REACH Practical Guide on Safe Use Information for Mixtures under REACH

The Lead Component Identification (LCID) Methodology

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WIR GESTALTEN ZUKUNFT.

This REACH Practical Guide on Safe Use Information for Mixtures under REACH and the Lead Component Identification (LCID) Methodology is a contribution to the CSR/ES Roadmap (action 4.4A; http://echa.europa.eu/regulations/reach/registration/information-requirements/chemical-safety-report/csr-es-roadmap)

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1 Introduction

The safe use of chemicals is one of the main objectives of REACH. Chemical safety assessments (CSA) of substances are the main source of this information. In a CSA the entire life cycle of a substance must be evaluated.

In many cases substances are used in mixtures during their life cycle. Therefore these uses have to be included in the CSA. But uses of substances in mixtures often imply changes in the conditions of use. These changes may be relevant to the operational conditions (OCs) and risk management measures (RMMs) derived for such uses.

Most chemical products are mixtures, which are usually formulated or produced directly in order to change certain properties and effects of substances or to achieve specific effects of the product. Mixtures may be formulated from substances or other mixtures but they are often a result of a production process (e.g., if a substance is manufactured in a solution).

The following sections address tasks and obligations of the different actors who handle such mixtures.

2 Supply chains and mixtures

A typical **supply chain** starts with the manufacturer of substances and ends with the final downstream user (DU) who applies a mixture in an industrial or professional application. This is illustrated in Figure 1. The structure of the supply chain can vary according to the different mixtures. It can be shorter or longer, and can involve distributors between each step. However, the main elements shown in Figure 1 are relevant for most mixtures.

The different actors shown in Figure 1 have different obligations under REACH regarding mixtures:

- **Manufacturers/importers of substances** have to register each substance manufactured/imported in volumes of 1 tonne or more per year and per legal entity. They have to generate a Chemical Safety Report (CSR) for those substances which they produce/import in quantities of 10 tonnes or more per year. The CSR has to include exposure scenarios (ESs) for all identified uses in case substances meet the criteria of Art. 14 of the REACH regulation.
- **Formulators** produce mixtures by formulating substances or other mixtures. If they do not manufacture or import the substances, they are only acting as downstream users under REACH.

  Mixtures from the first formulator can be used by a second formulator as a raw material for his mixtures. Several formulators can be involved until the end-use mixture is supplied to the final downstream user[1].

[1] Consumers are not considered as downstream users under REACH.

- **Final downstream users of chemical products** applying mixtures in industrial or professional applications have specific obligations under REACH. Consumers have no obligations since they are not downstream users under REACH.
- **Distributors** can be involved several times in the supply chain; they are not considered downstream users.

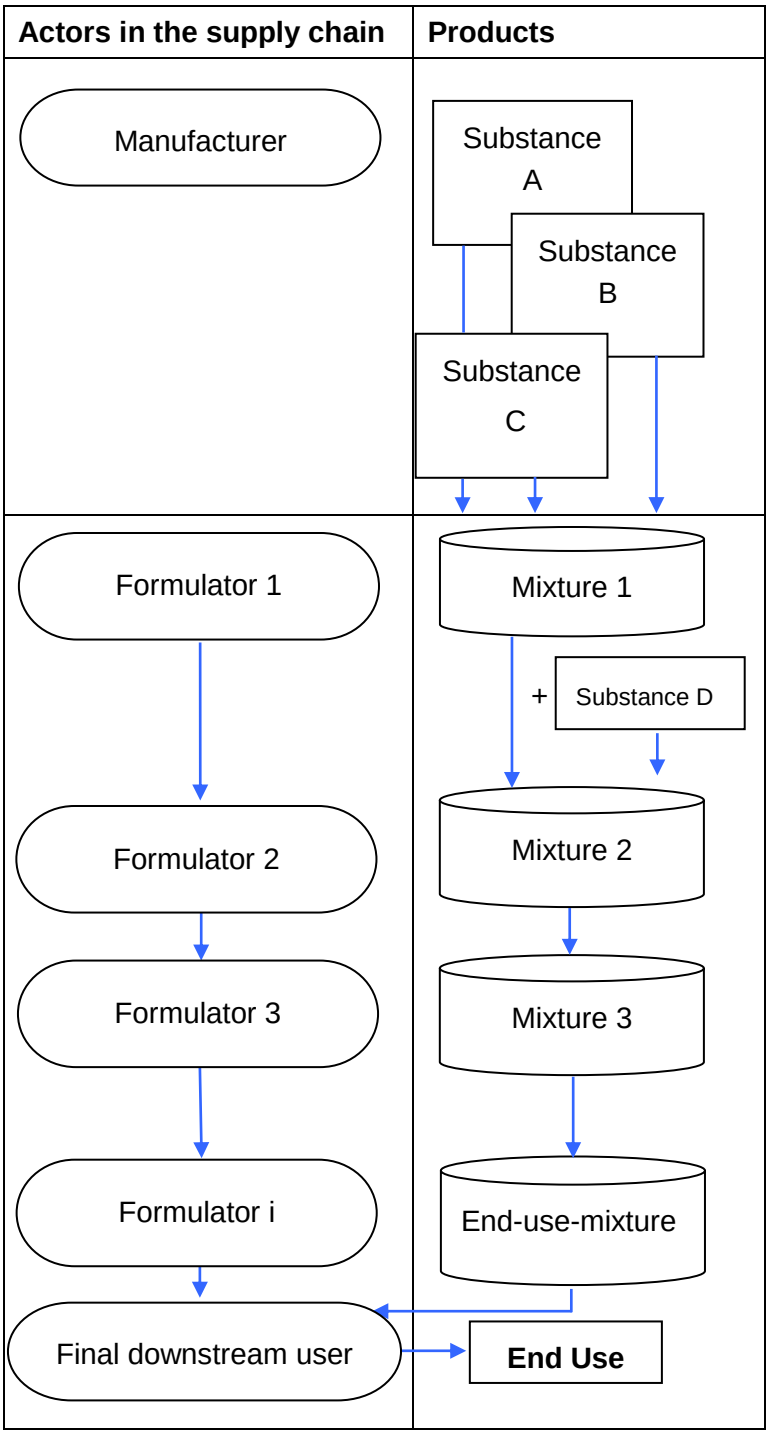

Figure 1 Supply chain mixtures

3 REACH obligations for actors dealing with substances in mixtures and mixtures themselves

REACH obligations for manufacturers, formulators and the final downstream users differ according to their role and are described in further detail in this chapter. In advance it is helpful to get an overview of which type of documents related to a substance (especially for the classified substances) and which documents related to a mixture can be expected to be handled by the different actors in the supply chain.

(Please note: Not all of these documents are obligatory for each substance; for example, CSRs are only required for substances produced/imported in quantities of 10 tonnes or more per year per registrant; downstream user chemical safety reports (DU CSRs) are only required for uses which are not covered by the exposure scenario (ES) of the supplier and if exemptions cannot be applied).

REACH documents that have to be prepared for the registration by the manufacturer/ importer (M/I) related to a hazardous substance:

- registration dossier;
- chemical safety report[2] (CSR), which documents the chemical safety assessment (CSA) of the substance. It is part of the registration dossier, if required per REACH Art. 14.1;
- exposure scenarios (ESs) for the identified uses of the substance (part of the CSR), if required according to REACH Art. 14.4; and
- extended safety data sheet (eSDS), with one or more exposure scenarios as annexes to the eSDS, if required under REACH Art. 14.4 and Art. 31.7 (only if the substance is placed on the market in the EU).

REACH documents that may be prepared or forwarded by downstream users related to a mixture classified as hazardous:

- safety data sheet (SDS) for the mixture, including safe use information (related to the intended downstream uses);
- exposure scenarios for substances in the mixture, if required according to REACH Art. 31.7;
- conditions of safe use for the mixture as part of one's own assessment or safety data sheet according to REACH Art. 31.2 sentence 2[3]);

[2] A chemical safety report is required for substances with a tonnage of 10 tonnes per year and more per manufacturer/importer and is part of the registration dossier

[3] If the safety data sheet is developed for a mixture and the actor in the supply chain has prepared a chemical safety assessment for that mixture, it is sufficient if the information in the safety data sheet is consistent with the chemical safety report for the mixture instead of with the chemical safety report for each substance in the mixture.

- downstream user notification to ECHA of uses not covered by exposure scenarios received from suppliers, if required according to REACH Art. 38;
- downstream user chemical safety report (DU CSR) for one or more hazardous substances in the mixture (Art. 37.4 REACH) (if the use is not covered by the ES of the supplier or if the supplier advises against this use, unless exemptions according to REACH Art. 37.4 are applicable); and
- chemical safety report for the mixture (Art. 31.2 sentence 2 REACH) (no REACH requirement, optional).

Nearly all REACH obligations are related to substances as such or as part of a mixture – but not to mixtures themselves. With regards to mixtures, Title IV of REACH sets requirements for the communication in the supply chain including creating safety data sheets for mixtures.

Three main obligations are important for actors handling substances in mixtures:

1. Chemical safety assessment (CSA) of substances (M/I)

This requirement only refers to manufacturers and importers who have to register substances. (In certain cases, downstream users may develop their own CSA, if their uses are not covered by the exposure scenarios which they received from their suppliers.)

The CSAs prepared have to cover all identified uses during the substance's complete life cycle[4] including manufacture of the substance in the EU (REACH Art. 14.4 and Annex I) and being part of a mixture.

Chapter 4.4 of this document addresses the question on how the registrant can take into account when his substance becomes part of a mixture when performing the chemical safety assessment.

2. Check of downstream user (DU) whether his uses are covered by exposure scenarios

The obligations to assess whether one's own uses[5] are covered by exposure scenarios which have been received applies to **any** downstream user, independent of whether they receive the substance on its own or in a mixture (see Figure 2). This includes the first actor who is producing a mixture as well as follow-up formulators and finally the (industrial or professional) user of the end-use mixture[6].

A downstream user has to check whether his own conditions of use are covered by the OCs and RMMs described in the exposure scenarios he receives (REACH Art. 37.4). Note: Fig-

[4] In line with REACH Art. 14.2, uses in mixtures where the concentration of a given substance is below the CLP threshold limits do not need to be taken into account.

[5] Registrants **should** include uses of **all** of their customers/downstream users in their registrations. However, these checks are a means for downstream users to verify that their uses have been covered and if not, an opportunity to communicate these gaps with their suppliers.

[6] See ECHA Guidance for Downstream Users Version 2.1 (Oct. 2014), 1.2.2. The role of downstream users in supply chains, pp. 18-20

ures of this guidance reference this as “DU check conditions of use.” Please be aware that this assessment of the downstream user has nothing to do with the compliance check done by the European Chemicals Agency (ECHA) related to registration dossiers.

If his use is not covered or his conditions of use differ from those described in the exposure scenario, he has five options:

- contact the supplier to have the use/conditions of use included;
- implement the conditions of use described in the exposure scenario;
- change to a supplier who provides the substance with a safety data sheet and exposure scenario that covers his use;
- find a substitute for the substance; or
- prepare his own CSA, unless exemptions according to REACH Art. 37.4 are applicable.

The downstream user’s assessment as to whether his uses are covered, its consequences and the related time frames, is described in further detail in Chapter 4 of the ECHA Guidance for downstream users.

3. Inclusion of information in safety data sheets (SDS) (M/I, DU)

Any downstream user shall include (or be consistent with) relevant information from received exposure scenarios, and use other relevant information from the safety data sheets supplied to him, when compiling his own safety data sheet for identified uses (REACH Art. 31.7, 2nd sentence).

This requirement refers to anyone who receives safety data sheets and is required to develop a safety data sheet for his substance or mixture that includes identified uses. This is especially the case for formulators producing mixtures who must supply corresponding safety data sheets to customers. The following Figure 2 describes the main tasks for formulators and final downstream users receiving SDSs from their suppliers. Final downstream users of an end-use mixture do not need to prepare safety data sheets and therefore are not affected by this obligation. Details on what DUs should consider relevant information to forward on to their customers from supplier ESs, and possible options on how to forward that information are discussed in Chapter 5.

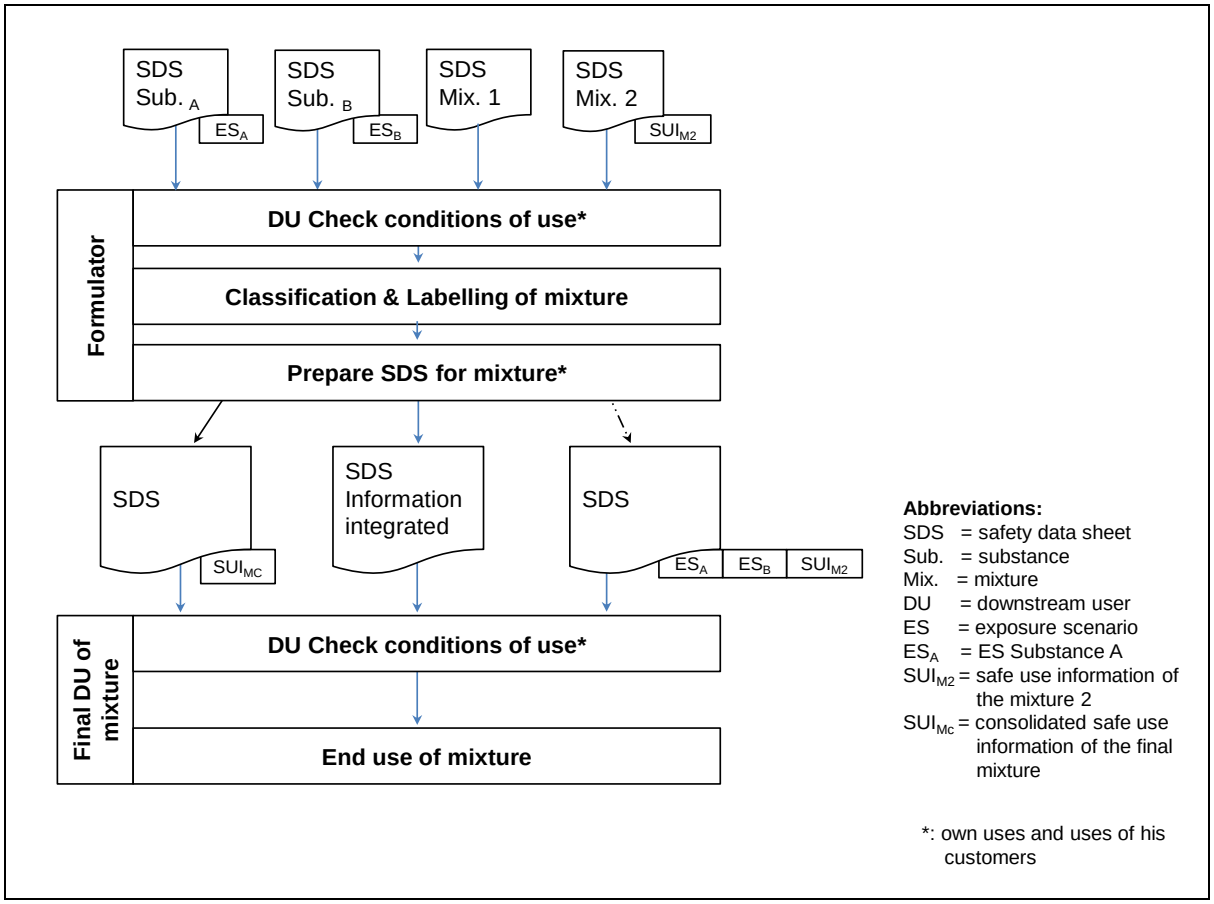

Figure 2 Main tasks for a formulator and final downstream user receiving safety data sheets.
Both actors (the formulator and the final downstream user of the mixture) have to implement the operational conditions (OCs) and the risk management measures (RMMs) related to their own uses. The second part of the figure illustrates three options to include safe use information from safety data sheets of substances into the safety data sheet of the mixture. See Chapter 5 for details.

The task of preparing an SDS for a mixture is illustrated in Figure 3. It is described in detail in Chapter 6 of this document.

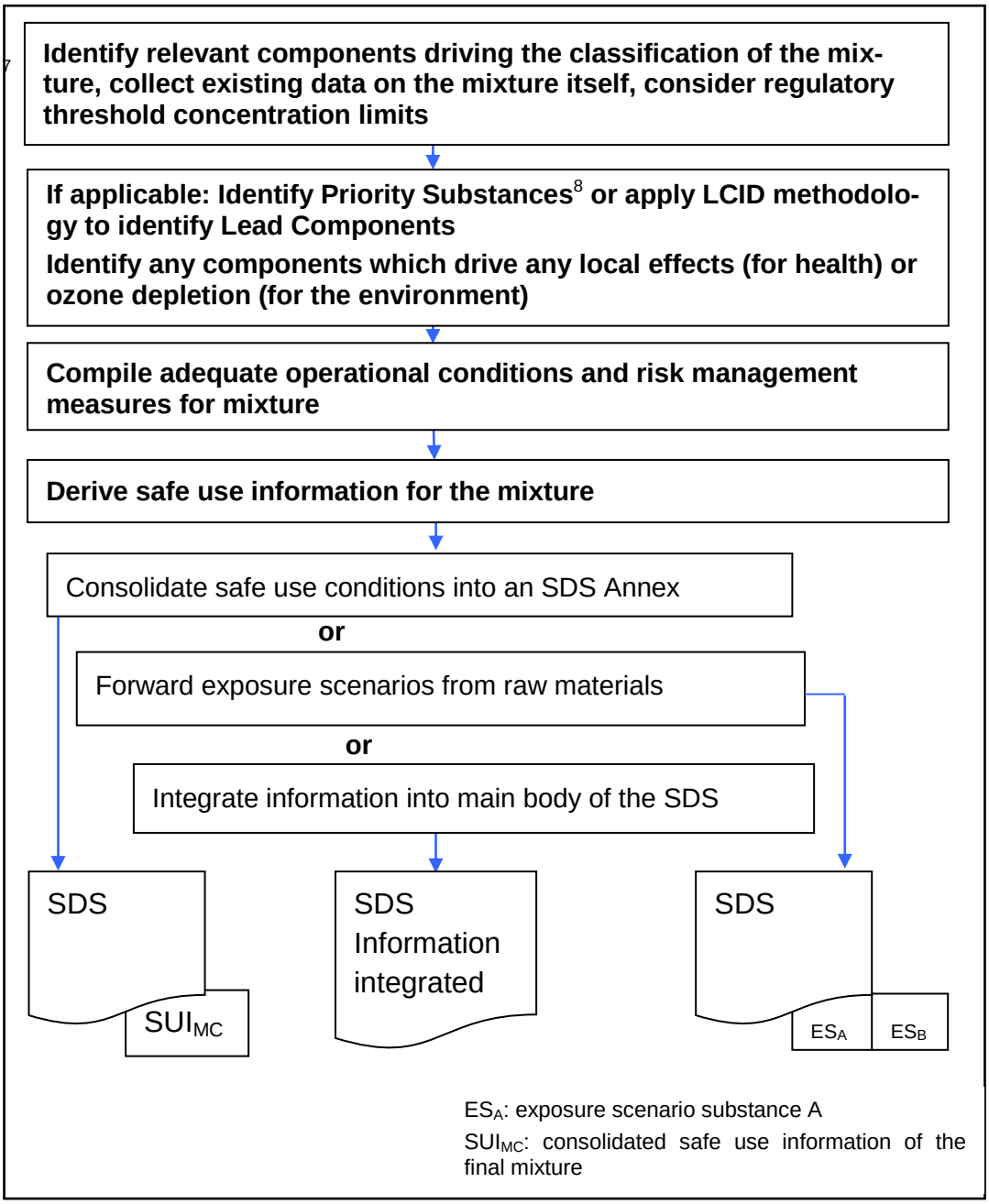

Figure 3 Main tasks for a downstream user preparing a safety data sheet for a mixture. The second part of the figure illustrates three options to include information from safety data sheets of substances into the safety data sheet of the mixture. Remark for the third option: it might be necessary to modify exposure scenarios of substances before forwarding them. See Chapter 5 for details.

[7] Priority Substances: For health hazards these are carcinogens and mutagens; for environmental hazards these are chemicals classified as PBTs (persistent, bioaccumulative, toxic substances) and/or vPvBs (very persistent, very bioaccumulative substances).

4 REACH and formulators

Formulators who do not import or manufacture substances, but produce mixtures from substances, are downstream users under REACH. Therefore they have to fulfil the obligations REACH defines for downstream users.

Some of these obligations are identical for all downstream users, independent of whether they are formulators or users of a mixture. Some obligations are specific to formulators.

4.1 Tasks for formulators under REACH

Formulators who produce mixtures by formulating many raw materials (substances or mixtures) have the following specific tasks and obligations within the supply chain:

- Review the sections on hazard identification and, if available, exposure scenario information as soon as new/revised (extended) SDSs on substances (components for mixtures) are received.
- Classify and label the mixtures: assess the hazardous potential of the mixtures. This includes consideration (based on experience, knowledge or monitoring data) to substances where exposure during use may occur above Occupational Exposure Limits (OELs) or because of their physico-chemical characteristics (e.g., volatility) despite being present at below regulatory threshold limits.
- Describe OCs and RMMs to handle the mixtures in a safe way[8].
- Prepare safety data sheets for products if supplied to customers. These safety data sheets should contain all the information necessary to handle the mixtures safely.

Under REACH, as in the past, SDSs for mixtures are required only if mixtures are classified as hazardous according to the CLP Regulation (REACH Art. 31.1 (a)).

In addition, SDSs for mixtures are required upon a customer's request for non-classified mixtures:

- if the mixture contains at least one hazardous or PBT/vPvB[9] substance or Substance of Very High Concern (SVHC)[10] in concentrations above the limits defined in REACH Art. 31.3; or
- if it contains a substance for which a community workplace exposure limit exists.[11]

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[8] The Regulation on Classification, Labelling and Packaging defines the legal obligations for the hazard assessment of mixtures apart from REACH.

[9] PBT: persistent, bioaccumulative, toxic; vPvB: very persistent, very bioaccumulative

[10] SVHC: Substance of Very High Concern; included in the REACH Candidate List for the authorisation procedure

[11] REACH Art. 31.3 refers to safety data sheets which have been requested by the customer.

Safety data sheets do not need to be supplied where hazardous substances or mixtures offered or sold to the general public are provided with sufficient information to enable users to use them safely (REACH Art. 31.4) unless a downstream user or distributer has requested such information.

4.2 Obligations for formulators under REACH

REACH has defined new obligations for formulators and partly changed the conditions for existing and continuing tasks.

Formulators have to check whether their uses – and should also check whether the foreseeable uses of their customers – are covered by the exposure scenarios which they receive.[12]

An extended SDS (eSDS) for a substance supplied to formulators contains exposure scenarios (ESs) if an exposure assessment was mandatory for the registration of the substance. Formulators have to assess whether their uses, and should assess whether the (foreseeable) uses of their customers, are covered by the exposure scenarios of the substances.

If the exposure scenarios of the substances do not cover the uses of the mixtures yet, the formulator has several possible follow-up tasks. At least one actor in the supply chain has to do the exposure assessment, the risk characterization and the identification of the conditions of safe use if no exemption according to Art. 37.4 is applicable. The downstream user has the right to communicate his use to the supplier to make it an identified use (REACH Article 37.2.)[13] In order to do so the formulator has to provide sufficient information to allow the supplier to prepare an exposure scenario. Alternatively the downstream user may also consider preparing his own DU CSR (e. g. if he does not want to disclose his specific operational conditions to his supplier).

Formulators will be receiving more information on their substances under REACH and will have to check whether classification and labelling of their mixtures must change. Nonetheless, an SDS will need to be updated to meet REACH Annex II and CLP classification requirements.

More and more information on the hazardous properties of substances will become available as the 2018 registration deadline of substances approaches. Classification and labelling of

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[12] Art. 37.4 of the REACH regulation refers to uses of a downstream user and obliges him to prepare a chemical safety report for uses not covered by an exposure scenario received, if no exemption applies. Whereas the check of their own use by the formulator is mandatory, the check of uses by their customers is recommended. See also ECHA Guidance for Downstream Users Version 2.1 (Oct. 2014) Chapter 4.2: "*In order to compare your use(s) and your conditions of use with the information in the exposure scenario, you may need to collect information on your own use(s), and the foreseeable uses of your products by your customers.*"

[13] For reasons of protection of human health or the environment, the registrant can decide not to include it as an identified use (REACH Art. 37.3). In this case, he shall inform ECHA and the downstream user and may not supply the substance to any DU without informing them on the rationale.

substances may change due to new information available or changes to regulations (CLP Regulation).

More information on the safe use of substances will be communicated through the supply chain, especially safe limit values (e.g., DNELs, PNECs) for the substances. To an increasing degree, safety data sheets for substances will contain exposure scenarios as annexes describing the conditions of safe use. Subsequently, safety data sheets of mixtures classified as hazardous will be modified to take into account information contained in the exposure scenarios of its component substances.

Formulators shall include (or be consistent with) relevant information from exposure scenarios of the substances received and use other relevant information from the safety data sheets supplied to them on components when compiling the safety data sheet for their products (REACH Art. 31.7).

This requirement refers to all actors of the supply chain which are compiling safety data sheets. It is of specific relevance to formulators because they have to handle information from all of the substances that they use to make their products.

Chapter 5 addresses the process on how to include the information from exposure scenarios of substances into the safety data sheet of a mixture.

4.3 Tips to cope easier with the obligations under REACH

- Only perform a downstream user check if concentrations of substances in a mixture are above the limit concentrations under REACH Art. 14.2.
- When compiling an SDS for a mixture:
  - Use limit concentrations of REACH Art. 14.2 to focus on relevant substances of a mixture.
  - Consideration should be made, however, based on experience, knowledge or monitoring data, of some substances that despite being present at below these limits, exposure to them during use may occur above Occupational Exposure Limits (OELs) or because of their physico-chemical characteristics (e.g., volatility).

> **!** For many substances contained in mixtures in concentrations below 0.1% (e.g. Acute Tox. 1-3, Aquatic Acute 1, Aquatic Chronic 1) or 1% (Acute Tox. 4, Skin Corr./Irrit., Aquatic Chronic 2-4, Eye Dam./Irrit.) it **is not required** to perform a chemical safety assessment (REACH Art.14.2 and CLP Art. 11.3)**!** Exemptions from this general rule: For a particular substance, specific concentration limits can be defined in the Regulation (EC) No. 1272. In this case, if the concentration in the mixture is lower than the lowest substance-specific concentration limit (see REACH Art. 14.2), a CSA is not required (see Annex I of this guidance for details).

  - Decide which of the different ESs received are relevant for one's own use (and where appropriate, the use conditions of the mixture supplied).

  - Decide if a new ES for substances in the mixture is necessary or more appropriate.
  - Identify the presence of Priority Substances (above threshold values of REACH Art. 14.2.), see Chapter 7.
  - Identify the Lead Components[14] of the mixture (see Chapter 7) for each relevant exposure route for human health and the environment.
  - Compile the OCs and RMMs of the Priority Substances/Lead Components and components contributing to local effects for health or ozone depletion for the environment. Determine if the original OCs and RMMs of the Lead Components need to be adapted for the mixture to derive safe use information of the mixture

  Note: Presently only partial information will be available to the DU as eSDSs of substances will be received gradually. Case-by-case decisions will have to be made to decide when to update SDSs of mixtures.

- Information on substances should be carefully compiled and assessed by the supplier. Even if identical substances are supplied by different suppliers, classification and labelling and hazard data (e.g., DNELs, PNECs) should be identical (in practice this is often not the case today). This requires a careful check if such data are used by the next actor in the supply chain for his own assessments (see also Chapter 9.2). A plausibility check of the received ES data on raw materials – substances and mixtures – by the DU is very important and part of the legal obligations set in the CLP Regulation for the assessment of mixtures.
- In Section 15 of the SDS, it must be made clear whether the supplier has made a chemical safety assessment[15] for the given substance. In addition, it should state if an exposure scenario has been prepared. For mixtures, it is helpful to document for which substances in the mixture, CSR and ESs (or/and the CSR/safe use information or the mixture as such) have been prepared.
- The format for ESs for substances (used as substances for a mixture) is structured in a way that it is easy to find and select relevant sections for developing the safe use information of the mixture.
- Typically the ES of substances already cover the use of the substance in mixtures.
- Input parameters, applied methodology and results of the exposure assessment used in an ES should be documented in a transparent way to support the check of the next downstream user whether his uses are covered by the exposure scenario. Reference can be given to a website where these data are available. Safe use information of mix-

[14] Lead Component: Substance in a mixture that is relevant for deriving safe use information for a mixture; for details see Chapter 7.

[15] REACH Annex II Section 15.2 **Chemical safety assessment:** ***"****It shall be indicated if a chemical safety assessment has been carried out for the substance or the mixture by the supplier."*

tures should be clearly stated for the Lead Components of the mixture for the different exposure routes for human health and the environment, as applicable. While the latter is not a legal requirement, it is an essential element to allow downstream users to check whether their uses are covered and assessments of the next uses of the mixtures throughout the entire supply chain. In the standard format of exposure scenarios, Section 3 is foreseen as the location where information on prediction of exposure can be found.

- In the ES sometimes registrants give guidance to formulators on how to show that a use is covered, even if individual conditions of this use differ from the exposure scenario. This procedure is called “scaling”, if simple calculations are used. (It is described in Chapter 9).
- ES of substances only contain information relevant for the downstream user describing safe use and supporting the check whether the uses of the downstream user are covered. It is not required to list all information from the CSR in the ES. If additional information is required, e.g., on marine ecosystems, it can be given in more detail on a publicly available website.

4.4 Information to be given by formulators for the risk assessment of substances in mixtures

The chemical safety assessment of a substance should cover its entire life cycle. It has to consider the different exposure routes, the operational conditions and the risk management measures applied to the uses which have been identified.

In many cases, a registered substance is used by formulators for manufacturing mixtures. In general the registrant does not know the recipes of the mixtures in which his substance will be used further downstream in the supply chain. Therefore, he cannot take into account potential changes of the determinants of exposure for his substance if used in mixtures.

In general, the registrant assumes that the use of a substance in a mixture can be seen primarily as a dilution of the substance with other substances.

If substances with the same hazards and/or health or environmental effects are formulated together any additive, synergistic or antagonistic effects should be considered e.g., as described in Art. 12 c) of the CLP Regulation. If the manufacturer of the substance is not aware of such combinations (as will be often the case), he is not able to assess these additive effects. Then it becomes the task of the formulator to take his specific knowledge on the mixture into account. An increase of the solubility of a substance due to the presence of a carrier in a mixture, or the decrease of the irritating potential of mixtures of different surfactants, are examples of these cases.[16]

[16] Changes in bioavailability of metals due to the chemical bonding in an alloy, is an additional example.

However, if for specific uses it is well known that the substance behaves differently in a mixture (synergistic or antagonistic effects), this should be considered in the chemical safety assessment of the substance.

In some cases, these interactions are intended by the formulator. They are used to meet specific technical or functional properties of the mixture. If such changes are foreseeable and highly increase the exposure, the formulator might decide to inform his supplier or prefer to perform a DU CSA, if required. In case the registrant is informed he can consider these chemical interactions in the chemical safety assessment of the substance used for mixtures.

The following recommendations aim to support the communication between suppliers of substances and formulators, if required:

- Exposure scenarios for substances used in mixtures should state which concentration range is covered by the conditions of use. These conditions of use can be specified for different concentration ranges. Thereby it is ensured that the ES of a substance covers a broad range of uses. Furthermore it should be clear that these ranges only relate to mixtures in which the other components are inert and have no influence on the hazards or the other exposure determinants.
- Classification of a mixture can be different from the classification of its substances (e.g., a mixture with a content of 2% diethyl ether is not classified as flammable, whereas diethyl ether is classified as highly flammable). The supplier can describe specific OCs and RMMs for different results of classification of the mixture. This makes it easier for a formulator to identify the appropriate conditions of use for his mixture.
- Any downstream user has the right to make uses of a substance known to its suppliers[17]. In case an individual downstream user wants to make his use known to his supplier, the following information should be given to the supplier by the formulator:
    - The substance (e.g., name, CAS Number and relevant identifiers) used in mixtures.
    - Maximum concentration of the substances in mixtures or relevant concentration ranges, if the substance can occur in different concentrations in mixtures (as a consequence, the registrants could recommend specific sets of OCs and RMMs for these concentration ranges).
    - Changes in the determinants of exposure due to the use of the substance in mixtures, if relevant.

  Normally, this information is communicated as part of the exchange on general conditions of use. Use of a substance in a mixture can be considered as a specific condition of use of the substance.

[17] The information given should be in a way that a CSA is possible. REACH guidance provides a Use Descriptor System (UDS) which allows describing sectors of uses, processes, product and article categories in a harmonized way. Additional information on OCs and RMMs are of large value. Assignment of uses to the UDS is often called mapping. A template is available: http://echa.europa.eu/csr-es-roadmap/use-maps.

- Information should be part of the mapping of main uses. In many cases, the product categories already indicate that substances are used in mixtures.
- Representative exposure information within different industry sectors should be collected by sector groups.[18]

5 Safe use information for mixtures

5.1 Options for including safe use information in a safety data sheet

Annexes with safe use information for mixtures are one of several possibilities to include information on substances into safety data sheets of mixtures. (Under REACH there is no formal obligation for any actor of the supply chain to prepare an exposure scenario of a mixture).

If a registrant prepares an exposure scenario for a substance used in the supply chain, it is obligatory for him to communicate this exposure scenario. For downstream users who prepare their own safety data sheets, there is no legal obligation to prepare their own exposure scenarios as long as their uses are covered by the exposure scenarios of their suppliers. For them it is compulsory to **include** information which they have received in their own safety data sheets (REACH Art. 31.7, see Chapter 2). They can do this in several ways[19] :

1. **Annexing relevant exposure scenarios for the substances in the mixture**
   Exposure scenarios for relevant uses of relevant substances in the mixture are forwarded. In this case the downstream user can make use of the substance ES, e.g. when deriving safe use information for another mixtures formulated from this mixture.
   Note: Forwarding is only possible if the pieces of information in the exposure scenarios are aligned with each other and if there are no contradictions to the information in the SDS. In some cases it may be necessary to modify one or more of the received exposure scenarios of substances according to the specific conditions of use of the mixture. The modified exposure scenarios of the substances can be attached to the SDS of the mixture.
2. **Consolidating** the received exposure scenarios for substances into an SDS annex providing safe use information for the mixture. This information is typically structurally analogous to an ES.

[18] See also DUCC Activities – Use Communication and Use Mapping: http://www.ducc.eu/Activities.aspx and Cefic “Overview table on associations activities”: http://www.cefic.org/Industry-support/Implementing-reach/Guidances-and-Tools1/

[19] See ECHA Guidance on the compilation of safety data sheets, Version 3.1, Nov. 2015; Appendix 1: “Including relevant exposure scenario information into safety data sheets”.

3. **Extracting** the relevant information on OCs and RMMs from the received ESs, summarizing and including them in the related sections of the SDS for the mixture. (If the immediate downstream user is the formulator of a product to be offered or sold to the general public, he can use another option, e.g., extract, summarize and include the relevant information on OCs and RMMs in information for the general public. This is a fourth option).

The first option, just forwarding received exposure scenarios, seems to be simple, especially in cases of mixtures containing only a very limited number of hazardous substances.

Note: It has to be ensured that information in the exposure scenarios forwarded is consistent with the information in the safety data sheet of the mixture itself. In addition, it is possible that the ESs for the substances have to be modified in order to cover the specific properties of the mixture (see Chapter 8).

It is a company decision which of these options will be most appropriate for them. It may depend on their customers, and different options may even be used for different products. Some aspects that play a role in this decision include:

- If the mixture is an end-use product which is used under different conditions (e.g., adhesives), consolidation of information into an annex to the SDS for the different uses can be the best option. Here use-specific RMMs for each use are necessary. They might be described in use-specific annexes, while the main body of the SDS contains the information which is relevant for all users.
- For a mixture which has an end-use product with a well-defined user group, integration of information into the main body of the SDS might be the best way. OCs and RMMs can be described which are appropriate for this specific use. In such a case it is not necessary to define different OCs and RMMs for different conditions of use.
- As long as mixtures are further “processed” in the supply chain, in particular when used in other mixtures, supplying information in the form of an annex structured according to the ES format helps the subsequent actors in their task of identifying and including the relevant information for the substances received into their own safety data sheet. If compatible with the Sections 1 to 16 of the SDS it might be suitable just to forward the original substance ESs.
- If scaling is important for the downstream user, this information is more easily communicated in an annex structure according to the exposure scenario format than in the main body of the SDS.
- If industrial users with experience in workplace exposure control are interested primarily in the substance-specific data given in the main body of the safety data sheet, inclusion of information there seems more appropriate.
- In addition, the safe use of substances and mixtures will be considered more likely if the necessary information for this is provided in a structured way. This makes it easier for a downstream user to check whether he complies with the conditions of use which have been assessed as being safe.

- If applicable generic sets of safe use information are available for the mixtures' uses (e.g., typical OCs and RMMs in a sector), it might be easier to use these sets rather than to develop this information via a top-down approach (starting from ESs received from suppliers).

Remark: Annex II of this document gives an overview on the contents of an exposure scenario and the corresponding section of the safety data sheet. This provides guidance on how a downstream user may integrate the information from an ES into the safety data sheet of their mixture if this option is selected.

5.2 Approaches for developing safe use information for mixtures

Option A: Top-down approach – substance/components-based approach

Safe use information for the mixture is derived based on the exposure scenarios of the component substances received from suppliers. A key element of this approach is to identify the lead components of the mixture for the various exposure routes or pathways. This drives the selection of the relevant OCs and RMMs to determine the safe use information for the mixture. This approach is, despite some limitations, generally applicable and described in detail in Chapters 6 and 7 of this Practical Guide.

Option B: Bottom-up approach – mixture use based approach.

The starting points for a "mixture use" based approach are the composition and typical uses of the mixture. This approach is mainly used in a generic way. Sector groups derive safe use information for typical uses, compositions and hazard profiles for products within specific sectors.[20] Formulators can then use these predefined sets of safe use information for assessing their mixtures.

An advantage of this is that a large number of mixtures can be covered by a limited number of generic sets of realistic and consistent safe use information. This information can also be provided in sector-specific terminology.

It depends on the specific situation of an actor in the market which approach for developing safe use information for the mixture and which option for forwarding it to customers will be the most appropriate. It also depends on the number of hazardous substances in the mixture and the type of effects.

This information can then be consolidated in an annex to the SDS or extracted and integrated in Sections 1-16 of the SDS as discussed in Chapter 5.1.

Both bottom-up and top-down approaches are appropriate to fulfil REACH requirements related to safe use information for a mixture. In the case a suitable set of information from a bottom-up approach as provided by some industry sectors is available (use description, OCs

[20] See DUCC, December 2015, "Sector-specific approaches towards developing and communicating information for the safe use of mixtures": http://www.ducc.eu/Publications.aspx

and RMMs), formulators might conclude that it is the preferred option for elaborating the safe use information for a mixture.

6 Determining safe use information for inclusion in a safety data sheet of a mixture

Mixtures often consist of many substances. The task of including the relevant information from the exposure scenarios of the substances into the safety data sheet (SDS) of the mixture can be made easier if it is possible to concentrate on substances which determine the hazardous properties and/or the risk management measures (RMMs) of the mixture – and to sort out substances which are not relevant for OCs and RMMs as they are not determining risks related to the use of the mixture. In this context, for substance-rich mixtures, the following points are important:

- When assessing the mixture information, substance exposure scenarios only have to be included for substances that drive the hazards of the mixture classification.
- The decision as to which ES of a CSA for a specific substance in a mixture is relevant, should be reflected by the following questions
    - "does it require operational conditions (OCs) and risk management measures (RMMs) for the mixture itself?"
    - "are the RMMs not already triggered by other substances or the mixture itself (regardless if ES for these components are available)?".

  Processes and tools are being developed which help to identify the risk-determining substances (e.g., Priority Substances, Lead Components) for specific exposure routes and pathways.

The basic premise is that if the risks associated for the most hazardous component (e.g., Lead Component) are adequately controlled, then the risks from the other substances in the mixture are also controlled with regards to the same exposure route and/or pathway.[21]

Components for which additive principles may apply, are of similar structure, or cause similar toxicological effects via similar modes of action.

6.1 The process and its main steps

The main steps in preparing safe use information for the safety data sheet (SDS) of a mixture are shown in Figure 4. It includes the use of existing knowledge, the requirements for the classification and labelling of a mixture and also the new obligations under REACH. Figure 4

[21] More complex cases where this simple assumption is not valid are considered via an extended evaluation as explained in Chapter 8.

shows the whole process from the identification of the substance profile of the mixture and its hazard assessment to the preparation of the safety data sheet of the mixture.

Key elements of a formulators' mixture assessment when applying the Lead Component Identification (LCID) methodology

- Identify components of the mixture/formulation and associated data:
  - Concentrations, hazard classifications including associated reference values (DNELs, PNECs, NO(A)EL or NO(A)ECs etc. and/or surrogate information and cut-off criteria)
  - Exposure scenario(s) of relevant components for each applicable use
  - Collect data on mixture itself, or a surrogate, if available
- Classify the mixture
- Decide whether a sectorial "bottom-up approach" is applicable or whether the generally applicable "top-down" LCID methodology shall be applied
- Identify relevant components by applying the LCID approach:
  - Priority Substances (Carcinogen 1A, 1B, 2/Mutagen 1A, 1B, 2; PBT/vPvB ≥ 0.1%)
  - Components contributing to any local effects to human health (e.g., eye, skin, or respiratory tract irritation/corrosivity, skin or respiratory sensitisation[22]) and for the environment (e.g., ozone layer depletion)
  - Lead Components (identification via comparison of Lead Component Indicators of the mixture components based on DNELs/PNECS or surrogate information) and concentrations for all relevant exposure routes/pathways
  - Components for which additive principles may apply or are of similar structure, toxicological effects via similar modes of action
- Based on identification of the relevant components, identify relevant operational conditions and risk management measures for the relevant identified uses of the mixture
- Generate safe use information and decide whether to include it in Sections 1 - 16 of the SDS or added as an annex

Figure 4 Overview: Key elements in assessment of a mixture and generation of safe use information for the SDS

[22] See Chapter 7, Step H6

In Chapter 7, more details on the working steps are provided, including if test data on the mixture or a surrogate mixture is available, ensuring RMMs adequately cover all appropriate routes of exposure/pathways, and adding weight to substances for which additivity principles can be applied.

6.2 Approach for mixtures as a "raw material" for other mixtures

Often raw materials as provided to a formulator may itself be a mixture. Formulators should rely on information provided at the substance-level, and not the mixture-level, when elaborating safe use information for such mixtures (e.g., those that are formulated by using another mixture as raw material). In the safety data sheet for a mixture received by a supplier, the relevant substances and their corresponding concentrations are normally addressed in Section 3. These components were considered when classifying the raw material mixture and also have to be considered when classifying a mixture containing this mixture. The formulator should try to identify, to the extent possible, the components driving the hazard classifications (e.g., Priority Substances and Lead Components) for the raw material mixture, and derive their ultimate concentrations in the final mixture, to allow the application of the approach for deriving safe use information for the mixture as described in Chapter 7.

Even if the safe use information (OCs and RMMs) has been derived from a bottom-up approach, it is still imperative to attempt to identify those "Lead Components" which are responsible for driving the hazard classification.

7 Identification of Lead Components

7.1 Introduction

There is often no toxicity information available on mixtures as a whole, therefore, it has been a presumed assumption that the hazards posed from exposure to a mixture are often a sum of the hazards from exposure to its individual components over selected threshold levels. This approach has been taken when classifying hazards under the Dangerous Preparations Directive (Directive 1999/45/EC) and more recently the CLP Regulation (EC No. 1272/2008). With REACH, the concept of risk is taken into account by estimating exposure levels, under selected uses and operational conditions, to derive use-specific risk management measures (e.g., ventilation controls, personal protective equipment). Reliance on these assumptions, exposure estimates, and identified measures, serves as the basis for developing safe use information for mixtures.

Most of this information can be found on extended safety data sheets (eSDSs) from suppliers for each component of a mixture.[23] The safe use for mixtures is highly driven by those substances that drive the CLP classifications of the mixture, the so called “Lead Components”. The Lead Component is not necessarily the most hazardous substance in the mixture: other factors need to be considered such as the concentration in the mixture and the exposure route/pathway. The Lead Component Identification (LCID) methodology as described in this chapter principally counts only for the substances present in mixtures classified as hazardous in concentrations above the concentration limits set in Art. 14.2. (Note: Consideration should have been made when classifying the mixture, if there was the potential for exposure to substances despite being present at below these limits.)

Also important is the identification of Priority Substances: Carcinogens and mutagens for human health[24] and PBTs and vPvBs for the environment. Priority Substances, and further, Lead Components generally require the most stringent risk management measures. When these are applied it is assumed that they are also applicable for other hazardous components that may be present (worst case assumption). Special consideration must also be made for components which may drive local effects (e.g., eye/skin/respiratory tract damage/irritation or skin/respiratory tract sensitisation, drying and cracking of the skin), or as an ozone layer hazard.

It is important to note, that following this methodology does not absolve one of the responsibility for verifying that their uses and the uses of their DUs are covered by their supplier's REACH registration or eSDS. One is still required to do use coverage checks.

This chapter gives guidance on how to identify these Lead Components for the various exposure routes/pathways and based on this, how to derive the applicable OCs and RMMs to determine safe use information for the mixture.

In case a suitable set of safe use information from a bottom-up approach as provided by some industry sectors is available (use description, OCs and RMMs) formulators might prefer to build their mixture information on this specific groundwork instead of applying the entire LCID methodology.

Physical hazards are not addressed in this LCID methodology, however, when reviewing consolidation of OCs and RMMs the effects related to physico-chemical properties of the mixture must also be reviewed (e.g., flammability, reactivity, explosivity) and also aspiration

[23] Note: The quality of input data is expected to have been checked upfront; such checks are not part of the LCID methodology.

[24] Carcinogens and mutagens are generally assumed to have non-threshold effects. Contact to substances classified as carcinogens and/or mutagens should thus be minimized as much as possible. As a consequence, these types of components are considered Priority Substances. For all other systemic hazards, including reproductive toxicity, a DNEL can be derived. In the rare case that a DNEL is available for a carcinogenic or mutagenic substance, it may not be considered a Priority Substance and use of the DNEL should be applied in calculating its LCI.

hazards based on kinematic viscosity. Additional safe use statements associated with these hazards should also be addressed.

7.2 LCID methodology - Human Health hazards

The main steps in preparing safe use information regarding human health hazards for a mixture are shown in Figure 5. It includes the compiling of information including the CLP classification and labelling of a mixture, hazard data gathered under REACH (e.g., DNELs), local effects (e.g., irritation, corrosivity, sensitisation, drying and cracking of the skin) and specific conditions of use which affect exposure (e.g., formation of vapours, dusts, fumes, mists, aerosols, use as a solid/massive).

This methodology takes into account the following cases:

- Priority substances: Carcinogens and mutagens (CM; CLP Categories 1A, 1B and 2) that are non-threshold substances[25]
- Classified substances with DNELs[26]
- Classified substances which lack DNELs but have available other toxicity reference values (e.g., NO(A)ELs, NO(A)ECs, LD_{50}s, LC_{50}s or ATEs).
- Substances that have similar modes of action and similar biological effect, but differ in potencies as far as combined effects can be expected on the basis of dose/concentration addition

Once the DU determines which exposure scenarios, including contributing activities (process categories - PROCs) are applicable to their uses and, as appropriate, their customer uses, this data forms the basis for identifying the Lead Components which drive the safe use information for their mixture. Lead Components are identified then, per each relevant exposure route (e.g., inhalation and dermal routes for worker exposures). The RMMs then selected for safe use for the mixture are based on these Lead Components, specific to a given contributing activity (e.g., PROC). Safe use information relevant to the physical hazard classifications of mixtures (e.g., flammability, reactivity, explosivity) and aspiration hazards (due to their dependence on viscosity) are not addressed in the LCID methodology.

Note: Independent action (or simple dissimilar action) is the basic assumption in the LCID methodology. Independent action (response addition, effects addition) occurs if chemicals act independently from each other, usually through different modes of action that do not influence each other. With the LCID methodology an additional step also accounts for combined effects in case these are known or expected.

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[25] In rare cases where thresholds have been identified, they should be handled via the Lead Component Identification route)

[26] This includes substances that are reproductive toxicants (R; CLP Categories 1A, 1B and 2).

Mixtures where components interact in such a way that the combined biological effect is stronger (synergistic/potentiating) or weaker (antagonistic) than would be expected on the basis of dose/concentration addition or response addition, are not covered by this approach. However such kinds of interaction between chemicals are only expected in very rare cases (Directorate-General for Health & Consumers, 2012)[27]. If there is a potential for synergistic/ potentiating/antagonistic effects, evaluation of the properties of the mixture heavily relies on expert knowledge and can only be done on a case-by-case basis.

Figures 5a and 5b show the entire process, from the compilation of data requirements on the components of the mixture and its risk assessment to the preparation of the safe use information for integration, or as an annex, to the safety data sheet (SDS) of the mixture. The process for deriving the classification of the mixtures is out of scope of the LCID methodology; it is assumed that this has already been done prior to application of the methodology. In addition, it is also presumed that the decision has already been made that the “bottom-up” approach is not applicable for the mixture in question. In Table 1, more details on the working steps are provided.

Annex III includes test examples of applying the LCID methodology for deriving safe use information based on the human health hazard information provided on components of a mixture. This includes a template that describes the information/calculations used in the examples.

Annex IV is the technical documentation which provides the background, assumptions, and references for each of the steps of the LCID methodology as it pertains to human health hazards.

[27] European Commission, Directorate-General for Health & Consumers, SCHER/SCENIHR/SCCS 2012: Toxicity and Assessment of Chemical Mixtures

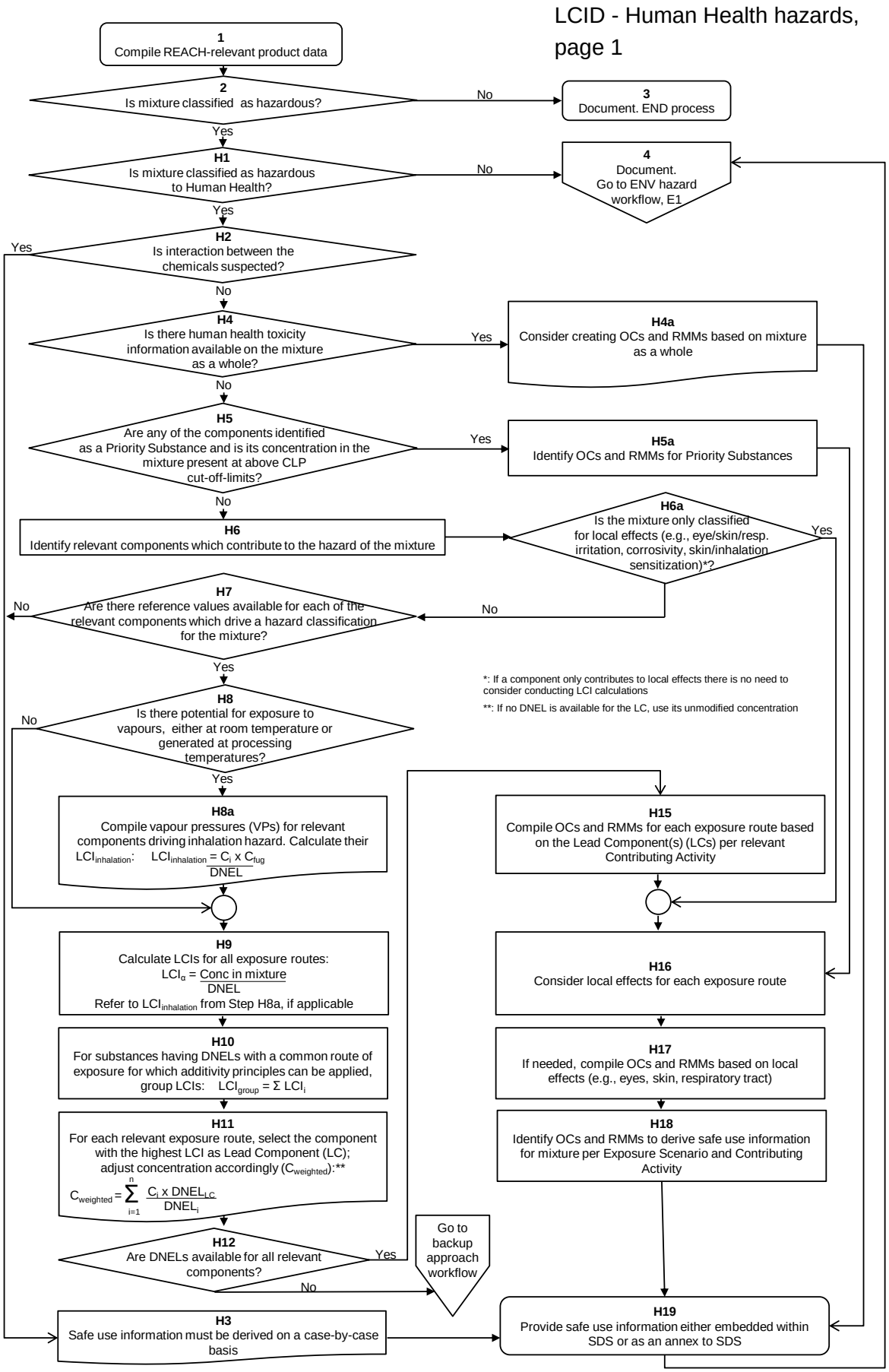
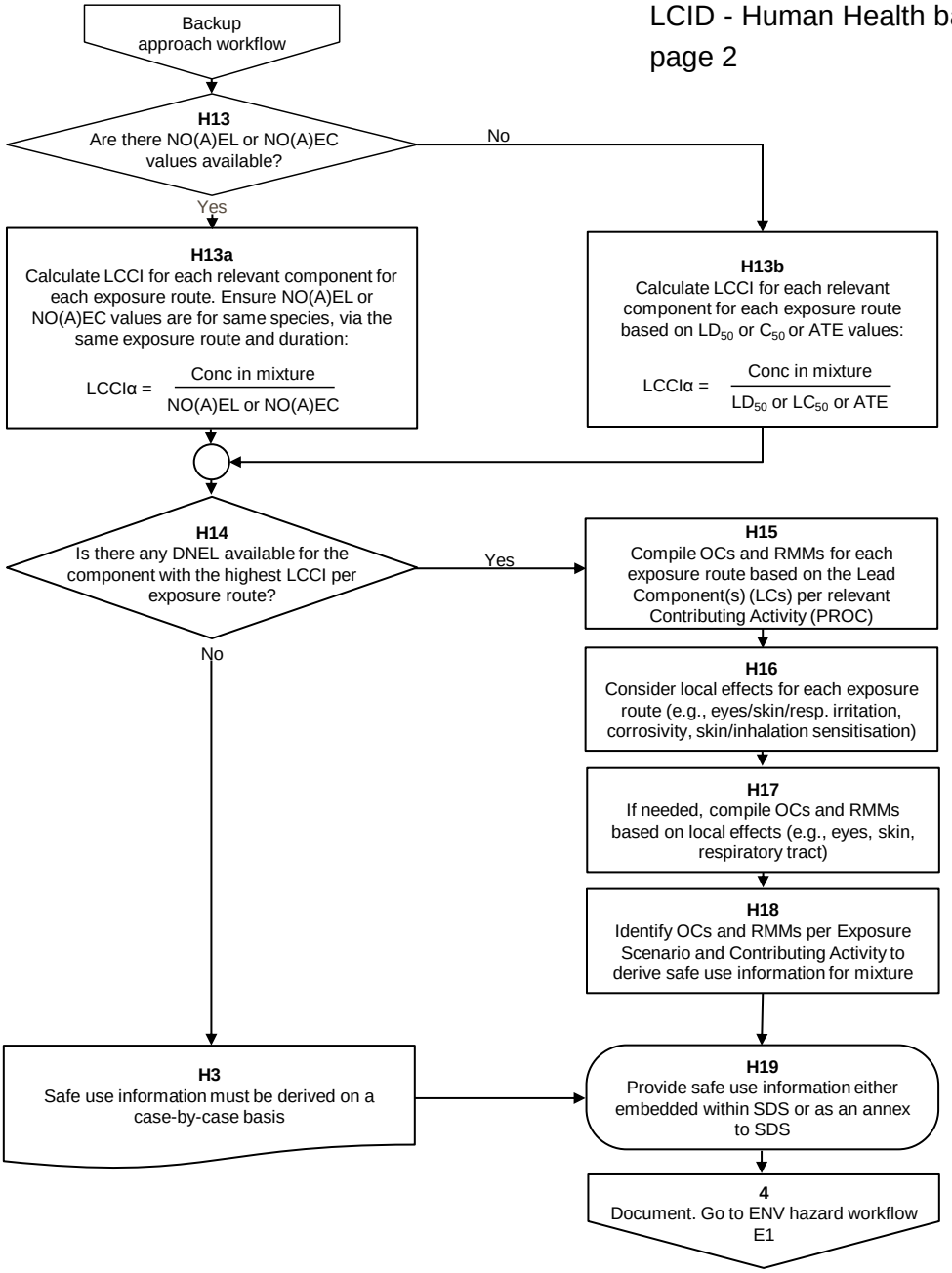


Figure 5a LCID methodology for generation of safe use information for mixtures - human health hazards



Legend Figures 5a and 5b:
ATE: Acute Toxicity Estimate
C_i: Concentration of the component i in the mixture
C_{fug}: Factor representing the potential effect of the vapour pressure (VP)
$C_{weighted}$: Adjusted concentration of the LC
DNEL: Derived No-effect Level
LC: Lead Component
LCI: Lead Component Indicator
LCCI: Lead Component Candidate Indicator
LCI_{max}: Maxímum LCI from the components of the LCI_{group}
LCI_{group}: Sum of the LCIs of the grouped components
LC_{50}: Lethal concentration resulting in 50% mortality of the experimental animals
LD_{50}: Lethal dose resulting in 50% mortality of the experimental animals
NOAEL: No-observed adverse effect level
NOAC: No-observed adverse effect concentration
OC: Operational Condition
PS: Priority Substance
RMM: Risk Management Measure
SDS: Safety Data Sheet

Figure 5b LCID methodology for generation of safe use information for mixtures, backup approach - human health hazards

Table 1: Explanation of the steps for generating safe use information regarding human health hazards for chemical mixtures

Step	Task	Comments
1	Compile REACH-relevant product data	Analysis begins by gathering all available and relevant information on both human health and environmental data for all individual components of the mixture as well as on the mixture itself. These are: • Identification of the chemical components[28] • Mixture composition (e.g., concentrations[29] for components) • CLP classification of the mixture (human health and environment) including identification of components which contribute to the hazard classification (ECHA, Guidance on the Application of the CLP Criteria, Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, 2013). Identifying components that are above limit concentrations of REACH Art. 14.2. consideration should also be given (based on experience, knowledge or monitoring data) to substances where exposure during use may occur above Occupational Exposure Limits (OELs) or because of their physico-chemical characteristics (e.g., volatility) despite being present at below regulatory threshold limits. • Physical form(s) for which there is a potential for exposure during use, including if processed at elevated temperatures or if sprayed or applied under pressure (e.g., vapour, dust, mist, aerosol, fume, gas); use as a solid/massive. • Toxicity and physico-chemical results of the mixture, as a whole, if available. CLP classification of the components: o Human Health (HH) hazard, including ▪ Carcinogen, Categories 1A, 1B or 2 (acc. to CLP) ▪ Mutagen, Categories 1A, 1B or 2 (acc. to CLP) o Environment (ENV) hazard, including ▪ Ozone layer hazard • Identification of components meeting the Persistent, Bioaccumulative, and Toxic (PBT) or very Persistent, very Bioccumulative (vPvB) criteria according to Annex XIII to REACH • Physico-chemical properties of individual components (e.g., vapour pressure, biodegradability) which drive

[28] Treat UVCB (Unknown or Variable composition, Complex reaction products or Biological materials) as if it is a single substance; use the DNELs that are associated with the UVCB for the LCID methodology calculations.

[29] If concentrations are provided by the supplier as a range, use the maximum concentration for all calculations in this LCID methodology.

Step	Task	Comments
		hazard classifications of the mixture • Reference values for all components which contribute to the hazard classification. Where available DNEL[30] values should be used. If all DNELs are lacking for a relevant component, then NO(A)ELs, NO(A)ECs, LD_{50}s, LC_{50}s, and ATE values should be considered. Also compile any associated occupational exposure limits (OELs) (e.g. MAKs, TLVs). • Exposure Scenarios (ESs), e.g., OCs including factors which could contribute to exposure and RMMs for components which drive hazard classifications of the mixture. Much of the data on individual components in the mixture can be found in the (e)SDSs provided from suppliers. Additional information can be found on ECHA's website of REACH-registered substances, as well as other publically/privately available resources. Note: The primary source of information should be the supplier's (e)SDS. If other data sources are used, ensure that the obtained data is relevant for the components used in the formulation of the mixture. Go to Step 2.
2	Is the mixture classified as hazardous?	Refer to the CLP hazard classification of the mixture and Section 2 of the SDS. Non-classified mixtures are considered non-hazardous as it applies to human health and the environment and, therefore, any use of the mixture is considered safe. However, this LCID methodology may be applied to unclassified mixtures. If a mixture does pose a hazard due to its volatility that should have been determined when classifying the mixture and addressed in Section 2 of the SDS. Hazard classification for the mixture is done prior to applying the LCID methodology. Note: Safe use information relevant to the physical hazard classifications of mixtures (e.g., flammability, reactivity, explosivity) and aspiration hazards (due to their dependence on viscosity) are not addressed in the LCID methodology. Yes/No decision. If yes, go to Step H1. If no, go to Step 3.
3	Document	The mixture is not classified as hazardous, either as a human health (HH) or environmental (ENV) hazard. Document this assessment and allow for easy access to enforcement authori-

[30] For purposes of applying the LCID methodology, the DNELs to use are the substance's systemic long-term DNEL values.

Step	Task	Comments
		ties, if required. Records should include date of review. END LCID methodology workflow[31].
H1	Is the mixture classified as hazardous to human health?	Refer to CLP hazard classification of the mixture. Yes/No decision. If yes, go to Step H2. If no, go to Step 4.
4	Document Go to ENV workflow, E1	Document the assessment that the mixture is not classified as a human health hazard and allow for easy access to enforcement authorities, if required. Records should include date of review. The mixture has, however, been classified as hazardous to the environment (ENV), therefore, go to Step E1.
H2	Is interaction between the chemicals expected?	Consider the potential for interactions between the components. Interaction is described as the combined effect of two or more chemicals as either stronger (synergistic, potentiating, supra-additive) or weaker (antagonistic, inhibitive, sub-additive, infra-additive) than would be expected on the basis of dose/concentration addition or response addition. Interactions may vary according to the relative dose levels, the route(s), timing and duration of exposure (including the biological persistence of the mixture components), and the biological target(s). Interaction considerations include: • Toxicokinetic interactions; a common cause of deviations from additivity. Examples are chemicals modifying the absorption of others (e.g., skin penetration enhancing substances in cosmetics) or chemicals competing for active transport mechanisms (uptake, clearance) • Metabolic interactions: chemicals modifying the metabolism of other mixture components • Toxicodynamic interactions: interactions between the biological responses resulting from exposure to the individual chemicals, for example resulting from similar targets (e.g., ligand-receptor interaction) (Directorate-General for Health & Consumers, 2012)[32] Evaluation of specific properties of mixtures relies heavily on expert knowledge of the formulator and/or a company/ consulting toxicologist to help make such determinations. If interaction is suspected, document the company's position and allow for easy access to enforcement authorities, if required. Yes/No decision. If yes, go to Step H3. If no, go to Step H4.

[31] If asked for an SDS upon request for an unclassified mixture, this LCID methodology may be applied.

[32] European Commission, Directorate-General for Health & Consumers, 2012, Toxicity and Assessment of Chemical Mixtures

Step	Task	Comments
H3	Safe use information must be derived on a case-by-case basis	The LCID methodology is not applicable if there are suspected interactions between the components or if the information available for the components is insufficient to select the Lead Component(s). Safe use information is therefore derived on a case-by-case basis and should be referred to an expert. Document the company's position and allow for easy access to enforcement authorities, if required. Go to Step H19.
H4	Is there human health toxicity information available on the mixture as a whole?	Has there been toxicity testing of the mixture as a whole? This refers to toxicity information, to the extent available that is applicable to the LCID methodology, e.g., Annex II of REACH. An assessment may also be based on data generated on a mixture of reasonably similar composition or a "surrogate mixture," e.g., a mixture close in composition (components and proportions) to the mixture under evaluation (see ECHA Guidance on CLP for details on bridging principles). Information may be available from the company's own testing of the mixture (e.g., for regulatory purposes), or through a supplier (through information provided on their (e)SDS or if the mixture is a commodity or formulation, through an industry sector organization or published literature. If the testing data set for the entire mixture is incomplete, follow the LCID methodology (e.g., test data on the mixture as a whole is available regarding acute toxicity, but lack of mixture test results for long-term toxicity). Document the company's position and allow for easy access to enforcement authorities, if required. Yes/No decision. If yes, go to Step H4a. If no, go to Step H5.
H4a	Consider creating OCs and RMMs based on mixture as a whole	Consider if any of the test results on the mixture as a whole can be used to derive safe use information. If data is lacking for some of the endpoints, consider following the LCID methodology to fill the gaps for the other exposure routes and/or health hazard endpoints and local effects. If this is the case, then go to Step H5. Document the company's position and allow for easy access to enforcement authorities, if required. Go to Step H19.
H5	Are any of the components identified as a Priority Substance and is its concentration in the mixture present above CLP cut-off limits?	Are there any components that have been identified as a carcinogen (Categories 1A, 1B or 2) or mutagen (Categories 1A, 1B or 2) (Priority Substance) present above CLP cut-off limits? In the rare case that a DNEL has been derived for the carcinogen or mutagen, then go to Step 6 and treat as any other toxicological hazard with a DNEL. Note: Reproductive toxicants are addressed like other target organ effects. Carcinogens and mutagens are generally assumed to have non-threshold effects. As a consequence, these

Step	Task	Comments
		types of components are considered Priority Substances. For all other systemic hazards, including reproductive toxicity, a DNEL can be derived. In the rare case that a DNEL is available for a carcinogenic or mutagenic substance, it may not be considered a Priority Substance and use of the DNEL should be applied in calculating its LCI. Yes/No decision. Document. If yes, go to Step H5a. If no, go to Step H6.
H5a	Identify OCs and RMMs for Priority Substances	Gather the relevant exposure scenario information (OCs and RMMs) for the Priority Substances. These can typically be found in a supplier's (e)SDS or be derived from the chemical substance's CSR (if available to you). Select the OCs and RMMs that are appropriate to how the **mixture** will be used (e.g., as a fuel, coating, adhesive). See Chapter 9 for further considerations when determining the appropriate OCs and RMMs for the mixture. Priority Substances generally require the most stringent RMMs. However, it is possible that they do not control adequately other components of the mixture having different physico-chemical properties which may affect exposure or are only protective for one route of exposure. If the Priority Substance only causes effects via one route of exposure consider LCI calculations for the remaining routes. See Text Example 1 (in Annex III) on deriving safe use information based on the presence of a Priority Substance in a formulation. Go to Step H16.
H6	Identify relevant components which contribute to the hazard of the mixture	Review the CLP classification of the mixture. Identify which components contribute to the health hazard classifications of the mixture (e.g., identify all components having at least one hazard classification that contributes to the mixture hazard classification). The hazard classifications of the individual components are typically available in Section 2 of the supplier's (e)SDS. Of this list, select all components that add to a systemic effect of the mixture (e.g., those classified for acute toxicity, reproductive toxicity, Specific Target Organ Toxicity Single/Repeated exposure (STOT SE/STOT RE Cat. 1+2), and STOT SE Cat 3 (drowsiness and dizziness). These components are further identified as **relevant components,** as these are the ones relevant for the DNEL-based calculations within the LCID methodology. Components that contribute to the hazard classifications of local effects (eye, skin, or respiratory tract irritation/corrosivity, skin or respiratory sensitisation) including EUH066 (dryness or cracking of the skin) are addressed in Step H16. Ensure that hazard classifications align with hazards identified in Section 2 of the SDS (including those that may be due to components below concentration but above consideration

Step	Task	Comments
		thresholds). If there are reasons to believe that components that do not drive the CLP classification and labelling criteria for the mixture (cf. REACH Article 31(3)) yet pose a risk to human health, they should be included in the calculation/selection of RMMs. Go to Step H6a.
H6a	Is the mixture only classified for local effects (e.g., eye/skin/resp. irritation, corrosivity, skin/inhalation sensitisation?	**If the mixture is only classified for local effects**, one does not have to identify any systemic Lead Components (e.g., do not need to calculate LCIs) and can directly address safe use information based on the components driving the local effects. If yes, go to Step H16. If no, go to Step H7.
H7	Are there reference values available for each of the **relevant components** which drive a hazard classification for the mixture?	Review all reference values for all relevant components which contribute to the hazard classification(s). These are all components that add to the systemic effects of the mixture (e.g., those classified for acute toxicity, reproductive toxicity and Specific Target Organ Toxicity Single/Repeated exposure (STOT SE/STOT RE Cat. 1+2). Where available, long-term systemic DNEL values should be used. Note: A long term systemic DNEL should protect against acute effects as well as long-term effects. If **all DNELs** are lacking for a relevant component, then NO(A)ELs, NO(A)ECs, LD_{50}s, LC_{50}s, and ATE values should be considered. These latter values may be used as back-up data to ensure that a potentially more toxic component is not missed when developing safe use information for the mixture based on the DNEL. Note: If a DNEL is missing for one route of exposure or only local DNELs are available, a valid reason for this omission may be presumed. Since exposure or systemic effects via this route were not considered relevant for the substance, they can also be presumed not relevant for the mixture and consequently the backup-approach should not be applied. On the other hand this does not mean that a DNEL for one route of exposure may be ignored because no classification for a systemic hazard for this route of exposure exists. For example, for a component that has been identified as a relevant component for acute inhalation toxicity, its inhalation and dermal DNELs must be taken into account, if both have been derived. If a **substance** is, however, **classified for local hazards only**, available DNELs should not be considered in the further process (see H6a). If a component has an OEL and has not been identified as a Lead Component, ensure that this component was included in the LCI calculation to avoid that a more hazardous component is missed. Reference values are typically found in either Sections 8, 11 and/or 12 of the (e)SDS. Additional information can be found on ECHA's website of REACH-registered substances, as well as other publically/privately available resources.

Step	Task	Comments
		Note: The primary source of reference values should be the supplier's (e)SDS. If other data sources are used, ensure that the obtained data is relevant for the components used in the formulation of the mixture. Yes/No decision. Document. If yes, go to Step H8. If no, go to Step H3.
H8	Is there potential for exposure to vapours, either at room temperature or generated at processing temperatures?	This step is designed to address the concerns for the potential for exposure to vapours under conditions of use including being evolved at elevated processing temperatures. If there is a possible exposure to vapours, then consider taking into account the effect of vapour pressure(s) (VP) on the exposure potential when calculating a component's Lead Component Indicator (LCI) value. Use information on the mixture may help make this determination. Review of OCs and RMMs in the applicable Exposure Scenarios (ESs) of the associated (e)SDSs can also assist in the decision of whether vapour exposure is of concern. If unsure if exposure to vapours is of concern, for example due to lack of information, compare the outcome of both considering and not considering an effect due to VP (see Steps H8a and H9 for details). Note: Any comparisons must be made on an equivalent basis, e.g., for each relevant component make the comparison of LCIs by factoring in the vapour pressure, or compare LCIs calculated without factoring in vapour pressure. Note: If the vapour pressures for all the relevant components are similar, then this step may not be necessary and one can skip to Step H9. The assumption for solid mixtures is that the mixture is homogeneous and there is no difference due to dustiness influencing the LCI calculation. Yes/No decision. Document. If yes, go to Step H8a. If no, go to Step H9.
H8a	Compile vapour pressures (VPs) for relevant components driving inhalation hazard. Calculate their $LCI_{inhalation}$	Compile the vapour pressures (in hPa) of the relevant components. These can typically be found in Section 9 of the (e)SDS. If VP(s) for different components were derived at different temperatures, a correction to the same temperature (25°C) is recommended. For each relevant component, a Lead Component Indicator (LCI) is calculated. The LCI is then calculated as follows: $$\mathrm{LCI_{inhalation}} = \frac{\mathrm{C_i \times C_{fug}}}{\mathrm{DNEL}}$$ Where:

Step	Task	Comments
		$LCI_{inhalation}$: LCI for inhalation C_i: Concentration of the component i in the mixture C_{fug}* = Factor representing the potential effect of the vapour pressure (VP) DNEL: Derived no-effect level long term systemic * The default value for C_{fug} is the VP (hPa). Different approaches to adjust the weighting of the VP relative to the other parameters in the equation are currently being explored (e.g., based on TRA fugacity) to better represent the effect of the VP on exposure potential. See Test Example 2 (in Annex III) for deriving LCI values incorporating vapour pressures in the calculations for deriving safe use information. Document. Go to Step H9.
H9	Calculate LCIs for all exposure routes. Refer to $LCI_{inhalation}$ from Step H8a, if applicable	The determination of the Lead Component (LC) for each route of exposure is based on the long term systemic DNEL values. A Lead Component Indicator (LCI) is calculated per route of exposure and per relevant component having a long term systemic DNEL for that route. That means that the LCI has to be calculated for **all** routes of exposure (for which this is possible), and it does not matter, if the component or mixture has actually been classified for this route. All components that do not have a long term systemic DNEL are ignored during this step, but will be dealt with at a later stage (Steps H12 – H14). Calculate LCI for each exposure route (e.g., inhalation, dermal, oral as applicable), using this equation: $$LCI_{\alpha} = \frac{C_i}{DNEL}$$ Where: LCI_{α}: LCI for route of exposure α Ci: Concentration of the component i in the mixture DNEL: Derived no-effect level long term systemic NOTE: $LCI_{inhalation}$s need **not** be calculated in this step if they were calculated in Step H8a **unless** one is unsure if the exposure to vapours is of concern or not. IF there is a concern about whether exposure to vapours is an issue, then calculate $LCI_{inhalation}$ in two ways, once using the equation in Step H8a and then again using the equation in Step H9 (e.g., including or not including a C_{fug} factor). See Test Example 2 and 3.1 (in Annex III) calculating LCIs based on DNELs to derive safe use information. Document. Go to Step H10.
H10	For substances having DNELs with a common route of exposure for which additivity principles can be applied, group LCIs.	Components, when present simultaneously in a mixture, may act in combination and cause potential adverse effects resulting in an additive effect. There is a major knowledge gap on exposure information to mixtures, their modes of action and their potencies. There is a consensus among the scientific community that a dose/concentration addition methodology should be applied as the default approach to evaluate the health risks of chemical mixtures (Directorate-General for Health &

Step	Task	Comments
		Consumers, 2012). In order to take into consideration the possible additive effects of the components in the mixture: For the following hazard classes additivity concepts are applicable (ECHA, Guidance on the Application of the CLP Criteria, Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, 2013): - Acute toxicity for the inhalation route, categories 1, 2, 3 and 4 (H330, H331, H332), - Acute toxicity for the dermal route, categories 1, 2, 3 and 4 (H310, H311, H312) - Acute toxicity for the oral route, categories 1, 2, 3 and 4 (H300, H301, H302) - STOT SE 3 for dermal route of exposure and inhalation (narcotic effects) (H336) Grouping may be considered if there are components in the mixture of similar structure, similar toxicological effects via similar modes of action (e.g., certain phthalates). The expert tool MiXie which is available on the website of IRSST[33] may also be used to identify components which exert a similar effect. Local effects, e.g., eye, skin and respiratory tract irritation/corrosivity, and skin/respiratory sensitisation are considered separately (see Step H16). Note: This subject will have to be assessed as new information becomes available. Sum the LCIs of these grouped components (LCIs calculated in Steps H8a and/or H9); this total represents LCI_{group}: $$\mathrm{LCI_{group}} = \sum_{i=1}^{n} \mathrm{LCI_i}$$ Grouping of chemicals should always be verified by an expert to ascertain that the most relevant LCI has been derived for $LCI_{group.}$ See Test Examples 3.1 and 3.2 (in Annex III) for example of grouping chemicals to derive safe use information. Document. Go to Step H11.
H11	For each relevant exposure route, select the component with the highest LCI as Lead Component (LC); adjust concentration accordingly	All comparisons are done separately per route of exposure so that a Lead Component (LC) for each route is defined for **all** relevant routes. If no components were grouped in Step H10, select the component with the highest LCI, per route, as calculated in Steps H8a or H9 as the Lead Component. If at least one LCI_{group} was derived in Step H10, compare the

[33] IRSST: Institut de recherche Robert-Sauvé et en sécurité du travail

Step	Task	Comments
	($C_{weighted}$)	LCI_{group} with the LCI_i of all other components of the mixtures which were **not part of a group** (those for which additivity principles cannot be applied). If the highest LCI is not an $LCI_{group,}$ then that component with the highest LCI is the Lead Component. If the highest LCI is an LCI_{group}, identify the component with the highest LCI within that group. This component becomes the Lead Component for that exposure route, but its concentration needs to be adjusted according to the following formula to account for all other components also contributing to this toxic effect (calculation of $C_{weighted}$). This concentration is needed to define the correct OCs and RMMs in Step H15. Calculation of $C_{weighted}$ $$C_{weighted} = \sum_{i=1}^{n} \frac{C_i \times DNEL_{LC}}{DNEL_i}$$ Where: C_i: Concentration of the components from the group identified under Step H10 for a given exposure route $DNEL_{LC}$: DNEL of the Lead Component $DNEL_i$: DNEL of the components from the group identified under Step H10 for a given exposure route Note 1: For inhalation, vapour pressures are not included in the calculation; they are only relevant when considering exposure potential and do not impact the overall toxicity of the components. In rare cases $C_{weighted}$ may exceed 100% because of worst case assumptions that are built upon each other (e.g., worst case exposure estimations, worst case concentration). In these circumstances, select the RMMs for the Lead Component at its concentration up to 100%. Note 2: In the case that a component needs to be included in the group, but no DNEL is available for this component, the unmodified concentration of this component can be added to the $C_{weighted}$ concentration as a worst case approach. Test Examples 3.1 and 3.2 (in Annex III) demonstrate calculation and use of $C_{weighted}$. Go to Step H12.
H12	Are DNELs available for all relevant components?	For all relevant components, check if there is at least one DNEL value available. This does not have to be a long term systemic DNEL, but can be a DNEL of any type and for any route of exposure. Note: If a manufacturer/importer registered a substance in a tonnage band of at least 10 tonnes per year, then all relevant DNELs should have been derived. Therefore, if a DNEL is missing there was probably a very good reason for this, e.g., exposure via this route of exposure was not considered relevant for this substance. Thus there is no need to include this route of exposure when identifying the Lead Component. The same holds true if only local acute DNELs are available; this means that systemic effects were not considered relevant for a REACH registration so they should not be considered relevant

Step	Task	Comments
		for the mixture. Yes/No decision. If yes, there is a DNEL available for all relevant components, continue to Step H15 to identify appropriate OCs and RMMs. If no, go to backup strategy described in Steps H13 (including H13a and H13b) - H14.
H13	Are there NO(A)EL or NO(A)EC values available?	NO(A)EL or NO(A)EC values may be used as a back-up approach, if no DNELs are available for one or more relevant component(s). NO(A)ELs and/or NO(A)ECs are typically found in Section 11 of a supplier's (e)SDS, or from publically/privately available resources. To ensure comparisons are equivalent, one must use NO(A)EL or NO(A)EC values from comparable experimental studies. This means that they are derived based on studies using the same species with exposures via the same route and same duration (e. g., 28-days repeated exposure study on rats via the oral route). Also **DO NOT** compare NO(A)ELs or NO(A)ECs with DNELs for the same route of exposure. Additionally, any comparisons must be made on an equivalent basis, e.g., NO(A)ELs with NO(A)ELs and NO(A)ECs with NO(A)ECs. Yes/No decision. If yes, comparable NO(A)EL or NO(A)EC values are available for all the relevant components for a given route of exposure (as per the conditions described above), then go to Step H13a. If no, go to Step H13b.
H13a	Calculate LCCI for each component for each exposure route. Ensure NO(A)EL/ NO(A)EC values are for the same species via the same exposure route and same duration of exposure	A Lead Component Candidate Indicator LCCI is calculated per component and per route of exposure: $$\mathrm{LCCI}_{\alpha} = \frac{\mathrm{C_i}}{\mathrm{NO(A)EL\ or\ NO(A)EC}}$$ Where: C_i : concentration of the component i in the mixture NO(A)EL: No-observed (adverse) effect level NO(A)EC: No-observed (adverse) effect concentration Document. Please see Test Example 4 (in Annex III) for use of NO(A)ECs in calculating LCCIs. Go to Step H14.
H13b	Calculate LCCIα based on LD_{50} or LC_{50} or ATE values	LD_{50} or LC_{50} or ATE values may be used as a back-up approach to calculate an LCCI, if no DNELs or NO(A)ELs or NO(A)ECs are available for one or more relevant component(s). LD_{50} or LC_{50} or ATE values are typically found in Section 11 of a supplier's (e)SDS, or from publically/privately available resources. **DO NOT** compare LD_{50}s with LC_{50}s. Any comparison must be made for the same route of exposure. If no LD_{50} or LC_{50} values are available, ATE values derived for the same route of exposure can be used for the calculation. The conversion of the classification to ATE values is based on Table 3.1.2

Step	Task	Comments
		of the CLP regulation (Regulation (EC) No 1272/2008). An LCCI is calculated per component and per route of exposure: $$\mathrm{LCCI}_{\alpha} = \frac{\mathrm{C_i}}{\mathrm{LD_{50}\ or\ LC_{50}\ or\ ATE}}$$ Where: Ci : Concentration of the component i in the mixture LD_{50}: Lethal dose resulting in 50% mortality of the experimental animals LC_{50}: Lethal concentration resulting in 50% mortality of the experimental animals ATE: Acute Toxicity Estimate Document. Please see Test Examples 5.1 and 5.2 (in Annex III) for use of LC_{50} and LD_{50} values in calculating LCCIs. Go to Step H14.
H14	Is there any DNEL available for the component with the highest LCI per exposure route?	The most reliable means of identifying Lead Component, for each relevant exposure route, is relying on the DNEL calculations. The alternative approaches (e.g., NO(A)ELs or NO(A)ECs and/or LD_{50} or LC_{50} or ATE values) should only be referenced to ensure that a potentially more toxic component is not missed when generating the safe use information. Be aware that this comparison is not fool-proof. If one has reasons to believe that a component is more toxic (e.g., would deserve a lower DNEL, if it had been derived), one should respond with a "No" to this question and continue with the case-by-case evaluation at Step H3. Reasons could be, for example, for a substance with a classification for reproductive toxicity or having a very low occupational exposure limit (OEL) value that this substance did not have a DNEL or NO(A)EL or NO(A)EC value covering this effect. So, for a component that has the highest LCCI for a given exposure route, based on either its NO(A)EL or NO(A)EC or LD_{50} or LC_{50} or ATE comparison, is there a DNEL available at all? Yes/No decision. If yes, go to Step H15. If no, then potentially a more toxic component would most likely be missed when compiling the safe use information. In that case, safe use information cannot be derived using the described methodology. Therefore safe use should be derived on a case-by-case analysis, go to Step H3.
H15	Compile OCs and RMMs for each ex-	In Step H11, for each route of exposure[34], a Lead Component (LC) has been identified. Compile the OCs/RMMs for each LC

[34] The relevant routes of exposure to consider are those exposure routes (e.g., dermal, inhalation, and/or oral) by which a worker or a consumer can be exposed under foreseeable conditions of use. Also consideration should be made on the components'/mixture's physical properties, including consideration of forms of application of the mixture which are beyond the "individual substance" scope generally applied. For example, consider the generation of fine dusts and fumes in processes in the metal industry and other industrial surroundings. Or exposure to mists or sprays as in applying paints. Also during the service life of many products (e.g., coat-

Step	Task	Comments
	posure route based on the Lead Component(s) (LCs) per relevant Contributing Activity (PROC)	based on the relevant exposure route. OCs and RMMs can typically be found in the supplier's (e)SDS or, if available, the CSR. Select the OCs and RMMs that are appropriate to how the **mixture** will be used (e.g., as a fuel, coating, adhesive). See Chapter 9 for further considerations when determining the appropriate OCs and RMMs for the mixture. When compiling this information, 3 cases are possible: • **Concentration of the LC equals the concentration provided in the eSDS:** Directly utilize the OCs and RMMs of the Exposure Scenario and Contributing Activity as provided by the supplier. If different LCs were identified for different routes of exposure, only copy those RMMs associated with the route for which the component was selected as LC. • **Concentration of the LC is significantly lower than the concentration given in the eSDS**: Either use the information unchanged (same as in the first case) or adapt the OCs/RMMs in the Exposure Scenario and Contributing Activity via scaling. • **Concentration of the LC is higher than the one provided in the eSDS:** This case can only occur if the Lead Component is part of a group (see Step H10) and its concentration was adjusted to account for additive effects. It requires that the recommended OCs/RMMs are reviewed to ensure the Exposure Scenario and Contributing Activity OCs and RMMs cover the adjusted concentration (e.g., $C_{weighted}$) (calculated in Step H11). In practice, the maximum concentration given in the scenario will often be the upper bound of the ECETOC-TRA concentration ranges, so an adjustment does not have to be done in all cases. Where the concentration was adjusted, but only in those cases, when it is increased to values above the boundaries given in the eSDS, does one need to ensure the Exposure Scenario and Contributing Activity OCs and RMMs cover the adjusted concentration (e.g., $C_{weighted}$). One quick solution prior to remodelling with ECETOC could be to check if the same PROC has already been calculated with a higher concentration. Go to Step H16.
H16	Consider local effects for each exposure route (e.g., eye/skin/respiratory tract irritation, corrosivity, skin/respiratory sensitisation) based on the Lead Components (LC)	Identify the presence of any components that may contribute to the hazard classifications of local effects (eye, skin, or respiratory tract irritation/corrosivity, skin or respiratory sensitisation) including EUH066 (dryness or cracking of the skin). Information on the potential presence of these hazards for components of the mixture can be found in their respective supplier's (e)SDSs. Note: Components classified as skin corrosion/irritation 1A, 1B, 1C (H314) pose as hazards to both the skin and the eyes, therefore RMMs to protect for exposure by both these routes

ings), processes such as grinding, sanding, or polishing or during recycling of coated objects, specific exposure conditions such as dust generation may occur which have to be considered specifically.

Step	Task	Comments
		should be considered. Go to Step H17.
H17	If needed, compile OCs and RMMs based on local effects (e.g., eyes, skin, respiratory tract)	If the CLP classification for the mixture includes any of the following hazard classes: eye irritation/damage, skin irritation/corrosion, skin sensitisation, respiratory sensitisation, respiratory irritation, dryness or cracking of the skin, then additional RMMs might have to be selected to protect against these effects. RMMs for eye protection should be selected based on the use of the mixture. Skin protection measures can also be derived based on the use of the mixture, but it must be ensured that the selected material protects the worker against all components in the mixture that cause this effect. For respiratory sensitisation and irritation, check if the RMMs for the inhalation route for these components were already included in the RMMs copied from the Lead Components. Add these RMMs, if this is not the case. Go to Step H18.
H18	Identify OCs and RMMs per Exposure Scenario and Contributing Activity to derive safe use information for mixture	Verify if the OCs and RMMs derived in the previous steps are sufficient to ensure safe use of the mixture. Expert judgment is recommended to select the final set of OCs and RMMs. If you have reasons to believe that components that do not drive the CLP classification and labelling criteria for the mixture (cf. REACH Article 31.3) yet present a risk to human health, they should be included in the selection of RMMs. Document and allow for easy access to enforcement authorities, if any changes to the OCs or RMMs were required. Go to Step H19.
H19	Provide safe use information either embedded within SDS or as an annex to SDS	See Chapter 5 and Annex II for details. Go to LCID Environmental methodology workflow (Step E1).

7.3 **LCID methodology - Environmental hazards**

The main steps in preparing safe use information regarding environmental hazards for a mixture are shown in Figures 6a and 6b. It shows the entire process, from the compilation of data requirements on the components of the mixture and its risk assessment to the preparation of the safe use information for incorporation or as an annex to the safety data sheet of the mixture. It also includes the requirements for the classification and labelling of a mixture and hazard data gathered under REACH (e.g., PNECs). This methodology also accounts for the presence of:

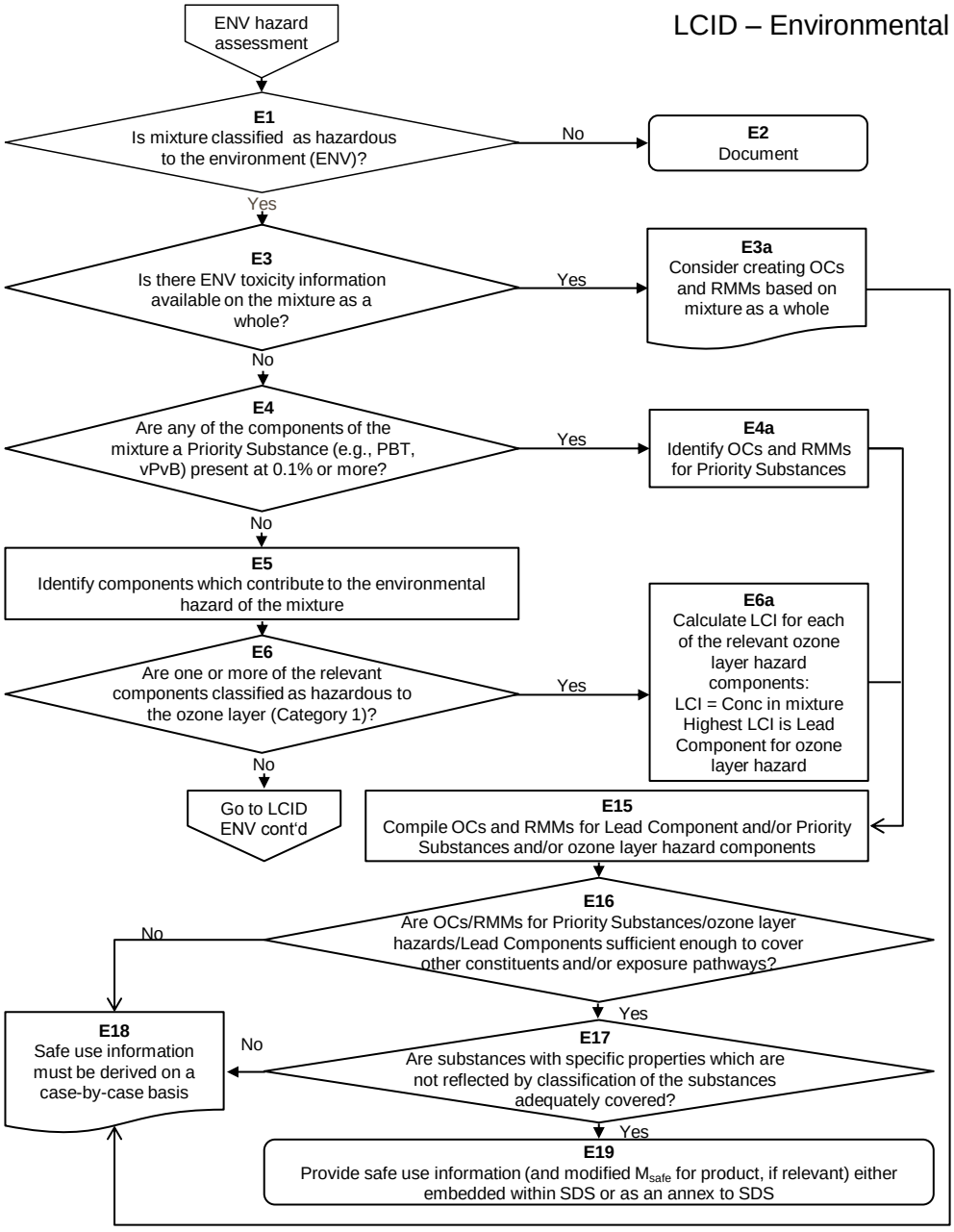
- Priority Substances (e.g., PBTs and vPvBs criteria according to Annex XIII to REACH)
- Substances of very high concern (SVHC) meeting the criteria set out in REACH Article 57 (if not already identified as a priority substance)
- Substances which lack PNECs but have available other relevant data (e.g., classification for environmental hazards, M-factors)
- Substances with environmentally relevant properties, e.g., biodegradability
- Substances that have been identified as ozone layer hazards
- Potential additive environmental effects

Note: Mixtures where components interact in such a way that the combined biological effect is stronger (synergistic, potentiating) or weaker (antagonistic) than would be expected on the basis of dose/concentration addition or response addition, are not covered by this approach. If there is a potential for synergistic/antagonistic effects, evaluation of the properties of the mixture heavily relies on expert knowledge and can only be done on a case-by-case basis.

In Table 2 more details on the working steps are provided.

Annex III includes test examples of applying the LCID methodology for deriving safe use information based on the environmental hazard information provided on components of a mixture. This includes a template that describes the information/calculations used in the examples.

Annex IV is the technical documentation which provides the background, assumptions, and references for each of the steps of the LCID methodology as it pertains to environmental hazards.



Legend Figures 6a and 6b
C_i: Concentration of the component i in the mixture
$C_{weighted}$: Adjusted concentration of the LC
LC: Lead Component
LCI: Lead Component Indicator
LCI_{max}: Maximum LCI from the components
M_{acute}: M-Factor for aquatic acute toxicity endpoint
$M_{chronic}$: M-Factor for aquatic chronic toxicity endpoint
MF: Modifying Factor
M_{safe}: Maximum daily tonnage of a component
OC: Operational Condition
PNEC: Predicted No-Effect Concentration
PS: Priority Substance
RMM: Risk Management Measure
SDS: Safety Data Sheet

Figure 6a LCID methodology for generation of safe use information for mixtures 1 – environmental hazards

LCID - Environmental hazards, page 2

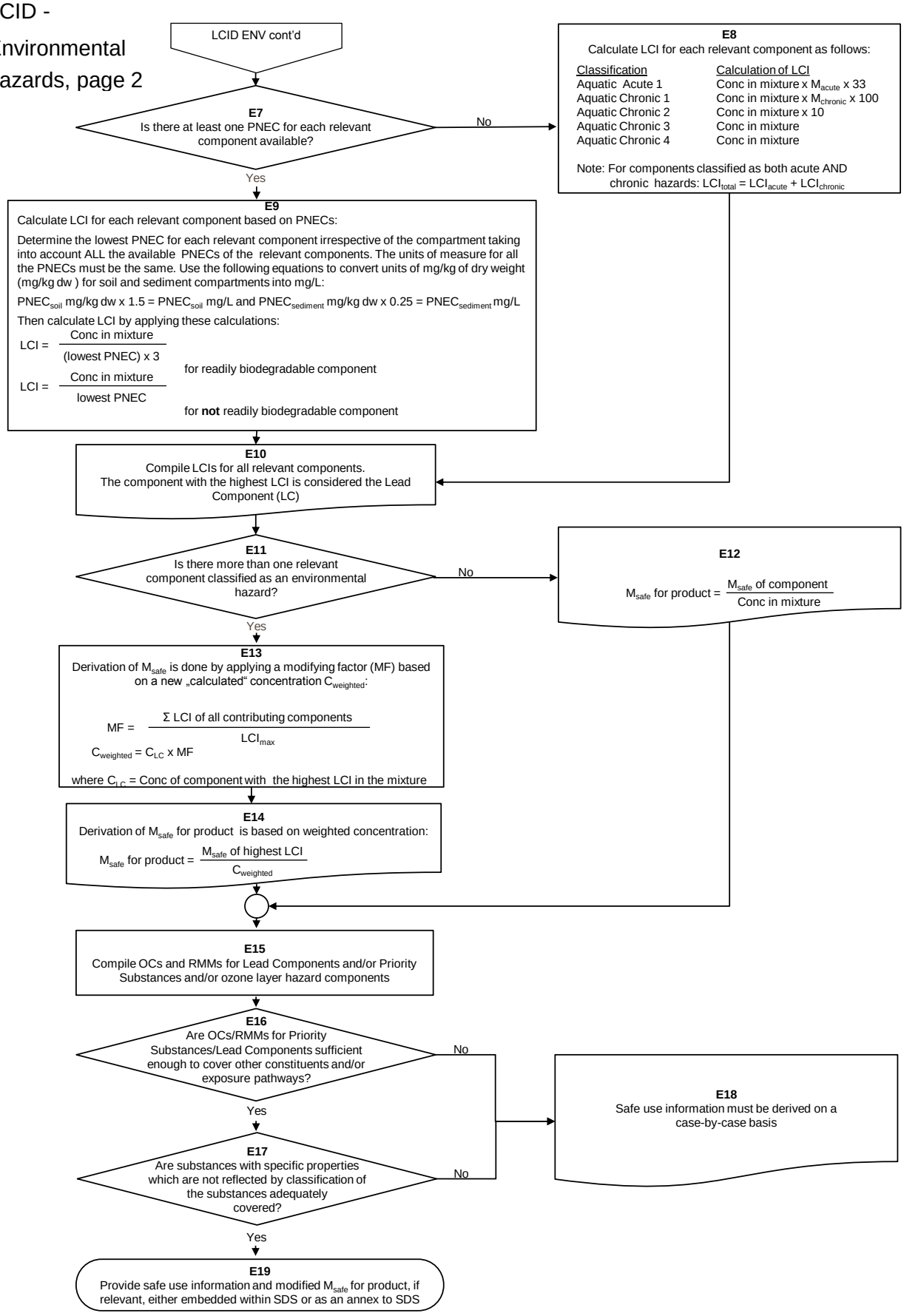


Figure 6b LCID methodology for generation of safe use information for mixtures, page 2 – environmental hazards

Table 2: Explanation of the steps for generating safe use information regarding environmental hazards for chemical mixtures

Step	Task	Comments
E1	Is the mixture classified as hazardous to the environment (ENV)?	Refer to CLP hazard classification of the mixture. Yes/No decision. If yes, go to Step E3. If no, go to Step E2.
E2	Document	If not classified as an environmental hazard, document for internal purposes and allow for easy access to enforcement authorities, if required. Records should include date of review[35]. END LCID methodology workflow.
E3	Is there ENV toxicity information available on the mixture as a whole?	Has there been toxicity testing of the mixture as a whole? An assessment may also be based on data generated on a mixture of reasonably similar composition or a "surrogate mixture", e.g., a mixture close in composition (components and proportions) to the mixture under evaluation. Can any of the test results be used to derive safe use information for the mixture as a whole? Information may be available from the company's own testing of the mixture (e.g., for regulatory or permitting purposes), or through a supplier (through information provided on their (e)SDS) or if the mixture is a common commodity or formulation, through an industry sector organisation or published literature. If the testing data set for the entire mixture is incomplete, can the data that is available be used to justify safe use recommendations for one or more of the environmental compartments? If data is lacking, consider following the LCID methodology to fill the gaps for the other compartments (e.g., test data on the mixture as a whole is available for air). Document the company's position and allow for easy access to enforcement authorities, if required. Yes/No decision. If yes, go to Step E3a. If no, go to Step E4.

[35] If asked for an SDS upon request for an unclassified mixture, this LCID methodology may be applied.

Step	Task	Comments
E3a	Consider creating OCs and RMMs based on the mixture as a whole	Consider creating safe use information based on the test data for the mixture as a whole; this is done on a case-by-case basis. If data is lacking, consider following the LCID methodology to fill the gaps for the other environmental compartments. If this is the case, then go to Step E4. Document the company's position and allow for easy access to enforcement authorities, if required. Go to Step E18.
E4	Are any of the components of the mixture a Priority Substance (e.g., PBT, vPvB) present at 0.1% or more?	Are there any components that have been identified as a PBT or vPvB present at 0.1% or more? Yes/No decision. Document. See Test Example 6 (in Annex III) for deriving safe use information for a mixture containing a PBT. If yes, go to Step E4a. If no, go to Step E5.
E4a	Identify OCs and RMMs for Priority Substances	Gather the relevant exposure scenario information (OCs and RMMs) on the Priority Substances. These can typically be found in a supplier's (e)SDS or from the chemical substance's CSR (if available). Priority Substances generally require the most stringent risk management measures. Go to Step E15.
E5	Identify components which contribute to the environmental hazard of the mixture	Review the CLP classification of the mixture. Identify which components are present above limit concentrations of REACH Art. 14.2. and contribute to the environmental hazard classification. These components are further identified as relevant components. The hazard classifications of the individual components are typically available from Section 3 of the supplier's (e)SDS. Go to Step E6.
E6	Are one or more of the relevant components classified as hazardous to the ozone layer (Category 1)?	Components depleting the ozone layer are considered separately as this is a very specific environmental effect in comparison with the other toxic endpoints related to the environment. Identify any relevant components that are hazardous to the ozone layer, as identified by the components CLP classification. Yes/No decision. Document. If yes, there is more than one relevant component that is classified as an ozone layer hazard, go to Step E6a. If no, go to Step E7.

Step	Task	Comments
E6a	Calculate LCI for each of the relevant ozone layer hazard component(s)	Calculate the LCI for each of the contributing ozone layer hazard components: LCI = Concentration in mixture The highest LCI is the Lead Component driving the ozone layer hazard classification. See Test Example 7 (in Annex III) for deriving LCI values for a mixture containing more than one ozone layer hazard component. Go to Step E15.
E7	Is there at least one PNEC for each relevant component available?	Determine if each relevant component has at least one PNEC, **irrespective of the compartment (e.g., air, water, soil, sediment)** taking into account **all** the available PNECs of the relevant components. Yes/No decision. If yes, go to Step E9. If no, then go to Step E8.
E8	Calculate LCI based on CLP-classification, concentration and M-factors	This is the backup approach in case the required set of PNECs (at least one PNEC per component) is not complete. Identify if any relevant components have associated M-factors. These can be typically found in either Section 2 of the (e)SDS of the component or in Section 3 of the (e)SDS for mixture components. M-factors have been incorporated into the calculation to account for a high individual toxicity of a component. Calculate the LCI taking into account CLP-classification, concentration and M-factors: Classification — Calculation of LCI Aquatic Acute 1 — Conc in mixture x M_{acute} x 33 Aquatic Chronic 1 — Conc in mixture x $M_{chronic}$ x 100 Aquatic Chronic 2 — Conc in mixture x 10 Aquatic Chronic 3 — Conc in mixture Aquatic Chronic 4 — Conc in mixture Contributions from both acute and chronic aquatic hazard classifications should be taken into account to identify the Lead Component (LC). Thus, for components classified as both acute AND chronic hazards: $LCI_{total} = LCI_{acute} + LCI_{chronic}$ Document. See Test Example 9 (in Annex III) for calculating LCIs based on classification and M-factors, when missing PNECs. Go to Step E10.

Step	Task	Comments
E9	Calculate LCI for each relevant component based on PNECs	Determine the lowest PNEC for each relevant component **irrespective of the compartment (e.g., air, water, soil, sediment)** taking into account **all** the available PNECs of the relevant components. 9.1 In order to determine which has the lowest PNEC, the units of measure for all the PNECs must be the same. Use the following equations to convert units of mg/kg of dry weight (mg/kg dw) for soil and sediment compartments into mg/L (Rationales for conversion factors are included in Annex IV): $PNEC_{soil}$ mg/kg dw x 1.5 = $PNEC_{soil}$ mg/L and $PNEC_{sediment}$ mg/kg dw x 0.25 = $PNEC_{sediment}$ mg/L Document, as necessary. 9.2 Determine whether the component is readily degradable or not. You have to take biodegradation into account. This information can be typically found in Section 12 of the (e)SDS of the component. 9.3 Calculate the LCI for each relevant component. If a component is readily degradable then: LCI = C / PNEC x 3 Otherwise apply this equation (not readily degradable: LCI = C / lowest PNEC Where: C = Concentration of component in the mixture PNEC = Predicted No-Effect Concentration Note: The higher the concentration of a relevant component in a mixture, the higher the contribution of this component to the potential hazard of the mixture is (the numerator); the lower the PNEC of a relevant component, the more hazardous the component is (the denominator). Document. See Test Example 9 (Annex III) for calculating LCIs based on PNECs. Go to Step E10.

Step	Task	Comments
E10	Compile LCIs for all components; the relevant component with the highest LCI is considered the Lead Component (LC)	Select the relevant component with the highest LCI as the Lead Component. The component with the highest LCI is deemed to have the highest impact on the potential environmental hazard of the mixture. It is judged that providing information on the safe use of this component will ensure safe use of the entire product mixture. Document the company's position and allow for easy access to enforcement authorities, if required. If there is more than one component that contributes to the environmental hazard classification of the mixture, then these calculated LCI values, including the LCI of the Lead Component, will be needed in Step E13. Go to Step E11.
E11	Is there more than one relevant component classified as an environmental hazard?	In order to calculate the M_{safe} for the product mixture, first determine if more than one component (beyond the Lead Component) has contributed to its CLP environmental hazard classification for the mixture. Yes/No decision. If yes, there is more than one relevant component that contributes to the environmental hazard classification of the mixture, go to Step E13. If no, there is only one component that contributes to the environmental hazard classification of the mixture, go to Step E12.
E12	Derive M_{safe} for product mixture if there is only one relevant component that drives the environmental classification of the mixture	Identify the M_{safe} value for the relevant component which drives the environmental hazard classification of the mixture. This can be typically found in the supplier (e)SDS or from the substance's CSR. The M_{safe} for the product can be derived using a linear relationship: M_{safe} product = M_{safe} component / C [36] Where: C = Concentration of component in the mixture The lower the concentration of this Lead Component in the mixture, the higher the resulting M_{safe} for the product. If there is no information on the M_{safe} of the Lead Component available, the daily site tonnage assumed for the Lead Component may be used as a surrogate. This amount is lower than the M_{safe}, therefore representing a conservative approach: $\text{Daily amount at site} = \frac{\text{Annual amount used at site}}{\text{emission days}}$

[36] It has to be assured that the concentration is considered appropriately, e.g. XY% must be used as 0.XY in the calculation.

Step	Task	Comments
		$M_{safe}\ product = Daily\ amount\ at\ site\ /\ C$ Document the company's position, and communicate to downstream users. Allow for easy access to enforcement authorities, if required. See Test Examples 8 and 9 (in Annex III) for deriving M_{safe} for product mixtures. Go to Step E15.
E13	Derivation of M_{safe} for the product mixture when more than one relevant component contributes to the environmental hazard classification of the mixture	Potential additive environmental effects may need to be addressed. For this purpose, a modifying factor (MF) is calculated to give more weight to the LCI of the Lead Component compared to the LCIs of the other contributing components. The MF is calculated using the following equation: $MF = \frac{\sum LCI}{LCI_{max}}$ Where the ΣLCI is the sum of the LCIs (including LCI_{max}) for all contributing components (as calculated in Step E10) and LCI_{max} is the LCI of the Lead Component. The LC and its associated LCI is identified in Step E10. Using the MF, the actual concentration of the Lead Component in the mixture is converted into a "$C_{weighted}$" concentration: A hypothetical concentration that accounts for the additive effects. $C_{weighted} = C_{LC} \times MF$ Where: C_{LC} = Concentration of the Lead Component MF = Modifying factor calculated above Document and use this value for Step E14. See Test Examples 8 and 9 (in Annex III) for deriving $C_{weighted}$ values. Go to Step E14.
E14	Derivation of M_{safe} for product is based on weighted concentration	So the M_{safe} value for the product can be calculated using the M_{safe} value of the Lead Component and the modified concentration (e.g., $C_{weighted}$ value) as follows: $M_{safe}\ product = \frac{M_{safe}\ LC}{C_{weighted}} \times 100\%$ Where: M_{safe} LC = M_{safe} of Lead Component $C_{weighted}$ = Calculated from Step E13 Use of $C_{weighted}$ takes into account potential additive effects. If there is no information on the M_{safe} of the Lead Component available, the daily site tonnage assumed for the Lead Component may be used as a surrogate. This amount is lower than the M_{safe}, therefore representing a conservative approach: $Daily\ amount\ at\ site = \frac{Annual\ amount\ used\ at\ site}{emission\ days}$ So the equation to calculate the M_{safe} value for the prod-

Step	Task	Comments
		uct using this surrogate value would be: $M_{safe}\ \text{product} = \text{Daily amount at site} / C$ Use expert judgment before issuing. Document the company's position, and communicate to downstream users. Allow for easy access to enforcement authorities, if required. Go to Step E15.
E15	Compile OCs and RMMs for Lead Component and/or Priority Substances and/or ozone layer hazard components	Determine the OCs and RMMs for the Priority Substances and/or Lead Components and/or ozone layer hazard and use these as safe use information for the mixture. The concentration of the Lead Component in the mixture, e.g., the reduced hazard potential of the mixture, is reflected in the increased M_{safe} of the product (compared to the M_{safe} of the pure Lead Component). A check should be performed to ensure that possible hazards arising from components causing risks to the environment that do not meet the CLP classification and labelling criteria for the mixture (cf. REACH Article 31.3, are adequately covered by the proposed OCs and RMMs. Evaluate the RMM for the Lead Component. If it only covers protection from one release pathway (e.g., air) but there is another component which triggers the need to reduce release to another pathway (e.g., water) then, one should ensure that RMMs for both types of releases are provided. Review if there are substance-specific RMMs that may address the Lead Component very efficiently but have no effect on the other components that are hazardous existing in the mixture. Expert judgment is recommended to check whether the final OCs/RMMs allow an adequate control of all environmental hazards. If not, additional or modified RMMs may have to be identified. For mixtures of volatile and non-volatile compounds which are assigned to more than one ERC (e.g. 4/5, 8a/8c, 8d/8f) it can be expected that compounds envisage a diverging environmental fate and are linked to independent RMMs (e.g. precipitation, neutralisation and filtration for non-volatile compounds on-site, biological degradation for volatile compounds at municipal STP). In these cases, it may be a reasonable option to determine one lead compound per assigned ERC. Document and allow for easy access to enforcement authorities, if required. Go to Step E16.
E16	Are OCs/RMMs for Priority Substances/ozone layer hazards/Lead Components	Ensure that risk management measures for Lead Components and Priority Substances cover protection against the other hazardous substances in the mixture. See Section 8. Extended evaluation of mixtures for more

Step	Task	Comments
	sufficient enough to cover other constituents and/or exposure pathways?	details. If yes, go to Step E17. If no, use expert judgement to add appropriate OCs and/or RMMs; then go to Step E18.
E17	Are substances with specific properties which are not reflected by classification of the substances adequately covered?	A check should be performed to ensure that possible hazards arising from components causing risks to the environment that do not meet the CLP classification and labelling criteria for the mixture (cf. REACH Article 31.3, are adequately covered by the proposed OCs and RMMs. If yes, go to Step E19 If no, use expert judgement to add appropriate OCs and/or RMMs; then go to Step E18.
E18	Safe use information must be derived on a case-by-case basis	The LCID methodology is not applicable and safe use information is therefore derived on a case-by-case basis and should be referred to an expert. Document the company's position and allow for easy access to enforcement authorities, if required.
E19	Provide safe use information and modified M_{safe} value for product, if relevant, either embedded within SDS or as an annex to SDS	See Chapter 5 and Annex II for details. Note: An M_{safe} is not meaningful for products that contain a PBT, vPvB or ozone hazard. For those cases, choose the OCs and RMMs that limit their releases as much as possible; for PBTs and vPvBs consider all exposure pathways, and for ozone hazards, via air. END

8 Extended evaluation of mixtures

It is acknowledged that the LCID methodology will not cover 100% of the cases and there are several decision points where it may be necessary to refer to expert judgement to derive safe use information for chemical mixtures. Experts in such disciplines as chemistry, human and environmental toxicology, industrial hygiene, process safety management, as well as those familiar with industrial applications, processes, and equipment would be qualified consultants to help derive such appropriate safety practices.

8.1 Interactions between substances of a mixture

Hazard assessment of formulations may differ from substance-based hazard assessments as some properties will change significantly when incorporated into a formulation. For example, hazards associated with dustiness and surface properties of particles (silicogenic particles) are negligible as long as these particles are integrated into a polymer matrix. Flammability of solids (aluminium, nitro cellulose) is not relevant below specific concentrations. Corrosiveness of organic acids and amines is lost due to buffering mechanisms of the formulation (antagonism). Classification derived from flash point may be overruled for water-based materials. On the other hand, under specific conditions, harmful properties may be enhanced in mixtures (synergism). Some substances, such as dimethyl sulfoxide may enhance skin penetrations of others, thus leading to higher toxicity after dermal exposure.

Discussions on how toxicity of chemical mixtures should be assessed are currently ongoing; there is no final agreement among the scientific community on the best practice for the assessment of interactions in a mixture. In conclusion it can be said that especially in the case of suspected synergistic, antagonistic or potentiation-type of interactions, the evaluation of specific properties of mixtures heavily relies on expert judgment, as the effects of a multitude of possible combinations of substances in a mixture cannot be anticipated. Moreover significant toxic interactions between chemicals are much less likely to occur at doses below the effect levels for individual component compounds than at higher doses (Directorate-General for Health & Consumers, 2012). Hence these properties of interactions between chemicals are not within the scope of the LCID methodology presented in Chapter 7.

9 Generation of suitable safe use information – additional options for DUs

The LCID methodology can support the formulator of a mixture by identifying the Priority Substances (PS) and Lead Components (LCs) for different exposure routes and pathways and, thus, indicates from which exposure scenarios (ESs) obtained from a supplier the OCs and RMMs for these routes need to be taken and reviewed.

However, the OCs and RMMs for the same substance can differ widely between DU companies. Neither the manufacturer of an individual substance nor the formulator, who places a

mixture containing this substance onto the market, can be expected to know the full range of all the details of uses/use conditions/OCs/RMMs to include in the CSA for the registration dossier.[37] Typically, the manufacturer and/or formulator will communicate in their exposure scenarios the safe conditions of use on the basis of standard and/or worst case assumptions for all identified uses. Adjustments of these generic OCs and RMMs as provided in eSDS annexes of substances may be performed by the DU applying either "scaling" (complying with scaling rules/boundaries set and communicated in the eSDS of the supplier) or performing a DU CSA.

Note: If the DU has evidence that he has implemented measures that are higher in hierarchy or more effective than those in the ES received, he can consider his use being covered by the supplier's exposure scenarios (e.g. containment instead of Local Exhaust Ventilation (LEV)). The same applies to uses of his formulation by customers.

This is a valid qualitative approach applicable in accordance with Art. 37.4(d) of the REACH regulation and also addressed in ECHAs' Guidance for Downstream Users.

Scaling

Scaling means the application of rather simple calculations based on the algorithms of the exposure assessment tool used for the CSA on which the eSDS ES information of a substance is based on.

Scaling may be done manually applying parameters and equations or by calculation tools, if the respective scaling information (including the relevant parameters, rules, references to tools etc.) is communicated to the formulator by the supplier. With these, the formulator can examine the appropriate OCs and RMMs for the use of the Lead Components in his mixture for his customers and whether they can be considered to be within the boundaries of the exposure scenario. Furthermore, the following principles and boundaries must be taken into consideration:

- Scaling can only be applied to **quantitative** determinants of exposure.
  In the case of RMMs, the effectiveness is therefore key information for the calculation. The type of measure can deviate from the measure described in the exposure scenario if this is considered in the scaling instructions in the eSDS. The DU/formulator must then verify that his RMMs have the appropriate effectiveness to fulfil the boundaries of scaling defined by the supplier.
- The scaling of an exposure determinant may affect different routes of exposure. This needs to be considered by the supplier when drafting scaling instructions for manual scaling as well as in IT tools. DUs/formulators might therefore receive scaling instructions

[37] The parallel CSR/ES Roadmap activity on the sector use maps package (= description of use plus exposure assessment inputs: SWEDs, SpERCs, SCEDs) is designed to provide the registrant with more realistic information from downstream sectors on uses/use conditions/OCs/RMMs to include in the CSA for the registration dossier. One intended outcome from their implementation is to lessen the need for scaling.

where the intended change of one parameter also triggers a change of another parameter.

- Suppliers might set boundaries to parameters (e.g., frequency of exposure or quantities used at a site) as strong deviations may result in a different type of exposure. DUs/formulators have to respect these boundaries.
- DUs/formulators also should note any restrictions on removal of a RMM provided by a supplier.
- If the supplier does not provide any scaling information including the relevant parameters in the SDS (e.g, in Section 4 of the ES), the formulator may not perform scaling.

The identification and determination of parameters and boundaries for scaling is still in progress and will be made available via ECHA and/or industry websites.

Downstream User Chemical Safety Assessment (DU CSA) for a Substance

If the DU/formulator concludes that his conditions of use cannot be covered by scaling (considering the defined principles and boundaries), he may contact his supplier and ask for inclusion of his set of operational conditions and risk management measures in the assessment and for an updated eSDS[38]. Another option is to perform a DU CSA.

Performing a DU CSA may be a challenge for many DUs due to availability of the most relevant substance-specific input data and the technical skills required. A concept is currently being developed for a "simplified DU CSA" based on the same algorithms used for scaling, but applicable if actual use conditions are beyond the defined boundaries of scaling.

A DU CSA is made by a downstream user for uses which are not covered by the exposure scenarios of the suppliers and therefore differs in scope and content from a CSA made by the registrant as part of the registration:

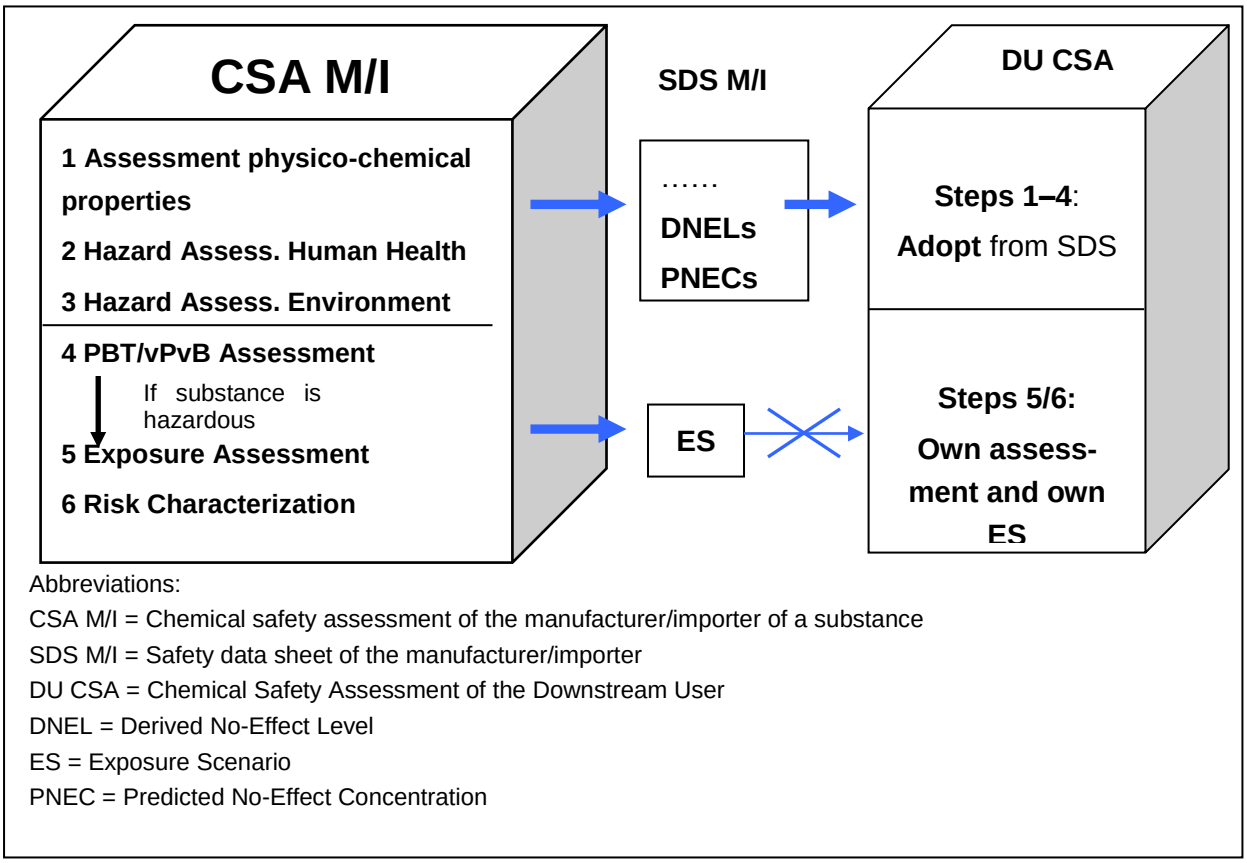
- The CSA of a registrant aims to describe conditions of safe use for all identified uses which are supported by the registrant. This CSA includes the complete assessment of the hazardous properties of the substance. For hazardous substances and for PBT/vPvB-substances, the CSA contains an exposure assessment and risk characterisation.
- The DU CSA concentrates on a specific use which has not been covered yet by the assessment of the supplier. For this use he performs an exposure assessment and risk characterisation. The downstream user usually does not have to re-assess the hazardous properties of the substances and the assessment of the PBT/vPvB properties. He can use the information on hazardous properties directly from the safety data sheet. This shall be stated in his CSR. Only in specific cases it might be necessary that the downstream user also performs a hazard assessment. This can be required if additional data on substance properties are necessary for the assessment of his use (e.g., long-term tox-

[38] For other options see Chapter 3, section "Check of downstream user (DU) whether his uses are covered by exposure scenarios."

icity for inhalation exposure), which were not part of the CSA of the registrant. Therefore in most cases, the downstream user CSA will be much shorter than the CSA of the registrant referring to the same substance (e.g. only Part B, Chapters 9 and 10 of a registrant's CSR format according to REACH Annex I).

- If the downstream user has different information on the hazards, he has to inform his supplier (and ECHA) and take this information into account for his own safety data sheet.

The following Figure 7 shows the relationship between the CSA of the registrant (manufacturer/importer M/I) and the downstream user CSA (DU CSA).



Abbreviations:
CSA M/I = Chemical safety assessment of the manufacturer/importer of a substance
SDS M/I = Safety data sheet of the manufacturer/importer
DU CSA = Chemical Safety Assessment of the Downstream User
DNEL = Derived No-Effect Level
ES = Exposure Scenario
PNEC = Predicted No-Effect Concentration

Figure 7 Relationship between the chemical safety assessment of a registrant (CSA M/I) and the chemical safety assessment of a downstream user (DU CSA). For his own assessment the downstream user can use relevant information from the extended safety data sheets which he has received.

In practice there are several ways to carry out a DU CSA which differ in their level of complexity. An ECHA practical guide for downstream users who have to perform a downstream

user chemical safety assessment (DU CSA) is available.[39] This practical guide describes different approaches that can be taken and indicates what needs to be documented in a DU CSR.

If a DU performs a DU CSA, the DU has the obligation to:

- implement the RMMs outlined in his DU CSR for his own uses and communicate the RMMs for the identified uses (in the supply chain) down the supply chain.
- report to ECHA and document the results of this assessment in his chemical safety report (DU CSR); he is not required to submit the CSR to ECHA (in contrast to the registrant's requirement of submitting a CSR to ECHA).

Finally note that the downstream user has one year commencing from the receipt of an eSDS with a registration number and an ES to perform his DU CSA.

When several substances in a mixture are used outside the conditions described in their respective substance-related exposure scenarios, and no exemptions according to REACH Art. 37.4 apply, the DU must carry out chemical safety assessments for each of these substances. As an alternative option, the DU can perform a chemical safety assessment (CSA) for the mixture as a whole.[40]

10 IT support for the compiling of safety data sheets for mixtures

Many companies generate SDSs for their chemical products in an automated process. This is especially the case for companies producing hundreds or thousands of products. Often SDSs are generated in more than 30 languages.

REACH requires including additional information from exposure scenarios of substances into the SDSs of mixtures. For an effective implementation of this requirement, it is necessary that it can also be done to a large extent automatically. "Manual" application of expert judgement should be minimized as much as possible. However, at least for a final check of the result of the automatic compilation process expert judgement is needed.

The tasks described above to generate safe use information for the safety data sheet of a mixture can be supported by IT systems. This is easier to do if the additional information in the exposure scenarios received and the safe use information for the mixture are structured in a uniform and modular way. The principal approach of generating safety data sheets in an automated process is illustrated in Figure 8.

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[39] Details on how to do a downstream user CSA are given in the ECHA Guidance for downstream users Chapters 5.3 and 5.4 (ECHA 2014, Version 2.1). The ECHA Practical Guide 17 "How to prepare a downstream user chemical safety report" is available in the internet: http://echa.europa.eu/documents/10162/13655/pg17_du_csr_final_en.pdf

[40] REACH Art. 31.2: "… If the safety data sheet is developed for a mixture and the actor in the supply chain has prepared a chemical safety assessment for that mixture it is sufficient if the information in the safety data sheet is consistent with the chemical safety report for the mixture instead of with the chemical safety report for each substance in the mixture."

Information on classification, labelling and packaging (CLP data) and exposure scenarios of raw materials are stored in a specific database (these raw materials are substances or mixtures). From this database information on substances is extracted and stored in a second database. Further databases contain standard phrases used for safety data sheets, description of the uses of the products, appropriate OCs and RMMs, recipes and physico-chemical data of the mixtures.

The safety data sheet for the mixture is generated based on the composition and physico-chemical data of the mixture.

Even today, the application of the CLP Regulation[41] to classify and label a mixture is done automatically in many cases. In a similar way, additional assessment steps such as the selection of Lead Components can be implemented in existing IT systems for the generation of SDSs of mixtures.

In addition, expert judgement which is needed for an advanced evaluation can be integrated if it refers to standard situations, e.g., substances with defined properties like carcinogenicity. These properties can be clearly identified from the results of the classification of the substance. In addition, further risk management measures for specific conditions of use (e.g., spray applications with aerosol formation) can be added automatically if this is indicated for a specific use in the underlying database.

[41] Until 1st June 2015 mixtures are classified according to the Dangerous Preparations Directive or CLP regulation; as from 1st of June 2015 they are to be classified according to CLP regulation

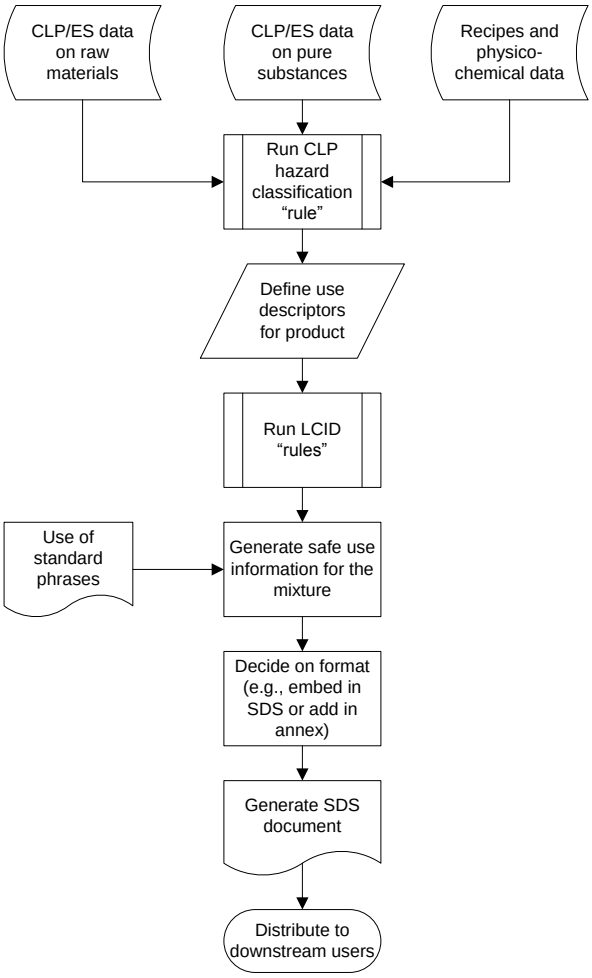


Figure 8 Elements of an IT system for the generation of extended safety data sheets (eSDS).

A decision tree delineating the LCID methodology in which an IT system may be based, can be found in Chapters 7.2 and 7.3.

During the development of this Practical Guide an Excel-based tool (Cefic/VCI Lead Component Identification (LCID) Template, v1.0) was developed to partially automate the LCID methodology and is available as a separate deliverable.

11 Glossary

AC	Article category
Additive effect	Any effect wherein two or more substances or actions used in combination produce a total effect, the same as the sum of the individual effects
ATE	Acute Toxicity Estimate
C_i	Concentration of the component i in the mixture
C_{LC}	Concentration of the lead component in the mixture
CLP Regulation	Regulation on classification, labelling and packaging of substances and mixtures, Regulation EC No 1272/2008
CMR	Substances which are carcinogenic, mutagenic or toxic to reproduction
Conditions of use	Conditions of use are operational conditions (OC, e.g. duration of activity) and risk management measures (RMMs, e.g. local exhaust ventilation)
CS	Contributing Scenario
CSA	Chemical safety assessment
CSR	Chemical safety report
DNEL	Derived No-Effect Level
Distributor	Only stores and places on the market a substance according to REACH Art. 3 No. 14
DPD	Dangerous Preparation Directive, Directive 99/45/EC; repealed with effect from 1 June 2015
DPD+ methodology	Method to identify lead components in mixtures based on the Dangerous Preparation Directive; with DNELs and PNECs becoming available and repeal of Directive 99/45/EC the method is replaced by the LCID methodology
DU	Downstream user according to REACH Art. 3 No. 13
ECETOC-TRA	Model for exposure estimation and risk description. TRA: “Targeted Risk Assessment”
ECHA	European Chemicals Agency
End-Use(r)	Final downstream use(r) in a supply chain
ES	Exposure Scenario
eSDS	Extended Safety Data Sheet
ERC	Environmental Release Category. Categories for release of chemical substances into the environment.
Exposure	Exponere (lat): to be set out; contact between a chemical substance or a physical or biological agent on the one hand and an organism or an environmental compartment on the other.
Formulator	Downstream user who formulates mixtures from substances or mixtures

GHS	Globally Harmonized System of Classification and Labelling. It is implemented in Europe by the CLP Regulation.
LC	Lead Component
LCCI	Lead Component Candidate Indicator
LCI	Lead Component Indicator
LCI_{α}	LCI for route of exposure α
LCI_{group}	Sum of the LCIs of the grouped components
LCI_{max}	Maximum LCI from the components of the LCI_{group}
LCID	Method to identify lead components in mixtures considering DNELs and PNECs available from registrations under REACH and classification of components according to CLP Regulation
LD_{50}	Lethal dose resulting in 50% mortality of the experimental animals
LC_{50}	Lethal concentration resulting in 50% mortality of the experimental animals
MAK	Maximum concentration of a chemical substance in the work place air which generally does not have known adverse health effects; in Germany: “Maximale Arbeitsplatzkonzentration”
MF	Modifying factor
M-factor	A multiplying factor that gives increased weight to substances classified as hazardous to the environment
M_{safe} value	Maximum daily tonnage of the substance guaranteeing safe use for a specific application
Mode of action (MoA)	Mode of action (MOA) is a biologically plausible sequence of key events leading to an observed effect, supported by robust experimental observations and mechanistic data.
NO(A)EL	No-observed (adverse) effect level
NO(A)EC	No-observed (adverse) effect concentration
OC	Operational condition (of use) such as duration and frequency of substance use, application temperature, state of aggregation of the substance
OEL	Occupational Exposure Limit
PBT	Persistent, bioaccumulative and toxic (substance)
PC	Product category
PEC	Predicted Environmental Concentration
PNEC	Predicted No-Effect Concentration
PROC	Process category
RCR	Risk Characterisation Ratio
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals. Regulation (EC) 1907/2006 that entered into force on 1 June 2007 in the European Union

RMM	Risk management measure (e.g. local exhaust, closed equipment, gloves of a certain specification, instructions).
SCED	Specific Consumer Exposure Determinant
SDS	Safety data sheet
Scaling	Here: Use of simple arithmetic operations, in order to be able to calculate with exposure estimates based on one's own specific input values
SpERC	Specific Environmental Release Category
STOT(-SE/RE)	Specific Organ toxicity (SE: Single Exposure; RE: Repeated Exposure)
SU	Sector of use
SVHC	Substance of very high concern
SWED	Sector-specific Workers Exposure Description
TLV	Threshold limit value
Use Descriptor System	System for the short description of uses. The abbreviations specified in this system can be used in the short title of an exposure scenario, in order to give a first indication, in which industries a substance is used, to which type of product it belongs, during which processes it is used and – if of importance – in which products it can appear later on.
vPvB	very Persistent and very Bioaccumulative (substance)

Annex I: Concentrations limits for substances in mixtures according to REACH Art. 14.2

Note: The wording of Article 14.2 is as follows:

"*A chemical safety assessment in accordance with paragraph 1 need not be performed for a substance which is present in a mixture if the concentration of the substance in the mixture is less than*

(a) the cut-off value referred to in Article 11, paragraph 3 of Regulation (EC) No 1272/2008;

(b) 0,1 % weight by weight (w/w), if the substance meets the criteria in Annex XIII REACH.';

The cut-off values referred to in Article 11 for health and environmental hazards are substantiated in Annex I CLP section 1.1.2.2.2.

(i) for substances where a specific concentration limit is set for the relevant hazard class or differentiation either in Part 3 of Annex VI CLP or in the classification and labelling inventory referred to in Article 42, and where the hazard class or differentiation is mentioned in Table 1.1, the lower of the specific concentration limit and the relevant generic cut-off value in Table 1.1; or

(ii) for substances where a specific concentration limit is set for the relevant hazard class or differentiation either in Part 3 of Annex VI CLP or in the classification and labelling inventory referred to in Article 42, and where the hazard class or differentiation is not mentioned in Table 1.1, the specific concentration limit set either in Part 3 of Annex VI CLP or in the classification and labelling inventory; or

(iii) for substances where no specific concentration limit is set for the relevant hazard class or differentiation either in Part 3 of Annex VI CLP or in the classification and labelling inventory referred to in Article 42, and where the hazard class or differentiation is mentioned in Table 1.1, the relevant generic cut-off value set out in that table; or

(iv) for substances where no specific concentration limit is set for the relevant hazard class or differentiation either in Part 3 of Annex VI CLP or in the classification and labelling inventory referred to in Article 42, and where the hazard class or differentiation is not mentioned in Table 1.1, the generic concentration limit for classification in the relevant sections of Parts 3, 4 and 5 of Annex I CLP.

(b) For aquatic environmental hazards in section 4.1 of Annex I CLP:

(i) for substances where an M-factor has been set for the relevant hazard category either in Part 3 of Annex VI CLP, or in the classification and labelling inventory referred to in Article 42, the generic cut-off value in Table 1.1 adjusted using the calculation set out in section 4.1 of Annex I CLP; or
(ii) for substances where no M-factor is set for the relevant hazard category either in Part 3 of Annex VI CLP or in the classification and labelling inventory referred to in Article 42, the relevant generic cut-off value set out in Table 1.1."

Table 1.1 - Generic cut-off values

Hazard class	***Generic cut-off values to be taken into account***
Acute Toxicity:	
— Category 1-3	*0,1 %*
— Category 4	*1 %*
Skin corrosion/Irritation	*1 % ([1])*
Serious damage to eyes/eye irritation	*1 % ([2])*
Hazardous to Aquatic Environment	
— Acute Category 1	*0,1 % ([3])*
— Chronic Category 1	*0,1 % ([3])*
— Chronic Category 2-4	*1 %*

([1]) Or < 1 % where relevant, see 3.2.3.3.1.
([2]) Or < 1 % where relevant, see 3.3.3.3.1.
([3]) Or < 0,1 % where relevant, see 4.1.3.1.

Note: Generic cut-off values are in weight percentages except for gaseous mixtures for those hazard classes where the generic cut-off values may be best described in volume percentages.

Table 4.1.3 - Multiplying factors for highly toxic components of mixtures

Acute toxicity	***M factor***	***Chronic toxicity***	***M factor***	
$L(E)C_{50}$ value (mg/l)		*NOEC value (mg/l)*	*NRD ([1]) components*	*RD ([2]) components*
$0,1 < L(E)C_{50} \leq 1$	*1*	*$0,01 < NOEC \leq 0,1$*	*1*	*—*
$0,01 < L(E)C_{50} \leq 0,1$	*10*	*$0,001 < NOEC \leq 0,01$*	*10*	*1*
$0,001 < L(E)C_{50} \leq 0,01$	*100*	*$0,0001 < NOEC \leq 0,001$*	*100*	*10*
$0,0001 < L(E)C_{50} \leq 0,001$	*1 000*	*$0,00001 < NOEC \leq 0,0001$*	*1 000*	*100*
$0,00001 < L(E)C_{50} \leq 0,0001$	*10 000*	*$0,000001 < NOEC \leq 0,00001$*	*10 000*	*1 000*
(continue in factor 10 intervals)		*(continue in factor 10 intervals)*		

([1]) Non-rapidly degradable.
([2]) Rapidly degradable.

Annex II: Integration of information from an exposure scenario in the main body of a safety data sheet

The following Table A.II.1 gives an overview on the contents of an exposure scenario and the corresponding section of the safety data sheet. This provides guidance on how a downstream user may integrate the information from ES into the safety data sheet of his mixture if this option (see option 3 in Chapter 5) is chosen by him.

Note: By integration of safe use information derived from exposure scenarios into the main body of the SDS it can become more difficult for the following downstream user to check whether his uses (and the uses of his customers, if applicable) are covered by the exposure scenario. (In Chapter 5 the different options have been described in detail).

In practice it is difficult to incorporate differentiated safe use conditions for different uses/ tasks into the main body of the SDS. In such cases, an annex to the SDS might be the preferred option. The core SDS should then deal with safety properties of the mixture "as is", and can include references to the annex for more detailed and use-specific conditions.

Table A.II.1 Content of the exposure scenario and the corresponding sections in the safety data sheet.[42]

ES section	SDS Section
Short title of the exposure scenario	1.2
Operational conditions and risk management measures	7 + 8
Control of workers exposure	
Product characteristic	7 + 8 + 9
Amounts used	7 + 8
Frequency and duration of use	7 + 8
Human factors not influenced by risk management	7 + 8
Technical conditions and measures at process level (source) to prevent release	7 + 8
Technical conditions and measures to control dispersion from source towards the worker	7 + 8
Organisational measures to prevent/limit releases, dispersion and exposure	(5, 6), 7+ 8
Conditions and measures related to personal protection, hygiene and health evaluation	(5, 6), 7, 8
Other conditions affecting workers exposure	7 + 8
Control of consumer exposure* ***** Note that specific information on **consumer** exposure in Section 8 of the SDS is not a legal requirement.	
Product characteristic	7 + 8 + 9
Amounts used	7 + 8
Frequency and duration of use	7 + 8
Other conditions affecting consumers exposure	7 + 8
Control of environmental exposure	
Product characteristic	7 + 8 + 9
Amounts used	7 + 8
Frequency and duration of use	7 + 8
Environmental factors not influenced by risk management	
Technical conditions and measures at process level (source) to prevent release	7
Technical onsite conditions and measures to reduce or limit discharges, air emissions and releases to soil	7 + 8
Organisational measures to prevent/limit release from site	6 + 7 + 8
Conditions and measures related to municipal sewage treatment plant	8 + 13
Conditions and measures related to external treatment of waste for	13

[42] Cited from the ECHA Guidance on the compilation of safety data sheets, page 109, table 1: Relationship between exposure scenario and SDS Sections (Version 3.1 from November 2015)

ES section	SDS Section
disposal	
Conditions and measures related to external recovery of waste	13
Other given operational conditions affecting environmental exposure	7

The following Table A.II.2 shows the link between sections of the safety data sheet and the content of the exposure scenario.

Table A.II.2 Content of the exposure scenario and the corresponding sections in the safety data sheet. Source: own compilation based on Table A.II.1.

Sections of the safety data sheet		Sections of the ES with relevant information for the section of the SDS
1.	IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING	
1.1	Product identifier	
1.2	Relevant identified uses of the substance or mixture and uses advised against	Whereas short titles of Exposure Scenarios shall allow differentiation between scenarios, Section 1.2 of the SDS shall only include a general description how the substance is used (“solvent”)
1.3	Details of the supplier of the safety data sheet	
1.4	Emergency telephone number	
2.	HAZARDS IDENTIFICATION	
3.	COMPOSITION/INFORMATION ON INGREDIENTS	Concentration of substance in mixture or article
	Substances presenting a health or environmental hazard in concentrations above the concentration limits according to REACH Annex II, No. 3.2.a	
	Substances for which there are community workplace exposure limits	
	PBT and vPvB substances	
	Substances in mixtures not classified (see REACH Annex II, No. 3.2.2	
	Classification of the above substances	
	Name, registration number, EINECS or ELINCs number, if available, of the above substances. CAS Number and IUPAC name may also be helpful.	
4.	FIRST AID MEASURES	
5.	FIRE-FIGHTING MEASURES	
6.	ACCIDENTAL RELEASE MEASURES	
7.	HANDLING AND STORAGE	
7.1	Precautions for safe handling	
7.2	Conditions of safe storage	

Sections of the safety data sheet		Sections of the ES with relevant information for the section of the SDS
7.3	Specific end use(s)	Ensure consistency with Section 1.1 Short titles of Exposure Scenario
8.	EXPOSURE CONTROLS/PERSONAL PROTECTION	Duration and frequency of use for which the ES ensures control of risk
8.1	Control parameter	Duration and frequency of use for which the ES ensures control of risk
8.2	Exposure controls	Physical form of product in which the substance is contained Surface area per amount of article containing the substance (if applicable) Concentration of substance in mixture or article Other operational conditions determining exposure, e.g. temperature, capacity of receiving environment (water flow; room size x ventilation rate)
8.2.2.2	Occupational exposure controls	Occupational measures following the hierarchy of Directive 98/24/EC: type and efficiency of single options or combination of options on exposure to be quantified; options to be phrased as instructive guidance
Optional: Consumer related exposure controls		Consumer-related measures: type and efficiency of single options or combination of options on exposure to be quantified; options to be phrased as instructive guidance
8.2.3	Environmental exposure controls	Environment-related measures: type and efficiency of single options or combination of options on exposure to be quantified; options to be phrased as instructive guidance
9.	PHYSICAL AND CHEMICAL PROPERTIES	Physical form of product in which the substance is contained
9.1	Information on basic physical and chemical properties	
9.2	Other information	
10.	STABILITY AND REACTIVITY	
10.1	Reactivity	
10.2	Chemical stability	
10.3	Possibility of hazardous reactions	
10.4	Conditions to avoid	
10.5	Incompatible materials	
10.3	Hazardous decomposition products	
11.	TOXICOLOGICAL INFORMATION	
12.	ECOLOGICAL INFORMATION	
12.1	Toxicity	

Sections of the safety data sheet		Sections of the ES with relevant information for the section of the SDS
12.2	Persistence and degradability	
12.3	Bioaccumulative potential	
12.4	Mobility in soil	
12.5	Results of PBT and vPvB assessment	
12.6	Other adverse effects	
13.	DISPOSAL CONSIDERATIONS	Waste-related measures needed to ensure control of risk at the different life cycle stages of the substances (including mixtures or articles at the end of service life)
14.	TRANSPORT INFORMATION	
15.	REGULATORY INFORMATION	
16.	OTHER INFORMATION	

In the SDS the focus is on information related to the hazards posed by the substances. The ES contains additional information on exposure and exposure assessment to address risks. In addition, the ES contains guidance on scaling. Therefore, there is no direct correspondence between the following information from the ES and sections in the SDS at present:

- Section 1: Description of activities/process(es) covered in the ES
- Section 3: Prediction of exposure
- Section 4: Guidance to downstream users to evaluate whether he works inside the boundaries set by the ES

Note: If one or more exposure scenarios have been integrated into the main body of the safety data sheet, the following remark should be given in the SDS (Phrase available in EuPhraC: http://www.esdscom.eu/english/euphrac-phrases/):

"*This safety data sheet contains an ES in an integrated form. Contents of the exposure scenario have been included into Sections 1.2, 8, 9, 12, 15 and 16 of this safety data sheet."*

or

"*This safety data sheet contains more than one ES in an integrated form. Contents of the exposure scenarios have been included into Sections 1.2, 8, 9, 12, 15 and 16 of this safety data sheet."*

Annex III: Test examples applying the Lead Component Identification (LCID) methodology

The LCID methodology to derive safe use information for mixtures, based on exposure scenarios provided by suppliers of its components, was tested by using practical examples.

The templates included in this annex can be used to demonstrate how the LCID methodology can be applied in practice, as well as test one's understanding by making comparisons of one's results with the ones provided in these examples.

Blank templates for applying the human health and the environmental part of the LCID methodology workflow are provided as well as to test examples including the following mixture formulations:

Example No.	Description of Mixture Example Characteristics
1	Presence of a health hazard priority substance
2	Presence of components with DNELs
3.1 and 3.2	Application of grouping where a few of the components have similar toxic endpoints by similar modes of action
4	At least one relevant component having no DNEL so NO(A)EL values are considered in identifying lead components
5.1 and 5.1	At least one relevant component having no DNEL so LD_{50} values are considered in identifying lead components
6	Presence of an environmental priority substance
7	Presence of an ozone hazard
8	Presence of components missing PNECs so environmental classifications are used to identify lead components
9	Presence of components with PNECs and grouping is applied to derive a weighted concentration

Please note the colour coding of the tables:

Colour	Explanation
	These are headers and noteworthy explanations
	These are descriptions of data to be entered on the components of the mixtures, as available. This data is used to identify and perform calculations to determine the presence of priority substances, lead components, and components contributing to causing local effects or ozone depletion to derive safe use information for the mixture. Sources include exposure scenarios provided from suppliers as well as information from the user (e.g., formulation, use descriptors).
	Description of data that requires to be derived, applying calculations and logic from the LCID methodology
	Applicable results, including results of calculations leading to determination of priority substances, lead components, components whose toxicological endpoints are grouped, and components contributing to local effects.
	Applicable final modified OCs and RMMs for the Mixture

Annex III.1 – Human Health

Template-Description of Data Fields for Human Health Hazards

Description of data	**Data fields – Human Health**			***Comments***
CLP Health Hazard Classification of mixture	Listing of CLP Health Hazard Classification of mixture For example: Cancer 1A, STOT RE 1, Skin Sens. 1, Skin Corr. 1B, Eye Dam. 1			*CLP health hazard classification of mixture*
(Relevant) components	Component 1	Component 2	Component X_y	*List of relevant components-those components that contribute to the CLP health hazard classification of the mixture; can include other components (e.g., those with OELs, sensitising agents); if confidentiality is of concern then just generic identifiers may be used, e.g., Component A, Component B, etc.*
Relevant CAS No. (if available)	XXXX-XX-X	XXXX-XX-X	XXXX-XX-X	*XXXX-XX-X*
Concentration of component	X%	X%	X%	*X%*
Health Hazard CLP classification of relevant component	CLP classification of Component 1	CLP classification of Component 2	CLP classification of Component X_y	*CLP health hazard classification of Component*
	CLP classification of Component 1	CLP classification of Component 2	CLP classification of Component X_y	*CLP health hazard classification of Component*
	CLP classification of Component 1	CLP classification of Component 2	CLP classification of Component X_y	*CLP health hazard classification of Component*
	CLP classification of Component 1	CLP classification of Component 2	CLP classification of Component X_y	*CLP health hazard classification of Component*
	CLP classification of Component 1	CLP classification of Component 2	CLP classification of Component X_y	*CLP health hazard classification of Component*
Relevant local effects	Local effects from exposure to Component 1	Local effects from exposure to Component 2	Local effects from exposure to Component X_y	*Local effects (e.g., eye, skin, respiratory tract irritation/damage, corrosivity; skin and respiratory tract sensitisation) from exposure to Component;* *For example:* *Skin Sens. 1*
Health Hazard Priority Substance (yes/no)	Identification of a Priority Substance, if applicable	Identification of a Priority Substance, if applicable	Identification of a Priority Substance, if applicable	*Identify if Component is a Priority Substance (e.g., carcinogen or mutagen), above threshold levels (> 0.1%) present in formulation.*

Description of data	Data fields – Human Health			*Comments*
DNEL inhalation (mg/m³)	DNEL inhalation for Component1	DNEL inhalation for Component 2	DNEL inhalation for Component X_y	*Derived No Effect Level (DNEL), for the inhalation route, if applicable, provided by supplier of Component*
DNEL dermal (mg/kg bw day)	DNEL dermal for Component 1	DNEL dermal for Component 2	DNEL dermal for Component X_y	*DNEL, for the dermal route, if applicable, provided by supplier of Component*
DNEL oral (mg/kg bw day) (if applicable, e.g., consumer)	DNEL oral, if applicable, for Component 1	DNEL oral, if applicable, for Component 2	DNEL oral, if applicable, for Component X_y	*DNEL, for the oral route, if applicable, provided by supplier of Component*
Vapour Pressure at 25°C (hPa)	Vapour pressures (VP) of Component 1 if drives inhalation hazard classification	VP of Component 2 if drives inhalation hazard classification	VP of Component X_y if drives inhalation hazard classification	*Vapour pressures (VP) (in hPa) of the relevant components driving the inhalation hazard classifications (except sensitisation and irritation which are handled separately). If VP(s) for different components were derived at different temperatures, a correction to the same temperature (25°C) is recommended.*
LCI (DNEL) - inhalation	LCI (DNEL) - inh for Component 1	LCI (DNEL) - inhalation for Component 2	LCI (DNEL) - inh for Component X_y	*Calculation of the LCI based on DNEL is: "Concentration/DNEL inhalation (mg/m³)" for the inhalation route for the Component OR if there is the potential for exposure to vapours of this Component, the LCI is calculated as follows: "Concentration x Vapour Pressure/DNEL inhalation (mg/m³)"*
LCI (DNEL) - dermal	LCI (DNEL) - dermal for Component 1	LCI (DNEL) - dermal for Component 2	LCI (DNEL) - dermal for Component X_y	*Calculation of the LCI based on DNEL is: "Concentration"/"DNEL dermal (mg/kg bw day)" for the dermal route for the Component*
LCI (DNEL) - oral	LCI (DNEL) oral, if applicable, for Component 1	LCI (DNEL) oral, if applicable, for Component 2	LCI (DNEL) oral, if applicable, for Component X_y	*Calculation of the LCI based on DNEL is: "Concentration"/"DNEL dermal (mg/kg bw day)" for the oral route for the Component*
Grouping - by route of exposure	Yes or No, given exposure route	Yes or No, given exposure route	Yes or No, given exposure route	*Yes or No response If there are components having common endpoints via the same route of exposure and contribution to the CLP hazard classification of the mixture they should be grouped together to account for additive effects and thus, give more weight to this route of exposure and endpoint than would ordinarily be given if*

Description of data	Data fields – Human Health			*Comments*
				addressed individually.
LCI_{group} (DNEL), by route of exposure	LCI_{group} calculation, by exposure route	LCI_{group} calculation, by exposure route	LCI_{group} calculation, by exposure route	*Identify and group the components that have a similar endpoint and/or a common toxic effect for a given exposure route. Sum their LCIs to calculate LCI_{group}:* $LCI_{group} = \Sigma LCI_i$ *Where LCI_i: Lead Component Indicators*
$C_{weighted}$ of LC - by route of exposure (%)	$C_{weighted}$, by route of exposure (%)	$C_{weighted}$, by route of exposure (%)	$C_{weighted}$, by route of exposure (%)	*Calculation of $C_{weighted}$* $C_{weighted} = \Sigma (C_i \times DNEL_{LC} / DNEL_i)$ *Where: C_i: Concentration from the components of the LCI_{group} $DNEL_{LC}$: DNEL of the Lead Component $DNEL_i$: DNEL from the components of the LCI_{group}* *Note: In the case that a component needs to be included in the group, but no DNEL is available for this component use its unmodified concentration.*
Are there DNELs available for all the relevant components? (yes/no)	Yes/No, identify those missing DNELs			*The most reliable means of identifying Lead Component (the component with the highest LCI), for each relevant exposure route, is relying on the DNEL calculations. If there were no DNELs available for all relevant components, then alternative approaches e.g., LCCIs based on NO(A)ELs/NO(A)ECs and/or LD50/LC50/ATE values) should be conducted to ensure that a potentially more toxic component is not missed when generating the safe use information.*
NOAEC inhalation (mg/m^3)	NOAEC, inhalation for Component 1	NOAEC, inhalation for Component 2	NOAEC, inhalation for Component X_y	*No observed (adverse) effect concentration*
NOAEL dermal (mg/kg bw day)	NOAEL, dermal for Component 1	NOAEL, dermal for Component 2	NOAEL, dermal for Component X_y	*No-observed (adverse) effect level*
NOAEL (oral) (mg/kg bw day)	NOAEL, oral for Component 1	NOAEL, oral for Component 2	NOAEL, oral for Component X_y	*No-observed (adverse) effect level*
LCCI (NOAEC) - inhalation	LCCI, inhalation for Component 1	LCCI, inhalation for Component 2	LCCI, inhalation for Component X_y	*An LCCI is calculated per component and per route of exposure:* *$LCCI_\alpha$: C_i / NO(A)EL or*

Description of data	Data fields – Human Health			*Comments*
LCCI (NOAEL) - dermal	LCCI, dermal for Component 1	LCCI, dermal for Component 2	LCCI, dermal for Component X_y	*NO(A)EC* *Where:* *C_i: Concentration of the component i in the mixture* *NO(A)EL: No-observed (adverse) effect level* *NO(A)EC: No-observed (adverse) effect concentration*
LCCI (NOAEL) - oral	LCCI, oral for Component 1	LCCI, oral for Component 2	LCCI, oral for Component X_y	
LC50 (inhalation) (mg/m³)	LC50, inhalation for Component 1	LC50, inhalation for Component 2	LC50, inhalation for Component X_y	*Lethal concentration resulting in 50% mortality of the experimental animals*
LD50 (dermal) (mg/kg bw day)	LD50, dermal for Component 1	LD50, dermal for Component 2	LD50, dermal for Component X_y	*Lethal dose resulting in 50% mortality of the experimental animals*
LD50 (oral) (mg/kg bw day)	LD50, oral for Component 1	LD50, oral for Component 2	LD50, oral for Component X_y	*Lethal dose resulting in 50% mortality of the experimental animals*
LCCI (LC50) - inhalation	LCCI, inhalation for Component 1	LCCI, inhalation for Component 2	LCCI, inhalation for Component X_y	*A Lead Component Candidate Indicator (LCCI) is calculated per component and per route of exposure:* *$LCCI_\alpha$: C_i / LD_{50} or LC_{50} or ATE* *Where:* *Ci : Concentration of the component i in the mixture* *LD50: Lethal dose resulting in 50% mortality of the experimental animals* *LC50: Lethal concentration resulting in 50% mortality of the experimental animals* *ATE: Acute Toxicity Estimate*
LCCI (LD50) - dermal	LCCI, dermal for Component 1	LCCI, dermal for Component 2	LCCI, dermal for Component X_y	
LCCI (LD50) - oral	LCCI, oral for Component 1	LCCI, oral for Component 2	LCCI, oral for Component X_y	
Lead Component for relevant exposure routes	Lead Component for given route	Lead Component for given route	Lead Component for given route	*For each relevant exposure route, select the component with the highest LCI (based on DNELs) as the Lead Component (LC), check that no other component without an LCI value has a higher LCCI value (result from the backup approach) for possible consideration in deciding safe use.*
Exposure Scenario (ES)	Relevant Exposure Scenario (ES) Title Title of Exposure Scenario (ES). The rows above pertain to ALL the Contributing Scenarios under this ES. There are varying Operational Conditions (OCs) and Risk Management Measures (RMMs) for each of the Contributing Scenarios (CS) that must be derived.			*Relevant Exposure Scenario Title*
Contributing Scenario (CS)	Relevant Contributing Scenario (CS) Title			*Relevant Contributing Scenario Title (PROC)*

Description of data	**Data fields – Human Health**			***Comments***
Operational Conditions (OCs)	OCs relevant to the Contributing Scenario (CS) of Component 1	OCs relevant to the Contributing Scenario (CS) of Component 2	OCs relevant to the Contributing Scenario (CS) of Component X_y	*Operational Conditions (OCs) relevant to the Contributing Scenario (CS) of the Component* *For example:* *5 days per week; > 4h per day*
Risk Management Measures (RMMs)	RMMs relevant to the Contrib-uting Scenario (CS) of Compo-nent 1	RMMs relevant to the Contrib-uting Scenario (CS) of Compo-nent 2	RMMs relevant to the Contrib-uting Scenario (CS) of Compo-nent X_y	*Risk Management Measures (RMMs) relevant to the Contributing Scenario (CS) of the Component* *For example:* *LEV, resp. protection, safety goggles, suitable working clothes, gloves*
Modified OCs for the Mixture	OC - Safe use information for the Mixture For example: Indoor 5 days per week; > 4h per day			*Need to review the OCs for Priority Substance(s), or Lead Components, and local effect contributors for each exposure route to determine the most strin-gent ensuring they cover all other relevant components.*
Modified RMMs for the Mixture	RMM - Safe use information for the Mixture For example (see CS for specific information): Local exhaust ventilation (LEV), e.g. 90 %, respiratory protection, e.g. 95 %, suitable gloves according to EN 374 (e.g. with specific activity training), safety goggles, suitable working clothes			*Need to review the RMMs for Priority Substance(s), or Lead Components, and local effect contributors for each exposure route to determine the most strin-gent ensuring they cover all other relevant components.* ***Ensure that RMMs for local effects are covered.***

Test Example 1: Presence of a health hazard priority substance

Description of data	Data Test Example 1			Comments
CLP Health Hazard Classification of mixture	Carc. 1A (H350), STOT RE 1 (H372), Skin Sens. 1 (H317), Skin Corr. 1B (H314), Eye Dam. 1 (H318)			
Relevant components	Nickel monoxide	Barium oxide	Strontium oxide	
Relevant CAS No. (if available)	1313-99-1	1304-28-5	1314-11-0	
Concentration of relevant component	10	20	10	
Health Hazard CLP classification of relevant component	H350; Carc. 1A	H302; Acute. Tox. 4 (oral)	H314; Skin Corr. 1B	*Note: A carcinogen has been identified; Nickel monoxide is a Priority Substance; therefore there is no need to do any LCI calculations requiring DNELs or other reference values. Highlighted in RED in the columns under the respective component, are the classifications of the individual Component which contributes to the CLP hazard classification of the mixture. This includes those which contribute to local effects (e.g., irritation, corrosivity, sensitisation).*
	H273; STOT RE 1	H314; Skin Corr. 1A	H318; Eye Dam.1	
	H317; Skin Sens. 1	H318; Eye Dam. 1		
Relevant local effects	Skin Sens. 1	Skin Corr. 1A Eye Dam. 1	Skin Corr. 1B Eye Dam.1	*Listing of local effects for each Component.*
Health Hazard Priority Substance (yes/no)	Yes			*Indicate with a yes, if component has been identified as a Priority Substance (e.g., carcinogen, mutagen)*
DNEL inhalation (mg/m³)				*No need to gather data on DNEL as a priority substance has been identified.*
DNEL dermal (mg/kg bw day)				
DNEL oral (mg/kg bw day) (if applicable, e.g., consumer)				
Vapour Pressures at 25°C (hPa)				
LCI (DNEL) - inhalation				
LCI (DNEL) - dermal				
LCI (DNEL) - oral				
Grouping - by route of exposure				*Not needed as priority substance has been identified*
LCI_{group} (DNEL) - by route of exposure				
$C_{weighted}$ of LC - by route of exposure (%)				

Description of data	Data Test Example 1			*Comments*
Are there DNELs available for all the relevant components? (yes/no)	Not relevant	Not relevant	Not relevant	*Priority Substance is driving the hazard*
Backup-calculation: Not needed, because a priority substance has been identified. All corresponding lines have been omitted from this example to improve readability.				
Lead Component for relevant exposure routes				
Exposure Scenario	Distribution of substance			
Contributing Scenario	PROC 8b			
Operational Conditions (OCs)	**Indoor 5 days per week; > 4h per day**	**Indoor 5 days per week; > 4h per day**	**Indoor 5 days per week; > 4h per day**	
Risk Management Measures (RMMs)	**Local exhaust ventilation, respiratory protection, safety goggles, suitable work-ing clothes, gloves**	**Gloves, safety goggles**	**Gloves, safety goggles**	
Modified OCs for the Mixture	**Indoor 5 days per week; > 4h per day**			*The OCs for Nickel monox-ide were selected because it was identified as a Priority Substance e.g., carcinogen), which takes precedence over the other components. As a carcinogen, it is as-sumed that the OCs are the most stringent and should be protective of the hazards from the other components. The OCs for the other relevant components should be reviewed for confirmation.* *As it is so happens in this case, the other components also contribute to the hazard classification for the mixture (e.g., local effects), but in this case, they both have similar sets of OCs as compared to the Priority Substance so there is adequate coverage for all health hazards.*

Description of data	Data Test Example 1	Comments
Modified RMMs for the Mixture	**Provide local exhaust ventilation, wear respiratory protection, wear safety goggles, wear suitable working clothes, wear gloves**	*The RMMs for Nickel monoxide were selected because it was identified as a Priority Substance (e.g., carcinogen) which takes precedence over the other components. As a carcinogen, it is assumed that the RMMs are the most stringent and should be protective of the hazards from the other components. The RMMs for the other relevant components should be reviewed for confirmation. In reviewing the local effects from exposure to this mixture, it was identified that Nickel monoxide is a skin sensitiser and both Barium oxide and Strontium oxide are corrosive to the skin and cause eye damage. Therefore, RMMs should take into account protection to these hazards. In this case skin and eye protection RMMs for Nickel monoxide adequately protected for these hazards as well.*

Test Example 2: Presence of components with DNELs

Description of data	Data Test Example 2			Comments
CLP Health Hazard Classification of mixture	Flam. Liq. 2 (H225); Acute Tox. 3 (oral) (H301) + Acute Tox. 3 (dermal) (H311) + Acute Tox. 3 (inhalation) (H331); Eye irritation 2 (H319); STOT SE 3 (H336 (drowsiness/dizziness)); STOT SE1 (H370)			
Relevant components	Methanol	2-Propanol	Ammoniumacetate	
Relevant CAS Nos. (if available)	(CAS 67-56-1)	(CAS 67-63-0)	(CAS 631-61-8)	
Concentration of relevant component	40	55	5	
Health Hazard CLP classification of relevant component	H225; Flam. Liq. 2	H225; Flam. Liq. 2	not classified	
	H301; Acute Tox. 3 (oral)	H319; Eye Irrit. 2		*Only the classifications highlighted are relevant. The derivation of safe use information for physical hazard classifications (e.g., flammability, reactivity, aspiration hazards) are not addressed in the LCID methodology.*
	H311; Acute Tox. 3 (dermal)	H336; STOT SE 3 (drowsiness/ dizziness)		

Description of data	Data Test Example 2			*Comments*
	H331; Acute Tox. 3 (inhalation)			
	H370; STOT SE 1			
Relevant local effects	None	Eye Irrit. 2	None	*2-Propanol contributes to the local effects CLP hazard classification of the mixture.*
Health Hazard Priority Substance (yes/no)	No	No	No	
DNEL inh (mg/m³)	260	500		*The DNEL for Ammonium acetate is not relevant because it does not contribute to the hazard classification of the mixture.*
DNEL dermal (mg/kg bw day)	40	888		
DNEL oral (if applicable, e.g., consumer)	N/A	N/A		
Vapour Pressures at 25°C (hPa)	169,6	43		
LCI (DNEL) - inhalation	40*169.6 / 260 = 26.1	55*43 / 500 = 4.73		*LCI = Conc x VP / DNEL*
LCI (DNEL) - dermal	40 / 40 = 1.0	55 / 888 = 0.06		*LCI = Conc / DNEL*
LCI (DNEL) - oral	N/A	N/A		
Grouping - by route of exposure				*Not needed - no common hazard*
LCI_{group} (DNEL) - by route of exposure				
$C_{weighted}$ of LC - by route of exposure (%)				
Are there DNELs available for all the relevant components? (yes/no)	Yes	Yes		
Backup-calculation: Not needed, because DNELs are available for all relevant components. All corresponding lines have been omitted from this example to improve readability.				
Lead Component for relevant exposure routes	Lead Component for inhalation and dermal exposure routes			*Methanol is Lead Component - inhalation (26.1); Methanol is Lead Component - dermal (1.0)*
Exposure Scenario				
Contributing Scenario				
Operational Conditions (OCs)	**Indoor 5 days per week; > 4h per day**	**Indoor 5 days per week; > 4h per day**		
Risk Management Measures (RMMs)	**Local exhaust ventilation**	No local exhaust ventilation		
	Gloves tested to EN 374	**Safety googles**		

Description of data	Data Test Example 2	*Comments*
Modified OCs for the Mixture	**Indoor 5 days per week; > 4h per day**	*From Methanol as Lead Component - inhalation*
Modified RMMs for the Mixture	**Provide local exhaust ventilation, wear gloves tested to EN 374, wear safety googles**	*From Methanol as Lead Component - inhalation and 2-Propanol for local effects (Eye Irrit. 2. Note RMM from 2-Propanol for drowsiness or dizziness is covered by OCs from Methanol. Together, RMMs for the components cover also the local effects of the mixture.*

Test Example 3.1 and 3.2: Application of grouping where a few of the components have similar toxic endpoints by similar modes of action

Description of data	Data Test Example 3.1			*Comments*
Classification	Acute Tox. 3 (inhalation) (H331) + Skin Irrit. 2 (H315) + Eye Dam. 1 (H318)			
Relevant components	Component 1	Component 2	Component 3	
Relevant CAS No. (if available)				
Concentration of relevant component	50	30	20	
Health Hazard CLP classification of relevant component	H 331; Acute Tox. 3 (inhalation)	H332; Acute Tox. 4 (inhalation)	H319; Eye Irrit. 2	
	H 318; Eye Dam. 1	H315; Skin Irrit. 2	H312; Acute Tox. 4 (dermal)	
Priority Substance (yes/no)	No	No	No	
DNEL inhalation (mg/m³)	2	10		
DNEL dermal (mg/kg bw day)	N/A	N/A		
DNEL oral (mg/kg bw day) (if applicable, e.g., consumer)	N/A	N/A	N/A	
Vapour Pressures at 25°C (hPa)	N/A	N/A	N/A	

Description of data	Data Test Example 3.1			*Comments*
LCI (DNEL) - inhalation	50 / 2 = 25.0	30 / 10 = 3.0		*LCI = Conc / DNEL* *Both Components 1 and 2 meet the additivity criteria via inhalation and contribution to the CLP hazard classification of the mixture (inhalation); thus, these should be grouped together to account for additive effects and thus, give more weight to this route of exposure and endpoint than would ordinarily be given if addressed individually. Also this information is used to identify a modified concentration ($C_{weighted}$) to determine appropriate OCs and RMMs for the mixture based on threshold cutoffs, for example for selected Personal Protective Equipment (PPEs).* *For example there may be a variance in duration or ventilation requirement dependent of concentration in a mixture (cut-off at < 25% concentration).*
LCI (DNEL) - dermal	N/A	N/A		
LCI (DNEL) - oral	N/A	N/A	N/A	
Grouping - inhalation	Yes, inhalation	Yes, inhalation		*Both Components 1 and 2 have common endpoints via inhalation and contribution to the CLP hazard classification of the mixture (inhalation)*
LCI_{group} (DNEL) - inhalation	28,0			$LCI_{group} = \Sigma\ LCI_i$ *25 + 3 = 28*
$C_{weighted}$ of LC - inhalation (%)	56,0			$C_{weighted} = \Sigma\ C_i \times DNEL_{LC} / DNEL_i$ *(50 x 2 / 2) + (30 x 2 / 10) = 56*
Are there DNELs available for all the relevant components? (yes/no)	Yes	Yes		
Backup-calculation: Not needed, because DNELs are available for all relevant components. All corresponding lines have been omitted from this example to improve readability.				
Lead Component for relevant exposure routes	Lead Component by inhalation route			*Component 1 has the largest LCI*
Relevant local effects	Eye Dam. 1	Skin Irrit. 2	Eye Irrit. 2	*Components 1, 2, and 3 contribute to the local effects CLP hazard classification of the mixture.*
Exposure Scenario				
Contributing Scenario				
Operational Conditions (OCs)	**> 4h; up to 100%**	**> 4h; up to 100%**	**> 4h; up to 100%**	
Risk Management Measures (RMMs)	**Provide local exhaust ventilation (LEV) 90% + Wear**	Provide local exhaust ventilation (LEV)		

Description of data	Data Test Example 3.1			Comments
	Respiratory protection equipment			
	Wear eye glasses	**Safety googles**	**Wear eye glasses**	
	Gloves tested to EN 374	**Wear chemical resistant gloves**	**Wear suitable gloves tested to EN374.**	
Modified OCs for the Mixture	**5 days per week; > 4h per day**			*From Component 1 which is the Lead Component by inhalation.*
Modified RMMs for the Mixture	**Provide local exhaust ventilation (LEV) 90%, wear respiratory protection equipment, wear eye glasses, wear chemical resistant gloves**			*From Component 1 which is the Lead Component by inhalation, and all three Components which contribute to the local effects hazard classification of the mixture. The RMMs cover all local effects of the mixture.*

Description of data	Data Test Example 3.2			Comments
CLP Health Hazard Classification of mixture	Acute Tox.. 3 (H331 (inhalation) + H311 (dermal) + H301 (oral)); STOT SE 3 (H336 – drowsiness/ dizziness); STOT SE 2 (H371 (oral, dermal, inhalation)); STOT RE 2 (H373 (inhalation)); Skin Corr. 1B (H314); Repr. 2 (H361d)			
Relevant components	Component 1	Component 2	Component 3	
Relevant CAS Nos. (if available)				
Concentration of relevant component	5	30	65	
Health Hazard CLP classification of relevant component	H225; Flam. Liq. 2	H225; Flam. Liq. 2	H301; Acute Tox. 3 (oral)	
	H301; Acute Tox. 3 (oral)	H361d; Repr. 2	H311; Acute Tox. 3 (dermal)	
	H311; Acute Tox. 3 (dermal)	H304; Asp. Tox.. 1;	H331; Acute Tox. 3 (inhalation)	
	H331; Acute Tox. 3 (inhalation)	H373; STOT RE 2 (inhalation)	H373; STOT RE 2 (oral, dermal, inhalation)	
	H370; STOT SE 1	H315; Skin Irrit. 2	H314; Skin Corr. 1B	
		H336; STOT SE 3		
Relevant local effects	None	H315; Skin Irrit. 2	H314; Skin Corr. 1B	*Components 2 and 3 contribute to local effects*
Priority Substance (yes/no)	No	No	No	
DNEL inhalation (mg/m³)	260	192	8	
DNEL dermal (mg/kg bw day)	40	384	1,23	
DNEL oral (mg/kg bw day) (if applicable, e.g., consumer)	N/A	N/A	N/A	
Vapour Pressures at	169,6	37,86	0,47	

Description of data	Data Test Example 3.2			*Comments*
25°C (hPa)				
LCI (DNEL) - inhalation with VP	3,26	5,92	3,82	*Components 1 and 3 meet the additivity criteria via inhalation and contribution to the CLP hazard classification of the mixture (inhalation):* *LCIgroup = Σ LCIi* *Acute toxicity for the inhalation route, categories 1, 2, 3 and 4 (H330, H331, H332)* *Component 3 is designated as Lead Component, because it has the highest LCI of the group (Components 1 &3) and because the LCI of the group (see below) is higher than the one or Component 2.*
no VP	0,02	0,16	8,13	
LCI (DNEL) - dermal	0,13	0,1	52,8	
LCI (DNEL) - oral	N/A	N/A	N/A	
Grouping - inhalation	Yes, inhalation	No, inhalation	Yes, inhalation	
LCI Grouping (DNEL) inhalation	7,1			*LCIgroup = Σ LCI_i* *3.26 + 3.82 = 7.08*
$C_{weighted}$ of LC - inhalation (%)	65,2			*$C_{weighted}$ = Σ C_i x $DNEL_{LC}$ / $DNEL_i$* *(5 x 8 / 260) + (65 x 8 / 8) = 65.2*
Grouping - dermal	Yes, dermal	No, dermal	Yes, dermal	*Components 1 and 3 meet the additivity criteria via dermal route of exposure and contribution to the CLP hazard classification of the mixture (dermal):* *LCIgroup = Σ LCI_i* *Acute toxicity for the dermal route, categories 1, 2, 3 and 4 (H310, H311, H312)*
LCI Grouping (DNEL) dermal	53,0			*LCIgroup = Σ LCI_i* *0.13+52.8 = 52.9*
$C_{weighted}$ of LC - dermal (%)	65,2			*$C_{weighted}$ = Σ (C_i x $DNEL_{LC}$ / $DNEL_i$* *(5 x 1.23 / 40) + (65 x 1.23 / 1.23) = 65.2*
Lead Component for relevant exposure routes			Lead Component by inhalation and dermal route	*Acute toxicity for the inhalation route, categories 1, 2, 3 and 4 (H330, H331, H332),*
Exposure Scenario	Distribution			
Contributing Scenario	Proc 8a			
Operational Conditions (OCs)	**5 days per week; > 4h per day**	**5 days per week; 8h per day**	**5 days per week; ≤8 h per day**	

Description of data	Data Test Example 3.2			*Comments*
Risk Management Measures (RMMs)	**Provide local exhaust ventilation (LEV) 90%**	**Provide a good standard of general ventilation (not less than 3 to 5 air changes per hour) or wear a respirator conforming to EN140 with type A filter or better**	**Provide local exhaust ventilation (LEV) 90%**	
		Wear gloves (TypeEN374)	**Wear suitable gloves tested to EN374.**	
Modified OCs for the Mixture	**5 days per week; ≤8 h per day**			*From Component 3 which is the Lead Component by inhalation and dermal route*
Modified RMMs for the Mixture	**Provide local exhaust ventilation (LEV) 90%, wear gloves (TypeEN374)**			*From Component 3 which is the Lead Component. Additionally, RMMs for local effects of component 2 were considered, but inhalation RMMs were not added to the mixture, because they are less strict than those of the Lead Component.*

Test Example 4: At least one relevant component having no DNEL so NO(A)EL values are considered in identifying lead components

Description of data	Data Test Example 4			*Comments*
CLP Health Hazard Classification of mixture	Flam. Liq. 2 (H225); Actue Tox. 4 (oral) (H302); Eye Dam. 1 (H318); Acute Tox. 3 (inhalation) (H331); STOT SE 3 (drowsiness/dizziness) (H336); STOT RE 2 (H373)			
(Relevant) components	Component 1	Component 2	Component 3	
Relevant CAS No. (if available)				
Concentration of component	70	20	10	
Health Hazard CLP classification of relevant component	H302, Acute Tox. 4 (oral)	H225; Flam. Liquid 2	H225; Flam. Liquid 2	*Only the classifications highlighted are relevant. The derivation of safe use information for physical hazard classifications (e.g., flammability, reactivity, aspiration hazards) are not addressed in the LCID methodology.*
	H373; STOT RE 2	H318; Eye Damage 1	H336; STOT SE 3 (drowsiness/ dizziness)	
		H336; STOT SE 3 (drowsiness/dizziness)	H332; Acute Tox. 4 (inhalation)	

Description of data	Data Test Example 4			*Comments*
		H331; Acute Tox. 3 (inhalation)		
Relevant local effects		H318; Eye Dam. 1		*Component 2 contributes to the local effects CLP hazard classification of the mixture.*
Health Hazard Priority Substance (yes/no)	No	No	No	
DNEL inhalation (mg/m³)	60	Not available	Not available	
DNEL dermal (mg/kg bw day)	106	Not available	Not available	
DNEL oral (mg/kg bw day) (if applicable, e.g., consumer)	Not available	Not available	Not available	
Vapour Pressure at 25°C (hPa)				*For this example, the vapour pressure is not relevant due to low VPs of all components and thus no likely exposure to vapour.*
LCI (DNEL) - inhalation	70 / 60 = 1.17	Not available	Not available	*LCI = Conc / DNEL*
LCI (DNEL) - dermal	70 / 106 = 0.66	Not available	Not available	*LCI = Conc / DNEL*
LCI (DNEL) - oral	Not available	Not available	Not available	
Grouping - by route of exposure				
LCI_{group} (DNEL), by route of exposure				
$C_{weighted}$ of LC - by route of exposure (%)				
Are there DNELs available for all the relevant components? (yes/no)	No, only for component 1			*Missing DNELs for Components 2 and 3.*
NOAEC inhalation (mg/m³)	5000	3000	10800	
NOAEL dermal (mg/kg bw day)	250	150	500	
NOAEL (oral) (mg/kg bw day)	Not available	Not available	Not available	
LCCI (NOAEC) - inhalation	70 / 5000 = .014	20 / 3000 = .0067	10 / 10800 = .0009	*LCCIα = Conc / NO(A)EL or NO(A)EC*
LCCI (NOAEL) - dermal	70 / 250 = .28	20 / 150 = .13	10 / 500 = .02	*LCCIα = Conc / NO(A)EL or NO(A)EC*
LCCI (NOAEL) - oral	Not available	Not available	Not available	
LC50 (inhalation) (mg/m³)	Not available	Not available	Not available	
LD50 (dermal) (mg/kg bw day)	Not available	Not available	Not available	
LD50 (oral) (mg/kg bw day)	Not available	Not available	Not available	
LCCI (LC50) - inhalation				
LCCI (LD50) - dermal				

Description of data	Data Test Example 4			Comments
LCCI (LD50) - oral				
Lead Component for relevant exposure routes	Lead Component for inhalation and dermal routes of exposure	Eye Damage		*Component 1 also has the highest LCCI value.*
Exposure Scenario (ES)				
Contributing Scenario (CS)				
Operational Conditions (OCs)	**Indoor 5 days per week; > 4h per day**	Not available	Not available	
Risk Management Measures (RMMs)	**Local exhaust ventilation Gloves tested to EN 374**	Not available	Not available	
Modified OCs for the Mixture	**5 days per week; > 4h per day**			*From Component 1 which is the Lead Component by inhalation.*
Modified RMMs for the Mixture	**Provide local exhaust ventilation, wear gloves tested to EN 374, wear tightly fitting safety goggles**			*From Component 1 which is the Lead Component by inhalation, and Components 2 which contributes to the local effects hazard classification of the mixture. Safety goggles were included based on the mixture classification*

Test Example 5.1 and 5.2: At least one relevant component having no DNEL so LD_{50} values are considered in identifying lead components

Description of data	Data Test Example 5.1			Comments
CLP Health Hazard Classification of mixture	Acute Tox.. 4 (oral, dermal, inhalation) (H302/H312/H332), STOT RE 1 (H372), STOT SE 3 (H336; drowsiness/dizziness) (H336), Eye irrit. 2 (H319)			
(Relevant) components	Component 1	Component 2	Component 3	
Relevant CAS No. (if available)				
Concentration of component	70	20	10	
Health Hazard CLP classification of relevant component	H336; STOT SE 3 (drowsiness/ dizziness)	H301; Acute Tox. 3 (oral)	H312; Acute Tox. 4 (dermal)	
	H319; Eye Irrit. 2	H311; Acute Tox.. 3 (dermal)	H336; STOT SE 3 (drowsiness/ dizziness)	
		H331; Acute Tox.. 3 (inhalation	H335; STOT SE 3 (irrit.)	
		H372; STOT RE 1	H319; Eye Irrit. 2	

Description of data	Data Test Example 5.1			Comments
Relevant local effects	Eye Irrit. 2		Eye Irrit. 2 STOT SE 3 (irrit.)	*Components 1 and 3 contribute to the local effects CLP hazard classification of the mixture.*
Health Hazard Priority Substance (yes/no)	No	No	No	
DNEL inh (mg/m³)	305	50	Not available	
DNEL dermal (mg/kg bw day)	44	40	Not available	
DNEL oral (mg/kg bw day) (if applicable, e.g., consumer)	Not available	Not available	Not available	
Vapour Pressure at 25°C (hPa)				*For this example, the vapour pressure is not relevant due to low VPs of all components and thus no likely exposure to vapour.*
LCI (DNEL) - inhalation	70 / 305 = 0.23	20 / 50 = 0.4	Not available	*LCI = Conc / DNEL*
LCI (DNEL) - dermal	70 / 44 = 1.6	20 / 40 = 0.5	Not available	*LCI = Conc / DNEL*
LCI (DNEL) - oral	Not available	Not available	Not available	
Grouping - by route of exposure				
LCI_{group} (DNEL), by route of exposure				
$C_{weighted}$ of LC - by route of exposure (%)				
Are there DNELs available for all the relevant components? (yes/no)	No, only for components 1 and 2			*Component 3 does not have a DNEL available, but does have both an LD_{50} dermal value as well as LC_{50} inhalation*
NOAEC inhalation (mg/m³)	Not available	Not available	Not available	
NOAEL dermal (mg/kg bw day)	Not available	Not available	Not available	
NOAEL (oral) (mg/kg bw day)	Not available	Not available	Not available	
LCCI (NOAEC) - inh				
LCCI (NOAEL) - dermal				
LCCI (NOAEL) - oral				
LC50 (inhalation) (mg/m³)	20	3	3	
LD50 (dermal) (mg/kg bw day)	2000	300	1100	
LD50 (oral) (mg/kg bw day)	Not available	Not available	Not available	
LCCI (LC50) - inhalation	70 / 20 = 3,5	20 / 3 = 6.67	10/3 = 3.33	*$LCCI\alpha$ = Conc / LC_{50}*
LCCI (LD50) - dermal	70 / 2000 = 0,035	20 / 300 = 0.067	10 / 1100 = 0.009	*$LCCI\alpha$ = Conc / LD_{50}*
LCCI (LD50) - oral	Not available	Not available	Not available	

Description of data	Data Test Example 5.1			Comments
Lead Component for relevant exposure routes	Lead Component dermal	Lead Component inhalation		*Component 2 is the Lead Component via the inhalation and Component 1 via the dermal exposure route, assuming that Component 3 does not cause systemic effects after repeated exposure that were not covered by the acute classification or which are not more severe than those of component 1+2. Regardless of the result of the backup (LC/LD_{50}) approach, the DNEL based comparison is considered more reliable and the LC is always determined based on that calculation.*
Exposure Scenario (ES)				
Contributing Scenario (CS)				
Operational Conditions (OCs)	**Indoor 5 days per week; > 4h per day**	**Indoor 5 days per week; > 4h per day**		
Risk Management Measures (RMMs)	**Local exhaust ventilation Wear safety glasses**	**Local exhaust ventilation (90%) Wear respiratory protection equipment Gloves tested to EN 374**		
Modified OCs for the Mixture	**Indoors 5 days per week; > 4h per day**			*From Component 1 and 2 which are the Lead Components by inhalation and dermal route of exposure.*
Modified RMMs for the Mixture	**Provide local exhaust ventilation (LEV) 90%, wear respiratory protection equipment, wear safety glasses**			*From Component 1and 2 which are the Lead Components by inhalation and dermal exposures routes, and Components 1 and 3 which contribute to the local effects hazard classification of the mixture.*

Test Example 5.2

Description of data	Data Test Example 5.2			Comments
CLP Health Hazard Classification of mixture	Acute Tox. 4 (oral, dermal, inhalation) (H302/H312/H332), STOT RE 1 (H372), STOT SE 3 (drowsiness/dizziness) (H336), Eye Irrit. 2 (H319)			
(Relevant) components	Component 1	Component 2	Component 3	
Relevant CAS No. (if available)				
Concentration of component	20	40	40	

Description of data	Data Test Example 5.2			*Comments*
Health Hazard CLP classification of relevant component	H336; STOT SE 3 (drowsiness/ dizziness)	H301; Acute Tox.. 3 (oral)	H310; Acute Tox.. 2 (dermal)	
	H319; Eye Irrit. 2	H311; Acute Tox. 3 (dermal)	H331; Acute Tox. 3 (inhalation)	
		H331; Acute Tox. 3 (inhalation)	H335; STOT SE 3 (irrit.)	
		H372; STOT RE 1	H319; Eye Irrit. 2	
Relevant local effects	Eye Irrit. 2		Eye Irrit. 2 STOT SE 3 (irrit.)	*Components 1 and 3 contribute to the local effects CLP hazard classification of the mixture.*
Health Hazard Priority Substance (yes/no)	No	No	No	
DNEL inhalation (mg/m³)	260	260	Not available	
DNEL dermal (mg/kg bw day)	80	40	Not available	
DNEL oral (mg/kg bw day) (if applicable, e.g., consumer)	Not available	Not available	Not available	
Vapour Pressure at 25°C (hPa)				*For this example, the vapour pressure is not relevant due to low VPs of all components and thus no likely exposure to vapour.*
LCI (DNEL) - inhalation	20 / 260 = 0.08	40 / 260 = 0.15	Not available	*LCI = Conc / DNEL*
LCI (DNEL) - dermal	20 / 80 = 0.25	40 / 40 = 1.0	Not available	*LCI = Conc / DNEL DNELs not available for Component 3; only LC50 and LD50 values available*
LCI (DNEL) - oral	Not available	Not available	Not available	
Grouping - by route of exposure				
LCI_{group} (DNEL), by route of exposure				
$C_{weighted}$ of LC - by route of exposure (%)				
Are there DNELs available for all the relevant components? (yes/no)	No, only for components 1 and 2			*Component 3 does not have a DNEL available, but does have both an LD50 dermal value as well as LC50 inhalation*
NOAEC inhalation (mg/m³)	Not available	Not available	Not available	
NOAEL dermal (mg/kg bw day)	Not available	Not available	Not available	
NOAEL (oral) (mg/kg bw day)	Not available	Not available	Not available	
LCCI (NOAEC) - inhalation				
LCCI (NOAEL) - dermal				
LCCI (NOAEL) - oral				
LC50 (inhalation) (mg/m³)	3	3	5	
LD50 (dermal) (mg/kg bw day)	600	300	50	

Description of data	**Data Test Example 5.2**			***Comments***
LD50 (oral) (mg/kg bw day)	Not available	Not available	Not available	
LCCI (LC50) - inhalation	20/3 = 6.67	40 / 3 = 13.3	40 / 5 = 8.0	*LCCIα = Conc in mixture / LC_{50}*
LCCI (LD50) - dermal	20/600 = 0.03	40 / 300 = 0.13	40 / 50 = 0.8	*LCCIα = Conc in mixture / LD_{50}*
LCCI (LD50) - oral	Not available	Not available	Not available	
Lead Component for relevant exposure routes		**Lead Component, inhalation**	**Lead Component Candidate, dermal**	***No DNELs are available for Component 3. Based on LCCIs, Component 2 is the Lead Component via inhalation and Component 3 for dermal exposure route. Once a DNEL is derived, there is a chance that the dermal LCI might also be higher for Component 2. A long-term DNEL is believed to be also protective for acute effects.***
Exposure Scenario (ES)				
Contributing Scenario (CS)				
Operational Conditions (OCs)	Indoor 5 days per week; > 4h per day	Indoor 5 days per week; > 4h per day	Indoor 5 days per week; > 4h per day	
Risk Management Measures (RMMs)	Local exhaust ventilation Wear safety glasses	Local exhaust ventilation Gloves tested to EN 374	Local exhaust ventilation Wear gloves tested to EN 374 Wear safety glasses	
Modified OCs for the Mixture				
Modified RMMs for the Mixture				***Case by case evaluation required. No dermal LC determined***

Annex III.2 – Environment

Template-Description of Data Fields for Environmental Hazards

Description of data	**Data fields – Environment**			***Comments***
CLP Environmental Hazard Classification of mixture				*CLP environmental classification of mixture*
(Relevant) components	Component 1	Component 2	Component X_y	*List of relevant components, those components that contribute to the CLP environmental hazard classification of the mixture; if confidentiality is of concern then just generic identifiers may be used, e.g., Component A, Component B, etc.*
Relevant CAS No. (if available)	XXXX-XX-X	XXXX-XX-X	XXXX-XX-X	*XXXX-XX-X*
Concentration of relevant component	X%	X%	X%	*X%*
Environmental CLP classification of relevant component	CLP classification of Component 1	CLP classification of Component 1	CLP classification of Component 1	*CLP environmental classification of Component*
PBTs? vPvBs?	Identify if PBT or vPvB	Identify if PBT or vPvB	Identify if PBT or vPvB	*Identify if Component is a Priority Substance e.g., Persistent, Bioaccumulative, Toxic substance (PBT), very Persistent, very Bioaccumulative (vPvB) substance above threshold level (≥ 0.1%) present in formulation.*
Hazardous to the Ozone Layer category 1 (yes/no)	Yes/No	Yes/No	Yes/No	*Identify any relevant components that are hazardous to the ozone layer, as identified by the components CLP classification.*
LCI (Ozone) - env	LCI (ozone) for Component 1	LCI (ozone) for Component 2	LCI (ozone) for Component X_y	*Calculate the LCI for each of the contributing ozone hazard components:* *LCI = Concentration in mixture*
Lead Component for Ozone Hazard	Lead Component for Ozone Hazard	Lead Component for Ozone Hazard	Lead Component for Ozone Hazard	*The highest LCI is the Lead Component driving the ozone hazard classification.*
Lowest $PNEC_{Compartment}$ available	$PNEC_{compartment}$ for Component 1	$PNEC_{compartment}$ for Component 1	$PNEC_{compartment}$ for Component 1	*Identify lowest PNEC for each component regardless of compartment (e.g., air, water, soil)*

Description of data	Data fields – Environment			*Comments*
Convert PNEC units to mg/L	PNEC $_{compartment}$ for Component 1	PNEC $_{compartment}$ for Component 1	PNEC $_{compartment}$ for Component 1	*Convert to like units (mg/L)* *Use the following equations to convert units of mg/kg of dry weight (mg/kg dw) for soil and sediment compartments into mg/L:* *$PNEC_{soil}$ mg/kg dw x 1.5 = $PNEC_{soil}$ mg/L* *and* *$PNEC_{sediment}$ mg/kg dw x 0.25 =$PNEC_{sediment}$ mg/L*
Biodegradeable status	Readily biodegradable or not	Readily biodegradable or not	Readily biodegradable or not	*Identify if Component is readily biodegradeable or not.* *Yes is if component is "Readily biodegradeable" and "No" if substance is "No biodegradation observed", "Readily biodegradeable but failing 10 day window", " Ïnherently biodegradeable".*
LCI (PNEC) - env	LCI (PNEC) - env for Component 1	LCI (PNEC) - env for Component 2	LCI (PNEC) - env for Component X_y	*Calculate the LCI for each relevant component.* *If a component is readily biodegradable then:* *LCI = C / PNEC x 3* *Otherwise apply this equation:* *LCI = C / lowest PNEC* *Where:* *C = Concentration of component in the mixture* *PNEC = Predicted No-Effect Concentration*

Description of data	Data fields – Environment			*Comments*
LCI (classification) - env	LCI (classification) - env for Component 1	LCI (classification) - env for Component 2	LCI (classification) - env for Component X_y	*Calculate the LCI taking into account CLP-classification, concentration and M-factors:* *For Aquatic Acute 1:* *LCI = Conc in mixture x M_{acute} x 33* *For Aquatic Chronic 1:* *LCI = Conc in mixture x $M_{chronic}$ x 100* *For Aquatic Chronic 2:* *LCI = Conc in mixture x 10* *For Aquatic Chronic 3:* *LCI = Conc in mixture* *For Aquatic Chronic 4:* *LCI = Conc in mixture* *Contributions from both acute and chronic aquatic hazard classifications should be taken into account to identify the Lead Component (LC).* *Thus, for components classified as both acute AND chronic hazards:* *LCI_{total} = LCI_{acute} + $LCI_{chronic}$*
M-factors, if relevant	M_{factor} for Component 1	M_{factor} for Component 2	M_{factor} for Component X_y	Identify if any relevant components have associated M-factors. M-factors take into account any high individual toxicity of a component. This is a multiplying factor (M-factor) that gives increased weight to substances classified as hazardous to the environment.
Lead Component for env	Lead Component for environment	Lead Component for environment	Lead Component for environment	*Select the relevant component with the highest LCI as the Lead Component.* *The component with the highest LCI is deemed to have the highest impact on the potential environmental hazard of the mixture.* *It is judged that providing information on the safe use of this component will ensure safe use of the entire product mixture.*
Is there more than one relevant component classified as an environmental hazard? (yes/no)	Yes/No	Yes/No	Yes/No	*Identify with a yes or no if the Component contributes to the environmental hazard classification of the mixture.*

Description of data	Data fields – Environment			*Comments*
Modifying factor (if there is more than one relevant component)	Calculated Modifying factor if there is more than one component contributing to the environmental hazard classification of the mixture.			*Modifying factor (MF) is calculated using information for all contributing relevant components. It is calculated using the following equation: $MF = \Sigma LCI / LCI_{max}$ where the ΣLCI is the sum of the LCIs for all contributing components and LCI_{max} is the LCI of the Lead Component.*
$C_{weighted}$ - env (%)	$C_{weighted}$, env (%)			*Using the MF, the actual concentration of the Lead Component in the mixture is converted into a "$C_{weighted}$" concentration: A hypothetical concentration that accounts for the additive effects.* *$C_{weighted} = C_{LC} \times MF$* *Where:* *$C_{LC}$ = Concentration of the Lead Component* *MF = Modifying factor calculated above* *Note: Ensure you convert the CLC value from % to its decimal value (e.g., 9.4% to 0.094).*
M_{safe} (per component) (kg/day)	M_{safe} for Component 1	M_{safe} for Component 2	M_{safe} for Component X_y	*Identify the M_{safe} value for the relevant components which drive the environmental hazard classification of the mixture. This can be typically found in the supplier (e)SDS or from the substance's CSR.*
M_{safe} for product (kg/day)	M_{safe} for product			*The M_{safe} value for the product can be calculated using the M_{safe} value of the Lead Component and the modified concentration (e.g., $C_{weighted}$ value) as follows:* *M_{safe} product = M_{safe} LC / $C_{weighted}$* *Where:* *M_{safe} LC = M_{safe} of Lead Component* *$C_{weighted}$ =See above calculation* *Use of $C_{weighted}$ takes into account potential additive effects.*
Exposure Scenario (ES)	Relevant Exposure Scenario (ES) Title. The rows above pertain to ALL the Contributing Scenarios under this ES. There are varying Operational Conditions (OCs) and Risk Management Measures (RMMs) for each of the Contributing Scenarios (CS) that must be derived.			*Relevant Exposure Scenario Title*
Contributing Scenario (CS)	Relevant Contributing Scenario (CS) Title			*Relevant Contributing Scenario Title (PROC)*

Description of data	Data fields – Environment			*Comments*
Operational Conditions (OCs) for Ozone Hazard	OCs relevant to Ozone Hazard classification of Component 1	OCs relevant to Ozone Hazard classification of Component 2	OCs relevant to Ozone Hazard classification of Component Xy	*Risk Management Measures (OCs) relevant to a Component being an Ozone Hazard.*
Risk Management Measures (RMMs) for Ozone Hazard	RMMs relevant to Ozone Hazard classification of Component 1	RMMs relevant to Ozone Hazard classification of Component 2	RMMs relevant to Ozone Hazard classification of Component Xy	*Risk Management Measures (RMMs) relevant to a Component being an Ozone Hazard.*
Operational Conditions (OCs) - env	OCs relevant to the Contributing Scenario (CS) of Component 1	OCs relevant to the Contributing Scenario (CS) of Component 2	OCs relevant to the Contributing Scenario (CS) of Component X_y	*Operational Conditions (OCs) relevant to the Contributing Scenario (CS) of the Component, including protection of local effects.*
Risk Management Measures (RMMs) - env	RMMs relevant to the Contributing Scenario (CS) of Component 1	RMMs relevant to the Contributing Scenario (CS) of Component 2	RMMs relevant to the Contributing Scenario (CS) of Component X_y	*Risk Management Measures (RMMs) relevant to the Contributing Scenario (CS) of the Component, including protection of local effects.*
M_{safe} for product (kg/day)	**M_{safe} value for product**			*For a mixture having a single component contributing to environmental hazard classification of the mixture:* *M_{safe} for product = M_{safe} of Component/Conc* *For mixture having several components contributing to the environmental hazard classification of the mixture:* *M_{safe} for product = M_{safe} of highest $LCI/C_{weighted}$*
OCs for the Mixture	**OC - Safe use information for the Mixture** **For example:** **Amounts used - Maximum daily site tonnage (kg/d): 400000** **Frequency of use: Continuous release.** **Duration of use (Emission Days/year): 300** **Environmental factors not influenced by risk management: Local freshwater dilution factor: 10.** **Local marine water dilution factor: 100.** **Other Operational Conditions of use affecting environmental exposure: Manufacturing is made in a closed process. Release fraction to air: 1.00E-03. Release fraction to wastewater: 3.00E-03. Release fraction to soil (regional only): 1.00E-04.**			*Need to review the OCs for Priority Substance(s), Lead Components or ozone hazards to determine the most stringent ensuring they cover all other relevant components.*

Description of data	Data fields – Environment	*Comments*
RMMs for the Mixture	**RMM - Safe use information for the Mixture** **For example:** **Prevent discharge of undissolved substance to waste water or recover from wastewater.** **A leak prevention plan is needed to prevent low level continual releases Bund storage facilities to prevent soil and water pollution in the event of spillage. Site should have a spill plan to ensure that adequate safeguards are in place to minimize the impact of episodic releases.** **Conditions and measures related to municipal sewage treatment plant: Estimated substance removal from wastewater via domestic sewage treatment (%): 87.3. Total efficiency of removal from wastewater after onsite and offsite (domestic treatment plant) RMMs (%): 87.3.** **Conditions and measures related to external treatment of waste for disposal: External treatment and disposal of waste should comply with applicable local and/or national regulations.**	*Need to review the RMMs for Priority Substance(s), Lead Components or Ozone Hazards to determine the most stringent ensuring they cover all other relevant components.*

Test Example 6: Presence of an environmental priority substance

Description of data	Data Test Example 6			*Comments*
CLP Environmental Hazard Classification of mixture	Aquatic Acute 1 (H400), Aquatic Chronic 1 (H410)			*Not really necessary since presence of a PBT is identified.*
(Relevant) components	Component 1	Component 2	Component 3	
Relevant CAS No. (if available)				
Concentration of relevant component	30	2,5	20	
Environmental CLP classification of relevant component	Not relevant as Priority substance is identified	Aquatic Acute 1 Aquatic Chronic 1 additionally: definitive PBT substance	Not relevant as Priority substance is identified	
PBTs? vPvBs?	No	Yes	No	*Component 2 is a Priority Substance (PBT substance)*
Hazardous to the Ozone Layer category 1 (yes/no)	No	No	No	
LCI (Ozone) - env				
Lead Component for Ozone Hazard				
Lowest $PNEC_{Compartment}$ available				
Convert PNEC units to mg/L				
Biodegradeable status				
LCI (PNEC) - env				
LCI (classification) - env				
M-factors, if relevant				

Description of data	Data Test Example 6			Comments
Lead Component for env		Lead Component for environment		
Is there more than one relevant component classified as an environmental hazard? (yes/no)				
Modifying factor (if there is more than one relevant component)				
$C_{weighted}$ - env (%)				
M_{safe} (per component) (kg/day)				
M_{safe} for product (kg/day)	M_{safe} for product			
Exposure Scenario (ES)	Relevant Exposure Scenario (ES) Title			
Contributing Scenario (CS)	Relevant Contributing Scenario (CS) Title			
Operational Conditions (OCs) for Ozone Hazard				
Risk Management Measures (RMMs) for Ozone Hazard				
Operational Conditions (OCs) - env		**OC1, OC2 for Component 2**		*OCs for Component 2 - PBT*
Risk Management Measures (RMMs) - env		**RM1 for Component 2**		*RMMs for Component 2 - PBT*
M_{safe} for product (kg/day)	**Not applicable**			*No M_{safe} as there is no M_{safe} for a PBT substance; "rule of minimization" for releases applies - also for the mixture*
Modified OCs for the Mixture	**Operational Condition 1 of component 2 (OC1) and operational Condition 2 of component 2 (OC2)**			*OCs for Component 2 - PBT*
Modified RMMs for the Mixture	**Risk Management Measure 1 of component 2 (RM1)**			*RMMs for Component 2 - PBT*

Test Example 7: Presence of an ozone hazard

Description of data	Data Test Example 7			Comments
CLP Environmental Hazard Classification of mixture	**Ozone 1 (H420)**			
Relevant components	Component 1	Component 2	Component X_y	
Relevant CAS No. (if available)	XXXX-XX-X	XXXX-XX-X	XXXX-XX-X	
Concentration of relevant component	20%	X%	10%	
Environmental CLP classification of relevant component	Ozone 1		Ozone 1	
PBTs? vPvBs?	No	No	No	

Description of data	**Data Test Example 7**			***Comments***
Hazardous to the Ozone Layer category 1 (yes/no)	yes	no	yes	
LCI (Ozone) - env	20 (Concentration)	Not applicable	10 (Concentration)	*LCI for ozone hazards = Concentration* *Components 1 and 3 are ozone hazards (Ozone 1)*
Lead Component for Ozone Hazard	Lead Component for Ozone Hazard			*Component 1 has the highest LCI (20 vs. 10) and is, therefore, the Lead Component for ozone hazards*
Lowest $PNEC_{Compartment}$ available	Not available	Not available	Not available	
Convert PNEC units to mg/L				
Biodegradeable status				
LCI (PNEC) - env				
LCI (classification) - env				
M-factors, if relevant				
Lead Component for env				
Is there more than one relevant component classified as an environmental hazard? (yes/no)				
Modifying factor (if there is more than one relevant component)				
$C_{weighted}$ - env (%)				
M_{safe} (per component) (kg/day)				
M_{safe} for product (kg/day)				
Exposure Scenario (ES)	Relevant Exposure Scenario (ES) Title Title of Exposure Scenario (ES). *The rows above pertain to ALL the Contributing Scenarios under this ES. There are varying Operational Conditions (OCs) and Risk Management Measures (RMMs) for each of the Contributing Scenarios (CS) that must be derived.*			
Contributing Scenario (CS)	Relevant Contributing Scenario (CS) Title			
Operational Conditions (OCs) for Ozone Hazard	**OCs relevant to Ozone Hazard classification**			
Risk Management Measures (RMMs) for Ozone Hazard	**RMMs relevant to Ozone Hazard classification**			
Operational Conditions (OCs) - env	**OCs relevant to Ozone Hazard classification**			*OCs Component 1 - Lead Component for ozone hazard*
Risk Management Measures (RMMs) - env	**RMMs relevant to Ozone Hazard classification**			*RMMs Component 1 - Lead Component for ozone hazard*

Description of data	Data Test Example 7	*Comments*
M_{safe} for product (kg/day)	**Not applicable**	*No M_{safe} as there is no M_{safe} for a PBT substance; "rule of minimization" for releases applies - also for the mixture*
Modified OCs for the Mixture	**Operational Conditions relevant to ozone hazard classification of Component 1**	*OCs for Component 1 - ozone hazard*
Modified RMMs for the Mixture	**Risk Management Measures relevant to ozone hazard classification of Component 1**	*RMMs for Component 1 - ozone hazard*

Teat Example 8: Presence of components missing PNECs. So environmental classifications are used to identify lead components

Description of data	Data Test Example 8			*Comments*
CLP Environmental Hazard Classification of mixture	Aquatic Acute 1 (H400), Aquatic Chronic 1 (H410)			
Relevant components	Cyclohexane	n-Hexane	Naphtha, hydrotreated light	
Relevant CAS No. (if available)	110-82-7	92112-69-1	8030-30-6	
Concentration of relevant component	30	2,5	20	
Environmental CLP classification of relevant component	Aquatic Acute 1 Aquatic Chronic 1	Aquatic Chronic 2 (H411)	Aquatic Chronic 2 (H411)	
PBTs? vPvBs?	No	No	No	
Hazardous to the Ozone Layer category 1 (yes/no)	No	No	No	
LCI (Ozone) – env.				
Lead Component for Ozone Hazard				
Lowest $PNEC_{Compartment}$ available	Not available	Not available	Not available	
Convert PNEC units to mg/L				
Biodegradeable status				
LCI (PNEC) - env				
LCI (classification) - env	(30 x 1 x 33) + (30 x 1 x 100)= 990+3000= **3990**	(2.5 x 10) = 25	(20 x 10) = 200	*Aquatic Acute 1: LCI = Conc in mixture x M_{acute} x 33* *Aquatic Chronic 1: LCI = Conc in mixture x $M_{chronic}$ x 100* *Aquatic Chronic 2: LCI = Conc in mixture x 10* *Components classified as both acute AND chronic hazards: $LCI_{total} = LCI_{acute} + LCI_{chronic}$*
M-factors, if relevant	M_{acute} = 1; $M_{chronic}$ = 1			

Description of data	Data Test Example 8			Comments
Lead Component for env	Lead Component for env			*Cyclohexane is the Lead Component with the highest LCI (3990)*
Is there more than one relevant component classified as an environmental hazard? (yes/no)	Yes	Yes	Yes	
Modifying factor (if there is more than one relevant component)	(3990+25+200) / 3990 = 4215 / 3990 = 1.06			$MF = \sum LCI / LCI_{max}$
$C_{weighted}$ - env (%)	30x 1.056 = 31.68%			$C_{weighted}$ = conc LC x MF
M_{safe} (per component) (kg/day)	1250	2800	33000	
M_{safe} for product (kg/day)	1250/0.3168 = 3945.7 kg/d			M_{safe} prod = M_{safe} LC / $C_{weighted}$
Exposure Scenario (ES)				
Contributing Scenario (CS)				
Operational Conditions (OCs) for Ozone Hazard				
Risk Management Measures (RMMs) for Ozone Hazard				
Operational Conditions (OCs) - env	**OC1, OC 2**			OCs for Component 1
Risk Management Measures (RMMs) - env	**RM1, RM2, RM3**			RMMs for Component 1
M_{safe} for product (kg/day)	**3945.7 kg/d**			
Modified OCs for the Mixture	**Operational Condition 1 of Component 1 (OC1), Operational Condition 2 of Component 1 (OC 2)**			OCs for Component 1 - Lead Component
Modified RMMs for the Mixture	**Risk Management Measure 1 of Component 1 (RM1), Risk Management Measure 2 of Component 2 (RM2), Risk Management Measure 3 of Component 3 (RM3)**			RMMs for Component 1 - Lead Component

Test Example 9: Presence of components with PNECs and grouping is applied to derive a weighted concentration

Description of data	Data Test Example 9			Comments
CLP Environmental Hazard Classification of mixture	Aquatic Acute 1 (H400), Aquatic Chronic 1 (H410)			
Relevant components	Component 1	Component 2	Component 3	

Description of data	**Data Test Example 9**			***Comments***
Relevant CAS No. (if available)				
Concentration of relevant component	30	2,5	20	*These components were selected from the formulation as those contributing to the environmental hazard classification for the mixture.*
Environmental CLP classification of relevant component	Not relevant for PNEC approach	Not relevant for PNEC approach	Not relevant for PNEC approach	
PBTs? vPvBs?	No	No	No	
Hazardous to the Ozone Layer category 1 (yes/no)	No	No	No	
LCI (Ozone) - env				
Lead Component for Ozone Hazard				
Lowest $PNEC_{Compartment}$ available	$PNEC_{freshwater}$ = 0.0112 mg/L	$PNEC_{soil}$ = 0.03 mg/kg	$PNEC_{sediment}$ = 0.004 mg/kg	*Identify lowest PNEC for each component regardless of compartment (e.g., air, water, soil)*
Convert PNEC units to mg/L	0.0112 mg/L	0.03 x 1.5 = 0.45 mg/L	0.004 / 4 = 0.001 mg/L	*Convert to like units (mg/L)* *Use the following equations to convert units of mg/kg of dry weight (mg/kg dw) for soil and sediment compartments into mg/L:* *$PNEC_{soil}$ mg/kg dw x 1.5 = $PNEC_{soil}$ mg/L* *and* *$PNEC_{sediment}$ mg/kg dw x 0.25 =$PNEC_{sediment}$ mg/L*
Biodegradeable status	Readily biodegradable	Not readily biodegradable	Not readily biodegradable	
LCI (PNEC) - env	30/(0.0112 x 3) = 893.9	2.5/0.45 = 5.5	20/0.001 = **2000**	*If a component is readily biodegradable (as for Component 1), apply this equation to calculate LCI:* *LCI = Conc / (PNEC x 3)* *Otherwise apply this equation (for Components 2 & 3):* *LCI = Conc in mixture / lowest PNEC*
LCI (classification) - env				
M-factors, if relevant				
Lead Component for env			Lead Component	*Component 3 has the highest LCI (2000) and therefore is the Lead Component (LC) for the environment.*

Description of data	**Data Test Example 9**			***Comments***
Is there more than one relevant component classified as an environmental hazard? (yes/no)	Yes	Yes	Yes	*Components 1, 2 and 3 are all CLP- classified as Environmental Hazards.*
Modifying factor (if there is more than one relevant component)	MF = (893.9 + 5.5 + 2000) / 2000 = 2898 / 2000 = 1.45			*Modifying factor (MF) is calculated using information for all contributing relevant components.*
$C_{weighted}$ - env (%)			20 x 1.45 = 29 %	*Since there is more than one component contributing to the hazard classification need to calculate Cweighted (%):* $C_{weighted}$ *= Conc LC x MF*
M_{safe} (per component) (kg/day)	1250 kg/d	2800 kg/d	33000 kg/d	*Identify the* M_{safe} *value for the relevant component which drives the environmental hazard classification of the mixture.* *This can be typically found in the supplier (e)SDS or from the substance's CSR.* *If there is no information on the* M_{safe} *of the Lead Component available, the daily site tonnage assumed for the Lead Component may be used as a surrogate.*
M_{safe} for product (kg/day)	33000 / 0.29 = 113793 kg/d			M_{safe} *product =* M_{safe} *LC /* $C_{weighted}$
Exposure Scenario (ES)				
Contributing Scenario (CS)				
Operational Conditions (OCs) for Ozone Hazard				
Risk Management Measures (RMMs) for Ozone Hazard				
Operational Conditions (OCs) - env			**OC1, OC 2, OC 3 for Component 3**	*OCs 1-3 for Component 3*
Risk Management Measures (RMMs) - env			**RM1, RM2 for Component 3**	*RMMs 1-2 for Component 3*
M_{safe} for product (kg/day)	**113793 kg/d**			
OCs for the Mixture	**Operational Condition 1 of Component 3 (OC1), Operational Condition 2 of Component 3 (OC 2), Operational Condition 3 of Component 3 (OC 3)**			*OCs for Component 3 - Lead Component*
RMMs for the Mixture	**Risk Management Measure 1 of Component 3 (RM1), Risk Management Measure 2 of Component 3 (RM2)**			*RMMs for Component 3 - Lead Component*

Annex IV: LCID methodology – Underlying principles and rationales

Human Health – Underlying principles of and rationale for the steps for generating safe use information regarding human health hazards for chemical mixtures

Step	Task	Justification
1	Compile REACH-relevant product data	Analysis begins by gathering all available and relevant information on both human health and environmental data for all individual components of the mixture as well as on the mixture itself. This information forms the basis for identifying what hazards are associated with the components, their potential contribution to the hazards of the mixture, and the potential health and environmental risks for which Operating Conditions (OCs) and Risk Management Measures (RMMs) would constitute safe use for the mixture under various exposure and contributing scenarios.
2	Is the mixture classified as hazardous to human health?	Non-classified mixtures are considered non-hazardous as it applies to human health and the environment and, therefore, any use of the mixture is considered safe. This is in alignment with REACH, where no exposure assessment or risk management measures have to be defined for non-classified substances. The same logic is used for mixtures. For classification criteria, refer to the CLP hazard classification of the mixture. The EU regulation on classification, labelling and packaging ("CLP Regulation") uses internationally agreed classification criteria and labelling elements to contribute towards global efforts to protect humans and the environment from hazardous effects of chemicals.
3	Document	Documentation of this assessment should be readily available both internally and to enforcement authorities, if required.
H1	Is the mixture classified as a hazard to human health?	The Lead Components are derived separately for human health (HH) and the environment. Following the reasoning behind Step 2, all uses of the mixture are considered safe for HH, if it is not classified as hazardous for HH. In this case, the assessment would only be performed for the environmental hazard(s).
4	Document Go to ENV hazard assessment, E1	Documentation of this assessment should be readily available both internally and to enforcement authorities, if required.
H2	Is interaction between the chemicals expected?	Interactions between different components of the mixture are not covered by the LCID method and require a

		case-by-case assessment. Interaction is described as the combined effect of two or more chemicals as either stronger (synergistic, potentiating, supra-additive) or weaker (antagonistic, inhibitive, sub-additive, infra-additive) than would be expected on the basis of dose/concentration addition or response addition. Interactions may vary according to the relative dose levels, the route(s), timing and duration of exposure (including the biological persistence of the mixture components), and the biological target(s) (Directorate-General for Health & Consumers, 2012).
H3	Safe use information must be derived on a case-by-case basis	Case-by-case evaluation is required, if the LCID methodology is not applicable for a mixture. This can either be due to interactions of the components of the mixture or in most cases because no DNEL, that is also no exposure assessment, is available for a potential Lead Component. See Step H14 on more details when this is the case.
H4	Is there human health toxicity information available on the mixture as a whole?	An assessment may also be based on data generated on the mixture itself or a mixture of reasonably similar composition or a "surrogate mixture," e.g., a mixture close in composition (components and proportions) to the mixture under evaluation (Directorate-General for Health & Consumers, 2012). Whole-mixture approaches have the advantage of accounting for any unidentified materials in the mixture and for any interactions among mixture components (Boobis AR, 2011)[43]. They have been used for poorly characterised but stable mixtures, for effluent toxicity assessments and for specially designed mixtures. But care must be taken that the available data is sufficient to evaluate repeated dose effects of the mixture and that the dose, duration, observation or analysis do not render the results inconclusive. Also, this approach may not be applied if the mixture contains components classified as carcinogenic, mutagenic or toxic to reproduction.
H4a	Consider creating OCs and RMMs based on mixture as a whole	Available information on the mixture may be sufficient to derive safe use information for the mixture.
H5	Are any of the components identified as a Priority Substance and is its concentration in the mixture above CLP cut-off limits?	Carcinogens and mutagens present at relevant concentrations are of particular significance for human health assessments. If present in a mixture, these substances are major drivers to consider in health risk assessments and are often decisive for further action. Carcinogens and mutagens are generally assumed to have non-threshold effects. Contact to substances classified as carcinogens and/or mutagens should thus be minimized as much as possible. As a consequence,

[43] Boobis AR, 2011: Boobis AR, Budinsky R, Collie S, Crofton K, Embry M, Felter S, Hertzberg R, Kopp D, Critical analysis of literature on low-dose synergy for use in screening chemical mixtures for risk assessment, Crit Rev Toxicol, 41, 369-383.

		these types of components are considered Priority Substances. For all other systemic hazards, including reproductive toxicity, a DNEL can be derived. Also, it may be the case that the RMMs for a substance causing reproductive toxicity are for exposure to high levels only, thus the RMMs could be less stringent than those for another hazard-driving component, e.g., acutely toxic components of the mixture. It is therefore important to compare all components for which a no-effect level can be derived in order to find the most hazardous and to apply the necessary RMMs. In the rare case that a DNEL is available for a carcinogenic or mutagenic substance, it may not be considered a Priority Substance.
H5a	Identify OCs and RMMs for Priority Substances	The aim of OCs/RMMs for carcinogenic and/or mutagenic substances is to minimize exposure as much as possible. Most likely, the same measures as recommended for these types of substances will have to be applied to a mixture containing these substances.
H6	Identify relevant components which contribute to the hazard of the mixture	If the mixture would be non-classified, all uses would be considered safe. In agreement with this logic, all components, which do not lead to or contribute to the classification of the mixture, will not be considered for the identification of the Lead Component. Thus, they are not considered relevant in the scope of this method. Also, all components that only contribute to a classification for local effects (e.g., skin irritation/corrosion, eye irritation/ damage, skin sensitisation, respiratory sensitisation, dryness and cracking of the skin) should not be considered as relevant components for the Lead Component calculation. These effects are covered in additional steps (H16 and H17) to ensure that the conditions of use based on the Lead Components also protect against all local effects. This is necessary because the identification of the Lead Component(s) is based on reference values derived for systemic toxicity, which most likely do not cover local effects. Reference values for local effects are usually not available. In conclusion, relevant components in the context of the LCID methodology are those that contribute to at least one hazard classification of the mixture other than a classification for local effects.
H6a	Is the mixture only classified for local effects (e.g., eye/skin/resp. irritation, corrosivity, skin/inhalation sensitisation?	If the mixture is only classified for local effects, then one does not need to identify Lead Components for systemic effects. All calculations for LCIs can be skipped and safe use information can be derived based on the components that drive the local effects classification.
H7	Are there reference values available for each of the relevant components which drive a hazard classification for the mixture?	LCID aims to identify the component(s) that is/are mostly responsible for the hazardous properties of the mixture. Reference values, e.g., DNELs, NOAEL/Cs, LD_{50} or LC_{50}s are used for the comparison of the components. DNELs are used for the derivation of the Lead Component, whereas other data can be used to derive a Lead Component Candidate Indicator (LCCI)

		in the backup approach. Calculation according to LCID is possible as long as at least one of the above mentioned values is available for all relevant components (for a definition please see Step H6) for all relevant routes of exposure, e.g., those routes for which exposure is expected for either workers or consumers. If the classification does not apply to one route of exposure, this route must in most cases still be considered relevant. If for example a component is classified for acute inhalation toxicity, but not for acute dermal toxicity, this might well be because only an inhalation study exists, but not a study via the dermal route. As long as a DNEL was derived for a route of exposure, a hazard via this route should be assumed, and the DNEL value should be used to calculate an LCI.
H8	Is there potential for exposure to vapours, either at room temperature or generated at processing temperatures?	This step is designed to address the concerns for the potential for exposure to vapours under conditions of use including being evolved at elevated processing temperatures. If there is a possible exposure to vapours, then consider taking into account the effect of vapour pressure(s) (VP) on the exposure potential when calculating a component's Lead Component Indicator (LCI) value. Use information on the mixture may help make this determination. Review of OCs and RMMs in the applicable Exposure Scenarios (ESs) of the associated (e)SDSs can also assist in the decision of whether vapour exposure is of concern. If unsure if exposure to vapours is of concern, for example due to lack of information, compare the outcome of both considering and not considering an effect due to VP (see Steps H8a and H9 for details). Remark: The assumption for solid mixtures is that the mixture is homogeneous and there is no difference due to dustiness influencing the LCI calculation.
H8a	Compile vapour pressures (VPs) for relevant components driving inhalation hazard. Calculate their $LCI_{inhalation}$	Exposure to substances through inhalation of vapours is highly driven by the volatility of substances. This means that when identifying the Lead Component, the differences in volatility between substances in the mixture should be taken into account. This is done through applying a factor (C_{fug}) which represents the potential effect of volatility via exposure through inhalation of vapours. By applying this additional factor one will minimize the possibility of a non-volatile substance (one for which it is anticipated that there would be no exposure through inhalation) would be identified as the Lead Component. In other words, using this factor would give greater weight to components for which exposure to vapours is more likely. However it is acknowledged that using the VP as such may lead to the fact that the identification of the Lead Component is strongly driven by its VP. Thus, components with high VPs have a much greater advantage of being identified as Lead Components, irrespective of the reference values used in the equation. This is particularly true when the range of VPs between components in the mixture is extremely wide.

		The default value for C_{fug} is the VP (hPa) at 25°C. Different approaches to adjust the weighting of the VP, relative to the other parameters in the equation, are currently being explored (e.g., based on TRA fugacity) to better represent the effect of the volatility on exposure potential.
H9	Calculate LCI for all exposure routes. Refer to $LCI_{inhalation}$ from Step H8a, if applicable	The determination of the Lead Component (LC) for each route of exposure is based on the long term systemic DNEL values for workers (inhalation and dermal) or consumers (oral). These values were selected because the long term systemic DNELs are the most common type of DNEL to be derived, and therefore, there is likely data available for as many of the components as possible. Also, in deriving a long term DNEL there is less uncertainty and therefore, less non-substance specific variation, as compared to, for example, a short term DNEL. Local effects are covered separately and thus this calculation focuses on systemic effects. Worker DNELs were selected whenever possible because they are more common and, since there is usually a constant factor between worker and consumer DNELs, this choice does not affect the result of the calculation.[44] DNEL values can be directly compared between components. Differences for example in exposure duration and absorption have already been accounted for during the derivation, which makes them not only the best value to use for the exposure assessment, but also for a comparison of the toxicological potency of different substances. For this reason the LC is always selected by the DNEL-based LCI values: $$\mathrm{LCI}_{\alpha} = \frac{\mathrm{C_i}}{\mathrm{DNEL}}$$ This calculation is performed for all relevant components only (see Step H6 for a definition and justification). It is assumed that the provided data are correct and complete. So, if a DNEL is missing for one route of exposure or only local DNELs are available, a valid reason for this omission is presumed. Since exposure or systemic effects via this route were not considered relevant for the substance, they are also presumed not relevant for the mixture. In conclusion, a component will not become the Lead Component for a route of exposure where no long term systemic DNEL has been provided

[44] Consumer DNELs are only used for the calculation of the oral lead component, since no worker DNELs are available for this route of exposure. For all other routes, the worker DNELs are used, because:
- they are more often available,
- worker and consumer DNELs usually differ by a constant factor,
- the DNEL is only used to identify the Lead Component, the absolute value of the LCI is irrelevant.
- Since the hazard is the same for worker and consumer, the same LC should be derived, and two separate calculations (one with worker and one with consumer DNELs) are not necessary.

		and no LCI_{α} is calculated. NOAELs or NOAECs and LD_{50} or LC_{50} values are only used if no DNEL at all is available for at least one relevant component, and only as a backup check to ensure that no potentially more toxic component is missed during the DNEL-based comparison.
H10	For substances having DNELs with a common route of exposure for which additivity principles can be applied, group LCIs.	Substances, when present simultaneously in a mixture, may act in combination and cause potential adverse effects resulting in an additive response. There is a major knowledge gap on exposure information to mixtures, their modes of action and their potencies. There is a consensus among the scientific community that a dose/concentration addition methodology should be applied as the default approach to evaluate the health risks of chemical mixtures (Directorate-General for Health & Consumers, 2012). A common toxic effect may refer to identical target organs, identical cell types affected, identical pathology or identical biological/biochemical responses. However most of these effects are unknown or not made available for all the relevant components of a mixture. Therefore the hazard classification identified according to the CLP regulation seems to be the best accessible information source to identify similar endpoints between relevant components contributing to the hazard(s) of a mixture. For the following hazard classes additivity concepts are applicable (ECHA, Guidance on the Application of the CLP Criteria, Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, 2013): - Acute toxicity for the inhalation route, categories 1, 2, 3 and 4 (H330, H331, H332), - Acute toxicity for the dermal route, categories 1, 2, 3 and 4 (H310, H311, H312) - Acute toxicity for the oral route, categories 1, 2, 3 and 4 (H300, H301, H302) - STOT SE 3 for dermal route of exposure and inhalation (narcotic effects) (H336) Grouping may be considered if there are components in the mixture of similar structure, similar toxicological effects via similar modes of action (e.g., certain phthalates). Local effects, e.g., eye, skin and respiratory tract irritation/corrosivity and skin/respiratory sensitisation are considered separately (see Step H16). Note: This subject will be assessed as new information becomes available.
H11	For each relevant exposure route, select the component with the highest LCI as Lead Component (LC); adjust concentration accordingly ($C_{weighted}$)	The ultimate goal of the LCID method is to provide safe use information for the mixture. The required RMMs for a component are more severe the lower the DNEL and the higher the concentration of this component. Consequently, when using the RMMs from the component having the highest quotient of concentration and DNEL (LCI), these RMMs should be sufficient

		to also protect against all other components of the mixture (excluding local effects, which are treated separately). This approach is similar to that of DPD+ (Cefic/DUCC, 2009)[45]**.** Thus the component with the highest LCI is considered the Lead Component. In the special case that components were grouped in Step H10 based on a common toxic effect, the LCI of the group is used when selecting the highest value instead of the LCIs of the individual components. If the highest LCI is an $LCI_{group,}$ the component with the highest LCI within that group is defined as the LC, but for the subsequent selection of RMMs (see Step H15) the concentration of this component has to be adjusted to reflect additive effects of the other members of the group. The contribution of each group member depends on its LCI relative to the LCI of the Lead Component. All comparisons are done separately per route of exposure so that a Lead Component (LC) is defined for **all** relevant routes.
H12	Are DNELs available for all relevant components?	As stated in Steps H9 and H11, the LC is the component with the highest LCI based on the calculation using the DNELs. If this calculation could be performed for all relevant components and all relevant routes of exposure, e.g., all required DNELs were available, no further calculations have to be performed. If this calculation could only be done for some of the relevant components, **there is a chance** that one of the remaining components is more relevant to the selection of the safe use conditions for the mixture (e.g., it is more toxic and present at a sufficiently high concentration) than the currently selected LC based on DNELs. For these cases a back-up approach was implemented deriving LCCIs to compare the components of the mixture based on their NOAEL or NOAEC or LD_{50} or LC_{50} values. Caution must be taken, however, when using the results from the backup calculations because effects that would be covered by the DNEL might not be addressed by NOAEL or NOAEC or LD_{50} or LC_{50} values. These might be effects on reproduction or systemic toxicity not observed after single exposure. This is also part of the reason why the backup calculations are not used to derive the LC (the LC is always based on the DNEL), but rather is done as a check if a DNEL was not available for a component that may be more responsible for the toxicity of the mixture than the LC based on a DNEL.
H13	Are there NO(A)EL or NO(A)EC values available?	Since NO(A)EL or NO(A)EC values are derived in repeated dose studies, which means longer exposure times and more detailed examinations compared to

[45] Cefic/DUCC, June 2009, REACH: Exposure scenarios for preparations – Methodology for the identification of substances that represent the dominant risks to human health and the environment and the drivers for risk management measures

		acute toxicity studies, they are the preferred option for the backup calculations deriving LCCIs. But in order for this approach to work, these values must be available for all relevant components, especially those for which no DNELs were available. Otherwise the same components missing from the DNEL-based comparisons would also be missed using this calculation. To ensure comparisons are equivalent, one must use NO(A)EL or NO(A)EC values from comparable experimental studies. This means that they are derived based on studies using the same species with exposures via the same route and same duration (e.g., 28-days repeated exposure study on rats via the oral route).
H13a	Calculate LCCI for each component for each exposure route. Ensure NO(A)EL/NO(A)EC values are for the same species via the same exposure route and same duration of exposure	The same logic is used as for the DNEL-based calculation, assuming that a component has more influence on the toxic effects of the mixture the higher its concentration and the lower its NOAEL or NOAEC.
H13b	Calculate LCCIα based on LD_{50}/LC_{50}/ATE values	The same logic is used as for the DNEL-based calculation, assuming that a component has more influence on the toxic effects of the mixture the higher its concentration and the lower its LD_{50} or LC_{50} or ATE. As is the case when using NOAEL or NOAEC values, an LD_{50} or LC_{50} or ATE should be available for all relevant components. But if a component is not classified for acute toxicity for one or more routes of exposure, its acute toxicity does not drive the toxicity of the mixture and it can be omitted from the calculation. Thus, for these routes of exposure no LD_{50} or LC_{50} or ATE values are required for non-classified components.
H14	Is there any DNEL available for the component with the highest LCI per exposure route?	The most reliable means of identifying the Lead Component, for each relevant exposure route, is based on the DNEL calculations. The alternative approaches (e.g., NO(A)ELs or NO(A)ECs and/or LD_{50} or LC_{50} or ATE values) should only be referenced to ensure that a potentially more toxic component is not missed when generating the safe use information. If there is a DNEL available for the component with the highest LCCI in the NOAEL or NOAEC or LD_{50} or LC_{50} calculation, it was already considered during the DNEL-based identification of the Lead Component, though it will not necessarily be the Lead Component for this route of exposure. For reasons stated in Step H9, any type of DNEL will be sufficient. If for a component with the highest LCCI in the NOAEL or NOAEC or LD_{50} or LC_{50} calculation no DNEL is available, this component should not be ignored when deriving the safe use information for the mixture. It might well become the “real” LC once the DNELs are derived. But simply using this component as the new LC does not work because firstly, it is not entirely certain that it will become the “true” LC and secondly, if no DNELs have been derived there will be no exposure scenarios from which safe use information can be copied. Therefore the safe use information can only be

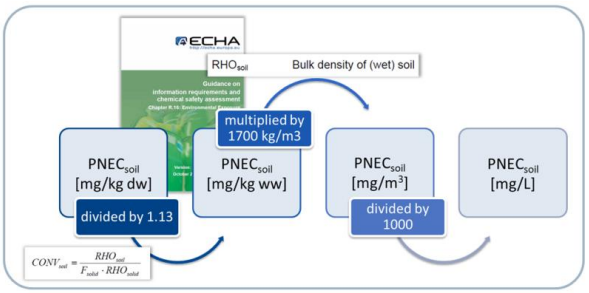
		derived case-by-case. Also be aware that the alternative approaches using NO(A)ELs or NO(A)ECs and/or LD_{50} or LC_{50} or ATE values might miss toxic endpoints which would lead to a low DNEL, if it was derived (e.g., reproductive toxicity).
H15	Compile OCs and RMMs for each exposure route based on the Lead Component(s) (LCs) per relevant Contributing Activity (PROC)	The required RMMs for a component are more severe the lower the DNEL and the higher the concentration of this component. Consequently, when using the RMMs from the Lead Component, these RMMs should be sufficient to also protect against all other components of the mixture (excluding local effects, see next steps). In the special case that additive effects are expected, these are accounted for by adjusting the concentration of the LC for which safe use has to be ascertained. When different scenarios are combined to fit into Sections 7/8 of the SDS or whenever there are different safe use conditions from two LCs for different routes of exposure, the worst case is selected to ensure safe use of the mixture under all circumstances.
H16	Consider local effects for each exposure route (e.g., eye/skin/respiratory tract irritation, corrosivity, skin/respiratory sensitisation) based on the Lead Components (LC)	Local effects are usually assessed qualitatively, which means that no DNELs are derived. They are also not covered by the long term systemic DNELs used in the LCI calculation. Thus, they are considered separately to ensure sufficient protection.
H17	If needed, compile OCs and RMMs based on local effects (e.g., eyes, skin, respiratory tract effects	RMMs for local effects can most easily be selected based on the use of the mixture and the components that contribute to these effects.
H18	Identify OCs and RMMs per Exposure Scenario and Contributing Activity to derive safe use information for mixture	All relevant OCs and RMMs of the Priority Substance(s) or Lead Component(s) and/or local effects hazards, for each exposure route, are considered in deriving safe use information for the mixture (e)SDS. Consider applying the strictest of the OCs and RMMs, unless professional judgment dictates otherwise.
H19	Provide safe use information either embedded within SDS or as an annex to SDS	Derivation and communication of safe use information is the purpose of the LCID methodology. It is up to the author of the SDS to decide how this is passed on along the supply chain.

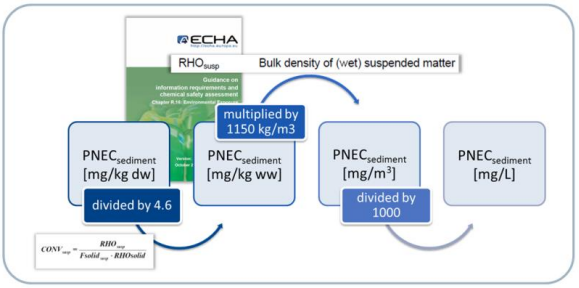
ENV – Underlying principles of and rationale for the steps for generating safe use information regarding environmental hazards for chemical mixtures

Step	Task	Justification
E1	Is the mixture classified as hazardous to the environment (ENV)?	Non-classified mixtures are considered non-hazardous to the environment, therefore any use of the mixture is considered safe for the environment.
E2	Document	Documentation of this decision should be readily available internally and accessible to enforcement authorities, if required.
E3	Is there ENV toxicity information available on the mixture as a whole?	If information on the mixture as such is available, the application of LCID may not be required.
E3a	Consider creating OCs and RMMs based on the mixture as a whole	Available information on the mixture may be sufficient to derive safe use information for the mixture.
E4	Are any of the components of the mixture a Priority Substance (e.g., PBT, vPvB) present at 0.1% or more?	PBT and/or vPvB substances at relevant concentrations are of particular significance for environmental assessments (REACH Article 14.1). If present in a mixture, these substances drive the environmental risk and are decisive for further action.
E4a	Identify OCs and RMMs for Priority Substances	The aim of OCs/RMMs for PBT and/or vPvB substances is to exclude any release resulting from the use of those substances or to reduce emissions as far as possible. Most likely, the same measures as recommended for these pure substances will have to be applied to a mixture containing this substance (ECHA, Guidance on information requirements and chemical safety assessment. Chapter R.11: PBT Assessment, 2012) (Regulation (EC) No 1907/2006 Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Article 60: Granting of authorisations).
E5	Identify components which contribute to the environmental hazard of the mixture	If the mixture is classified as non-hazardous, all uses would be considered safe. In agreement with this logic, all components, which do not lead to, or contribute to, the classification of the mixture will not be considered for the identification of the safe use information of the mixture. Thus, they are not considered relevant in the scope of this method.
E6	Are one or more of the relevant components classified as hazardous to the ozone layer (Category 1)?	LCID also accounts for components depleting the ozone layer. However, components depleting the ozone layer are considered separately, as this is a very specific environmental effect in comparison with the other toxic endpoints related to the environment. If more than one of those substances is contained in a mixture, a Lead Component needs to be identified.
E6a	Calculate LCI for each of the relevant ozone layer hazard component(s)	The component hazardous to the ozone layer with the highest concentration in the mixture is considered to have the highest impact on the ozone depleting potential of the mixture – and is therefore identified as the Lead Component relating to this effect.
E7	Is there at least one PNEC for each relevant	In case the full set of PNECs for all compartments is communicated by suppliers, the most critical one – irrespective

<table>
<tr><td></td><td>component available?</td><td>of the compartment – may be used. For the purpose of registration under REACH, a registrant is obliged to submit the full set of PNECs – or a justification, why some or all of them have not been derived. This full set of information is provided to ECHA via the dossier and the CSR. In the SDS, however, only (mostly) the relevant information is passed on. Some registrants have decided to provide all PNECS, others only those that have been derived (and do or do not state a reason why the remaining ones are not conveyed); others just state the most critical one. So in any case there is good reason to believe that the quality of this PNEC information is sufficient to be used in the LCID methodology – and favoured over the classification approach. So (at least) one PNEC per relevant component is deemed sufficient to run the LCID methodology.</td></tr>
<tr><td>E8</td><td>Calculate LCI based on CLP-classification, concentration and M-factors</td><td>As apparent from the following chart, the backup approach for the environment is almost identical to DPD+ (Cefic/DUCC, 2009)[46] the only difference being the expression of the same content in terms of products instead of quotients. This is due to M-factors, which take into account the presence of highly toxic (to the environment) components.
<table><tr><th>LSI DPDplus</th><th>Classification</th><th>Classification</th><th>LSI CLPplus</th></tr><tr><td>C_i / (0.25% x 3*)</td><td>R50</td><td>Aquatic Acute 1</td><td>$C_i \times M_{acute} \times 33$</td></tr><tr><td>$C_i$ / 0.25%</td><td>R50/53</td><td>Aquatic Chronic 1</td><td>$C_i \times M_{chronic} \times 100$</td></tr><tr><td>$C_i$ / 2.5%</td><td>R51/53</td><td>Aquatic Chronic 2</td><td>$C_i \times 10$</td></tr><tr><td>C_i / 25%</td><td>R52/53</td><td>Aquatic Chronic 3</td><td>C_i</td></tr><tr><td>C_i / 25%</td><td>R53</td><td>Aquatic Chronic 4</td><td>C_i</td></tr></table>■ C_i = concentration of substance in mixture
■ *correction factor of 3:
in order to reflect increased removal efficiency of R50 vs R50/53 substances
Please note:
Never mix both approaches (PNEC and classification) to identify the lead component of a mixture. It is either one or the other without any exception.</td></tr>
<tr><td>E9</td><td>Calculate LCI for each relevant component based on PNECs</td><td>PNECs for different compartments may come in different units of measure (mg/L vs mg/kg dw). In order to enable a proper comparison, these units need to be aligned.
The following equations are based on ECHA guidance (ECHA, Guidance on information requirements and chemical safety assessment. Chapter R.16: Environmental Exposure Estimation, October 2012) for converting to common units for PNEC values for soil and sediment, respectively:</td></tr>
</table>

[46] Cefic/DUCC, 2009: REACH: Exposure scenarios for preparations - Methodology for the identification of substances that represent the dominant risks to human health and/or the environment and the drivers for risk management measures





The equation to determine the Lead Component Indicator is:

LCI = Conc in mixture / PNEC

The higher the concentration of a component in a mixture (the numerator), the higher the component contributes to the potential hazard of the mixture

The lower the PNEC of a component (the denominator), the more hazardous the component.

Applying principles of the predecessor of the LCID methodology, DPD+ (Cefic/DUCC, 2009), to identify lead substances in preparations, readily degradable substances received a “bonus” factor of 3 for the following reason:

> “*R50 substances undergo rapid degradation and do not bioaccumulate. Hence, their risk to the environment is lower than that of substances labeled R50/53. According to Chapter R16 of the ECHA Guidance on Information Requirements and Chemical Safety Assessment readily degrading substances degrade in a wastewater treatment plant to a degree of 67% whilst R50/53 labeled substances may not be affected (no degradation). This corresponding difference in the risk indicator can be accounted for by a correction factor of 3 in order to reflect the increased removal efficiency of a municipal wastewater treatment plant for readily degrading substances. Please note that this factor is not used for ac-*

		tual risk assessment but for discriminating between substances according to their risk. *The LSI algorithm for substance labeled R50 is then:* *$LSI = C_i / C_L \times 3$.* *Where:* *C_i = Concentration of component in the mixture* *C_L = Concentration Limit is where a dilution has no longer to be classified"* Based on these previous recommendations, this similar approach has also been taken into account when developing the LCID environmental methodology. Accordingly, the equation for the identification of Lead Components (for readily degradable substances) reads: LCI = C / PNEC x 3 Where: C = Concentration of component in the mixture PNEC = Predicted No-Effect Concentration
E10	Compile LCIs for all components; the relevant component with the highest LCI is considered the Lead Component (LC)	The component with the highest LCI is deemed to have the highest impact on the potential environmental hazard of the mixture. Providing information on the safe use of this component in the mixture will ensure safe use of the entire product.
E11	Is there more than one relevant component classified as an environmental hazard?	It is acknowledged that further components classified as hazardous to the environment (beyond the Lead Component identified in the process described above) and contained at relevant concentrations, may contribute to the environmental hazard of the mixture. This aspect is taken into consideration by LCID.
E12	Derive M_{safe} for product mixture if there is only one relevant component that drives the environmental classification of the mixture	In case there are no other components classified as hazardous to the environment present in the mixture at relevant concentrations, the M_{safe} of the product can be calculated using a linear relationship. The lower the concentration of the lead substance in the product, the higher the resulting M_{safe} for the product.
E13	Derivation of M_{safe} for the product mixture when more than one relevant component contributes to the environmental hazard classification of the mixture	Potential additive environmental effects may need to be covered (Directorate-General for Health & Consumers, 2012)[47]. This is done by division of the sum of all environmental LCIs by the maximum LCI. The resulting Modifying Factor (MF) reflects the relationship between the Lead Component identified and the further, environmentally relevant components. The MF therefore is an indication to which degree the Lead Component is representative for the environmental hazard of the entire mixture. Using the MF, the actual concentration of the lead component in the mixture is converted into "$C_{weighted}$": a hypothetical concentration of the Lead Component that also ac-

[47] European Commission, Directorate-General for Health & Consumers, 2012, Toxicity and Assessment of Chemical Mixtures

		counts for the additive effects of the other components contributing to the environmental hazard of the mixture.
E14	Derive M_{safe} for product based on weighted concentration	The derivation of the M_{safe} for the product follows the same approach as described under Step E11 – this time using the hypothetical concentration $C_{weighted}$ (derived via the MF) in order to also cover potential additive effects.
E15	Compile OCs and RMMs for Lead Component and/or Priority Substances and/or ozone layer hazard components	All relevant OCs and RMMs of the Priority Substance(s) or Lead Component and/or ozone layer hazard are transferred to the mixture (e)SDS. Any duplication should be removed. Consider applying the strictest of the OCs and RMMs, unless professional judgment dictates otherwise.
E16	Are OCs/RMMs for Priority Substances/ozone layer hazards/Lead Components sufficient enough to cover other constituents and/or exposure pathways?	Priority Substances and Lead Components generally require the most stringent risk management measures. However, if these measures are substance-specific or specific to a given exposure pathway, it is possible that they do not adequately control the exposure to other hazardous substances of the mixture which have different physico-chemical properties.
E17	Are substances with specific properties which are not reflected by classification of the substances adequately covered?	This step is aimed to take into account additional substance-specific information which may be available.
E18	Safe use information must be derived on a case-by-case basis	If the OCs and RMMs for Priority Substances/Lead Components are not sufficient enough to cover other constituents and/or exposure pathways, then a case-by-case evaluation is required using expert judgement.
E19	Provide safe use information and modified M_{safe} value for product, if relevant, either embedded within SDS or as an annex to SDS	Derivation and communication of safe use information is the purpose of the LCID methodology. It is up to the author of the SDS to decide how this is passed on along the supply chain.