Future Perspectives

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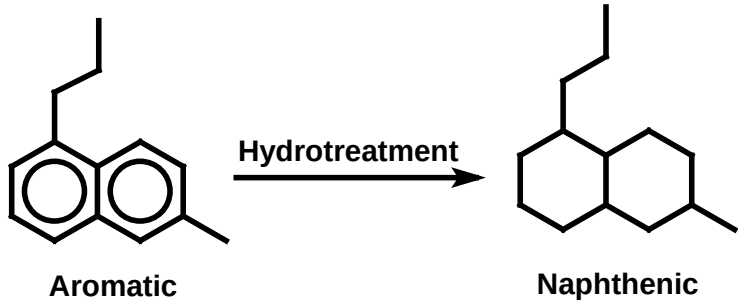
Future perspectives

- Where do we come from ?
- Where are we now ?
- Are we there yet ?
- Where are we heading ?

Where do we come from ?

- Petroleum substances are UVCBs: complex hydrocarbon *substances* with *variable composition*
- There is a wide range of products that are primarily marketed based on their *physico-chemical properties*
- These specifications *limit* the chemical variability and allow grouping → categories, based on physico-chemical characteristics & refining process

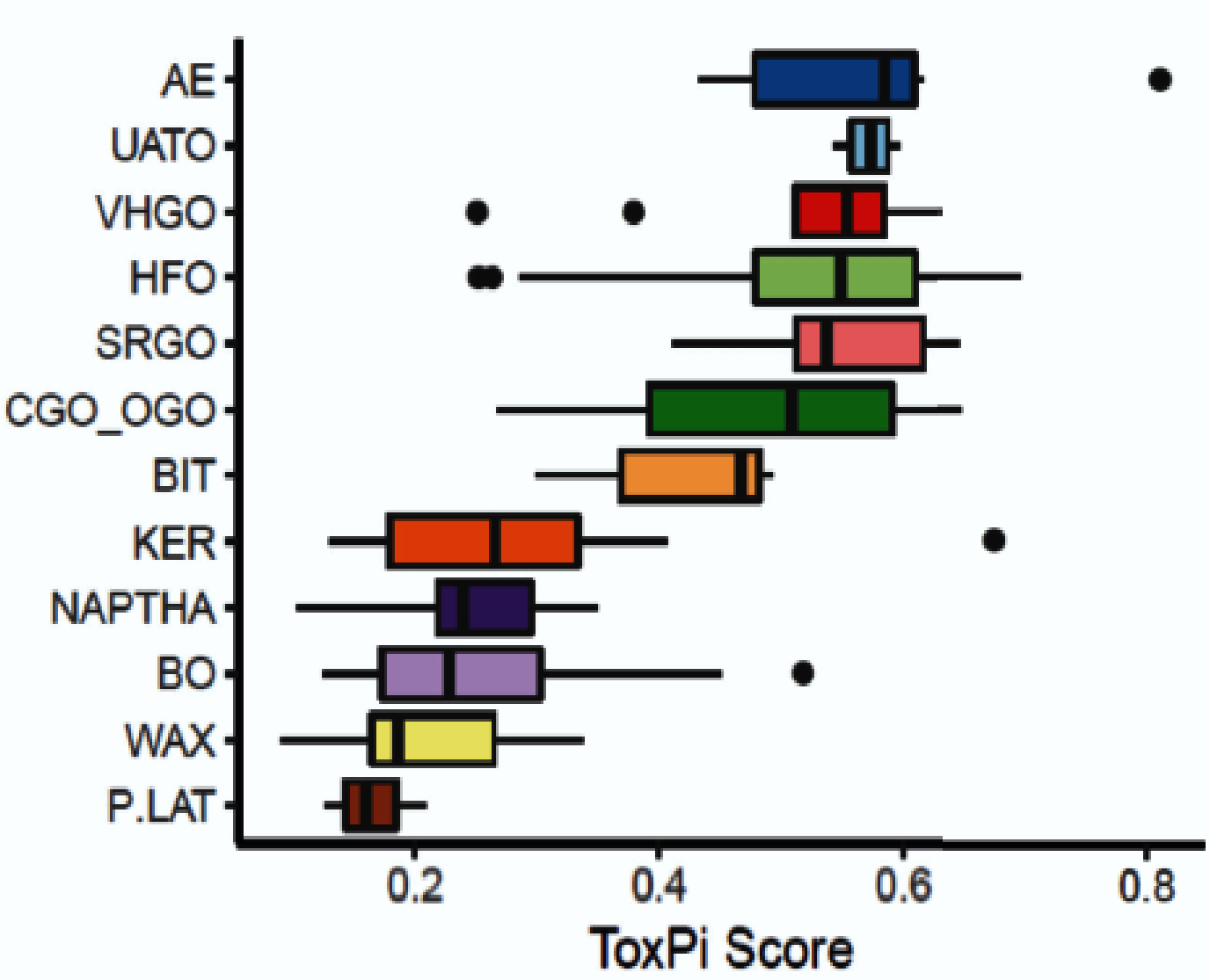


- Petroleum substance categories have been applied in regulatory context for a long time (EU: DSD, 67/548/EEC & ESR, 793/93/EEC; USEPA: HPV program '98)
- Since 2002, we've worked with the European Chemicals Bureau (TC-NES) on the methodology for risk assessment of petroleum substance categories: a risk assessment was done on the LBPN category, according to the TGD for the ESR with Finland as sponsoring Member State
- Similar risk assessment were done on other categories (kerosine, gas oil, bitumen) → same approach applied in REACH dossiers

Where are we now ?

- REACH is now in place and dossier evaluations ongoing → triggered questions from ECHA on robustness of categories
- Questions about chemical similarity → saturated hydrocarbons – which typically form the bulk of the bioavailable substances in the various petroleum categories – determine the physico-chemical properties to a very large extent, whereas other groups of constituents, such as PAH, which may be present at (much) lower levels may pose human health hazards
- This sparked off the idea to *add a biological component* to the other criteria that define a category → CatApp
- CatApp is *not* about hazard assessment, but about *grouping based on biological response*, i.e. adding a biological dimension to the physico-chemical dimension/refining history → broad range of systems and genes to cover a large biological spectrum

Are we there yet ?



- CatApp shows that also from a bio-logical perspective the petroleum substances are a continuum
- There are clear differences in biological activity between the various categories
- Categories may (partially) overlap but some are distinct from one another
- The CatApp data are fully consistent with the prevailing hypothesis on the contribution of certain PAH in the hazard of petroleum substances

Where are we heading ? (1)

Petroleum complex substances

Petroleum complex substances are generally defined by manufacturing and processing conditions, hydrocarbon chemistry (e.g., aliphatic hydrocarbons, aromatic hydrocarbons), physico-chemical properties such as boiling range or carbon-number range, and common use categories. An example of the grouping of petroleum complex substances, developed for the purposes of the Existing Substances Regulation and also used for classification and labelling purposes, is given in Comber and Simpson (2007). According to this approach, petroleum complex substances are grouped according to the process by which they are manufactured, on the assumption that substances within each group (or sub-group) have similar physico-chemical properties and therefore similar intrinsic hazard properties. Within this approach, two substances and a class of chemicals (DMSO extractable PAHs) were used as markers for carcinogenicity, i.e. the presence of one of these substances at a specified level was used to indicate and classify for carcinogenicity. For other classification endpoints read-across between members of the categories has been used and more recently supported by QSAR.

The approach adopted for the petroleum complex substances has more general applicability to UVCBs and should be considered by other industries for which it may be applicable.

ECHA, REACH Guidance on information requirements and chemical safety, Chapter R.6 (2008)

Where are we heading ? (2)

- Our current approach, as shown in CatApp, has wider applicability than just petroleum substances, but should also be applicable to other (types of) UVCBs → LOA consortium
- Potential further analyses on the data generated under CatApp:
- Linking CatApp data to chemical data other than polyaromatics
- Filtering out the gene responses/gene expressions that directly relate to the presence of PAH and investigate whether the remaining data allow (further) confirmation/differentiation of the grouping
- Link the data to other research programmes (e.g. reprotox programme at WUR; 3R-ToxFlow) to formulate hypotheses on potential toxic pathways
- Ultimate goal: select reasonable worst-case substance in each defined category to conduct *in vivo* testing to fulfil REACH requirements

Thank you for your attention

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Cat-App

www.concawe.eu/cat-app