17 July 2014

2014 SID Workshop – Substance Sameness

Introduction

This document is addressed to the attention of the participants of the workshop on substance identification and substance sameness organised by ECHA on 6-7 October 2014. It provides important background information as well as key considerations on the complex concept of substance sameness, which will be the focus of the workshop. It also describes, in generic terms, a possible solution for a systematic approach to assess whether substances can be registered together. This document has been written with the aim to facilitate as far as possible the development and possible exchange of views in advance of and during the workshop.

Substance sameness to be addressed at the workshop

The concept of sameness is multiple as it cannot be addressed without defining precisely the context. "Everything is the same – everything is different". Substance sameness in practice can essentially be understood in terms of "administrative sameness" and "hazard sameness".
When considering the registration process under REACH, the administrative sameness refers to the principle which entitles the joint submission of information in a registration. In other words, substances administratively the same are substance which can be registered together.
The hazard sameness on the other hand is about judging to which extent the hazard information on a sample of a substance describes the properties of another substance.
When looking at the crossover of these two concepts, a systematic correlation between administrative sameness and hazard sameness cannot be defined. Substances administratively the same do not necessarily have the same hazard properties. *Vice versa*, substances presenting the same hazard properties are not necessarily the same.

The sameness concept to be addressed at the workshop is the administrative sameness. In simple terms, one important objective of the workshop is to address the current uncertainties in answering the question "who can register together?".

Substance sameness – an analysis of the current state of play

The Guidance for identification and naming of substances under REACH and CLP provides comprehensive criteria for registrants to establish substance sameness between well-defined substances. In line with the Guidance, well-defined substances can be considered the same provided they consist of the same main constituents. Therefore, for well-defined substances, their composition determines sameness. The Guidance underlines that the identification of the main constituents is based on the 80% and 80-10% "rules of thumb". In line with these conventions, assessing whether 2 substances can be registered together may lead to three different conclusions:

- The substances can definitely be registered together as they consist of the same main constituents;
- The substances can definitely not be registered together as they do not consist of the same main constituents;
- The joint registration of the substances is plausible, if justifiable.

These conventions must be understood in light of the objective pursued by the joint registration process, in particular being able of identifying and sharing relevant data for all

substances to be registered jointly so that risks associated to these substances can be assessed and appropriate risk management measures recommended. The 80% and 80-10% rules accordingly set an acceptable presumption that the properties of compositions presenting the same main constituents can be addressed jointly. This presumption does not mean that the hazard properties and classification and labelling of substances registered together are necessarily the same. Other characteristics such as the impurity profile can for example influence the properties of the substances. It rather reflects a regulatory acceptance that the identity of the main constituents defines a common baseline for sharing relevant data and determining the hazards. Additional considerations on other characteristics of the substances, such as the impurity profile, will then need to be taken into consideration for the determination of the hazard properties in full.

Based on these considerations, an acceptable justification for registering substances together would be expected to consist of a demonstration that they can be considered sharing an equivalent baseline (as defined by the main constituents). The Guidance confirms this principle by acknowledging that acceptable justifications need to demonstrate that the baseline is typically the same or that baselines only qualitatively the same do not lead to a difference in the properties.

For UVCB substances, the Guidance does not define precisely the common baseline which entitles the joint registration of substances. The Guidance instead provides selected clear-cut examples where two UVCB substances cannot be considered the same. The Guidance also highlights the determinant role of the source and manufacturing process for determining whether two UVCB substances can no-longer be registered together. In line with the Guidance, "*any significant change of source or process would be likely to lead to a different substance that should be registered again*".

Whilst it may be possible to establish from the Guidance when certain UVCB substances can definitely not be registered together, the borderline which separates UVCB substances presumed to be the same from other UVCB substances cannot be easily predicted. Also the Guidance does not define a general derogation for registering together UVCB substances as it does for well-defined substances. Such derogation has however been introduced behind Recital 45 of the REACH Regulation.[1] The derogation in the Recital makes considerations on the properties of substances. An analogy with the derogation for registering together well-defined substances can therefore be drawn.

Overall, despite the lack of comprehensive set of criteria currently available in the Guidance for determining whether two UVCB substances can be registered together, it can reasonably be anticipated that assessing the sameness for this type of substances necessarily also leads to one of the three different conclusions:

- The substances can definitely be registered together;
- The substances can definitely not be registered together;
- The joint registration of the substances is plausible, if justifiable.

Resolving the current uncertainties on substance sameness between UVCB substances can therefore be achieved in practice by defining the boundaries between these three possible scenarios. The solution proposed to be considered for the workshop has been designed to meet this objective.

[1] Recital 45 of the REACH Regulation: "*The European Inventory of Existing Commercial Chemical Substances (EINECS) included certain complex substances in a single entry. UVCB substances (substances of unknown or variable composition, complex reaction products or biological materials) may be registered as a single substance under this Regulation, despite their variable composition, provided that the hazardous properties do not differ significantly and warrant the same classification*".

Requirements on the specifications of the substance sameness principles

When addressing the current uncertainties on substance sameness, certain principles must be taken into account.

First, it needs to be borne in mind that conventions on substance identification and substance sameness have been established over the past 30 years since the entry into operation of the notification scheme under the Directive 67/548/EEC. It is therefore important to ensure that the specifications of the substance sameness principles do not result in the re-definition of established substance sameness principles.

It must also be ensured that that the specifications of the substance sameness principles do not introduce any discrimination between the different substance types. The specifications should therefore not set any more lenient or more stringent criteria for UVCB substances than for well-defined substances.

Finally, it has to be recognised that exceptional conventions have been adopted for certain substances. For example, inorganic catalysts are exceptionally regarded as mixtures according to the Guidance. These exceptions should not dictate the specifications of the substance sameness principles.

Proposed approach

The Guidance specifies that "*when checking whether or not the substances from different manufacturers/importers can be regarded as the same, some rules should be respected. These rules which were applied for establishing EINECS should be regarded as a common base for identifying and naming a substance and thus finding a potential co-registrant of this particular substance*". The EINECS reporting rules are therefore presented as necessary conditions for establishing whether two substances can be registered together. It is proposed to use the EINECS reporting rules as the starting point for addressing the uncertainties on substance sameness and to structure the specifications of the UVCB substance sameness principles around these rules.

Looking back at the rules for reporting substances for EINECS, two main observations can be made.

Firstly, the EINECS reporting rules included six different methods for depicting UVCB substances out of which four methods can be considered relevant for defining the general substance sameness principles:[2]

- Structural representation of the constituents
- Reaction scheme (including essentially the identity of the reactants and the reaction type)
- Process output (including the identity of the precursors, the technology (method of preparation; process terms) and the typical composition)
- Combination of the abovementioned methods

Secondly, the substance, its constituents or precursors had to be specified as precisely as possible.

[2] See chapter 4.3.7 of the document available at http://bookshop.europa.eu/en/reporting-for-the-einecs-inventory-pbCB3281423/

When considering the use of the abovementioned methods for depicting UVCB substances, this second observation implies that there is a priority order between them; the composition of the substance itself (i.e. the structural representation) is the favoured way of depicting UVCB substances, followed by the reaction scheme, including the identity of the reactants, and finally the process output.

Taking into account the objective of setting the boundaries between substances which can be definitely/never/plausibly registered together and the rules for reporting the substances for EINECS, the substance sameness principles proposed to be followed would be based on the following:

- An approach for depicting UVCB substances according to the priority order
  1) Structural representation
  2) Reaction scheme
  3) Process output.

  The depiction should aim at representing the identity of the substance in full. If necessary, the three depiction methods should be combined for this purpose.
- The principle that UVCB substances considered to be the same must necessarily consist of the same (combination of) depiction(s).
- The principle that UVCB substances consisting of the same (combination of) depiction(s) cannot necessarily always be registered together without sufficient explanation demonstrating that the set of hazard data included in the registration duly cover the UVCB substances registered together.

  This can for instance refer to a situation where certain depictions such as depiction based on structural representation may be the result of justifiable deviations from the rules (as in the case of well-defined substances). This can also be the case where significant uncertainties exist in the compositional differences between substances. In particular, the more the depiction of substances depends on the methods of lower priority order (down to relying solely on the process output depiction), the higher these uncertainties are in practice.

  In such situations, even though registering substances together is plausible, transparency in the documentation of the hazards for the substances covered by the registration must prevail to ensure that the objective pursued by the registration process is fulfilled. Taking also into account the Recital 45 for UVCB substances, the transparency sought for should enable to demonstrate that hazard information included in the registration duly cover the UVCB substances registered together.

Separate considerations on the method of depicting, whether partly or fully, UVCB substances as well as the substance sameness boundaries resulting from the depictions are briefly provided thereinafter. Illustrative examples for the depiction of substances are included as an annex to this note.

Structural representation

A structural representation should reflect the existence of one or more predominant constituents or groups of constituents. To ensure coherence with the substance sameness principles established for well-defined substances, the determination of the structural representation is proposed to be based around the 80% and 80-10% rules.[3]

[3] Note that these thresholds have been taken into account in the OECD Guidance for characterising oleochemical substances for assessment purposes (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)6&doclanguage=en) and in the interpretation of the scope of entries in the No-Longer Polymer (NLP) list (see page 11 of the publication available at http://publications.jrc.ec.europa.eu/repository/bitstream/111111111/8721/1/6863%20-%20NLPFIN%20March1.pdf).

For example, the level of esterification of a UVCB substance obtained from an esterification reaction provides a structural representation. Based on the 80% and 80-10% rules, "diesters" would constitute a structural representation when the UVCB substance consists of ≥80% of such group of constituents.

A UVCB substance with a different structural representation of the level of esterification, e.g. "monoesters" could definitely not be registered together with "diesters".

A UVCB substance for which the structural representation of the level of esterification as "diesters" is a result of a deviation from the rules (e.g. because the concentration level of diesters overlaps the 80% threshold) could not be registered together unless a proper justification is provided.

Reaction scheme

The depiction based on the reaction scheme requires specifications of the identity of the reactants and the reaction type. Substances which depiction relies solely or partly on a reaction scheme can definitely not be considered the same if they do not share both the same reactants and reaction type.

However, it should be recognised that chemistry may allow reactions involving different reactants or reaction types to lead to the same substances. For example, esters can be obtained from the parent carboxylic acid or from the parent acyl chloride. In this situation, the depiction according to the reaction scheme needs to take into account the multiplicity of chemistry. Accordingly, the use of an acyl chloride instead of a carboxylic acid would not as such be a reason for considering that the representations of the reaction scheme of the esterification are different.

There may be situations where deviations for the identification of the reactants are applied. For example, a deviation from the 80% and 80-10% rules for the identification of a well-defined starting material may be invoked. Registering together the substance obtained for this starting material with substances where no deviation was applied would then require a proper justification to be provided.

Process output

Substances which depiction relies solely or partly on a process output necessarily need to have in common the identity of the precursors and the technology to be considered the same. The definition of the precursor must accommodate the inherent variability of a manufacturing process. For example, the use of secondary sources which identity cannot be predicted over time may not necessarily need to be defined precisely.

As explained earlier, the further the depiction of substances relies on descriptions as a process output, the higher the uncertainties are with respect to the similarities between substances. It is expected that registering together substances with such depictions cannot be considered without sufficient explanation demonstrating that the set of hazard data included in the registration duly cover the UVCB substances registered together.

Concluding remarks

The proposed substance sameness approach consists of a predictable tiered approach, based on established methods used to depict UVCB substances and introduced at the time of reporting substances for EINECS. The tiered approach allows the prioritisation of considerations on the composition of substances for determining whether they can be registered together. It is designed to answer the question on whether UVCB substances can definitely, never or plausibly (if justified) be registered together, as it can currently be done for well-defined substances.

An important aspect of the approach is the additional necessary step expected to be completed when registering substances together is not definite but only plausible. This step should aim at ensuring transparency in the documentation of the properties of the substances registered together. This is especially critical whenever it cannot be presumed that the properties of substances will be sufficiently constant within the permissible variations in the composition. This step falls in-between substance identification and hazard documentation. The expected level of detail and the format for providing this information still needs to be addressed. In particular, it needs to be determined how far the information must include in practice distinct considerations at the level of each individual endpoint. The 2014 workshop will be an opportunity to share views and ideas on this matter.

Annex: Illustrative examples of substance representations

Please note that the examples provided in this annex are purely theoretical. They are not intended to represent characteristics of substances actually manufactured or imported or to reflect accurate chemical processes. These examples do not set any precedent in the determination of the registration obligations under REACH with regard to substance identification and the joint submission of information.

Depiction based on one structural representation only:
A UVCB substance of known but variable composition, which consists of a set of specific linear alkylamine constituents at a concentration within the 10-80% concentration threshold, can be depicted by the identity of these predominant constituents.

An example of such depiction would be the structure corresponding to the following constituents "C8-C18(even numbered) alkylamines".

Considering such structural representation as sufficient to represent the substance would imply that it depicts the substance in full. Accordingly, the 6 individual structures behind this representation should represent a significant part of the substance composition. In line with the representation of well-defined mono-constituents, an overall representation of 80% of the composition would suffice.

Any substance presenting a different structural representation, such as a UVCB alkylamine represented by a different (e.g. broader, narrower) carbon number range could normally not be registered together. The same apply to any substance requiring additional depictions.

Depiction based on one structural representation and a reaction scheme:

A UVCB substance consisting predominantly of mono- and di-alkyl butanedioate and where the contribution of the alkyl substituent is depicted by the structural representation of the alcohol precursor would overall be depicted by:

- The structural representation referring to the level of esterification: mono- and di-;
- The reaction scheme (esterification) which would also embed the structural representation of the dicarboxylic acid and the alcohol.

An example is the substance represented as "C8-C18(even numbered) fatty alcohol, mono- and di-esters with butanedioic acid". This representation would normally set the expectation that the mono- and di-esters both contribute to 10-80% of the composition. It would also be expected that the starting materials can only be depicted as C8-C18(even numbered) fatty alcohol.

Any substance depicted by a different structural representation (e.g. mono-esters, di-esters) could not be registered together as a baseline. The same would apply to substances obtained from an alcohol precursor with a different structural representation (e.g. C10-C20(even numbered) fatty alcohol).

It should be noted that, in borderline cases where e.g. the substance may inherently consist predominantly of either mono-esters only (i.e. the mono-esters are present at >80%) or both mono-and di-esters (i.e. both the mono-esters and the di-esters are present at 10-80%) from one batch to another, a deviation from the rules is necessary. The deviation must be applied for depicting the substance either as the monoesters or the mono- and di-esters. The deviation must be justified.

It is also worth mentioning that, in this specific case, a structural representation alone would not be considered appropriate to describe the substance. In particular, the structural representation of the carbon number distribution could not reasonably be made without making reference to the actual alcohol precursor used.

Depiction based on one structural representation and a description of a process output

A UVCB substance is obtained from complex chemical process allowing the full extraction of the sterols present as such or as esters in sunflower oil. The substance is characterised by the systematic predominance of a specific sterol, in this case stigmast-5-en-3-β-ol (contributing to 10-80% of the composition), as well as a complex combination of other partially unknown sterols.

A structural representation as sterols including the predominance of stigmast-5-en-3-β-ol can be achieved for this substance. However, this structural representation is not sufficient for the full representation of the substance since the sterols other than stigmast-5-en-3-β-ol are only described in generic terms. Reference to the source used is necessary for distinguishing this complex set of sterols from any other sterol-containing UVCB substance.

It should be noted that the representation by a reaction scheme in this case is not relevant. The reaction scheme must aim at representing the identity of the constituents through chemical reactions. In this case, the substance is rather defined as deriving from a chemical refining process.

The substance would in this case be depicted as sterols from sunflower oil, with the predominance of stigmast-5-en-3-β-ol embedded in the depiction. Any sterol-based UVCB substance obtained from a different source could normally not be registered together. Any sterol-based UVCB substance obtained from sunflower oil but presenting a different structural representation (e.g. where stigmast-5-en-3-β-ol would not be predominant or where additional or other sterols would also be predominant) could not be registered together. Any substance which does not predominantly consist of sterols only could not be registered together.