Read-across Estimates of Aquatic Toxicity for Selected Fragrances

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Summary — Read-across as a non-animal testing alternative for the generation of risk assessment data can be useful in those cases where quantitative structure–activity relationship (QSAR) models are not available, or are less well developed. This paper provides read-across case studies for the estimation of the aquatic toxicity of five different fragrance substances, and proposes a pragmatic approach for expressing uncertainty in read-across estimates. The aquatic toxicity estimates and their uncertainties are subsequently used to estimate fresh water compartment Predicted No-Effect Concentrations (PNECs), with their two-sided 90% Confidence Intervals (CIs). These PNECs can be used directly in risk assessment. The results of the musk fragrance read-across cases (musk xylene, musk ketone and galaxolide) are compared to experimentally derived PNEC values. The read-across estimates made by using similarity in a hypothesised mechanism of action for (acute) toxicity of musk xylene gave a PNEC of 2μg/L (90% CI 0.0004–13.5μg/L) with the Species Sensitivity Distribution (SSD) approach. This estimated value is 1.8 times above the experimentally-based fresh water PNEC of 1.1μg/L. For musk ketone and galaxolide, the PNEC values based on the SSD approach and employing a toxicity mechanism-based read-across were 2.0 times greater, and 4.9 times below the experimentally derived PNEC values, respectively.

Key words: aquatic toxicity, andrane, coconut aldehyde, fragrances, galaxolide, musk ketone, musk xylene, PNEC, QSAR, read-across, risk assessment, Species Sensitivity Distribution, SSD, uncertainty.

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Introduction

The European Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulations advocate the use of non-animal testing methods (1), but guidance is needed on how these methods should be used. The EU FP7 CADASTER (CAse Studies on the Development and Application of In Silico Techniques for Environmental Hazard and Risk Assessment) project aims to provide practical guidance on integrated risk assessment by carrying out full hazard and risk assessments based on non-animal testing data, such as QSARs, for chemicals belonging to four compound classes — (benzo)triazoles, polybrominated diphenyl ethers (PBDEs), perfluorinated substances and fragrances (2). In contrast to the other three CADASTER compound classes, the fragrances group is characterised by its diversity of chemical structures. This class of compounds does not share a single specific chemical functionality, but instead, shares its pattern of use, i.e. all the substances are used as fragrances. Therefore, no specific QSAR models that are applicable to the (whole) class of fragrances are available. Broadly applicable QSAR models, which are considered valid for organic chemicals in general, could be used for the prediction of fragrance toxicity. For instance, the ECOSAR model, developed by the US Environmental Protection Agency (EPA), can be seen as this type of more-generalised model (3).

Another option is to use case-specific read-across to generate estimates of (aquatic) toxicity. Read-across is generally defined as a data gap-filling procedure, in which the property of a substance is considered to be equal to (the average toxicity of) sufficiently-similar and relevant analogue substances, for which experimental data are already available. Read-across as a non-testing method for the generation of toxicity data is explicitly mentioned in Annex XI of the REACH legislation (1). Guidance on how to apply read-across is given in a REACH-specific guidance document (4). Definitions for read-across, similar to the description shown above, are also provided in guidance documents from the EPA (5) and the Organisation for Economic Co-operation and Development (OECD; 6). A general description of the possibilities to use read-across within CADASTER was given in a CADASTER report (7).

Fragrances do possess a number of specific structural functionalities, which are often linked to the type of scent they are producing. These main functionalities comprise esters, aldehydes, nitro-musk, and polycyclic musks, and alcohols. If the