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

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## INTRODUCTION

**UVCBs present unique challenges to product registrants and regulators. Complex substances such as UVCBs are usually generated 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 constituents, some uncharacterized, whose concentrations may vary. One of the key questions related to UVCB risk assessment is:**

**"How can hazard data be best collected and interpreted, considering that substance composition can potentially vary from batch to batch, and that testing the whole UVCB substance does not necessarily reflect the behaviour of its constituents?" [1] To answer this question, the UVCB Committee of the Health and Environmental Sciences Institute (HESI) is building a tiered exposure-based approach based on the minimum level of information required for the ecological risk assessment of UVCBs.**

## BACKGROUND

- Two workshops organized by HESI's UVCB Committee resulted in the development of a **tiered, exposure-based ecological risk assessment framework** (Fig. 1) emphasizing the first step of the evaluation, or Tier 0.

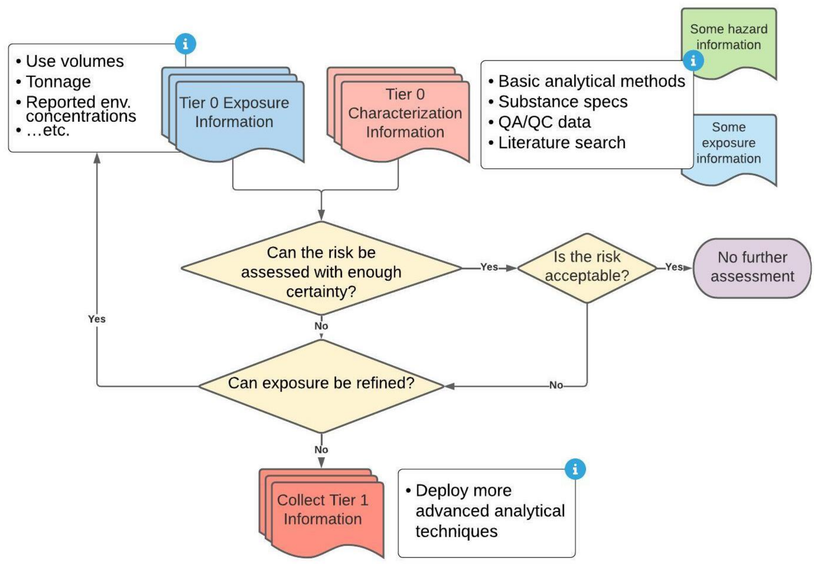


**Figure 1. General assessment framework**

- Case studies conducted to gather proof of concept for the risk assessment framework revealed the need for better access to **Tier 0 information** as well as a way to evaluate **substance complexity.**

### Tier 0 Data

Information necessary for the preliminary assessment of UVCBs without systematically resorting to full substance characterization. It includes basic compositional, structural, exposure and hazard information (Fig. 2), collected from simple analyses (e.g., Elemental analysis, HPLC, GC), substance specifications, QA/QC data, starting material and process information.

### Complexity or "difficulty to assess" UVCBs

This concept was defined as a composite of three characteristics of UVCBs substances:

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

- To address these needs, the committee decided to:
  - Create a database of Tier 0 data, to make this information more readily available to risk assessors
  - Develop a complexity evaluation scheme based on Tier 0 data, to allow for the rapid assessment and prioritization of UVCB substances, and determine which ones warrant further characterization.
  - Develop a guidance document to describe how to adapt our risk assessment framework to different types of UVCBs (Different chemistries and complexity) and systematically assess UVCBs in a tiered and fit-for-purpose fashion.

## TIER 0 INFORMATION PILOT DATABASE

A pilot database of Tier 0 information is being developed as a proof of concept for 100 UVCBs. The compiled information comprises substance identifiers, process information, chemical descriptors and properties, exposure information and other relevant publicly available information. (Fig. 2)

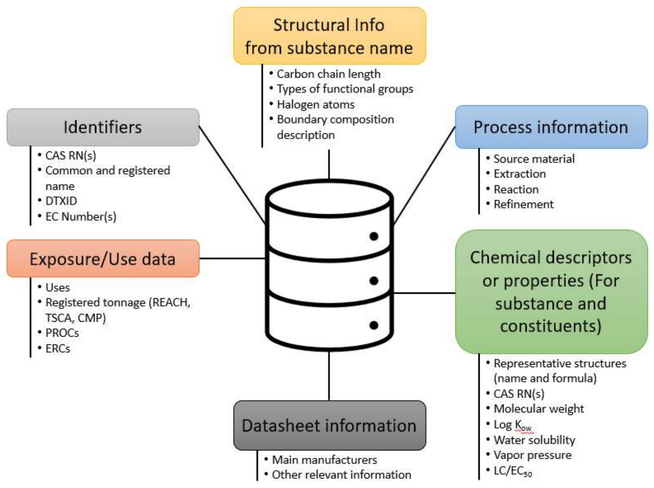


**Figure 2. Tier 0 information database**

Although the information relevant to this repository is not particularly sensitive and should be publicly available, the mining process is proving difficult and time consuming, and often leading to incomplete entries. The challenges encountered while populating this database are being documented, so the information can be made more readily available in the future, with the objective of centralizing it as well as facilitating and streamlining the Tier 0 risk assessment of UVCBs. Obtaining buy-in from industrial and regulatory partners will be key to facilitate the data collection process, and ultimately, realize of the full potential of such a repository of data.

## COMPLEXITY EVALUATION SCHEME

A complexity evaluation scheme is being developed, based on the qualitative scoring of the three criteria listed above to help risk assessors gauge the substance's difficulty to assess (low, medium, high) and decide on the level of substance characterization needed for the assessment (Table 1). Importantly, the three criteria evaluation largely relies on Tier 0 information.

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

| CAS# | Chemical Name | | Variability of Const. Conc | Diversity of Chem. Properties of Const | Belonging to Applicability Domain of Test Systems |
|---|---|---|---|---|---|
| 8027-33-6 | Alcohols, lanolin | Alcohols | | | |
| 85535-84-8 | Alkanes, C10-13, chloro | Chlorinated paraffins | | | |
| 68990-53-4 | Glycerides, C14-22 mono- | Glycerides | | | |
| 71888-89-6 | 1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters, C7-rich | Phthalates | | | |
| 8050-28-0 | Rosin, maleated | Resins & Rosins | | | |
| 71889-01-5 | Silane, chlorotrimethyl-, hydrolysis products with silica | Siloxane and Silanes | | | |

A guidance document will be developed to systematize the substance complexity evaluation, and suggest testing strategies depending on the level of complexity identified for each of the three criteria taken individually and as a whole.

## CONCLUSION AND FUTURE WORK

The proposed framework is a proof-of-concept for a tiered risk assessment approach of UVCBs. It relies on an initial basic substance characterization and exposure evaluation, and **aims to simplify the ecological safety evaluation of these substances, by shifting the focus from full substance characterization to a weight of evidence approach**. This Tier 0 evaluation can inform the initial screening and prioritization of UVCB substances, as well as the need for further testing, depending on the level of substance complexity.

A database of Tier 0 information is the linchpin to this framework as it will facilitate access to critical information necessary for the initial UVCB assessment, and more specifically for the characterization of substance complexity, in light of which assessors will be able to devise a testing and assessment strategy adapted to the substance.

Future initiatives by HESI's UVCB Committee will include:

- A manuscript highlighting the needs for a database of Tier 0 information as well as the challenges associated with this effort
- A guidance document to systematize the complexity evaluation and help assessors develop evidence-based assessment and testing strategies
- A workshop, which will be held in September 2023 to discuss the important issue of the whole substance vs. constituent approach, as well as the persistency question

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.

## Reference

[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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