DRAFT STRATEGY TO PREPARE UPGRADES OF UVCB INTERMEDIATES REGISTRATION DOSSIERS

N.B.: Red text refers to approaches / statements which need further discussion with EM secretariat, consultants and/or SCC TF. Blue text refers to items that require further action.

1. Introduction

1.1. Aim

This outline for an approach that could be followed by metals consortia to prepare dossier upgrades for their UVCB intermediates is the result from a brainstorming meeting held 19 January 2012 between EM secretariat (Hugo Waeterschoot & Violaine Verougstraete) and EPMF secretariat (Caroline Braibant & Katrien Arijs). The proposed approach will be discussed at an EM SCC Task Force meeting scheduled 1 March 2012 and will be further refined after additional input from EBRC and WCA.

1.2. Background

Following the release of an updated ECHA Guidance on intermediates in December 2010, the metals sector supported by EM has:

- Developed examples demonstrating how strictly controlled conditions (SCC) are implemented in the metals industry in light of the specificities of the materials processed, the process conditions and the risk management measures designed in accordance to both
- Developed tools to assist industry in the determination of either updates or upgrades requirements as well as in the preparation of each one of these:
    - ***Rigorous Containment Guide (RiCoG):*** an excel-based tool functioning as a questionnaire which allows companies to conduct a self reflection on whether their process takes place under rigorous containment (RiCo) and/or how it can be improved in order to meet RiCo conditions;
    - ***Appendix 2 and 3 best case templates*** containing detailed information, available to consortia to promote a coherent and consistent (internal) reporting on intermediates to facilitate high quality dossier update reporting;
    - ***Guidance on good quality workplace monitoring practices*** in order to support the above RiCo determination in dossier updates, or fulfil exposure data needs in dossier upgrades;
    - ***Decisive DNEL approach*** providing a selective tool to determine which driving constituents of a UVCB must be monitored when collecting / generating exposure data.
    - ***Metals Classification Tool (MECLAS):*** a web enabled tool originally developed for classification of complex materials in the metals sector containing a spectra of different metals (compounds) and minerals. This tool can also be used to determine which constituents drive the toxicity.
    - Improvements of existing ***metal specific exposure modelling tools*** such as MEASE, and SPERCs.

When preparing **upgrades** of their UVCB intermediate registration dossiers, registrants face the following challenges:

1. Can test waiving be applied and motivated?
2. How to perform read-across (which tool) and how to justify it appropriately?
3. How to identify and prioritise driving constituents for the effects assessment?
4. How to identify and prioritise driving constituents for the exposure assessment?
5. How to perform the risk characterisation and propose risk management measures and what iterations can be applied?

MECLAS can be used as a tool to identify those constituents that drive the toxicity (environmental and/or human health?). Tools to identify those constituents that drive the occupational exposure are still under development (no tool to identify drivers for environmental emission is under development yet). Basic principles are provided below:

- Environmental exposure and/or effects assessment: the concentration, possibly chemical speciation, M-factor, Transformation/Dissolution (T/D) data and GHS/CLP hazard categories of all relevant constituents need to be considered.
- Workplace exposure and/or human health effects assessment: the concentration, GHS/CLP hazard categories and DNEL (or OEL in the absence of DNEL) of all relevant constituents for each toxicity endpoint, exposure route and mode of action need to be considered.

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1.3. Structure of the document

The next chapters describe the underlying principles and methods that can be applied to conduct or justify UVCB intermediate assessments:

- Test waiving,
- Effects assessment,
- Validation testing (if relevant),
- Exposure assessment,
- Risk characterisation,
- Exposure scenario drafting, and
- Risk management measures.

The principles and methods applied will differ for the environmental and human health assessment. In each case, they will be illustrated by (real) examples.

The overall approach is based on the use of existing evidence from the Registration files of the constituents. It is therefore crucial to ensure a legitimate yet pragmatic access to the constituents' data sets, which is presented too. A standard approach between the metals Consortia seems most relevant to facilitate such exchanges.

While the approach was designed for UVCB intermediates, it is noted that several principles may also apply to simpler Multi Constituent Substances or other types of complex materials (e.g. alloys).

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2. Environmental exposure and effects assessment and risk characterisation of UVCB intermediates

2.1. Principles

Table 1. Principles of ecotoxicity and environmental fate, behaviour and exposure information requirements under REACH for a UVCB intermediate

	Background reasoning	Tool used/Information required
Test waiving[1]	- Inappropriate to test a complex mixture - Variability in composition across companies/streams and over time - Difficult to identify a representative sample - Test result may not be sufficiently protective nor contribute to improved safety	- Existence of registration dossier(s) on one or more of the constituents (if data already exists) - Existence of registration dossier(s) on all relevant substance(s) which can be used as a basis for read-across (shall be properly justified: basic principles summarised by EM) - Existence of 100 mg/l T/D information if no organics in play - What if organics?[2]
Effects assessment[1]	- Effects assessment of the intermediate will depend on effects of the different constituents (at this stage no cumulative, synergism/antagonism effects are considered[3]) - There are many constituents in the intermediate, how to identify the driving constituents, i.e. how to prioritise the effect assessment? => proposal to have a **prioritisation tool** based on: o Hazard values o Cut-off value of hazard category under CLP/GHS[4] (to cover DSD, still of application until 2015) of the constituent o (M-factor and/or TDp corrected) Concentration[5] of the constituent o Weight of evidence	- MECLAS for the prioritisation (includes cumulative effects) - Get access to registration files of driving constituents: Ecotoxicity Reference Values (ERVs) for water, soil, sediments, air[6], marine, Kd and dilution factor required (chronic[7] ERV of ion/metals[8])
Exposure assessment	- Exposure assessment of the intermediate will depend on exposure to intermediate constituents - How to identify driving constituents, i.e. how to prioritise the exposure assessment? => proposal to have a **prioritisation tool** based on: o Cut-off value of hazard category under GHS (to cover DSD, still of application until 2015) of the constituent o (M-factor and/or TDp corrected) Concentration[5] of the constituent o Volume of materials (for emissions to air only?[6])	- Emissions to water, soil, sediments, air[6] and sewage treatment plant for each compartment required (modelling possible) - SPERCs
Read-across / Risk Characterisation	- Site-specific local[9] assessment of each environmental compartment (water, soil, sediments, air[6] and sewage treatment plant) - Follow tiered approach: 1) Assume all constituent "X" emission results from Intermediate and use for RC calculation 2) If risk appears, attempt to allocate constituent "X" to specific sources in addition to Intermediate based on production volume 3) If risk subsists, measure constituent "X" released from each possible source at the source	- Emissions of (driving?) constituents transformed as total load into the environment (Toxic Unit Approach[10]) - PNEC for each driving constituent - Sum of individual RCR?
Validation testing	Most sensitive trophic level (Algae or Daphnia test in TDp solution)	
Exposure Scenario	Only one, covering the manufacture and use of the intermediate (even if it occurs at several steps on-site) How to cover transport? Exempt from REACH scope? Site-specific or Generic (for inclusion in joint CSR)	
Risk Management	To be completed	

[1] While test waiving is an administrative step, for which legal argumentation is needed, the effects assessment is part of the risk characterisation.
[2] Metals bound to organic compounds can (from an (eco)toxicity viewpoint) behave as a metal or as an organic compound. The latter is not covered by this approach, the first one is. For the environment, this can be easily assessed by checking if the substance dissociates in water solubilising the metal ion while the organic part does not express toxicity.
[3] Discussion point: cumulative effects are obligatory for hazard classifications but are not for risk assessments / characterisations (so far).
[4] GHS categories for the environment are recommended given aquatic acute 2 and 3 do not exist under CLP but do under GHS and could lead to risk scenarios.
[5] TDp corrected concentration to capture soluble fraction.
[6] Discussion point: should air be included?
[7] Environmental risk assessments are assessments of long-term impacts, need for chronic values.
[8] In environmental assessments of metals and their compounds, the ion is the toxicity driver.
[9] Regional assessments are not relevant as intermediates are short-life materials that are aimed to be transformed into another substance at the manufacture / use site, for which an individual local assessment is conducted.
[10] All ERVs translated in number of units in order to compare toxicants with different ERV and calculate total load into the environmental compartment (cf. 5.2 Toxic Unit Approach (Environmental endpoint)).

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2.2. Examples

Table 2. Examples of ecotoxicity and environmental fate, behaviour and exposure information requirements under REACH for a UVCB intermediate – to be further completed after agreement on principles

	Example of Flue dust 24 Constituents, oxides Fine powder Large surface	**Example of Matte** 20 constituents, sulphides Powder	**Example of Doré** 20 constituents, metallic Massive Low surface Antagonistic
Test waiving	No TDp available, oxide form dominates and all assumed to be soluble Reference files are registration dossiers of the ions	TDp for a reference sample available Unsure if Reference files for sulphides exists or are under development	TDp's for several reference samples are available Reference files for metallic forms available
Effects assessment	Hazard ID for classification: with MECLAS, identify driving constituents (prioritisation tool) based on: - EC_{50}s - Cut-off value of hazard category under CLP/GHS - (M-factor) corrected Concentration	Hazard ID for classification: with MECLAS, identify driving constituents (prioritisation tool) based on: - EC_{50}s - Cut-off value hazard category under CLP/GHS - (M-factor and TDp corrected) Concentration	Hazard ID for classification: with MECLAS, identify driving constituents (prioritisation tool) based on: - EC_{50}s - Cut-off value hazard category under CLP/GHS - (M-factor and TDp corrected) Concentration
	Effects assessment for risk characterisation: chronic based and using Assessment Factors for reference	Effects assessment for risk characterisation: chronic based and using Assessment Factors for reference	Effects assessment for risk characterisation: chronic based and using Assessment Factors for reference
Exposure assessment	Same prioritisation tool as for effects assessment SPERCS estimate (if relevant) as a first trigger by element		
Read-across / Risk Characterisation	RC per element + Toxic unit approach for cumulative effect (if needed)		RC per element
Validation testing			May be recommended to demonstrate "antagonistic release effect" of Cu/Ag
Exposure Scenario			
Risk Management			

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3. Workplace exposure and human health effects assessment and risk characterisation of UVCB intermediates

3.1. Principles

Table 3. Principles of human health toxicity and exposure information requirements under REACH for a UVCB intermediate

	Background reasoning	Tool used/Information required
Test waiving	- Inappropriate to test a complex mixture because of its variability in composition across companies/streams and over time - Difficult to identify a representative sample - Test result may not be sufficiently protective or contribute to improved safety (in case the reference sample is not based on a worst case scenario)	- Existence of registration dossier(s) on one or more of the constituents (if data already exists) - Existence of registration dossier(s) on all relevant substance(s) which can be used as a basis for read-across (shall be properly justified: basic principles summarised by EM) - Existence of dustiness information - Existence of bio-elution information (for read-across)
Effects assessment	- Effects of the intermediate will depend on effects of the different constituents (at this stage no cumulative, synergism/antagonism considered) - There are many constituents in the intermediate, how to identify the driving constituents, i.e. how to prioritise the effect assessment? => proposal to have a prioritisation for each relevant endpoint, relevant exposure route (inhalation, dermal, oral) in the form of a matrix based on: o Speciation[1] o Classification o Physical form (incl. dustiness) o (Bio-elution)	- Particle size, mode of action, toxicity reference values of all constituents (DNELs[2]) - MECLAS (classification) Get access to registration files of driving constituents: DNELs
Validation testing	Will depend on highest tonnage band to be registered, relevant endpoint(s) and exposure route(s)	
Exposure assessment	- Exposure will depend on exposure to constituents - How to identify driving constituents? Need to prioritise constituents for each endpoint, exposure route and mode of action based on: o MEASE estimate (if relevant as a first trigger) o Process (hot/cold) and associated emission potential o DNEL[2] o Dustiness o (Bio-elution corrected) Concentration[3]	- Process type (PROC code) required for the MEASE assessments - DNEL of all constituents - Exposure information required (modelling possible) - Decisive DNEL approach (as MECLAS does not take into account the process type)
Risk Characterisation	- Site and process/step specific; several processes with same operational conditions can be assessed jointly - Identify driving constituent for each endpoint, exposure route and mode of action, calculate RCR of each specific driving constituent, and assume the specific constituent's RCR is protective for the entire UVCB intermediate for that specific endpoint, exposure route and mode of action? - Size RCR? - Assessment of uncertainty - Follow tiered approach: 1) Assume all constituent "X" exposure (from all sources[4]) results from Intermediate and use for RC calculation 2) If risk appears, attempt to refine assessment by substance and allocate constituent "X" to specific sources / substances in addition to Intermediate	Is there a Toxic Unit approach for human health? If the same mode of action and/or target organ, probably yes.
Exposure Scenario	Several, for each process (step) involved in the manufacture and use of the intermediate How to address transport? Site-specific or Generic (for inclusion in joint CSR)	
Risk Management	To be completed	

[1] Need to have good knowledge/explanations about process steps/types as influences speciation (explain speciation is based either on measurements or on process knowledge).
[2] In the absence of DNELs, EU-wide OELs could be used for e.g. constituents which are not (yet) registered and for which a DNEL is not yet available.
[3] Assuming 100 % bioavailability unless dustiness information demonstrates no inhalation potential, and/or bio-elution information demonstrates reduced bioavailability.
[4] Occupational exposure monitoring is done using personal samplers which measure exposure from all process sources / substances the employee was exposed too that day.

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3.2. Examples

Table 4. Examples of human health toxicity and exposure information requirements under REACH for a UVCB intermediate – to be further completed after agreement on principles

	Example of Flue dust 24 Constituents, oxides Fine powder Large surface	**Example of Matte** 20 constituents, sulphides Powder	**Example of Doré** 20 constituents, metallic Massive Low surface
Test waiving			
Effects assessment			
Validation testing			
Exposure assessment			
Risk Characterisation			
Exposure Scenario			
Risk Management			

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4. Access to relevant data on constituents of UVCB intermediates

Each UVCB intermediate Registration Dossier contains a group of variable streams resulting from common process (steps). In the metals sector, the composition of UVCB intermediates is more variable than unknown, and the variability across metal sectors, companies and over time is very high in some cases.
Upgrading a UVCB intermediate Registration Dossier means fulfilling REACH Annex VII-X information requirements and preparing a CSA/CSR for a complex mixture of simple substances. This requires a complex mixture assessment and access to information on simple substances / constituents.

The information on constituents from existent Registration Dossiers / Dossiers under preparation which is needed includes:

- For the environment: Hazard category under GHS, ERV, Kd;
- For human health: Hazard category under GHS, mode of action, DNEL and how DNEL was derived

EBRC and WCA to translate in format in which information should be available on database.

Purchasing a Letter of Access (LoA) is justified in case (a) there is an intention to co-register; (b) access / use of the full dossier is needed or; (c) access / use of part of the dossier is needed (this is the case for UVCB intermediates). Therefore, a simple LoA-type access mechanism is needed to allow all concerned consortia to access part of the dossiers of the constituents to build UVCB intermediate dossier upgrades.
However, not all consortia are (currently) concerned and not all consortia need all files (need for consortia to list all relevant constituents – see also Annex 0

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Constituents present in UVCB intermediates across (non-ferrous) metals industry). Also, driving constituents will need to be identified in order to channel / filter data needs and identify those consortia which need to participate in the data access / sharing (urgent need to progress prioritisation tool for this too!).

The data access / sharing mechanism proposed would allow all (main) metal consortia secretariats to exchange necessary information on relevant constituents under an *ad hoc* data-sharing / confidentiality agreement. The data would be provided by the consultants involved in the (main) metals Registration Dossier preparation (EBRC, ARCHE, WCA, Exponent, ToxMinds, Len Levy, Environ, Dr. Knoell) and stored into a database containing only information that is relevant. The costs of the data-sharing could either be covered by each consortium or a common "fund" could be created by Eurométaux with contributions from concerned consortia to cover expenses of consortia not involved in UVCB intermediates. For the administration, supervision/guardianship of Eurométaux could be instated.

Legal aspects:

- Scope of data-sharing would be restricted to UVCB intermediate upgrades (to be defined);
- Confidentiality provision could be unlimited in time;
- Confidentiality/ownership rights?;
- Each consortium remains responsible for the quality of its information: only latest information would be used.

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5. Annexes

5.1. Read-across principles in metals industry: environment and human health - to be further completed

REACH Annex XI section 1.5 mentions:
*"Substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group, or "**category**" of substances. Application of the group concept requires that physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (**read-across** approach). This avoids the need to test every substance for every endpoint."*

Assumptions underlying the grouping of metal compounds[1]:

- Properties are likely to be similar or follow a similar pattern as a result of the presence of a common **metal ion** (or ion complex including a hydrated metal ion).
- It is the **bioavailability** of the metal ion (or a redox form of this ion) at target sites that in most cases determines the occurrence and severity of the effects to be assessed for the read-across of metal substances. Supporting information to assess the bioavailability of the metal ion at the target site can include information on a number of different factors (e.g. physico-chemical properties such as water solubility, degree of dissociation of the metal-containing compound, particle size and structure, in vitro solubility, in vivo data on systemic effects, toxicokinetics).

The following points could alter the assumption of commonality and should be considered[1]:

- **Chemical speciation and valency**: When selecting the appropriate source substance, the valence state and its influence on the assumption of commonality should be checked. For some metals (predominantly transition elements), the chemical speciation and in particular the different valencies may result in differences in mechanism of action and a variation in toxicological properties. In some cases, species may be interconvertible, in other cases there is little interconversion between the species.
- **Organometallic compounds** will generally have a different mode of action since the metal ion is not likely to be present in the same form as for inorganic compounds. In such cases, read-across between inorganic and organometallic compounds is not recommended, although read-across may well be appropriate between different organometallic compounds. On the other hand, especially for environmental risk assessment, if an organometallic compound degrades rapidly to its inorganic metal moiety, it can be assessed together with the inorganic metal moiety.
- **Metals**: Particular difficulties have been seen in evaluating the properties of metals on the basis of data for metal compounds. In some cases, read-across of properties from the metal compounds to the metal itself (metallic, zero-valent form) has been agreed, whilst for others it has not. These need to be evaluated on a case-by-case basis.
- **Metal containing UVCBs:** Some metal containing UVCB compounds may not be appropriate for consideration in a category approach, as their effects will not be expected to be adequately described by their metal content. These include compounds such as asphalt, frits and drosses. In cases where read-across is not considered appropriate, clear arguments should be put forward as to why the known hazard profile of the metal is not expected to be relevant (for example very low bioavailability).
- **Crystalline structure:** The crystalline structure of insoluble metal compounds could influence the hazard profile. If there is reason to believe that the crystalline structure influences significantly the effects of the compound to be assessed, this must be taken into account in the evaluation. An example is silica of which the crystalline and non-crystalline forms have a different hazard profile.

Preliminary evaluation of the category and read-across[1]:

- The **water solubility** of the metal compounds is often used as the starting point for establishing a category, as this provides a first indication of the availability of the metal ion in the different compartments of interest. The most simplistic approach to hazard evaluation is to assume that the specific metal-containing compound to be evaluated shows the same hazards as the most water-soluble compounds. This is a conservative approach, since systemic metal ion availability will normally be reduced with decreasing water-solubility and consequently reduced bioavailability. This simplistic approach can be refined for categories containing many substances by building subcategories based on water solubility, when data is available on trends with water solubility. This difference in trend is

[1] ECHA Guidance on Information Requirements and Chemical Safety Assessment – Chapter R6 – Section 6.2.5.6 Metals, metal compounds and other inorganic compounds (http://guidance.echa.europa.eu/)

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clearly recognised in evaluating the environmental hazards of metals and metal compounds, where the relevant hazards can be evaluated using TDp.

- Information from **other endpoints** could further support the systemic bioavailability assumptions (e.g. LD_{50} values). For endpoints where a threshold occurs, estimates of the systemic bioavailability (i.e. toxicokinetics) of the metal ion can be ascertained for representative members of each category in order to ascertain whether the bioavailability exceeds the threshold for the compounds.
- In addition to water solubility, phagocytosis, bioaccessibility in synthetic biological fluids, and organ deposition and clearance rates are relevant parameters to be considered.
- Where **toxicokinetic data** is available, this should be used as this provides relevant information on whether the source and target chemicals in question behave similarly as expected from read-across or whether there are biological differences that would bring into question the validity of the category hypothesis.
- Other factors may also need to be taken into account:
    - **Counter ions and other metal ions**: The assumption that the metal ion is responsible for the common property or effect implies that the toxicity of the counter ion or of other metals present in the compound will be largely irrelevant in producing the effects to be assessed. This assumption could be affected by interactions between the metal ion and other parts of the substance e.g. the counter ion. It is noted that in certain cases the effect of the counter ion in acute toxicity studies exert another effect than in repeated dose studies using lower dose levels. This could obscure the role of the metal ion in either the acute or repeated dose studies. The influence of the counter ion should be checked for each endpoint. If there is reason to believe that the counter-ion (such as cyanates, oxalates) or other metal ions present in the compound influence significantly the effects of the compound to be assessed and alter the assumption of commonality, this must be taken into account in the evaluation. One option may be to use the additive approach described in the foreword to Annex I, Directive 67/548/EEC, in the guidance to Note A.
    - **Crystalline structure**: The crystalline structure of insoluble metal compounds could influence the hazard profile. If there is reason to believe that the crystalline structure influences significantly the bioavailability and so the effects of the compound to be assessed, this must be taken into account in the evaluation.
    - **Particle size information**: Particle size information of the substance influences the deposition behaviour in the respiratory tract and potential toxic effects. Based on particle size distribution data, trends in deposition and potency of effects can be assessed for locally acting substances.
- If there is evidence that the crystalline structure and particle size influence significantly the bioavailability and so the severity of the effects of the compound to be assessed, this must be taken into account in a Weight of Evidence approach considering all available information (e.g. toxicokinetics).

Prioritisation effects assessment:

1. First assumption: all constituents may generate effects during production/use of the intermediate: need to know which substances are involved in production/use, over the process or a specific step, in which physical forms and which chemical speciation
2. Second assumption: common effects/endpoints should be assessed as cumulative effects as a first TIER (e.g. Toxic unit approach)
3. Prioritise and identify the drivers based on:
    a. Hazard profile (assumption that more dangerous substances are higher classified) of relevant speciation (or worst case if not classified as relevant speciation - if using worst case, it is important to demonstrate the reasoning you have used to decide that this is worst case)
    b. Cumulative effect of many individual elements recognising speciation, may be as important as the single effect of a more dominant component
    c. Physical form may also play a role in the effects assessment: massive vs. powders, fine powders vs. coarse
    d. Specific considerations to introduce if complex materials with matrix effect OR if specific mechanism of action

Speciation data issues:

- Not all companies have speciation data available -> some companies have XRFs: composition info can give info on speciation + speciation info is not always needed if you have process knowledge which may in general define the chemical speciation
- If available this information would be included in MECLAS if this tool was used for hazard classification

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Uncertainty and variability assessment:

- Difficult to find representative sample for UVCB intermediates -> compare margin of safety (as illustrated by the RCR) with margin of variability

Intermediate: name						
Composition	component A	component B	component C	component D	component E	component F
(%)						
Speciation						
Physical form						
Specific considerations: alloy, matrix?						

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Endpoint + exposure route	**Constituent A**			**Constituent B**			**Constituent C**		
	Classification A	Physical form A	To consider (bioavailability, mode of action)	Classification B	Physical form B	To consider (bioavailability, mode of action)	Classification C	Physical form C	To consider (bioavailability, mode of action)
Short-term effects, oral route (systemic and local effects)	Acute oral classification?	Not relevant in case particles cannot be ingested during normal handling and use		Acute oral classification?			Acute oral classification?		
Short term, inhalation route (systemic and local effects)	Acute inhalation classification?	Not relevant in case particles cannot be inhaled/respired during normal handling and use		Acute inhalation classification?			Acute inhalation classification?		
Short term, dermal route (systemic and local effects)	Acute dermal classification? Irritation?			Acute dermal classification? Irritation?			Acute dermal classification? Irritation?		
Long term, oral route (systemic and local effects)	Repeated dose classification by Oral route?	Not relevant in case particles cannot be ingested during normal handling and use		Repeated dose classification by Oral route?			Repeated dose classification by Oral route?		
Long term, inhalation route (systemic and local effects), oral	Repeated dose classification by Inhalation route ?	Not relevant in case particles cannot be ingested during normal handling and use (can we do this for hazard properties for effects assessment (not for classification)?).		Repeated dose classification by Inhalation route ?			Repeated dose classification by Inhalation route ?		
Long term, dermal route (systemic and local effects)	Repeated dose classification by Dermal route ?			Repeated dose classification by Dermal route ?			Repeated dose classification by Dermal route ?		

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Example to work out: Doré

Intermediate: Doré						
Composition	component A	component B	component C	component D	component E	component F
(%)						
Speciation						
Physical form						
Specific considerations: alloy, matrix?						

Endpoint + exposure route	**Constituent A**			**Constituent B**			**Constituent C**		
	Classification A	Physical form A	To consider (bioavailability, mode of action)	Classification B	Physical form B	To consider (bioavailability, mode of action)	Classification C	Physical form C	To consider (bioavailability, mode of action)
Short-term effects, oral route (systemic and local effects)	Acute oral classification?			Acute oral classification?			Acute oral classification?		
Short term, inhalation route (systemic and local effects)	Acute inhalation classification?			Acute inhalation classification?			Acute inhalation classification?		
Short term, dermal route (systemic and local effects)	Acute dermal classification? Irritation?			Acute dermal classification? Irritation?			Acute dermal classification? Irritation?		
Long term, oral route (systemic and local effects)	Repeated dose classification by Oral route?			Repeated dose classification by Oral route?			Repeated dose classification by Oral route?		
Long term, inhalation route (systemic and local effects), oral	Repeated dose classification by Inhalation route?			Repeated dose classification by Inhalation route?			Repeated dose classification by Inhalation route?		
Long term, dermal route (systemic and local effects)	Repeated dose classification by Dermal route?			Repeated dose classification by Dermal route?			Repeated dose classification by Dermal route?		

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5.2. Toxic Unit Approach (Environmental endpoint)

The Toxic Unit approach assumes that toxicity following exposure to multiple constituents is additive:

$$\text{Sum Toxic Units} = \sum \frac{ERV\ (X)}{Concentration\ (X)}$$

Why and when do we need a Toxic Unit (TU) approach?

- Why: to count for the cumulative effects of the different components in the mixture.
- When: in case the substances have a common mode of action (or always when this info is not available).

Example: One company is producing Ag, Flue dust and Cu -> Emission of e.g. Ag, Pb, Zn and Cu; Pb and Zn not prioritised with prioritisation tool (i.e. Ag and Cu are constituents of concern)

Ag production	Flue Dust production	Cu production

↓ 90% of total Ag emission
Ag
 	
RC done in Ag file
 	
Ag assessed as single/isolated load
	↓ 10% of total Ag emission
	Ag + Cu
	
	RC done in Flue Dust file
	
	Need to assess Ag and Cu load jointly: use tiered TU approach
	• Tier 1: compare total monitored concentration with TU to check for risk (assuming all Ag and Cu comes from flue dust production)
	  ○ Chronic ERV (Ag) = 0,08 µg/l
	  ○ Chronic ERV (Cu) = 8 µg/l
	  -> 1 unit of Ag is 100x more toxic then 1 unit of Cu
	• Tier 2: split Ag and Cu according to source; then apply TU
	• Tier 3: validation if needed (combined ecotox test)
		↓
		Cu
		
		RC done in Cu file
		
		Cu assessed as single/isolated load

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5.3. Metals processes and interference of speciation based on process knowledge

To be developed (2 pages: 1 flowsheet, 1 table)

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5.4. Constituents present in UVCB intermediates across (non-ferrous) metals industry

Table 5. List of constituents present in UVCB intermediates manufactured and used in the metals sector (to be completed by other sectors)

	Constituent	TRV - dissemination page	ERV - dissemination page	UVCB intermediates it is present in (Consortium)	Data-holder	Common hazard profile*	Authorisation
1.	**Ag**	DNEL inhal. longterm systemic	PNEC freshwater, marine, STP, sediment, soil	PM	PM		
2.	Ag chlorides			PM	PM		
3.	Ag nitrate (AgNO3)			PM	PM		
4.	Ag oxides (AgO, Ag2O)			PM	PM		
5.	Ag selenide (Ag2Se)			PM	PM+Se/Te		
6.	Ag sulphides			PM	PM		
7.	**Al**	DNEL inhal. longterm local	PNEC STP	PM			
8.	Al oxides (Al2O3)			PM			
9.	Al silicates (Al2SiO5)			PM			
10.	**As**	-	-	PM			
11.	As2O3	-	-	PM			
12.	As2O5	-	-	PM			
13.	**Au**	-	-	PM	PM		
14.	Au chlorides (AuCl4)	-	-	PM	PM		
15.	Au nitrate (AuNO3)	-	-	PM	PM**		
16.	Au sulphates (AuSO4)	-	-	PM	PM**		
17.	Au sulphides	-	-	PM	PM**		
18.	**B**	-	-	PM			
19.	Borates (Na2B4O7)	DNEL inhal. • acute local • longterm systemic • longterm local DNEL dermal longterm systemic	PNEC freshwater, marine, STP, sediment, soil	PM			
20.	**Ba**	-	-	PM			
21.	Ba oxides (BaO)	-	-	PM			
22.	Ba sulphates (BaSO4)	DNEL inhal. • longterm systemic • longterm local	PNEC freshwater, STP, sediment, soil	PM			
23.	**Bi**	DNEL inhal. longterm systemic	PNEC STP	PM			
24.	Bi arsenate (BiAsO4)			PM			
25.	Bi hydroxide (Bi(OH)2)			PM			
26.	Bi oxides (Bi2O3)			PM			
27.	**Ca**	DNEL inhal. • longterm local • acute local	-	PM			
28.	Ca chlorides (CaCl2)			PM			
29.	Ca oxides (CaO)			PM			
30.	Ca silicate (Ca2SiO4)			PM			
31.	**Cd**	DNEL inhal. longterm systemic	PNEC freshwater, marine, STP, sediment, soil, oral	PM			
32.	**Ce**	DNEL inhal. longterm systemic, DNEL dermal longterm systemic	PNEC freshwater, marine, STP	PM			
33.	**Co**	DNEL inhal.	PNEC	PM			

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	Constituent	TRV - dissemination page	ERV - dissemination page	UVCB intermediates it is present in (Consortium)	Data-holder	Common hazard profile*	Authorisation
		longterm local	freshwater, marine, STP, sediment, soil				
34.	Co sulphides			PM			
35.	**Cr**	DNEL inhal. longterm local	PNEC freshwater, sediment, soil	PM			
36.	Cr oxides (Cr2O3)			PM			
37.	Cr silicates (Cr2(SiO4)3)			PM			
38.	**Cu**	DNEL inhal. acute systemic, DNEL dermal • acute systemic • longterm systemic	PNEC freshwater, marine, STP, sediment, soil	PM			
39.	Cu arsenide			PM			
40.	Cu carbonates			PM			
41.	Cu hydroxide (Cu(OH)2)			PM			
42.	Cu nitrate (Cu(NO3)2)			PM			
43.	Cu oxides (CuO, Cu2O)			PM			
44.	Cu selenide (Cu2Se)			PM			
45.	Cu sulphates (Cu2SO4)			PM			
46.	Cu sulphides (CuS, Cu9S5)			PM			
47.	Cu telluride (Cu2Te)			PM			
48.	**Fe**	DNEL inhal. longterm local	-	PM			
49.	Fe oxides (FeO, Fe2O4, Fe3O4)			PM			
50.	Fe silicates (Fe2SiO4)			PM			
51.	Fe sulphides (FeS, FeS2)			PM			
52.	**Mg**	DNEL inhal. longterm systemic	PNEC freshwater, marine, STP, sediment, soil	PM			
53.	Mg chlorides (MgCl, MgCl2)			PM			
54.	Mg oxides (MgO)			PM			
55.	**Mn**	DNEL inhal. longterm systemic, DNEL dermal longterm systemic	PNEC freshwater, marine, STP, sediment, soil	PM			
56.	Mn oxides (MnO)			PM			
57.	**Ni**	DNEL inhal. • longterm systemic • longterm local • acute local • acute systemic DNEL dermal local	-	PM			
58.	Ni ferrites (NiFe2O4)	-	-	PM			
59.	Ni oxides (NiO)	-	-	PM			
60.	Ni sulphates (NiSO4)	DNEL inhal. • longterm systemic • longterm local • acute local	-	PM			

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	Constituent	TRV - dissemination page	ERV - dissemination page	UVCB intermediates it is present in (Consortium)	Data-holder	Common hazard profile*	Authorisation
		• acute systemic DNEL dermal longterm local					
61.	Ni sulphides (Ni3S2)	DNEL inhal. • longterm systemic • longterm local • acute local • acute systemic DNEL dermal longterm local	-	PM			
62.	**Pb**	-	PNEC freshwater, marine, STP, sediment, soil, oral	PM			
63.	Pb arsenide			PM			
64.	Pb arsenate (Pb3(AsO4)2			PM			
65.	Pb chlorides			PM			
66.	Pb hydroxide (Pb(OH)2)			PM			
67.	Pn nitrate (Pb(NO3)2)			PM			
68.	Pb oxides (PbO)			PM			
69.	Pb silicates			PM			
70.	Pb sulphates (PbSO4)			PM			
71.	Pb sulphides (PbS)			PM			
72.	**PGM (Pt, Pd, Rh, Ru, Ir)**	-	-	PM	PM		
73.	PGM chlorides (different oxidation states)			PM	PM		
74.	PGM chloro-complexes			PM	PM**		
75.	PGM nitrates			PM	PM		
76.	PGM sulphides			PM	PM		
77.	**Sb**	DNEL inhal. longterm local, DNEL dermal longterm systemic	PNEC freshwater, marine, STP, sediment, soil	PM			
78.	Sb arsenate (SbAsSO4)			PM			
79.	Sb hydroxide (Sb(OH)3)			PM			
80.	Sb oxides (Sb2O3)			PM			
81.	Sb sulphides			PM			
82.	**Se**	-	-	PM			
83.	Se oxides (SeO)	-	-	PM			
84.	**Si**	-	PNEC aqua (intermittent releases), PNEC STP	PM			
85.	Si oxides (SiO2)	DNEL inhal. longterm systemic	-	PM			
86.	**Sn**	DNEL inhal. • acute systemic • longterm systemic DNEL dermal • acute systemic • longterm systemic	-	PM			

	Constituent	TRV - dissemination page	ERV - dissemination page	UVCB intermediates it is present in (Consortium)	Data-holder	Common hazard profile*	Authorisation
87.	Sn oxides (SnO2)			PM			
88.	Sn silicates (SnSiO4)			PM			
89.	Sn sulphates (SnSO4)			PM			
90.	Sn sulphides			PM			
91.	**Sr**	-	-	PM			
92.	**Te**	-	-	PM			
93.	Te oxides (TeO2)	-	-	PM			
94.	**Ti**	-	PNEC freshwater, marine, STP, sediment, soil	PM			
95.	Ti oxides (TiO2)	DNEL inhal. longterm local	PNEC freshwater, marine, STP, sediment, soil	PM			
96.	**Zn**	DNEL inhal. longterm systemic, DNEL dermal longterm systemic	PNEC freshwater, marine, STP, sediment, soil	PM			
97.	Zn oxides (ZnO)			PM			
98.	Zn silicates (Zn3SiO410(0o)2			PM			
99.	**Zr**	DNEL inhal. longterm systemic, DNEL dermal longterm systemic	PNEC freshwater, marine, sediment, soil	PM			
100	Zr oxides (ZrO2)			PM			

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