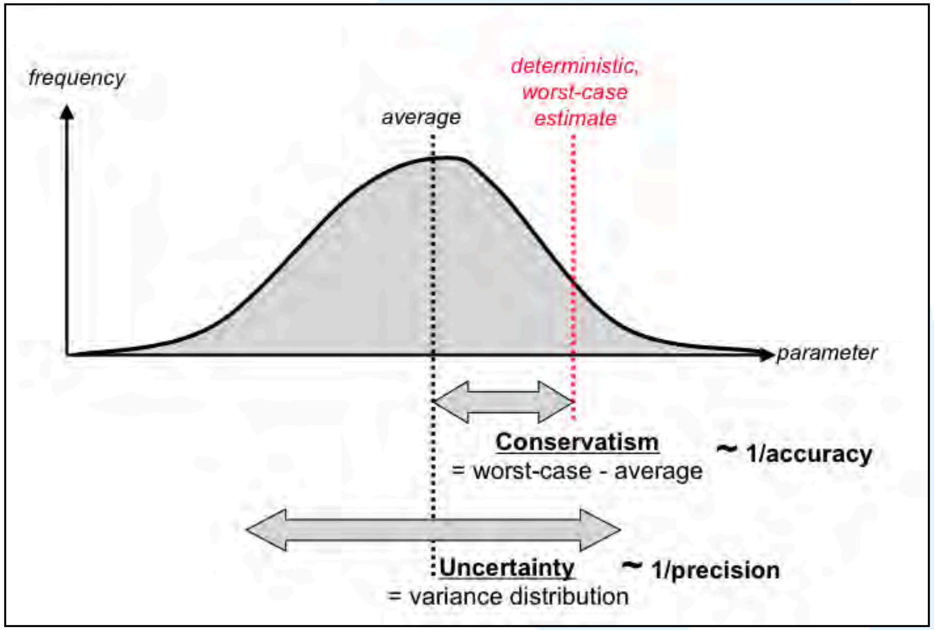
- **Review** of where and how uncertainty is addressed in the CSR to demonstrate robust risk conclusions
- **Recommendation** on the addition of uncertainty discussions or improvements to the existing ones
- Sections of the CSR: DNEL, PNEC, Exposure assessment (and risk characterisation)

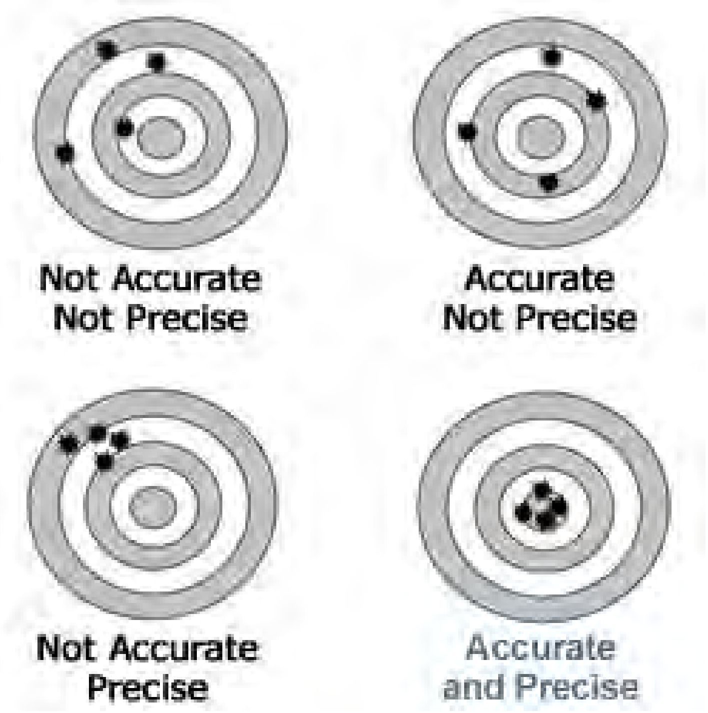
On-going work:

- Identification of **uncertainty sources**
- Assessment of **existing** uncertainty discussion for each source
- Type of **existing uncertainty analysis**
- Distinction **uncertainty / variability**
- Level of uncertainty: **Direction** and **Magnitude**

Uncertainty analysis: main principles

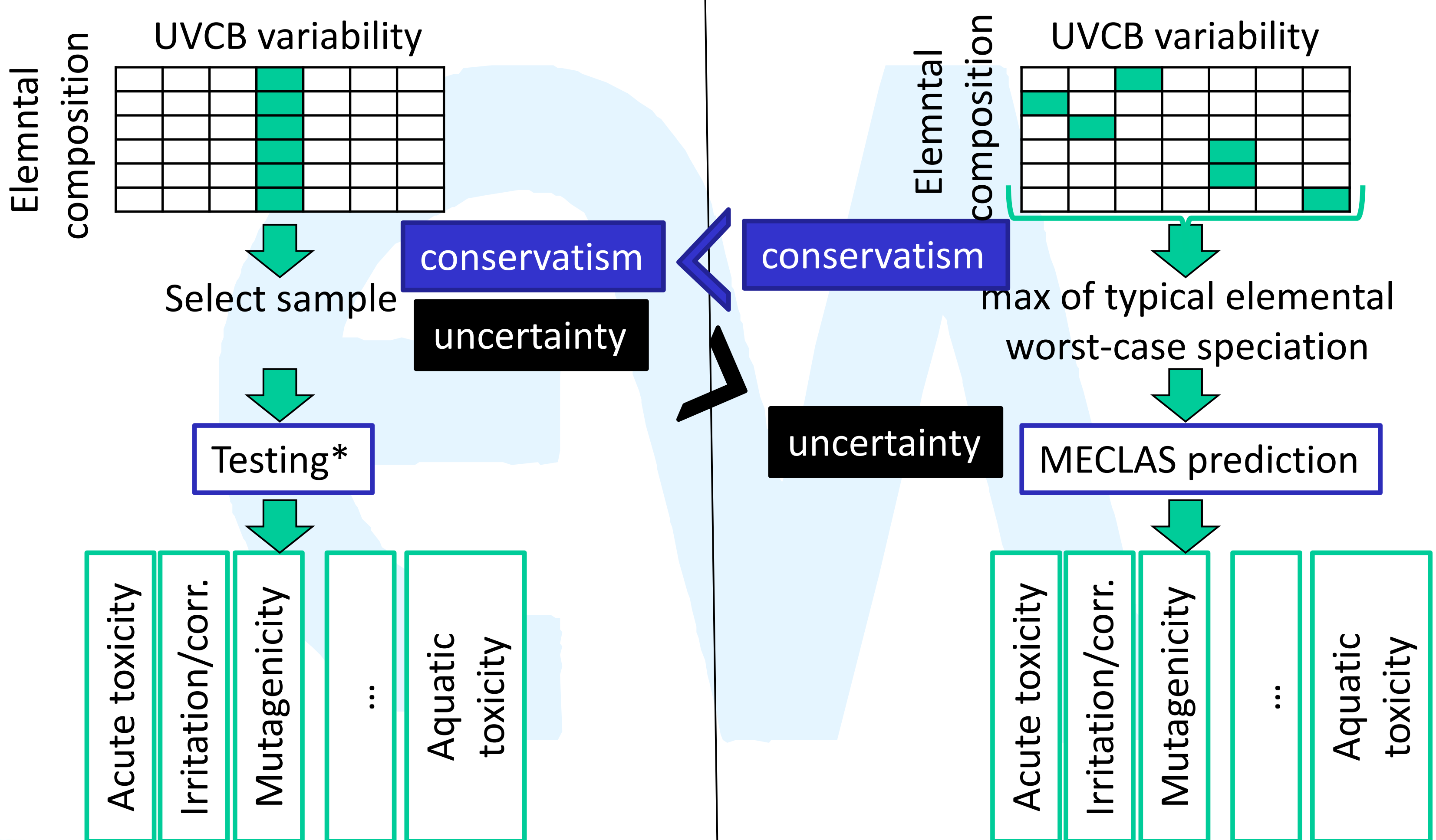
- Conservatism versus Accuracy
- Uncertainty (variability) versus Precision





Uncertainty analysis: main outcomes
Classification

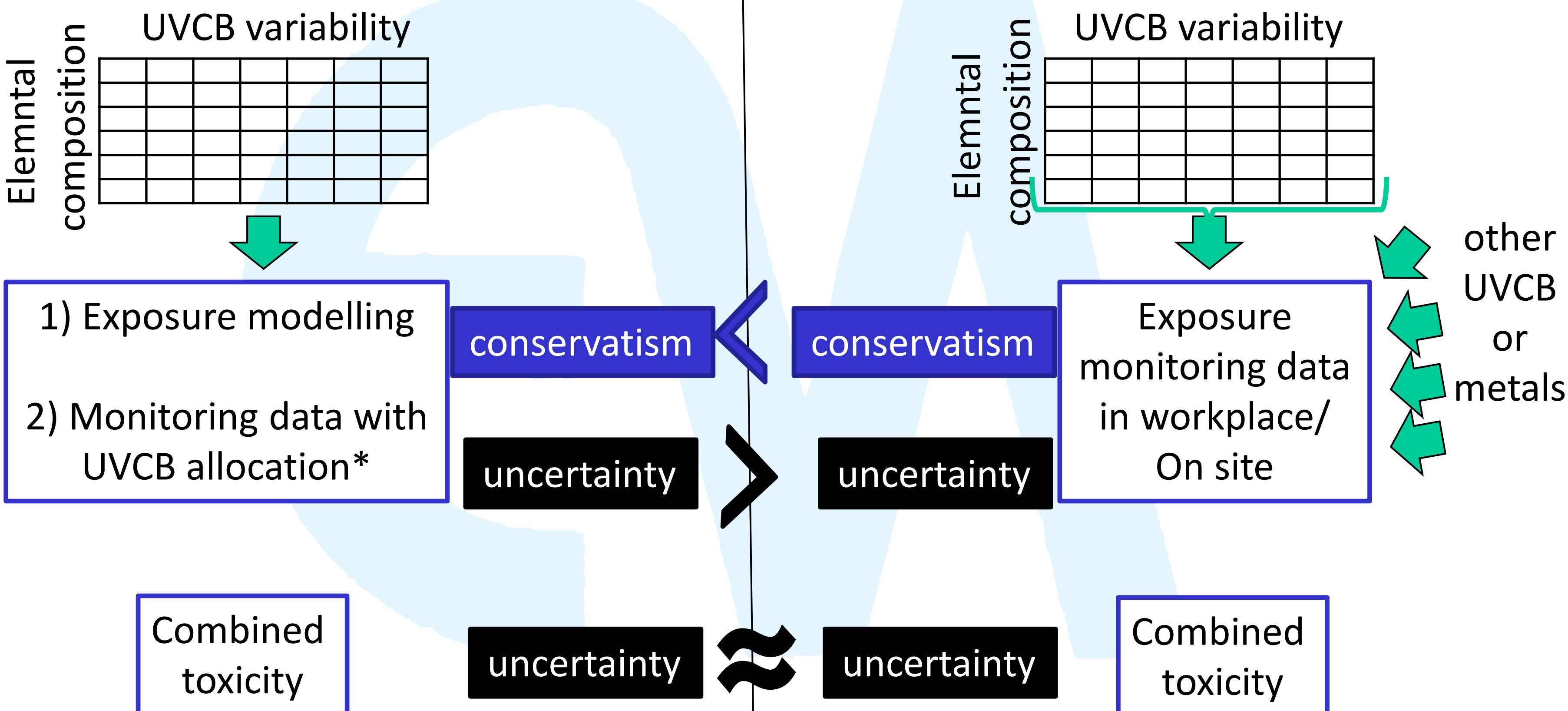
- Standard substance approach
- Inorganic UVCB approach



*Existing data are generally not available

Uncertainty analysis: main outcomes
Risk Assessment

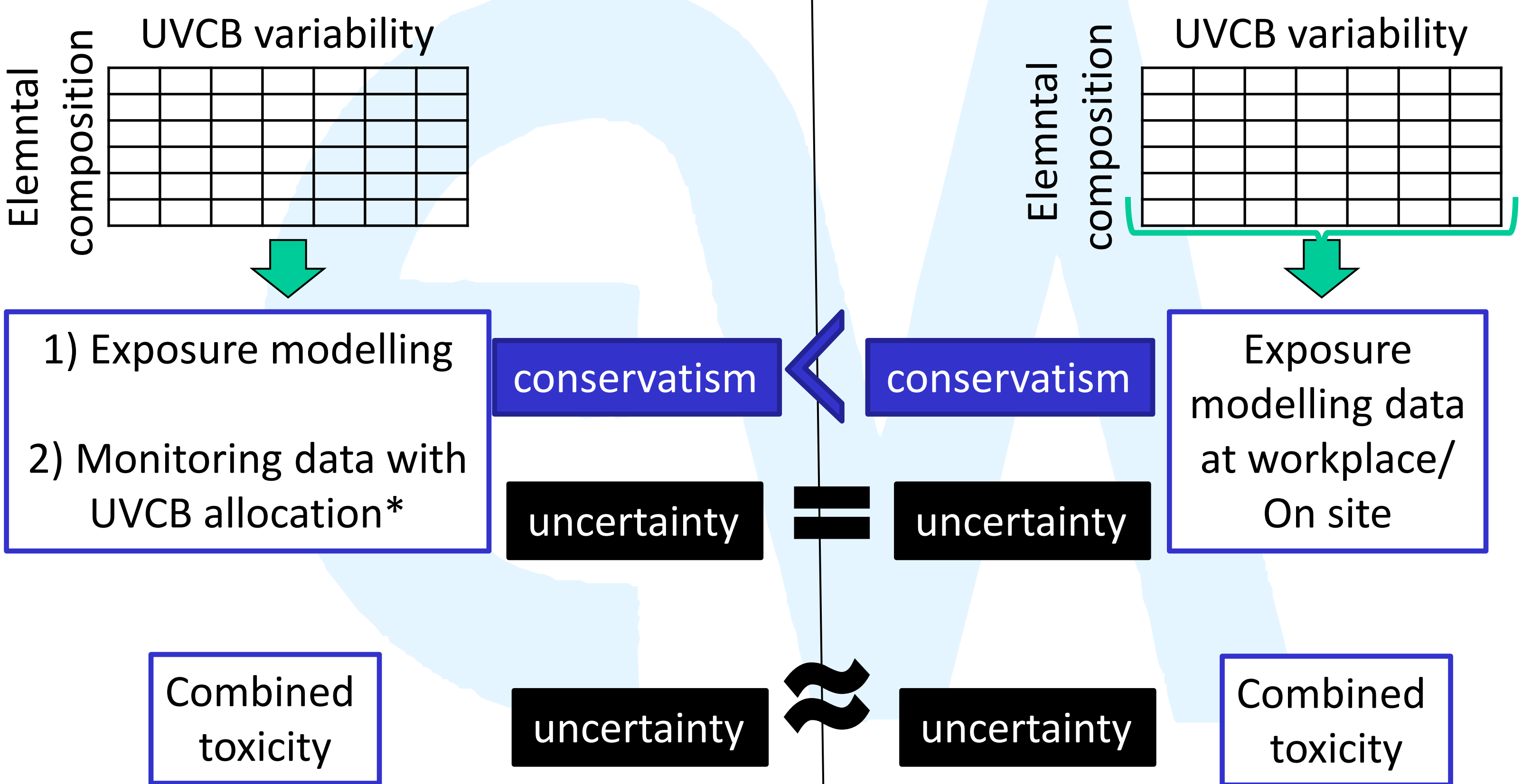
- Standard substance approach
- Inorganic UVCB constituent approach/monitoring



* Not common practice

Uncertainty analysis: main outcomes Risk Assessment

- Standard substance approach
- Inorganic UVCB constituent approach/modelling



* Not common practice

Combined toxicity

Way forward on combined toxicity
Introduction

- How to address co-exposure from several hazardous constituents

- Current recommendations (e.g. SCHER, ECETOC) propose that:
  - *In the case of **unknown** modes of action the dose/concentration **addition approach** is preferable.*
  - *In the case of chemicals with **independent** modes of action, the establishment of safe levels based on the **assessment of individual substances** appears to provide a sufficient safeguard*
- How to assess this for inorganic UVCBs?
  - interactions are difficult to assess and require expert judgment on a case-by-case basis

Way forward on combined toxicity
Current status

- We have **no definitive solution**
- Literature data on combined effects of metal and metal compounds is limited
- For **some** metals, there are indications of possible additive, synergistic or antagonistic behaviours when they are in presence of other specific substances
- Unfortunately such information is not readily available for **most** metals
- Research is on-going

Way forward on combined toxicity
Current status

- **Proposal:**
  - Whenever information on combined toxicity is available, this will be reflected in the risk assessment
  - ***If no information available, include a placeholder in our dossiers with reference to on-going research and some temporary ways forward***

Way forward on **environmental** combined toxicity
Specificities of metals

- Additivity, synergism, antagonism

- Most of data are on acute toxicity:
  - ➢ Chronic interactions?

- Most data are at higher concentrations:
  - ➢ What happens at low, environmentally “safe” levels?
    - e.g. of combined EQS?
    - At background levels?

Proposed way forward on environmental combined toxicity: Tier 0

- Assess and review literature data
- Use the sum of PEC/PNECs ratios as a first filter, to analyse whether there is a concern

➢ Easily a concern based on median ambient concentrations only

	Cu	Pb	As	Ni	Cd	Zn	
PEC freshwater (dissolved) µg.L-1	0,88	0,093	0,63	1,91	0,01	2,68	
PNEC freshwater (dissolved) µg.L-1	7,8	6,5	4,2	3,55	0,19	20,6	
RCR freshwater	0,11	0,01	0,15	0,54	0,05	0,13	**0,998**

to be updated

FOREGS

Proposed way forward on environmental combined toxicity: Tier 1

On-going research:

- Desktop analysis of existing data
  - Theoretical toxicity, evaluate SSDs and HC5s, evaluate data by species and conditions,…
- Experimental research
  - Interaction **at PNEC level between several metal**
- **Reseach and studies are on-going to refine the assessment and understand interactions better**

Proposed way forward on **human health** combined toxicity: Tier 0

Tier 0:

- Assess and review literature data: locate/identify existing data for inorganic UVCB constituents:
  - Target organs
  - Information on modes of action

- We could use the sum of RCRs of all constituents as first filter…

Proposed way forward on human health combined toxicity: Tier 1 – non CMR effects

Tier 1 step depends on the endpoint:

- **Acute toxicity** is generally associated with huge margins of safety:
  - Systemic: add RCRs, if threshold available
  - Local: add RCRs, if threshold available, or address via RMMs if peak exposures are expected
- **Sensitising / corrosive / irritating effects** are addressed by considering the applied strict RMMs on a qualitative basis (at the UVCB level)
- **Repeated dose, systemic effects/local effects**:
  - If same target organ: add RCRs
  - Otherwise: no combined toxicity assumed

Proposed way forward on human health combined toxicity: Tier 1 – CMR effects

- **Reproductive effects**
  - If same target organ: add RCRs
  - Otherwise: no combined toxicity assumed
- **Mutagenic effects:**
  - strict application of RMMs
  - can only be addressed on a qualitative basis
- **Carcinogenic effects:**
  - to be summed up by target organ, without distinguishing mode of actions

Way forward on human health combined toxicity
Specific considerations

- **Synergistic effects** can only be addressed if information is or becomes available
  - ➢ huge number of possible permutation of synergistic constituents

- Many **epidemiological studies** (metal industries) in workers may already involve co-exposures
  - ➢ to be checked on a case-by-case basis

- **Based on current knowledge, listing constituents target organs and apply the additivity approach is considered as a pragmatic way forward**

Questions and conclusions