

# AN APPROACH TO CHEMICAL CATEGORIES FOR ENVIRONMENTAL ENDPOINTS

Lapczynski, A. and Salvito, D.

Research Institute for Fragrance Materials, Woodcliff Lake, NJ USA.

## ABSTRACT

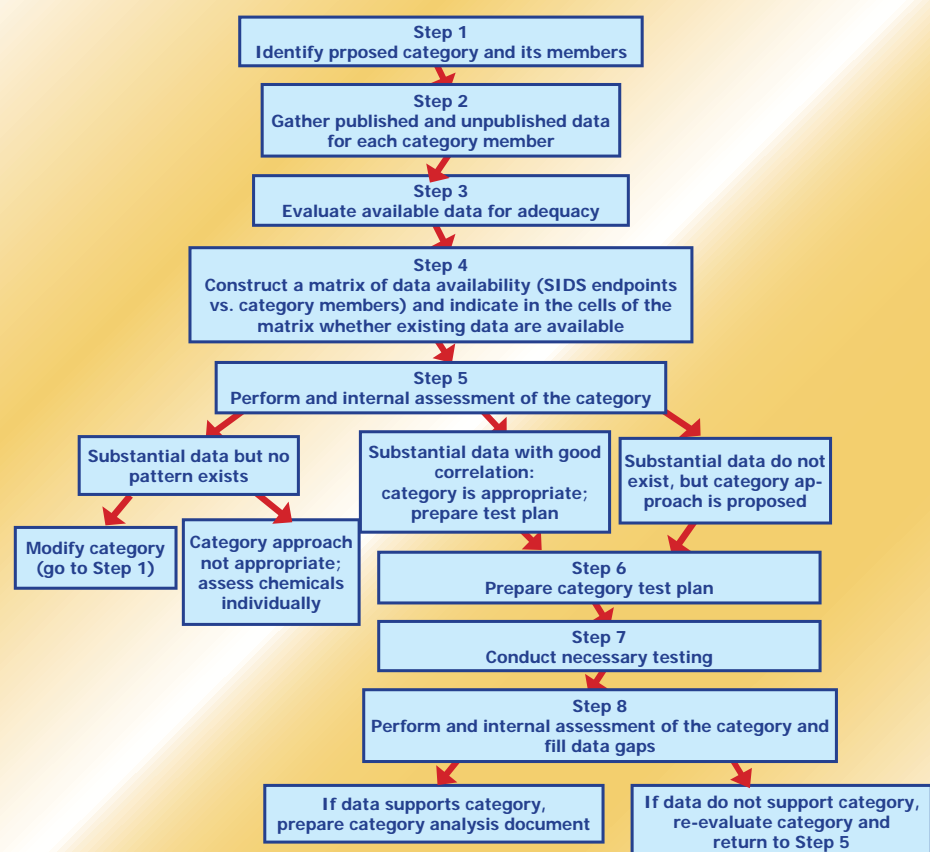
Chemical categorization is a well established process for grouping chemicals of similar structural moieties for the purpose of data gap filling. The guidance developed for REACH supports the use of chemical categories for these purposes. It requires the establishment of an hypothesis built around the physical-chemical and metabolic domain of the members of the group. Although this approach has been used by various regulatory agencies and industry for some time, it has not often been broadly applied for environmental endpoints. The numerous chemicals used in the preparation of fragrance compounds are represented by many different structural groups. Case studies from structural classes of fragrance materials will be provided as examples of categorization for environmental endpoints, particularly biodegradation and ecotoxicity. Subcategories are established based on potential chemical reactivity and metabolic pathways. Available data and tools (e.g., QSARs) will be used to validate the category domain and identify and fill data gaps.

## SOME PRINCIPLES

- Following OECD/RIP Guidance
- Begin with 2-D structural analogues
- Develop domain (structure/p-chem properties – incl. vp,  $K_{ow}$ , MW, water sol/functional groups/known metabolic pathways)
  - Do any materials “trouble” the domain?
- Develop analogue-data matrix
- Assess data quality

FIGURE 2 - PROPOSED PROCESS FOR DEVELOPING CHEMICAL CATEGORIES

### OECD Guidance - Flowchart



## KEY POINTS IN ESTABLISHING CATEGORIES

Form sub-categories based on:

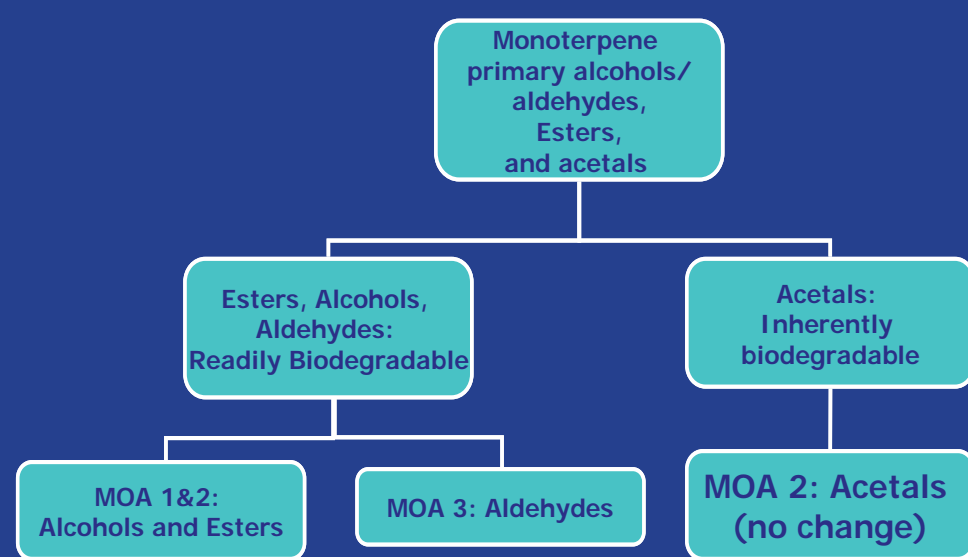
- Persistence (P): Breaks in biodegradability (ready vs inherent vs non-biodegradable materials)
- Bioaccumulation (B): Separate materials with known vs non or poorly metabolized materials
- Ecotoxicity (T): Separate via MOA (for FMs largely narcosis vs reactive toxicants)
  - MOA 1 and 2 can be grouped together

The RIFM database contains 2500 fragrance ingredients that are discrete organic chemicals representing over 23 different structural types (e.g. alcohols, esters, aldehydes, heterocycles).

In 2000, fragrance materials in the RIFM database were grouped according to structure-activity relationships. The fragrance structure – activity groups were developed through a collaboration of REXPAN and industry scientists and formed the basis of the REXPAN human health and environmental assessments. By grouping similarly structured materials and understanding the toxicology of key compounds within a group, structure – activity relationships were developed to assess members within a group.

Based on the original RIFM groups, a group of monoterpenes could be subclassed based on their biodegradability and ecotoxicological mode of action (MOA).

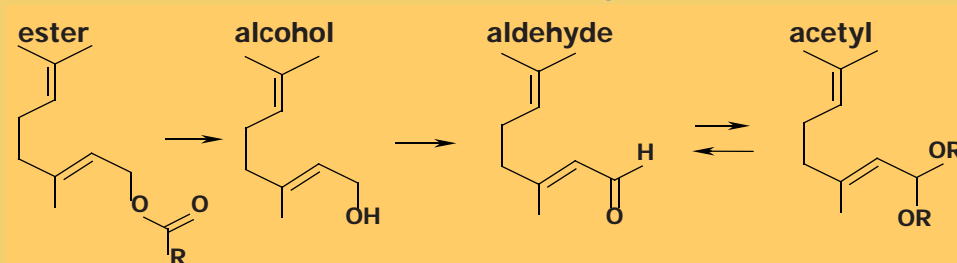
## HIERARCHICAL STRUCTURE



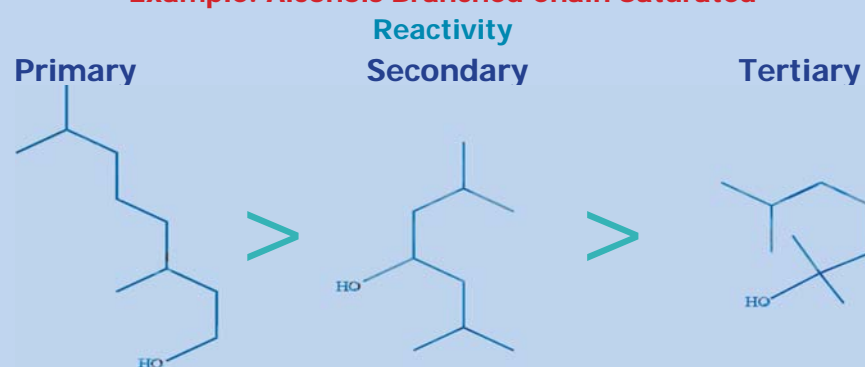
This structure also implies separation of subclassification of organic chemicals based on metabolic pathway and reactivity.

## Example-Monoterpene alcohols, aldehydes, esters and acetals

### Metabolic Pathway



## Example: Alcohols Branched Chain Saturated



## SUMMARY

This approach was applied to the RIFM database establishing a 1st tier of refinement to the original classes.

The usefulness of categorization to assess hazard properties and perform risk assessment will result in a reduction in animal testing and provide adequate information for these assessments.

## REFERENCES

Organisation for Economic and Cooperation Development. 2005. Manual for Investigation of HPV Chemicals. Chapter 3.2: Guidance on the Development and Use of Chemical Categories in the HPV Chemicals Programme.

Verhaar HJM, van Leeuwen CJ and Hermens JLM. 1992. Classifying environmental pollutants. 1. Structure-activity relationships for prediction of aquatic toxicity. Chemosphere 25: 471-491.