A tiered assessment framework for ecological risk assessment of Unknown or Variable composition, Complex reaction Products, or Biological materials (UVCBs)

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INTRODUCTION

Complex substances such as multi-constituent substances (MCS) and UVCBs usually result from the industrial processing or extraction of natural substances or from chemical reactions. Because of the nature of source materials, and the potential variability inherent to production processes, these substances can contain many, sometimes uncharacterized constituents, whose concentrations may vary. As a result, UVCB/MCS risk assessment presents unique challenges to product registrants and regulators alike.

With substance composition potentially varying from batch to batch, and when testing the whole UVCB substance does not necessarily inform the behavior of its constituents, or reveal the presence of risk drivers, how can hazard data be best collected and interpreted?[1]

To answer these questions, the UVCB Committee of the Health and Environmental Sciences Institute (HESI) is building an exposure-based tiered approach considering the minimum level of information required to perform a robust ecological risk assessment.

METHOD

Two workshops (one in person and one remote) convening stakeholders from government, academia, and industry, with a wide variety of expertise, were organized by HESI to discuss the challenges pertaining to the risk assessment of UVCBs.

- The first workshop focused on the development of a tiered substance characterization approach with emphasis on defining the first step of the evaluation, or Tier 0.
- The second workshop, a series of remote meetings, revolved around the development of three case studies designed to test the risk assessment framework developed by integrating the exposure component to the characterization approach developed in the first workshop. The three substances of interest were Cedar Oil, Alkyl Dimethyl Benzyl Ammonium Chlorides (ADBAC), and Hydrogenated Resin Glycerol Ester.

RESULTS

Tier 0 characterization and exposure data

The first workshop led to the development of a tiered characterization framework, the principle of which is to only generate information necessary for a robust risk assessment, without systematically resorting to full substance characterization.

The first step of the assessment (Tier 0) considers basic and readily available substance characterization and exposure information. Tier 0 characterization information includes substance specifications, quality assurance data, and basic chromatographic and elemental data, while exposure information includes use/importation volumes and end uses (Figure 1). Tier 0 characterization also provides elements of information on exposure (e.g., range of K_{ow}) and hazard (e.g., problematic elements and moieties).

Tier 0 information is evaluated to determine whether more characterization information might be needed for a preliminary assessment. This first tier is critical to allow the rapid screening of UVCBs which may or may not need in-depth characterization.

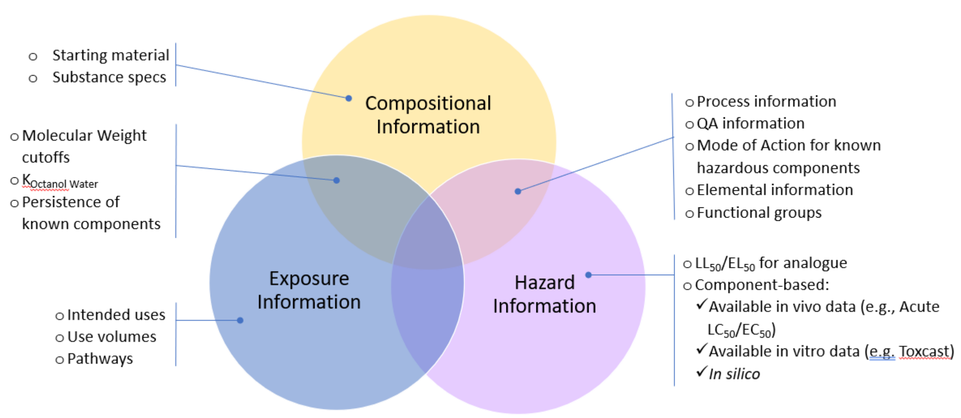

Figure 1. Tier 0 information

Tier 0 risk assessment framework

In the second workshop, a Tier 0 risk assessment framework based on the integration of Tier 0 compositional and exposure information was discussed and refined via the development of case studies involving the three substances of interest: Cedar Oil, Alkyl Dimethyl Benzyl Ammonium Chlorides, and Hydrogenated Resin Glycerol Ester. Figure 2 provides an example of the framework developed in the case of Cedar Oil.

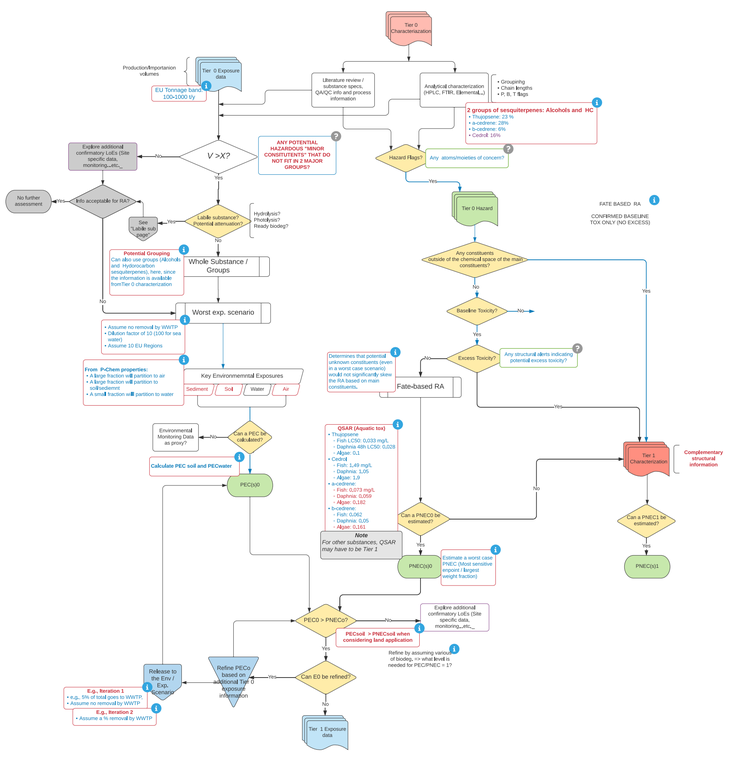

Figure 2. Example of UVCB (here, Cedar Oil) risk assessment framework.

Testing the framework on these three substances revealed that its application would depend on the type of UVCB substance (e.g., ionized, potential for persistence of some constituents, etc.). More specifically, the need for information beyond Tier 0, and the nature of that information, would be determined by one key characteristic of the substance, namely its complexity or "difficulty to assess".

Complexity and biodegradability evaluation

Complexity / Difficulty to assess

Defining the notion of "substance complexity" was deemed necessary so the UVCB risk assessment framework could be properly adapted to different substances, and so the information necessary for the risk assessment could be collected as needed.

Substance complexity, was defined as the combination of three characteristics:

1. **Variability** in constituent concentrations,
2. **Diversity** of chemistries and chemical properties of constituents, and
3. **Belonging to the applicability domain** of existing test models.

Substance complexity should be evaluated early in the risk assessment since it is likely to determine how thorough substance characterization will need to be. For that purpose, the committee has been developing a simple complexity evaluation scheme, based on the cumulative scoring of the three criteria listed above (see the Table below). This system could help risk assessors qualify the overall substance complexity level (low, medium, high) and decide on the level of substance characterization need for the assessment.

CAS#	Chemical Name		Variability of Const. Conc	Diversity of Chem. Properties of Const	Belonging to Applicability Domain of Test Systems	Complexity level
8027-33-6	Alcohols, lanolin	Alcohols	2	1	1	1.25
85535-84-8	Alkanes, C10-13, chloro	chlorinated paraffins	2	3	3	2.75
61789-01-3	Fatty acids, tall-oil, epoxidized, 2-ethylhexyl esters	Epoxides & glycidyl ethers	1	2	1	1.25
85203-81-2	Hexanoic acid, 2-ethyl-, zinc salt, basic	Fatty amides	1	1	2	1.5
68990-53-4	Glycerides, C14-22 mono-	Glycerides	2	1	1	1.25
71888-89-6	1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters, C7-rich	Phthalates	1	1	1	1
8050280	Rosin, maleated	Resins & rosins	3	3	2	2.5
71889-01-5	Silane, chlorotrimethyl-, hydrolysis products with silica	Siloxane and Silanes	1	1	3	2

Table 1. Example of substance complexity evaluation based on the evaluation of the three criteria of 1) Variability in constituent concentrations, 2) Diversity of chemistries and chemical properties of constituents, and 3) Belonging to the applicability domain of existing test models, as medium, low, and high.

Biodegradability evaluation

Although biodegradability testing provides data beyond "Tier 0", it could provide valuable exposure information, and (in combination with additional Tier 0 data) hazard information, and inform how to implement the framework, and what characterization strategy to deploy. Thus, biodegradability should be evaluated early into the risk assessment. The question of whether biodegradability should be tested on the whole substance or on representative structures should also be explored.

Conclusion

The proposed framework is a proof-of-concept for a tiered risk assessment approach of UVCBs. This method, which relies on an initial basic substance characterization and exposure evaluation, aims to simplify the safety evaluation of these substances, by shifting the focus from full substance characterization to a weight of evidence approach. Importantly, the evaluations of substance complexity and biodegradability are two important steps, which will determine the needed level of substance characterization.

Overall, this approach is expected to ensure that efforts and resources deployed for UVCBs risk assessment match actual needs and help streamline the risk assessment process.

References

[1] Salvito D, Fernandez M, Jenner K., Lyon DY, de Knecht J, Mayer P, MacLeod M, Eisenreich K, Leonards P, Cesnaitis R, León-Paumen M, Embry M, Deglin S. 2020. Improving the environmental risk Assessment of substances of unknown or variable composition, complex reaction products, or biological materials. Environ. Toxicol. Chem. 39,11:2097-2108

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