

Sufficiency of aquatic hazard data for environmental risk assessment in sediment and soil

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SUMMARY

Aquatic toxicity data are often the dominant or sole source of information on environmental hazards considered in regulatory risk assessments such as those performed under Registration, evaluation, authorisation and restriction of chemicals (REACH). An investigation into the sufficiency of aquatic hazard information for use in environmental risk assessment has therefore been performed.

Available substance toxicity data for the aquatic, terrestrial and sediment compartments from the European Chemicals Agency (ECHA) database of REACH registered substances has been compiled, along with physicochemical properties and predicted no effect concentrations (PNECs). Quantitative comparisons have been performed between experimental data from the aquatic compartment and that of the terrestrial or sediment compartments. Soil and sediment toxicity data and PNECs were converted from bulk mg/kg concentrations to pore water concentrations using equilibrium partitioning theory and compared with aquatic toxicity values. The analysis included both a direct comparison and an assessment of the influence of Verhaar class and various physico-chemical and environmental fate properties.

Direct comparisons of effects in aquatic species and effects in related taxonomic groups in soil or sediment revealed a large amount of scatter in the data and no clear trend. It can however perhaps be said that in most cases data are within two orders of magnitude of the 1:1 line, and that a higher proportion of the data are above, rather than below, the 1:1 line. The latter would indicate that the aquatic toxicity data are more conservative (i.e. lower effect concentration) than the terrestrial/sediment data after having been converted into pore water concentration. In the comparisons with physico-chemical and environmental fate properties, log K_{oc} was found in the first instance to have the most influence on the ratio of aquatic to terrestrial/sediment toxicity but this trend disappeared after some further data screening and the potential reasons for this are discussed. Several assumptions, limitations and potential confounding factors, which may have led to a poor correlation, were also identified and discussed.

Overall, the exercise highlighted the variability inherent to the database used, which is a collection of registration data. A high throughput approach has been applied in the current work. A thorough data quality/reliability analysis would have been optimal, but was outside of the scope of the current report. For any future assessment a more refined data analysis would need to be performed. The limitations and uncertainties in the dataset used limit the ability to draw meaningful conclusions on the mechanistic validity of the equilibrium partitioning theory. However, the results of this present analysis do not refute other equilibrium partitioning method (EPM) studies performed with more appropriate datasets that demonstrate that EPM is fit for purpose to support environmental risk assessments by extrapolating aquatic data to soil and sediment compartments when available information are limited or testing is not feasible. A number of suggestions for further work in this area have been made, including providing a clear rationale to support use of equilibrium partitioning theory for risk assessment.

1. INTRODUCTION

For the assessment of the potential effects of a chemical to the environment, there is much more data available on the aquatic toxicity than on the possible impact on species from other compartments such as soil and sediment. This is because basic environmental risk assessments typically rely on aquatic ecotoxicity data only. Furthermore, the scheme for classification and labelling for environmental hazards uses only aquatic hazard data (together with information on the environmental fate of a substance). Consequently, most information available on the environmental hazard of a chemical are studies performed in aquatic species. Results from non-aquatic testing are rather scarce for some chemicals in REACH.

However, a sound chemical safety assessment according to current understanding, and within present regulatory contexts, requires the coverage of environmental compartments including soil and sediment. In order to make best use of available information and to avoid unnecessary testing, knowledge about the extent to which aquatic hazard information is sufficient for managing risks in other compartments is essential. Currently, there is no clear consensus concerning this question.

This report aims to add scientific information to the discussion. A database of substances for which aquatic ecotoxicity data and soil and/or sediment ecotoxicity data are simultaneously available has been established. The sources of this information were dossiers that have been submitted by industry to support registrations of chemicals under Regulation (EC) No 1907/2006 (REACH). Those data are publicly available and disseminated via the web portal of the European Chemicals Agency (ECHA).

The compiled dataset has been used to address the extent to which the aquatic toxicity of a substance is representative of the effect of a substance towards soil and sediment organisms. Several approaches were applied. The most sensitive effect concentrations observed in aquatic studies were compared with effect concentrations in related taxonomic groups in soil or sediment tests (e.g. effects in aquatic algae vs terrestrial plants), both for acute and chronic exposures, and an attempt was made to reveal correlations. Furthermore, the performance of equilibrium partitioning methodology to extrapolate aquatic hazard information to the soil and sediment compartments – an approach typically used within regulatory frameworks such as REACH – was assessed for different trophic levels. For these purposes, different physico-chemical and environmental fate parameters, substance mode of action and other parameters were considered.

1.1 Terms of reference

The work is based on the following Terms of Reference (ToR):

- 1. Confirm the extent to which the existing system for describing the aquatic hazard of substances is protective for risks in the compartments water, soil, and sediment.
- 2. Explore parameters, e.g. physico-chemical properties, and their importance in the use of aquatic toxicity data to support risk assessment in soil and sediment.

3. Hold a workshop involving stakeholders to discuss the findings¹.

1.2 Expected outcome

- 1. A compilation of toxicity data from REACH database in soil and sediment along with toxicity data for exposure in water.
- 2. Definition of areas where the current aquatic hazard information is appropriate for triggering or waiving of environmental risk assessments.
- 3. Areas (compartments, substance classes, use patterns) identified where the current aquatic information may be insufficient for triggering environmental risk assessment and proposals on how to resolve this.

¹ The ECETOC Task Force attended and contributed to the ECHA Topical Scientific Workshop on Soil Risk Assessment. 7-8 October 2015. Helsinki. https://echa.europa.eu/nl/view-article/-/journal_content/title/topical-scientific-workshopon-soil-risk-assessment

2. METHODOLOGY

2.1 General introduction to the methodology

The aim of the work presented in this report was to investigate if environmental risk assessments for soil and sediment are sufficiently protective of these compartments if they are based on aquatic toxicity data only. When only aquatic toxicity data are available, the methodology that is generally used to assess the hazard towards the soil and sediment compartment is the equilibrium partitioning methodology (EPM).

In sediment (and soil) toxicity studies, relating the total concentration of the chemical in sediment (or soil) to the biological effect of concern has always been problematic (Di Toro et al., 1991). Di Toro et al., (1991) investigated several studies and observed that the toxicity of sediments could differ by a factor of 100 or more for the same total chemical concentration. As such, across different sediment types the observed toxicity could not be correlated to the total chemical concentration in sediment (e.g. as expressed in μg chemical/g sediment). On the other hand, it did prove possible to correlate the toxicity to the interstitial (i.e. pore water) concentration (e.g. as expressed in µg chemical/L pore water). Di Toro et al., (1991) also reported that effect concentrations found for pore water were essentially equal to those obtained from water-only exposures. The authors continue to explain that this can be rationalised by assuming chemical equilibrium between pore water and sediment organic carbon and that the concentrations in the pore water and the organic carbon are related by the partition coefficient K_{oc} . The reason why water-only effect concentrations and sediment exposure effect concentrations on a pore water basis seem to be equal is that the sediment-pore water equilibrium system provides the same exposure as the water-only system (see Figure 1; Di Toro et al., 1991). It is thereby important to note that in the sediment-pore water system exposure to the chemical occurs either from pore water (i.e. via respiration), from sediment carbon via ingestion, or from both. Thus, the pathway of exposure is deemed to be insignificant and the biological effect is produced by the chemical activity of the single phase or the sediment-pore water system in equilibrium (Di Toro et al., 1991). This theory – known as equilibrium partitioning methodology (EPM) - has been used to derive sediment quality standards from aquatic hazard data (van Beelen et al., 2003) and is also the method of choice under REACH (ECHA, 2008) to extrapolate the hazard of chemicals as assessed for aquatic organisms to the hazard towards soil and sediment organisms (in case experimental data on the latter are lacking).

One important observation relating to EPM is that difficulties arise for highly hydrophobic (or other strongly sorbing) chemicals when it comes to the determination of freely dissolved concentrations. The pore water concentration is essentially the sum of the freely dissolved concentration (i.e. the bioavailable fraction that represents the chemical activity) and the concentration of chemical complexed to dissolved organic carbon (DOC). The latter fraction is deemed not to be bioavailable (Di Toro et al., 1991). For highly hydrophobic chemicals, the fraction complexed to DOC can significantly influence the concentration measured in (pore) water, which is then no longer a good estimate of the chemical activity. This may play a role when using measured concentrations of highly hydrophobic chemicals in aquatic toxicity studies as well, which can make any estimates of sediment or soil toxicity through EPM highly uncertain.

Based on the above, the main strategy in the present study was to identify chemicals for which experimental ecotoxicity data exist both for aquatic organisms and sediment and/or soil organisms. The EPM was then used

to express the soil and sediment hazard data in mg chemical per L of pore water. This allows a direct comparison with the aquatic hazard data (expressed in mg chemical per L of water) and makes it possible to study any observed differences. Thereby, the potential influence of several physico-chemical and environmental fate parameters as well as mode of action was assessed.

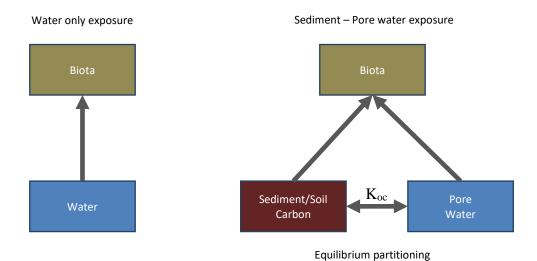


Figure 1. Diagram showing organism exposure routes for water-only exposures (left) and sediment exposures (right). Equilibrium partitioning refers to the assumption that an equilibrium exists between the chemical sorbed to the organic carbon in sediment or soil and the pore water whereby K_{oc} is the partition coefficient. Adapted from Di Toro et al., 1991

An additional concept used to explore the data and identify potential issues related to EPM, is chemical activity. Chemical activity is a concept introduced in 1907 by Gilbert N. Lewis (Lewis, 1907) and is similar to fugacity (Mackay et al., 2010). For a full definition, we refer to other sources (ECETOC (2014), Mackay et al. (2011), Mackay et al. (2010), Mayer and Reichenberg (2006)). As alluded to above, if an equal level of biological effect in a water-only and an equilibrated sediment-pore water system is observed, then the chemical activity of the test chemical in these two systems is expected to be equal. Therefore, the ecotoxicity data collected in the present study were also converted into chemical activity values.

2.2 Equilibrium partitioning theory: Examples from literature

The equilibrium partitioning methodology (EPM) or equilibrium partitioning (EqP) theory was developed around 1990 with the publication from Dominic Di Toro (Di Toro et al., 1991). The assumptions behind this model or theory are:

- A. The exposure of organisms in sediment and soil is mainly via the pore water in sediment or soil.
- B. The concentration in sediment or soil can be derived from the concentration in the aqueous phase (pore water) and the organic carbon normalised sorption coefficient (K_{oc}), assuming that the soil or sediment is in equilibrium with the pore water. K_{oc} values are often estimated from the octanol-water partition coefficient (K_{ow}).

C. Toxicity data in sediment or soil can be derived from experiments with benthic organisms in wateronly tests or from experiments with aquatic organisms assuming that the sensitivity of biota to toxicants in soil or sediment is similar to the sensitivity of aquatic organisms.

In the Di Toro paper, the EPM was successfully applied to different contaminants including classical chlorinated insecticides (DDT (dichlorodiphenyltrichloroethane), kepone, endrin), a number of polycyclic aromatic hydrocarbons (PAHs), organophosphate insecticides and pyrethroids. Since 1991, a number of studies have been published where the EPM was applied and some representative studies are presented in Table 1⁺. The majority of studies were with sediment (eighteen) and fewer with soil (six), and test chemicals mainly included polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs) and chlorinated insecticides. Other studies included pyrethroids, phthalate esters and surfactants. Some studies were focused on just one chemical while other studies included large data sets. Most of these publications confirm the validity of the equilibrium partitioning theory. In a number of cases, deviations from the EPM based predictions could be explained and the following examples are illustrative and insightful:

- i. In a number of cases, the EPM overestimated the toxicity to sediment dwelling species exposed to contaminants in sediment (Driscoll and Landrum, 1997). *Hyalella* is an epibenthic species and epibenthic species live on top of the sediments and are more exposed to the overlying water phase. If the system compartments (sediment, overlying water, organism, and pore water) are all in equilibrium, the concentrations (on a lipid weight basis) of hydrophobic organics in surface deposit and sub-surface feeders will likely be the same. However, if for example the concentration in the overlying water is lower than in the pore-water, the apparent sensitivity of surface deposit feeders will likely be lower. This situation may occur with chemicals that are relatively volatile or that are rapidly degraded in the overlying water phase. A study on the effect of an alcohol ethoxylate with the marine invertebrate *Corophium volutator* (a surface deposit feeder) has demonstrated that the outcome of the test was strongly affected by degradation of this chemical in the overlying water (Droge et al., 2008). This same mechanism may explain that toxicity to a species such as *Hyalella* is lower than predicted via equilibrium partitioning.
- ii. Inconsistent EPM toxicity predictions can result from the organic carbon normalised sediment sorption coefficient (K_{oc}) which are calculated from the octanol-water partition coefficient (K_{ow}). K_{ow}-based models are mainly developed for non-polar organic chemicals and are less suitable for complex molecules and ionised chemicals. The presence of soot in field sediment may also lead to inaccurate estimations of the sediment sorption coefficient because soot has a stronger sorption capacity than organic matter. Including sorption to soot may lead to results that are more consistent with calculations based on the equilibrium partitioning theory (Kukkonen et al., 2005). Also, actual measurement of pore water concentrations may lead to a better agreement of toxicity data (McDonough et al., 2010) or bioaccumulation data with EPM predictions (Kraaij et al., 2003, van der Heijden and Jonker, 2009).

[†] The literature was searched via Web of Science (December 11, 2019) with the following key words: "equilibrium partitioning theory and accumulation" and "equilibrium partitioning theory and toxicity". This resulted in 95 hits and a representative selection is included in Table 1

iii. Deviations of hazardous concentrations (HC), estimated from sensitivity distributions of toxicity data in sediment or soil, from aquatic HC values and EPM may also be caused by differences in sensitivity of aquatic and sediment/soil organisms. Differences in sensitivity can be large in particular for chemicals with a specific mode of action (Vaal et al., 1997). For the estimation of HC values of those chemicals it is important to include a representative sample of species with both target and non-target species (Golsteijn et al., 2013).

The literature examples of studies into equilibrium partitioning show that in general EPM is appropriate. Several studies with a relatively large number of chemicals support the validity of the approach (Golsteijn et al., 2013, Sverdrup et al., 2002, Verbruggen, 2012). Deviations from EPM can be expected for sediments that contain specific sorption phases such as soot or for chemicals that are beyond the domain of applicability of the K_{ow} models to predict K_{oc}. The EPM may also be less applicable to predict toxicity of organisms that live on top of the sediment. These deviations are often observed in cases where one of the three basic assumptions (A-C above) are not met.

Table 1. Representative examples of the application of the equilibrium partitioning methodology (EPM) in the prediction of toxicity in sediment or soil

Results	Type of chemicals	Reference
EPM was applied to derive sediment quality guidelines (SQGs) for thirty-	PAHs and other	(Burgess et al., 2013)
four polycyclic aromatic hydrocarbon (PAHs), thirty-two other organic	organic	
contaminants and seven metals. This study was a theoretical exercise	contaminants	
without a validation of the predictions.		
Exposure in sediment of Chironomus tentans or Hyalella azteca to high	Seven phthalate	(Call et al., 2001)
molecular weight phthalate esters did not affect survival and this was	esters	
consistent with water only tests and EPM. LC_{50} values in sediment for DBP		
(dibutyl phthalate) and <i>H. Azteca</i> were more than thirty times greater than		
predicted by EPM. This discrepancy may be related to the fact that H.		
azteca is an epibenthic species and not an obligative burrower. The LC_{50}		
values for DBP and C. tentans were within a factor of two of the values		
predicted by EqP theory.		
Toxicity of the polycyclic aromatic hydrocarbon (PAH) fluoranthene in	Fluoranthene	(Driscoll and
sediment to freshwater amphipods Diporeia spp. was consistent with EqP		Landrum, 1997)
predictions. EqP overestimated toxicity to Hyalella azteca. Again, this		
discrepancy may be related to the fact that <i>H. azteca</i> is an epibenthic		
species and not an obligative burrower.		
Results of toxicity studies with polychlorinated biphenyls (PCBs) and spiked	PCBs	(Fuchsman et al.,
sediments agreed with EPM predictions. Also, data for toxicity and benthic		2006)
community in eight PCB-contaminated sites agreed with EPM predictions.		
Pore water HC_{50} (hazardous concentrations for 50 % of the species) from		(Golsteijn et al., 2013)
soil toxicity tests for fourty-seven organic chemicals estimated with EPM		
were approximately a factor of three higher than freshwater \mbox{HC}_{50} values.		
The fourty-seven chemicals were grouped according to their mode of		
action using the Verhaar classification system into narcotic, reactive and		
specifically acting chemicals (Verhaar et al., 1992). A recommendation		
from this study is that for chemicals with specific mode of action, it is		

Results	Type of chemicals	Reference
important to include a representative sample of species with both target and non-target species to account for differences in sensitivity.		
Predicted pore water concentration with EPM for DDT, DDE (dichlorodiphenyldichloroethylene) and DDD (dichlorodiphenyldichloroethane) in contaminated field sediments agreed within one order of magnitude with measured pore water concentrations. Pore water LC ₅₀ for DDT and DDD were similar to LC ₅₀ values from water- only tests for <i>Hyalella Azteca</i> .	DDT, DDE and DDD	(Hoke et al., 1994)
Measured pore water concentrations in sediment and bioconcentration factors from pore water could very well predict the bioaccumulation in sediment of chlorobenzenes, PCBs and PAHs in Tubificidae. This indicates that EPM allows a correct representation of bioaccumulation in sediment.	Chlorobenzenes, PCBs and PAHs	(Kraaij et al., 2003)
Biota sediment accumulation factors (BSAF) with <i>Lumbriculus variegatus</i> and <i>Diporeia</i> species in seven sediments dosed with two PCBs and two PAHs were consistent with EPM based predictions if enhanced sorption to black carbon was taken into account.	PAHs and PCB's	(Kukkonen et al., 2005)
Equilibrium partitioning overestimated the toxicity of pyrene (LC_{50}) to <i>Diporeia spp</i> . in sediment with a factor ten. Difference may be due to the behaviour of <i>Diporeia</i> , differential particle-size distribution, and kinetic limitations.	Pyrene	(Landrum et al., 1994)
The bioconcentration factor of low-molecular-weight PAHs from water-only experiments were in the same range as bioaccumulation factors in field-soil experiments with earthworm <i>Lumbricus rubellus</i> , if concentrations were normalised to soil pore water, supporting the EPM theory. Results were less conclusive for benzo[a]pyrene.	PAHs (phenanthrene, fluoranthene, and pyrene, benzo[a]pyrene).	(Ma et al., 1998)
Pore water estimated LC_{50} s of cypermethrin in sediment for <i>Hyalella azteca</i> and <i>Chironomus tentans</i> were similar to effect concentrations from studies in water alone. This is in accordance with the EPM theory.	Cypermethrin (pyrethroid insecticide)	(Maund et al., 2002)
Predictions of toxicity to the freshwater benthic amphipod <i>Hyalella azteca</i> for thirty-four PAHs in sediment samples from twelve field sites were not consistent with EPM if organic carbon-based predictions of pore water concentrations were used. Including sorption to black carbon did not result in better predictions. Only direct measured pore water concentrations were consistent with observed toxicity.	Thirty-four PAHs	(McDonough et al., 2010)
No-effect concentrations (PNECs) in soil and sediment were estimated from aquatic PNECs based on the target lipid model (TLM) and EPM. A comparison with empirical chronic effect levels in soil and sediment showed that this approach was suitable for risk assessment.		(Redman et al., 2014)
Estimated pore water LC ₅₀ of C-12-2-LAS (linear alkylbenzene sulfonate) in a sediment toxicity test with the marine shrimp (<i>Corophium volutator</i>) corresponded well with LC ₅₀ values obtained from water-only exposure and this is in agreement with the EPM.	C12-LAS	(Rico-Rico et al., 2009)

Results	Type of chemicals	Reference
Interstitial water concentrations of fluoranthene predicted with the EPM were similar to measured interstitial concentrations in sediments. The EPM approach correctly predicted the toxicity in sediment toxicity assays with fluoranthene and <i>Hyalella azteca</i> , <i>Daphnia magna</i> , and <i>Chironomus tentans</i> for two out of the thee tested sediments.	Fluoranthene	(Suedel et al., 1993)
The results of a toxicity assay with the springtail <i>Folsomia fimetaria</i> and sixteen PAHs showed that toxicity was governed by the pore water concentration and this supports the equilibrium partitioning approach.	Sixteen PAHs	(Sverdrup et al., 2002)
Measured concentrations of a series of PCBs and chlorinated insecticides in two earthworm species (<i>Eisenia andrei</i> and <i>Aporrectodea caliginosa</i>) from a field contaminated site agreed with estimated concentrations using the EPM. The outcome varied with the model that was applied to estimate the organic carbon sorption coefficient.	PCBs and chlorinated insecticides	(Van der Wal et al., 2004)
Concentrations of PCBs in the lipids of macrophyte shoots from a field site corresponded with EPM predicted concentrations.	PCBs	(Vanier et al., 2001)
Equilibrium partitioning theory was used to derive no-effect levels (NELs) for sediments from aquatic NELs for compounds that act via narcosis. The aquatic NELs were calculated from a model based on the octanol-water partition coefficient (K_{ow}) and species sensitivity distributions for nineteen species.	Chemicals that act via narcosis	(van Leeuwen et al., 1992)
The equilibrium partitioning method was successfully applied to derive quality standards for PAHs in sediment and soil.	PAHs	(Verbruggen, 2012)

2.3 Data gathering

As explained in the introduction of the present report, a main objective of the work was to confirm the extent to which the existing environmental hazard assessment system mainly focused on the hazards of substances towards the aquatic compartment is sufficient to protect the other compartments (i.e. soil and sediment). As a starting point, it was thus needed to identify substances presenting data for at least two compartments; for instance, for both aquatic and terrestrial compartments or for both aquatic and sediment compartments.

Data was sourced via the eChemPortal (OECD, 2014), "a free publicly available access point to information stored across multiple online databases on chemical properties and direct links to collections of information prepared for government chemical review programmes at national, regional, and international levels. The development and maintenance of this resource is under the responsibility of The Organisation for Economic Co-operation and Development (OECD). Access to information on existing chemicals, new industrial chemicals, pesticides and biocides is provided."

In November 2014, 824 153 substances and 822 671 endpoints were covered by the eChemPortal across 30 databases, including the European Chemicals Agency's Dissemination Portal of information on chemical substances registered under REACH (ECHA CHEM). ECHA CHEM contains robust study summaries of all testing data submitted during the registration of substances under REACH and is, to date, the most comprehensive publicly disseminated database of property data for industrial chemicals. This was the primary source of information for the work set out in the present report and was chosen as it represents a recent and comprehensive collection of data. It is also highly relevant as it contains data on chemicals that are currently in commerce. However, it should also be highlighted that this database was not designed to support modelling studies, so the conclusions of work done with this database are limited by the types of data available.

To access information in eChemPortal, two kinds of search can be performed, either using substance identifiers (e.g. search by chemical name, synonym name, CAS number, EC number, etc.), or using specific property criteria (e.g. search for a specific endpoint such as short-term toxicity to fish or toxicity to terrestrial plants).

For the purpose of the present work, the 'property search' was used in order to collect aquatic, terrestrial and sediment toxicity data. A separate search was performed for each compartment focusing on the following endpoints:

- Aquatic compartment:
 - Short-term toxicity to fish,
 - Long-term toxicity to fish,
 - Short-term toxicity to aquatic invertebrates,
 - Long-term toxicity to aquatic invertebrates,
 - Toxicity to aquatic algae and cyanobacteria,
 - Toxicity to aquatic plants other than algae,
 - Toxicity to microorganisms.
- Sediment compartment: only one endpoint called 'Sediment toxicity'.
- Terrestrial toxicity:
 - Toxicity to soil macro-organisms except arthropods,
 - Toxicity to terrestrial arthropods,
 - Toxicity to terrestrial plants,
 - Toxicity to soil microorganisms.

2.4 Data preparation

The resulting Excel database was converted into several tab-delimited text files. As such, separate text files were generated for the physico-chemical and environmental fate data, the aquatic toxicity data, the soil

toxicity data, the sediment toxicity data and the PNEC values. These text files were then further processed using the R statistical program (R Core Team, 2015).

A list of unique CAS numbers was extracted from the database and used as input in EPI Suite[™] (US EPA, 2012) in order to generate SMILES (simplified molecular-input line-entry system) codes for each substance. When a CAS number was missing in the database of EPI Suite[™] (or if the CAS number was reported as incorrect), we did not attempt to acquire the SMILES code via a different method.

2.4.1 Addition of mode of action

The resulting list of SMILES codes was used as input in ToxTree (Patlewicz et al., 2008) in order to generate the mode of action of the substances in the database according to the Verhaar classification scheme (Verhaar et al., 1992). This scheme appoints a chemical to one of 5 different aquatic modes of action:

- 1) Class 1 or "inert" chemicals, which are nonpolar narcosis or baseline toxicity,
- 2) Class 2 or "less inert" chemicals, which are the polar narcotics,
- 3) Class 3 or "reactivity" chemicals, which are typically non-selectively, covalently reactive with protein moieties,
- 4) Class 4 or "specifically-acting" chemicals, which specific reactivity with receptors,
- 5) Class 5 or "unclassified" chemicals.

The SMILES codes were also used as input for ECOSAR, a model part of EPI Suite[™] (US EPA, 2012). In ECOSAR, a model used to predict aquatic toxicity of chemicals, the chemical of interest is first assigned to a chemical class based on its structure. The aquatic toxicity is then predicted using the model for this specific chemical class. This chemical class was extracted from the output of ECOSAR and was used mainly to support the Verhaar classification. In this way, whenever a substance was assigned Verhaar Class 5 and was categorised as a "neutral organic" by ECOSAR, the Verhaar Class 5 was substituted by a Verhaar Class 1. The actual aquatic toxicity predictions made by ECOSAR were not used in this study.

2.4.2 Physico-chemical and environmental fate data

2.4.2.1 Data clean-up and unit conversion

As a first step, all empty records (i.e. entries lacking a numerical value) were deleted. In the initial raw database, all endpoints were present as a single string of text (see column "Value" in Table 2 for examples). As such, the numerical data had to be extracted from this string, effectively separating them from the qualifiers and units. Whenever a range was reported, the average value was calculated for use in the data analysis. Values reported as lower or greater than were removed, as these could potentially skew the results of any statistical analysis. An additional selection was performed by removing entries with data type indications such as "Calc NS", "Calc disregarded", "Exp disregarded", "NS NS" etc. (i.e. data indicated as not having been considered for actual use in

the registration dossier or for which this was not specified). The data preparation steps specific to the different physico-chemical and environmental fate parameters are described below.

Some K_{ow} data entries lacked information on whether the displayed value was logarithmic or not, in which case they were removed. For the K_{oc} data, entry types in which the text strings " K_{oc} ", " K_p " and " K_d " appeared were retained. Where multiple K_{oc} entries were available, an average was used.

Unit conversions were applied so that vapour pressure data were expressed in Pa, Henry's Law constants were expressed in Pa m³ mol⁻¹ and water solubility data were expressed in mg L⁻¹.

Table 2. Examples of entries in selected columns of the datasheets containing physico-chemical/environmental fate parameters

Parameter*	Study Result Type	Value	Туре
Octanol-water partition coefficient	(Q)SAR	316	Kow
Octanol-water partition coefficient	experimental result	ca1.41 ca0.3	$\log K_{ow}$
Organic carbon-water partition coefficient	other: publication	> 202.7 < 456.7	K _{oc}
Organic carbon-water partition coefficient	other: literature review	> 5.37	log K _{oc}
Vapour pressure	other: handbook value	0.00000257 hPa	-
Vapour pressure	no data	0.0106 mm Hg	-
Henry's Law constant	estimated by calculation	0.0154 atm m ³ /mol	-
Henry's Law constant	other: expert judgement	0.00428 Pa m ³ /mol	-
Water solubility	other: secondary source	< 0.00001 mg/L	-
Water solubility	read-across	0.59 0.62 mg/L	-

* This column does not appear as such in the datasheet

2.4.2.2 Data gap filling

As physico-chemical and environmental fate data were missing for a substantial number of chemicals, in part due to the data clean-up described in the previous section, but mostly because these data were not present in the extracted database, values derived from quantitative structure-activity relationships (QSARs) were generated in order to fill the data gaps. To this end, the QSAR models present in EPI Suite[™] (US EPA, 2012) were used in batch mode, using the SMILES code as input. The individual models used are listed in Table 3. As the models in EPI Suite[™] are not suitable for metals and metal compounds, no QSAR data were generated for these substances.

Parameter	Model Name	Version
Kow	KOWWIN	v1.68 (September 2010)
K _{oc}	KOCWIN	v2.00 (September 2010)
Water solubility	WSKOWWIN	v1.42 (September 2010)
Vapour pressure	MPBPWIN	v1.43 (September 2010)
Henry's Law constant	HENRYWIN	v3.20 (March 2011)

Table 3. EPI Suite[™] models used to fill gaps in the physico-chemical/environmental fate dataset

2.4.3 Ecotoxicity data

The ecotoxicity data required some initial clean-up and preparation steps similar to the physico-chemical and environmental fate data: all incomplete records (in this case, records lacking a reported effect concentration) were deleted and the numerical data had to be separated from qualifiers and units (see Tables 4 and 5 for examples of aquatic and soil ecotoxicity entries, respectively). Entries for which no unit was reported were also removed. Values reported as lower or greater than were removed, as these could potentially skew the results of any statistical analysis.

2.4.3.1 Aquatic toxicity data

All aquatic toxicity data were converted into mg L⁻¹. To convert data expressed on a molar basis, the molecular weight as extracted from the EPI Suite[™] software was used.

After unit conversion, the aquatic toxicity dataset was split into separate datasets for fish, invertebrates, algae, aquatic microorganisms and other aquatic plants. Following these initial steps, each new dataset was further separated into subsets for acute and chronic data based on test duration (e.g. 72h, 3d, ...) and endpoint (e.g. EC₅₀, NOEC, ...).

For algae, test durations of 72 and 96 hours were retained for both acute and chronic endpoints. For the acute subset, all entries clearly indicating a half maximal effective concentration (EC_{50}) or half maximal lethal concentration (LC_{50}) were retained (including variations such as ErC_{50} and EbC_{50} which are indicative of the measured effect). For the chronic subset, no-observed effect concentrations (NOEC) and 10% effect concentrations (EC_{10}) were retained (including variations such as ErC_{10} , EbC_{10} , NOECr, etc.).

For invertebrates, test durations from 2 days up to 4 days were retained for the acute endpoints and further including all endpoints indicating a half maximal effective or lethal concentration. For the chronic endpoints, only the endpoint was filtered, retaining EC_{10} and NOEC values.

For acute fish studies, a test duration of 4 days was retained. Further filtering steps on the acute and chronic fish data were similar to the invertebrates' dataset.

Test organism Duration		Nominal/Measured	Endpoint	Effect concentration
Daphnia magna	48 h	Nominal	EC ₅₀	140 mg/L
Crangon crangon	96 h	meas. (TWA)	LC ₅₀	> 100 mg/L
Danio rerio	6 d	meas. (not specified)	other: LC ₂₀	>= 0.71 <= 1 mg/L
Daphnia sp.	48 h	no data	other: MATC	ca. 270 μg/L
Lemna minor	7 d	meas. (arithm. mean)	NOEC	5.3 other: ppm
Salmo salar	6 wk	meas. (initial)	LOEC	162 μmol/L

Table 4. Examples of entries in selected columns of the datasheets containing aquatic toxicity data

2.4.3.2 Soil and sediment toxicity data

As for the physico-chemical, environmental fate and aquatic toxicity data, empty records (i.e. lacking a reported effect concentration) were removed and the numerical values were extracted from the "Effect concentration" field (see Table 5). Only those entries including a specification on whether the endpoint was expressed based on wet or dry weight were retained. Furthermore, only those datapoints for which the unit allowed a conversion into mg kg⁻¹ dry weight were retained. For both soil and sediment data, no specific selection was made in terms of test duration as this would have reduced the number of available datapoints considerably.

Wet weight to dry weight conversion was done using the general methodology and characteristics of soil and sediment as outlined in REACH guidance document R.10 (ECHA, 2008). As such, chemical concentrations in soil on a wet weight basis were converted to dry weight basis by multiplication by a factor 1.13; for sediment, this factor was equal to 4.6.

To make the distinction between acute and chronic data, the endpoint was used (e.g. EC_{50} and LC_{50} values as acute, NOEC and EC_{10} values as chronic).

Test organism	Duration	Nominal/Measured	Endpoint	Effect concentration
Eisenia fetida	48 h	Nominal	LC ₅₀	1 other: 10 μg/cm ²
Lactuca sativa	14 d	meas. (not specified)	EC ₅₀	< 100 other: ug/g soil
other: Earthworm	14 d	Estimated	LC ₁₀₀	60.037 other: mg/l
Folsomia candida	4 wk	meas. (initial)	NOEC	100 mg/kg soil dw
Trogoderma granarium	7 d	no data	other: LD ₉₅	229.7 other: g/m ³
Folsomia sp.	21 d	meas. (arithm. mean)	EC ₁₀	ca. 24 mg/kg soil ww

Table 5. Examples of entries in selected columns of the datasheets containing terrestrial (soil) toxicity data

2.4.3.3 PNEC values

Empty records were removed and the numerical values were extracted from the "PNEC value" field, as for the ecotoxicity and physico-chemical and environmental fate data. PNEC values for the aquatic compartment were all converted to mg L⁻¹, PNEC values for sediment and soil were converted to mg kg⁻¹ dry weight.

2.4.4 Composition of the database

2.4.4.1 Types of chemical compounds

Chemical compounds present in the database were classified according to two well-known classification profilers relating to mode of action; these being ECOSAR (US EPA, 2012) and Verhaar (Verhaar, 1992, Enoch, 2008).

Fifty-nine ECOSAR classes were represented in the database. The most represented class is the neutral organics which cover 23.3% of the substances. 10.2% of the substances from the database belong to the esters class. Six classes each contain between 1 and 5% of the substances from the database (aliphatic amines, amides, inorganic compounds, phenols, aromatic triazines, acrylates). All other classes are represented at less than 1%. Finally, 38.6% of the substances could not be profiled according to ECOSAR classification.

According to Verhaar classification, 33.1% of the substances from the database were not within the scope of this classification scheme. 12.5%, 3.8%, 6.3%, 0.9% and 43.5% of the substances belong to classes 1 to 5, respectively (see Section 2.4.1 for class definitions). This distribution refers to the entire database prior to screening. The unassigned entries could be UVCBs, metal-organic salts, or other special compound types not in the original classification scheme.

2.4.4.2 Types of ecotoxicological data

The kinds of ecotoxicological data available in the database are presented in Table 6.

Compartment	Total number of datapoints (before cleanup)	Total number of datapoints (after cleanup)	Experimental data (%)	Read across (%)	QSAR/ Calculated (%)	Other (%)
Aquatic	69819	65596	69.2	26.6	1.1	3.1
Sediment	5211	3669	83.4	16.5	0.0	0.1
Terrestrial	29357	21012	66.8	33.00	0.0	0.3

Table 6. Numbers, percentages and types of ecotoxicological data contained in the database

As can be seen in Table 6, the clean-up exercise leads to a reduction of 14110 datapoints for the three environmental compartments (representing a reduction of 13.5% compared to the whole initial database). After this step, aquatic ecotoxicity data are the most represented (65596 data; corresponding to 72.7% of the database), followed by terrestrial data (23.3%) and sediment data (4.1%). The partitioning between the different kinds of data (i.e. experimental, read across, QSAR/calculated, other) tends to be similar between the different environmental compartments. Experimental results appear to be the most represented followed by read across. QSAR/calculated and data indicated as "Other" occur at only a minor percentage. It should be noted that the statistics in Table 6 were produced when data on organism groups that were not used for subsequent statistical analysis (e.g. fish, bacteria) were still included.

2.4.4.3 Types of physico-chemical and environmental fate data

The types of physico-chemical and environmental fate data in the database are presented in Table 7.

Parameter	Total data number (before cleanup)	Total data number (after cleanup)	Experimental data (%)	Read across (%)	QSAR/Calc (%)	Other (%)
K _{ow}	3067	2098	42.6	2.7	54.4	0.3
K _{oc}	5622	4068	47.9	4.5	33.2	14.4
Henry's Law constant	678	589	12.7	0.8	80.3	6.1
Vapour pressure	2699	1841	80.4	1.6	16.6	1.4
Water solubility	3066	1849	66.2	1.0	31.6	1.2

Table 7. Numbers, percentages and types of physico-chemical/environmental fate data contained in the database

As can be deduced from the above table, the clean-up exercise leads to a reduction of 4687 datapoints for all the physico-chemical and environmental fate endpoints (representing a reduction of 31.0% compared to the whole initial database). A notable difference with the ecotoxicity data as presented in the previous section, is that with the exception of vapour pressure and water solubility the percentage of experimental data is lower (i.e. between roughly 12 and 50% for Henry's Law constant, K_{ow} and K_{oc}). The percentage obtained through QSAR/calculation is high for Henry's Law constant, which is presumably often derived through calculation based on vapour pressure and water solubility. For all physico-chemical and environmental fate endpoints, it is noteworthy that read-across seems to be used only rarely.

It should be noted that the data presented in Table 7 were generated prior to application of the data gap filling strategy explained in Section 2.4.2.2. As such, the data in Table 7 only cover the data present in the registration dossiers and do not include any of the additional QSAR data that were generated for the purpose of this specific study.

2.4.4.4 Expression of the ecotoxicological data: nominal versus measured concentrations

For each environmental compartment, a closer look was taken at the way the ecotoxicological data were expressed with respect to nominal *versus* measured concentrations. This information is provided in Table 8.

Compartment	Proportion of data expressed in nominal concentration (%)	Proportion of data expressed in measured concentration (%)
Aquatic	28.1	58.6
Sediment	22.6	76.0
Terrestrial	50.8	42.8

Table 8. Proportions of ecotoxicological data expressed in nominal versus measured concentrations

Note that the rows corresponding to the different compartments do not present a total equal to 100% because for some data, there was no information about the way the concentration was expressed.

The numbers in Table 8 are global ones covering the whole set of data for each compartment (both acute and chronic data and all the trophic levels). It thus appears that concentrations are more often expressed on a measured basis when performing aquatic and sediment ecotoxicity studies, and they are more often expressed on a nominal basis when performing terrestrial ecotoxicity studies. However, by going beyond these figures, it appears that the way to express the results is highly endpoint-dependent. For instance, by looking at aquatic ecotoxicity studies, it appears that results from studies on micro-organisms are mainly expressed on a nominal basis (*ca*. 67% of the studies, compared to *ca*. 10% on a measured basis). This is not surprising given that standard test guidelines on aquatic micro-organisms do not recommend a mandatory analytical monitoring of the test chemical. In contrast, results from chronic studies on fish are mainly expressed on a measured basis (*ca*. 83% of the studies, compared to 9.6% on a nominal basis). The same endpoint-dependency is observed for terrestrial ecotoxicity with, for instance, results from acute studies on soil invertebrates more often expressed on a nominal basis (72.8% of the studies) and results from chronic studies on honey bees more often expressed on a measured basis (75.2% of the studies). Endpoint-dependency is also true for sediment where results from acute studies are often expressed on a nominal basis (62.5% of the studies), while results from chronic studies are often expressed on a measured basis (86.8% of the studies).

2.4.4.5 Methodologies of PNEC derivation

Table 9 presents the existing PNEC derivation methodologies and their proportions of use for the different environmental compartments. These different methodologies are defined below:

- Assessment factors method: It consists to calculate the PNEC by dividing the lowest short-term L(E)C₅₀ or long-term NOEC value by an appropriate assessment factor. This method is applicable to all compartments (i.e. water, soil, sediment...), where ecotoxicological data are available for the considered compartments. The assessment factors to apply are defined in the ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.10 Characterisation of dose [concentration] - response for environment (ECHA, 2008). These assessment factors reflect the degree of uncertainty in extrapolation from laboratory toxicity test data for a limited number of species to the 'real' environment. For example, an assessment factor of 1000 should be used if an aquatic dataset contains only acute data for the three trophic levels (*i.e.* fish, aquatic invertebrates, algae), while an assessment factor of 10 should be used if chronic data are available for the three trophic levels. In this example, results of chronic tests trigger lower, and thus less severe, assessment factors than results of acute tests because they give a more realistic picture of effects on the organisms during their entire life cycle. As another example, an assessment factor of 100 should be used if a soil dataset contains chronic data for only one trophic level (e.g. terrestrial plants), while an assessment factor of 50 should be used if chronic data are available for two trophic levels (e.g. terrestrial plants and terrestrial invertebrates). To sum up, the wider the database, the lower will be the assessment factor and typically the less severe (*i.e.* the highest) will be the PNEC.
- Equilibrium partitioning method: Chapter R.10 of ECHA Guidance on Information Requirements and Chemical Safety Assessment (ECHA, 2008) defines this method as follows: "In the absence of any ecotoxicological data for sediment- or soil-dwelling organisms, the PNEC [*for these compartments*] may be provisionally calculated using the equilibrium partitioning method (EPM). This method uses the PNEC_{water} for aquatic organisms and the suspended matter/water and the soil/water partitioning coefficient as inputs." By

definition, this method is only applicable to soil and sediment compartments. The underlying calculation formulas are based on considerations from Section 2.1 and are the following:

$$PNEC_{sed} = \frac{Ksusp-water}{RHOsusp} \times PNEC_{water} \times 1000 \quad \text{and} \quad PNEC_{soil} = \frac{Ksoil-water}{RHOsoil} \times PNEC_{water} \times 1000$$

in which

- PNECwater is the PNEC for aquatic organisms derived using the assessment factor method (mg/L),
- RHO_{susp} and RHO_{soil} are the bulk densities of wet suspended matter and wet soil, respectively (kg/m³),
- $K_{susp-water}$ and $K_{soil-water}$ are the partition coefficients suspended matter-water and soil-water, respectively (m³/m³),
- *PNEC_{sed}* and *PNEC_{soil}* are respectively the PNEC for sediment- and soil-dwelling organisms derived using the equilibrium partitioning method (mg/kg ww).

Statistical extrapolation method (= sensitivity distribution method): Chapter R.10 of ECHA Guidance on Information Requirements and Chemical Safety Assessment (ECHA, 2008) defines this method as follows: "The sensitivity distribution methods are based on statistical calculations and usually require experimentally determined NOEC values for a number of species from different taxonomic groups [*at least 10 NOECs (preferably more than 15) for different species covering at least 8 taxonomic groups*]. These methods aim at calculating a concentration [*a PNEC*] which is assumed to protect a certain percentage (*e.g.* 95%) of the species of the ecosystem against toxic effects. [...] The main underlying assumptions of the statistical extrapolation methods are as follows: the distribution of species sensitivities follows a theoretical distribution function; the group of species tested in the laboratory is a random sample of this distribution. [...]. In general, the methods work as follows: long-term toxicity data are log transformed and fitted according to the distribution function and a prescribed percentile of that distribution is used as criterion [*for setting the PNEC*]." This method is applicable to all compartments (*i.e.* water, soil, sediment...) where sufficient ecotoxicological data are available.

PNEC derivation methodology	Freshwater	Saltwater	Freshwater sediment	Marine water sediment	Soil
Assessment factors	75.1	78.2	21.9	22.7	50.4
Equilibrium partitioning	Not applicable	Not applicable	60.9	60.7	26.9
Statistical extrapolation	19.1	16.3	9.5	9.2	14.8
Unknown methodology	5.9	5.4	7.7	7.5	8.4

Table 9. PNEC derivation methodologies and proportions of use for the different environmental compartments

The assessment factor method clearly appears to be the most common method when deriving a PNEC for the aquatic medium. In contrast, the equilibrium partitioning method is the most common one when deriving a PNEC for the sediment. The latter is probably due to the fact that sediment ecotoxicity data are only required in the highest REACH Annex (highest tonnage band). For soil, the assessment factor method is the most common one, even though PNEC derivation through equilibrium partitioning is also possible. Finally, whatever

the environmental compartment, statistical extrapolation is used at a non-negligible extent, even though this method requires a considerable number of ecotoxicological data.

2.5 Screening criteria for dataset refinement

After the initial data preparation steps described in Section 2.4, the data in the database were subjected to a limited number of selection and screening criteria. The goal of this further data selection/screening was to: (1) remove ecotoxicological data of which the reported endpoint (E(L)C50, NOEC, ...) was above the chemical's solubility in the respective matrix (see Section 2.5.1); (2) screen out chemicals with problematic values for K_{oc} and/or K_{ow} (see Section 2.5.2); and (3) make a selection of chemical types not/less suitable for application of EPM (see Section 2.5.3).

2.5.1 Chemical activity screening

All the ecotoxicity data were converted into chemical activity. For aquatic toxicity data, this was done using the following formula:

$$a = \frac{EC}{S_w}$$

in which

- *a* is the chemical activity,
- EC is the effect concentration (mg/L) and
- S_w is the water solubility of the respective chemical.

In case a substance is a solid at ambient temperature (here 20°C was used), the subcooled liquid state solubility should be used instead of the regular water solubility. To this end, additional data on the substances' melting point was needed, which was obtained from the MPBPWin model (v1.43) available in EPI SuiteTM (US EPA, 2012). If a substance's melting point was higher than the ambient temperature, its subcooled liquid state solubility S_{w.ss} was calculated as follows (Thomas et al., 2015):

$$S_{w,SS} = \frac{S_w}{F}$$

in which

• F is the fugacity ratio, estimated with the following equation:

$$F = e^{-6.79\left(\frac{T_M}{T} - 1\right)}$$

whereby

• T_M is the substance's melting point (units K),

• T is the ambient temperature (293 K).

The factor 6.79 is the ratio between the entropy of fusion at the melting point (DS; units J mol⁻¹ K⁻¹) and the gas constant (R; 8.314 J mol⁻¹ K⁻¹). In some cases, DS can be assumed to have a value of 56.5 J mol⁻¹ K⁻¹ (Thomas et al., 2015).

For soil and sediment toxicity data, the conversion was similar but instead of the water solubility (S_w) , the substance's solubility in soil (S_{soil}) or sediment $(S_{sediment})$ was used. S_{soil} and $S_{sediment}$ were calculated based on S_w , the organic carbon-water partition coefficient K_{oc} and the fraction of organic carbon in soil or sediment f_{oc} :

$$S_{soil/sediment} = K_{oc} \cdot f_{oc} \cdot S_w$$

In case a respective chemical's melting point was higher than the ambient temperature, $S_{w,ss}$ was used instead of S_w . To calculate the chemical activity of a chemical in soil or sediment, its concentration (e.g. its effect concentration) was divided by S_{soil} or $S_{sediment}$.

A chemical activity greater than 1 indicates a substance is present at levels above its solubility in the respective matrix (water, soil, sediment, ...). Effect concentrations with a chemical activity greater than 1 were therefore removed from the database.

2.5.2 Koc/Kow quality screening

A detailed quality assessment of physico-chemical and environmental fate data was outside the scope of this work, but a rough quality screening assessment was made on K_{oc} and K_{ow} values. To this end, the final K_{oc} and K_{ow} values obtained in the data preparation step (Section 2.4) were compared to modelled values obtained with KOCWIN and KOWWIN. Differences greater than 10-fold between the values from the database and the modelled values were used to screen for any potential anomalies.

As the initial number of chemicals was too large to assess each individual chemical's dataset for its suitability, large differences between observed and predicted K_{oc} and K_{ow} values, as well as abnormal differences between K_{oc} and K_{ow} values, were used to identify potential problem cases.

2.5.3 Chemical type screening

lonisable substances, reactive chemicals (which could lead to uncertainty on what exactly was tested) etc. were identified by their SMILES and were removed from the database. Sorption behaviour of ionisable substances can be much different than expected based on their K_{oc} values and ECHA guidance already specifically requests experimental soil toxicity data on such substances. This screening step was done simultaneously with the K_{oc} / K_{ow} quality screening described in Section 2.5.2 whereby based on chemical type, it was decided if the removal of substances with diverging data was justified or if a modelled value could be used.

2.6 Statistics

2.6.1 Data conversion – Equilibrium partitioning

In order to express all ecotoxicity data in similar units, soil and sediment ecotoxicity data were converted into mg L⁻¹ pore water, using the equilibrium partitioning methodology described in ECHA guidance documents R.10 (ECHA, 2008) and R.16 (ECHA, 2011).

Ecotoxicity data for soil expressed in mg kg⁻¹ soil dry weight, were converted using the following formula:

$$EC_{soil,pw} = \frac{EC_{soil} \cdot RHO_{soil}}{K_{soil,water} \cdot 1000} = \frac{EC_{soil} \cdot RHO_{soil}}{\left(\frac{K_{oc} \cdot f_{oc,soil}}{1000} \cdot f_{solid,soil} \cdot RHO_{solid}\right) \cdot 1000}$$

in which

- EC_{soil,pw} is the effect concentration in a soil organism expressed in mg L⁻¹ pore water,
- EC_{soil} is the effect concentration in a soil organism expressed in mg kg⁻¹ soil (wet weight),
- RHO_{soil} is the bulk density of wet soil (kg_{soil} m⁻³soil),
- K_{oc} is the organic carbon-water partition coefficient (L kg⁻¹),
- f_{oc,soil} is the weight fraction of organic carbon in soil solids (kg_{oc} kg_{solid}⁻¹),
- f_{solid,soil} is the volume fraction of solids in soil (m_{solid}³ m_{soil}⁻³), and
- RHO_{solid} is the density of the solid phase (kg_{solid} m_{solid}⁻³)

(see Table 10 for the values used for RHO_{comp} , $f_{oc, comp}$, $f_{solid, comp}$ and RHO_{solid}).

It should be noted that this formula deviates from the formula presented in the ECHA guidance documents in the sense that no repartitioning of the substance to air and water is assumed. In other words, the EC_{soil} is assumed to be a concentration in dry soil at equilibrium conditions. Therefore, the EC_{soil,pw} is calculated as the concentration that is expected in the pore water at the given concentration in dry soil assuming equilibrium. As such, two parts included in the formulas in the ECHA guidance documents are missing, namely the fraction of water in soil as well as the part describing the repartitioning of the substance into the air compartment. These two parts were left out for reasons of simplicity as well as to reduce the dependency on QSAR values for Henry's Law constant. For the latter, only few experimental values were available and with the inclusion of modelled data the risk of introducing too much uncertainty was high.

For sediment ecotoxicity data, the same formula as for soil was used with different values specific for the sediment compartment (see Table 10).

	Symbol	Value for soil	Value for sediment	Unit
Bulk density, wet	RHO _{soil or sed}	1700	1300	[kg _{soil/sed} m ⁻³ soil/sed]
Density of the solid phase	RHO _{solid}	2500	2500	[kg _{solid} m _{solid} -3]
Weight fraction of organic carbon	$f_{\text{oc,soil or sed}}$	0.02	0.05	[kg _{oc} kg _{solid} ⁻¹]
Volume fraction of solids	${f f}_{solids,soil\ or\ sed}$	0.6	0.2	$[m_{solid}^3 m_{soil/sed}^{-3}]$

Table 10. Characteristics of soil and sediment used in the equilibrium partitioning calculations (ECHA, 2008 & 2011)

2.6.2 Correlations/regressions

To investigate the influence of mode of action and physico-chemical and environmental fate parameters on the accuracy of the equilibrium partitioning methodology (EPM), the difference between aquatic effect concentrations in mg L^{-1} water and the effect concentrations for soil/sediment organisms in mg L^{-1} pore water was expressed as the ratio between these two:

$$\Delta EPM = Log \frac{EC_{aquatic}}{EC_{soil/sediment}}$$

with

- EC_{aquatic} as the effect concentrations for aquatic organisms and
- EC_{soil/sediment} as the effect concentration for either sediment or soil organisms.

This ratio was calculated per trophic level and separately for acute and chronic data (i.e. using EC₅₀ / LC₅₀ values for acute data and NOEC / EC₁₀ values for chronic data). That means that for a given chemical for which a complete aquatic and terrestrial/sediment dataset was available, algal data were compared with terrestrial plant data, whereas aquatic invertebrates were compared with sediment invertebrates and soil invertebrates (separately). The correlation of this ratio with physico-chemical and environmental fate parameters and mode of action (Verhaar class) was determined. This was done to identify characteristics of substances (if any) that help explain potential deviations of experimental soil and sediment toxicity data from what the EPM theory predicts.

2.7 Assumptions and limitations

A very large dataset has been gathered, processed and analysed. It should be recognised that a number of assumptions needed to be made for this work to be practically possible, and that there are also therefore some limitations associated with the findings. These are listed below:

1. The data from the ECHA CHEM database are accurate and reliable

The ECHA CHEM database has formed the primary source of information for this work set out in the present report. The information in this database is that which has been submitted by industry for registrations under REACH. In these registrations, the registrant is expected to review all available data and assess their reliability.

The database query was set to include all experimental results regardless of the Klimisch score. All the original data that have been collected have not been modified, other than to convert units and screen out unsuitable data. There is therefore the assumption that these data are reliable and have been accurately input reported into the ECHA database. This assumption was made for all data taken from the ECHA database, such as flags for analytical monitoring etc. This introduces some uncertainty into the present work. However, it is expected to be mitigated by the screening criteria applied to the database. Also, in the cases of multiple entries, the lowest toxicity values were used.

It must be recognised that this will not always be the case and that some inappropriate data will have been included in the dataset, due to both unreliability of studies as well as incorrect recording of data in registration dossiers. For instance, recording into an erroneous field, could have an impact on the content of the dataset because data were extracted with an automated tool thus assuming that the data was present in the right field. If data were recorded into an erroneous field, some data could have been omitted. It is not clear how often such issues occur.

In addition to the reliability of the data themselves and the way they were reported into the registration dossiers, attention must also be paid to the limitations that can arise from the way the threshold values, like PNECs, have been calculated. For example, some erroneous values could have been included in the dataset if the registrants did not apply correctly the ECHA R.10 guidance when selecting the assessment factors and/or the ecotoxicological data underlying the PNECs. This limitation is also applicable in the case of PNEC derived from the EPM if not calculated correctly or based on improper data.

Further examples of data quality issues that were evident in the dataset were where NOEC values from limit tests, where no toxic effects were observed, may have been used as point estimates for toxicity in the plots. This could give the indication that substances were toxic where no toxicity was observed, and lead to false conclusions. As was noted in section 2.4.2.1 values indicated as ">" or "<" were removed, but NOEC values that are equal to the highest dose tested should not be indicated with the ">" sign. As such, they would not be screened out with the automatic, high throughput approach used for this study.

The dose response and supporting study meta-data are also not available through the ECHA portal to critically evaluate the reported values.

Additionally, for some groups of compounds the dataset available for the full series of substances is included in each substance registration dossier. In these cases, the effect data for the substance could not be distinguished from the data for other related substances, and this could contribute to bias and/or artefacts in the plots. Overall, these situations are expected to be limited and unlikely to have a large impact on the overall conclusions from such a large dataset, but are still worthy of mention from the outset.

2. The substances included in the database are representative of the broad range of chemicals on the market

The following aspects in relation to the substances and data available on the ECHA CHEM database need to be recognised:

- a) REACH is an EU regulation and concerns substances manufactured or imported to the EU. Therefore, only these substances will have data on the ECHA CHEM database. It is reasonable to assume that the EU market will contain a sufficiently broad mix of chemicals used globally.
- b) The test requirements related to tonnage bands outlined in the REACH regulation only require data on sediment and long-term terrestrial toxicity for substances manufactured/imported at ≥ 1000 tonnes per annum. This means that the majority of these data are only expected to be available for such 'high tonnage' substances.
- c) The REACH regulation concerns industrial chemicals only, meaning that chemicals used in other sectors (e.g. pharmaceuticals and agrochemicals) are generally not included in the database.
- 3. Where QSAR were used to generate property data, the substances for which these were generated were within the applicability domains of the models

A full set of reliable physico-chemical property data were not available for all substances and in some cases data gaps were filled with QSAR in order to perform further calculations and analysis. In particular, log K_{oc} was essential to calculate the pore water concentrations for soil and sediment toxicity data in order to compare these with aquatic toxicity data. No assessment was made as to whether the substance was within the applicability domain of the models used. In reality, certain types of substances are likely to fall outside these applicability domains and some calculated physico-chemical properties may be unrealistic. This was evidenced in some of the plots, where extreme predicted log K_{oc} values for some substances resulted in outliers, with a large disparity between their aquatic effect concentrations and their pore water effect concentrations calculated based on EPM. This could be exacerbated where high K_{oc} substances were non-toxic in limit tests, whose data might have been taken as point estimates of toxicity (as mentioned under point 1), leading to significant extrapolations of values which already underestimate toxic concentrations. As discussed in Sections 2.5.2 and 2.5.3 large differences (greater than 10-fold) between observed and predicted K_{oc} and K_{ow} values, as well as abnormal differences between K_{oc} and K_{ow} values, were used to identify potential problem cases. Some of this uncertainty was mitigated through the chemical activity-based screening.

4. The EPM was appropriate to derive PNECs and effective pore water concentrations from soil and sediment data for all substances

EPM can be used to calculate pore water concentrations of substances, and to convert aquatic PNECs to soil or sediment PNECs, on the basis that exposure is due to the concentration of the substance in the aqueous (pore water) phase. This analysis assumes that the equilibrium partitioning method (EPM) is suitable for all substances in the database, whereas it is recognised that this is less well established for strongly lipophilic (log $K_{ow} > 5$) substances or substances with specific binding properties. However, prior work does suggest that the EPM method is applicable to higher log K_{ow} chemicals (Redman et al 2014; Verbruggen 2012). This analysis also assumes that all soils/sediments used in the available data will be of a standard organic carbon content because most data are expected to be developed with OECD-like standard methods. Any deviations from the standards assumed in the EPM calculation will result in a corresponding over/underestimation in the pore water concentration. The validity of this assumption will depend on the methods used in these experimental tests, and whether artificial or natural soils were used as the substrate. There are likely deviations from these assumptions (e.g. organic carbon contents deviating from standard values) that will contribute to the overall variability in the dataset used in this study.

5. The simplification of the equilibrium partitioning formula has no incidence on the results

As explained in Section 2.6.1, the applied equilibrium partitioning formula deviates from the one presented in the ECHA guidance documents in the sense that some equation parts are missing, namely the fraction of water in soil or sediment as well as the part describing the repartitioning of the substance into the air compartment. These parts were left out for reasons of simplicity (e.g., K_{oc} continues to be the main driver) as well as to reduce the dependency on QSAR values for Henry's Law constant for which only little experimental values were available. The simplified formula hence obtained allowed to convert soil and sediment ecotoxicity data in a similar unit (mg L⁻¹ pore water) to the aquatic ecotoxicity data. As indicated in Section 2.6.2, effect concentrations for aquatic organisms in mg L⁻¹ water and effect concentrations for soil/sediment organisms in mg L⁻¹ pore water were then processed to calculate a ratio which was correlated with physico-chemical parameters and mode of action (Verhaar class). In order to determine whether using the simplified formula had some incidence on the results, the correlation exercises were performed with both the simplified and full equilibrium partitioning formula (data not shown). This reveals that whatever the simplified or the full formula was used, the trends observed with respect to the correlations were the same; leading to the conclusions that there was no concern to use the simplified formula in this context.

6. Broad screening approaches used to 'clean' the database may have removed valid data that were incorrectly added

An extensive data clean-up exercise was performed (described in Section 2.4) to screen out data that was not suitable for the analysis. Reasons for excluding data included non-standard species and study durations, and lack of specifying wet weight/dry weight for effect concentrations in soil and sediment toxicity studies. If data were not recorded correctly in the ECHA database, as discussed in point 1 above, this could have led to valid data being removed.

7. Some experimental studies have been read-across to other substances, and these data have been counted multiple times

For purposes of the analysis, read-across data judged as suitable for a substance was treated in the same way as experimental data for that substance. This allowed more substances to be used in the comparison of aquatic toxicity and soil/sediment toxicity. However, it also led to cases where a single experimental result would have been used multiple times. This could have an effect of skewing the analysis, particularly if read-across was extensive. Analysis of the ECHA CHEM database performed by ECHA found that publicly available studies account for more than 60% of endpoint study records for terrestrial toxicity, and that in most cases the same publication was submitted multiple times for different substances, dossiers, or endpoint study records (Jevtić, 2015). In practice it is difficult to identify entries based on read-across. Obvious instances of read-across were removed, but otherwise this remains some source of uncertainty. The small size, and heterogeneous nature, of the final database used in the present work suggests that potential bias would be negligible.

8. A NOEC for a soil/sediment study is assumed to be a chronic endpoint

During the data clean-up, all NOECs for soil and sediment experimental studies were assumed to qualify as chronic endpoints. This was due to the fact that data could not be standardised by duration or guideline. In reality, some of these may have been reported in what are considered to be acute studies. The number of results from acute studies that have been identified as chronic results, or the impact of this, is not known. However, it is perhaps sensible to expect that these results would be less conservative than true chronic results, due to their shorter timescales and often more severe endpoints (e.g. lethality).

3. **RESULTS**

3.1 Outcome of data screening

As briefly highlighted in Section 2.1, if an aquatic and (for instance) a sediment dwelling organism are equally sensitive to a certain chemical and the same level of biological effect (e.g. 50% mortality) is observed in their respective test systems (i.e. a water-only exposure and a sediment-water system), then the chemical activity in both systems should be equal. Therefore, if the above holds true, EC_{50} s of a chemical for an aquatic and a soil species (for instance) are expected to be equal if converted to chemical activity. It should be stressed again that this is the main principle underlying the EPM. The calculation of chemical activity is relatively simple, as it is the ratio between a chemical's effect concentration and its solubility in the respective matrix (water, soil, sediment, etc.). Therefore, the conversion of the data into chemical activity was deemed useful for two purposes:

- 1. Following logically from the way it is calculated, a chemical activity greater than 1 indicates a substance would be present at a level exceeding its solubility, which is a direct indication of such a value's unreliability.
- 2. The effect concentrations as converted into chemical activity can be used to compare observations made about chemical activity in studies in which only carefully selected concentration data were used (i.e. values strictly indicative of freely dissolved concentrations).

Of course, an important requirement for the derivation of chemical activity is having a reliable concentration as a starting point, meaning a measured concentration that only includes the fraction of the chemical dissolved in the respective matrix. If that matrix is water for instance, this means that the concentration has to represent the freely dissolved concentration of the chemical.

Table 11 provides information on the total number of datapoints in each of the environmental toxicity datasets (aquatic, terrestrial and sediment) after the data preparation (see Section 2.4) and the results of the quality screening based on chemical activity (α , see Section 2.5.1). For those substances for which the chemical activity could be calculated, between roughly 15 and 30% of the datapoints had a corresponding value for α greater than 1.

Toxicity Data Type	Total Number of datapoints (after data preparation steps)	Total number of substances (after data preparation steps)	Number of substances with data at $\alpha \leq 1$	Percentage of datapoints with a $\alpha > 1^*$
Aquatic	51435	632	277	14.5
Terrestrial	17526	418	148	25.8
Sediment	3221	206	58	28.9

Table 11. Total number of datapoints and unique substances in the database (after data preparation steps) and the effect of the chemical activity screening on the number of substances remaining. The last column indicates the percentage of datapoints removed for further analysis due to having a chemical activity (α) greater than 1.

^{*}It was not possible to generate chemical activity data for all substances; to calculate the percentage of datapoints with $\alpha > 1$ such chemicals were not included

Studies in which chemical activity was used to investigate the aquatic toxicity of baseline toxicants, report that in general toxicity was exerted at chemical activity levels between 0.01 and 0.1 (Bobra et al. (1983), Reichenberg and Mayer (2006), Mayer and Reichenberg (2006)). This was found to apply for acute toxicity to algae (Mayer and Reichenberg, 2006), invertebrates (Bobra et al., 1983) and fish (Mayer and Reichenberg, 2006). Reichenberg and Mayer (2006) illustrated that this principle seems to hold for acute toxicity to tadpoles and mice, with exposure via the air in the case of the latter. In light of this, it is interesting to observe that in the current analysis the Verhaar Class 1 chemicals exerted acute toxicity generally between 0.01 and 0.1 for the aquatic algae and invertebrates (see Figure 2a). For plants and soil invertebrates, the majority of E/LC₅₀ values expressed as chemical activity were lower than 0.01 and higher than 0.1, respectively.

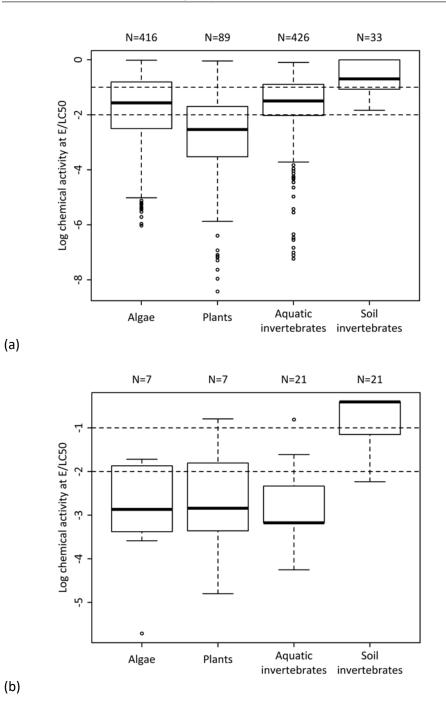


Figure 2. Boxplots (representing median, 1^{st} and 3^{rd} quartile; whiskers extend up to 1.5 times the interquartile range) of the logarithm of the chemical activity at E/LC_{50} of Verhaar Class I substances for different trophic levels in the aquatic and soil compartment. (a): Representing all effect concentration data. (b): Representing the finally retained effect concentration data (i.e. the lowest available effect concentrations). The two horizontal dashed lines indicate a chemical activity between 0.01 and 0.1. N: number of datapoints.

Assuming that the above-mentioned rule that baseline toxicants exert toxicity at chemical activities between 0.1 and 0.01 holds true, study design flaws could cause the observed deviation of the effect concentrations for plants and soil invertebrates, leading to the lower or higher chemical activities than normally expected for Verhaar Class I substances at acute toxicity levels. Nonetheless, while some study design flaws may lead to an

overestimation of the toxicity, the usual shortcomings such as the use of nominal exposure data or the failure to take into account fractions sorbed to DOC, would rather lead to an underestimation of the toxicity.

Interesting to note is also that the conservative practices used in risk assessments (i.e. the use of the lowest of the available and reliable effect concentrations) lead to the use of acute effect concentrations reflective of a chemical activity much below 0.01 (see Figure 2b). The same approach of selecting the lowest available effect concentration data was used when making comparisons between aquatic and soil or sediment studies (see Sections 3.2). Logically, the more toxicity values available, the higher the probability that the minimum value will significantly deviate from the mean. In other words, extremely low values are more likely to occur in larger datasets (Smith and Cairns, 1993). This is illustrated in the left graph of Figure 3 in which it is shown that while very low values can occur when a limited number of studies is available, this appears to more consistently occur as the number of available studies increases. It is potentially the combination of increased uncertainty due to experimental artefacts (see Section 2.7) and the practice in risk assessment of selecting the lowest (i.e. most conservative) value that is partly responsible for the trends observed in this study. In the right graph of Figure 3, the effect of using either the geometric mean or the arithmetic mean (rather than the minimum) of the available E/LC₅₀ values is illustrated. The geometric mean is an often-used summary statistic for ecotoxicity data (Stephen et al., 1985), but is also known to be biased low (Parkhurst, 1998). While this conservative property of the geometric mean can be desirable for environmental risk assessments, it may similarly lead to unrealistically low values that are less suitable to conduct analysis such as the one in this study. The arithmetic mean generally leads to higher and more realistic values. Whereas a more in-depth analysis of the underlying cause was outside of the scope of the work set out in the present report, it should be clear from these observations that the choice of the value used (i.e. minimum, geometric or arithmetic mean) can potentially have a significant impact on any analysis in which these values are used. It would therefore be highly recommended to include an assessment of the potential magnitude of this in any future studies.

This observation highlights that critical evaluation of EPM requires critical evaluation of the studies behind it.

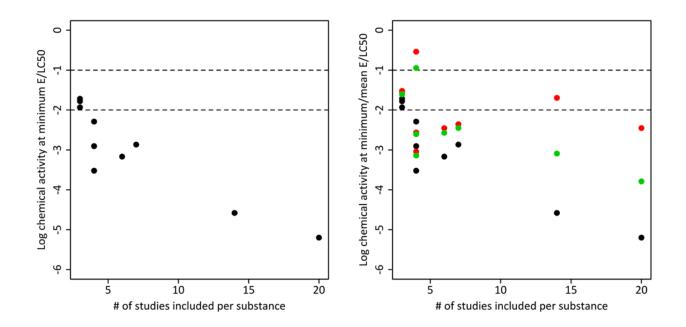


Figure 3. Left: Chemical activity of Verhaar Class I substances at minimum E/LC_{50} as derived from 72h and 96h algal growth inhibition studies plotted in function of the number of studies it was derived from (substances for which less than 3 algal studies were available are not included). Right: Same as the left graph, except the chemical activities were added in case the geometric mean (green) and the arithmetic mean (red) of the available E/LC_{50} s was used to derive it. In both graphs, the dashed lines indicate a chemical activity between 0.01 and 0.1.

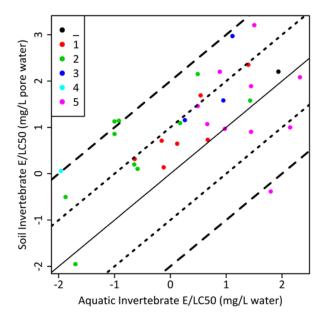
In addition to screening out effect concentrations at chemical activities greater than one, over all the datasets combined a further list of 46 chemicals was removed from the analysis based on the physico-chemical (i.e. removal of problem cases identified through anomalous K_{ow} and/or K_{oc} values) and chemical type (i.e. removal of ionisable and reactive chemicals) screening exercises described in Sections 2.5.2 and 2.5.3.

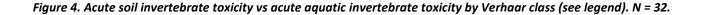
3.2 Direct comparisons of levels of toxicity in aquatic and soil/sediment compartments

In order to make a comparison of acute and chronic levels of toxicity shown by a chemical in water and soil/sediment, effect data available for substances in both compartments have been selected from the database. Where more than one effect value per compartment and exposure duration was available for a substance, e.g. from studies using different species and/or trophic levels, the lowest value obtained (i.e. indicating highest toxicity) was used for analysis. This was done in accordance with current environmental risk assessment practices and thus keep this study in line with the methodologies used for the regulatory submissions as prepared by the REACH registrants.

Direct comparisons have been made between aquatic toxicity and terrestrial/sediment toxicity to assess how comparable these results are. In order to do this, terrestrial and sediment toxicity results were converted into pore water concentrations using the methodology described in Section 2.6.1. For comparison purposes, taxa from the aquatic compartment have been grouped with similar taxa from the soil or sediment compartment, e.g. aquatic invertebrates with terrestrial invertebrates, aquatic algae with terrestrial plants, aquatic invertebrates with sediment invertebrates. In these comparisons, terrestrial/sediment toxicity (mg L⁻¹, pore water) was plotted against aquatic toxicity (mg L⁻¹) on a log scale. Lines representing 1:1 (solid line) and deviations of one and two orders of magnitude from parity (dotted lines) were included to aid the analysis. It should be noted that the number of substances presented in the graphs (Figures 4 to 9) is much lower than may be expected based on the numbers shown in Table 11. This is because only one value per substance and per taxa was retained (i.e. the lowest, reliable value) and because not all substances for which algal toxicity data are available do not necessarily all have data on terrestrial plants.

In general, there is a large amount of scatter in the data, as shown in the example plots (Figures 4 to 9), meaning that no clear trend is apparent. In addition, colour coding for Verhaar class does not reveal a clear dependence on Verhaar class. However, it can perhaps be said that in the majority of cases, data are within two orders of magnitude of the 1:1 line, and that a higher proportion of the data are generally above, rather than below, the 1:1 line. The latter would indicate that the aquatic toxicity data are more conservative (i.e. lower effect concentration) than the terrestrial/sediment data after having been converted into pore water concentration. This observation applies to both soil and sediment compartments and for all included trophic levels. This may be caused (partly) by the use of conservative risk assessment practices as described in Section 3.1 and with the fact that in general aquatic toxicity data are more prevalent. As such, by using the lowest available effect concentration there is an increased probability of ending up with aquatic toxicity data that are more conservative than the corresponding soil/sediment toxicity data.





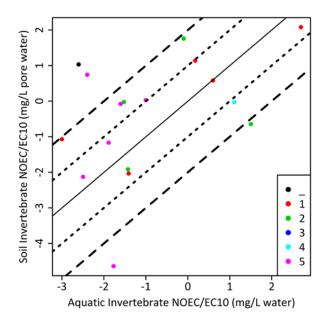


Figure 5. Chronic soil invertebrate toxicity vs chronic aquatic invertebrate toxicity by Verhaar class (see legend). N = 17.

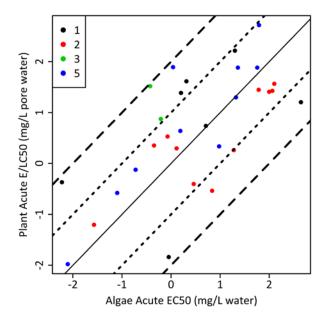


Figure 6. Acute plant toxicity vs acute algal toxicity by Verhaar class (see legend). N = 30.

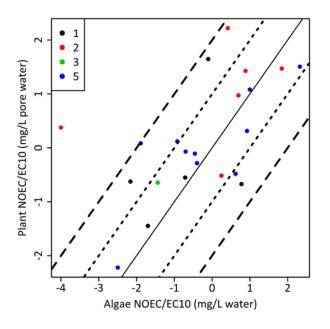


Figure 7. Chronic plant toxicity vs chronic algal toxicity by Verhaar class (see legend). N = 23.

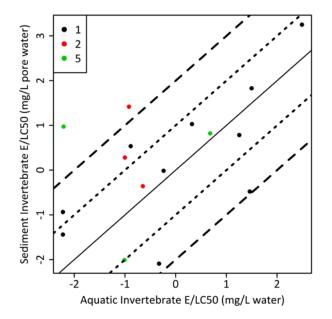


Figure 8. Acute sediment invertebrate toxicity vs acute aquatic invertebrate toxicity by Verhaar class (see legend). N = 17.

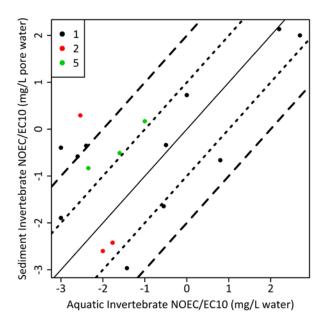


Figure 9. Chronic sediment invertebrate toxicity vs chronic aquatic invertebrate toxicity by Verhaar class (see legend). N = 18.

The findings of this comparison are that toxicity in one compartment is generally indicative of toxicity in other compartments. However, the spread of the data makes it difficult to be conclusive about the relationship between aquatic and terrestrial/sediment toxicity data. In order to dig deeper into this relationship, an investigation into the influence of various physico-chemical and environmental fate properties was conducted and is discussed in Section 3.3.

Direct comparisons have also been used to compare PNEC for soil/sediment derived using two methodologies: namely, the assessment factor method and the equilibrium partitioning method (Table 12, see also section 2.4.4.5 for the definitions of both methods). For a given substance, when a soil/sediment PNEC derived from soil/sediment toxicity data using the assessment factor method (PNEC.AF) was available, an alternative PNEC (PNEC.EPM) was calculated through application of the EPM to the PNEC_{aquatic} of this substance. Such an approach was applied for the soil, the freshwater sediment and the marine sediment compartments. It should be noted that in accordance with the ECHA guidance on information requirements and chemical safety assessment (Chapter R.10: Characterisation of dose [concentration]-response for environment) the PNEC_{soil or sediment} derived through the EPM was further divided by a factor of 10 for substances with either a log K_{oc} > 4, or a log K_{ow} > 5 in order to take uptake via ingestion of sediment or soil into account.

Compartments	Percentage of substances for which PNEC.EPM < PNEC.AF	Magnitude of the difference between PNEC.AF and PNEC.EPM
Soil	64.3 %	≤ 10 for 57.1 % of the substances
		> 10 for 42.9 % of the substances
Freshwater sediment	52.4 %	≤ 10 for 53.4 % of the substances
		> 10 for 46.6 % of the substances
Marine sediment	58.8 %	≤ 10 for 52.9 % of the substances
		> 10 for 47.1 % of the substances

Table 12. Direct comparison of PNEC.AF and PNEC.EPM	for the different compartments
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When PNEC for a given substance was derived using both methods, Table 12 shows that PNEC.EPM is lower than PNEC.AF, and thus apparently more conservative, for 64.3, 52.4 and 58.8% of the substances for soil, freshwater sediment and marine sediment, respectively. Reciprocally, it can be deduced from these percentages that PNEC.EPM are higher, and thus apparently less conservative, than PNEC.AF for 35.7%, 47.6% and 41.2% of the substances, respectively. In order to go beyond those considerations, a further look has been given to the magnitude of the difference between PNEC.AF and PNEC.EPM for a same substance. In a first instance, it has to be determined from which magnitude it could be considered that both PNEC are significantly different. For example, it appeared that the magnitude of the difference between PNEC.AF and PNEC.EPM is inferior or equal to a factor of 10 for 57.1% of the substances in the case of the soil compartment. Similar percentages were found for the freshwater (53.4%) and marine (52.9%) sediment. For all compartments, the majority of cases in which a factor of 10 was exceeded, was in the case in which PNEC.EPM was in fact more conservative (see Figure 8).

In any case, it is difficult to establish the significance of the difference between PNEC.AF and PNEC.EPM as they could have been derived from different sizes of datasets. In other words, PNEC.AF are derived by dividing terrestrial/sediment toxicity data by appropriate assessment factors (specific to the considered compartment and determined based on the size of the respective dataset), while PNEC.EPM are calculated from PNEC_{aquatic} which are themselves derived by dividing aquatic toxicity data by other assessment factors (specific to the water compartment and determined based on the size of the size of the size of the aquatic dataset). If the aquatic and terrestrial/sediment toxicity datasets contain more or less important levels of data, the assessment factors used to derive the PNEC_{soil or sediment}.AF and the PNEC_{aquatic} can be significantly different. Indeed, the aquatic toxicity dataset is often more consequent than the terrestrial/sediment one. Therefore, the assessment factor used to derive the PNEC_{soil or sediment}.EPM. Such a difference in the applied assessment factors could account for the final difference between PNEC.AF and PNEC.EPM; making the significance of a magnitude factor of 10 questionable.

Furthermore, worst-case PNEC.AF could have been derived based on the results of limit tests where no adverse effect was observed. In such cases, the NOEC used to derive the PNEC (= the NOEC to which the assessment factor was applied) are sometimes "artificially" set at the unique concentration tested during the limit assay (*e.g.* 1000 mg/kg sediment) in spite of the absence of effects at this concentration. In reality, effects could have occurred at considerably higher concentrations if such dose levels had been tested. Such a case

could result in relatively low PNEC.AF values, whereas no toxicity is expected. As explained in Section 2.7 (point 1), there may also be some cases where PNEC.AF could have been derived using improper methodology.

Thus, conclusions from this PNEC comparison should be considered with caution.

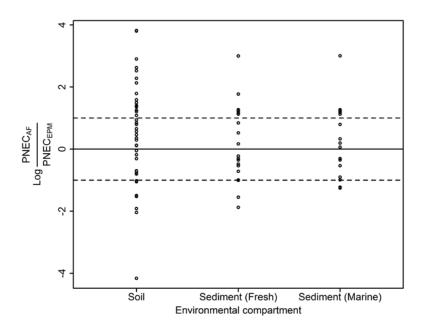


Figure 10. Distribution of the log ratio of PNEC.AF and PNEC.EPM for the different environmental compartments. The dashed lines indicate a difference of 1 order of magnitude from parity.

3.3 Correlations of aquatic and terrestrial/sediment toxicity ratio with physico-chemical and environmental fate properties

A number of correlations of the ratio between aquatic and terrestrial/sediment toxicity against various physico-chemical and environmental fate properties (K_{oc}, K_{ow}, vapour pressure and water solubility) have been investigated. Again, terrestrial and sediment toxicity results have been converted into pore water concentrations using EPM in order to compare directly with aquatic toxicity data (see Section 2.6.1). For comparison purposes, taxa from the aquatic compartment have again been grouped with similar taxa from the soil and sediment compartments.

Comparing the ratio of aquatic to terrestrial/sediment toxicity against certain physico-chemical and environmental fate properties is useful to establish whether these properties have a bearing on this relationship. It should be noted that the influence of these physico-chemical and environmental fate properties on the overall toxicity of the test substances is not shown in these plots; only the toxicity of the aquatic compartment relative to the terrestrial/sediment compartment. In other words, these plots illustrate whether an increase in a physico-chemical and environmental fate property causes the apparent sensitivity in one compartment to change in comparison to the other.

A number of example plots are presented in this report (Figures 11 to 14) and the correlations are briefly discussed in the text. Note: For interpretation of the graphs, the line y = 0 represents where the E/LC_{50} for terrestrial organism (mg L⁻¹ pore water) is equal to the E/LC_{50} for the aquatic organism (mg L⁻¹). This can therefore loosely be described as the point at which toxicity in one compartment becomes more significant (or sensitive) than the other. Below 0 the E/LC_{50} of the aquatic compartment is lower, and therefore the toxicity greater, than that of the terrestrial compartment, and vice versa.

It should be noted that initially some moderate to strong correlation was observed between the ratio of aquatic to terrestrial/sediment toxicity and several physico-chemical and environmental fate parameters (Log K_{oc} , Log K_{ow} , water solubility and vapour pressure). This was most pronounced for Log K_{oc} for which example plots are included below (Figure 11). This correlation seemed to suggest that as Log K_{oc} increased, the toxicity to soil and sediment organisms seemed to increase and eventually exceed the toxicity towards aquatic organisms. This observation initiated the further data screening steps described in Section 2.5, in which effect concentrations at chemical activities exceeding one were excluded from the analysis as well as specific substances deemed to be unsuitable for application of EPM (e.g. ionisable substances). As a result of this screening, the correlations became statistically insignificant (Figures 12 to 14). Nonetheless, a significant amount of noise is still present in the data as can be seen in Figures 12 to 14. As such, the ratio between aquatic and soil/sediment toxicity data spans several orders of magnitude.

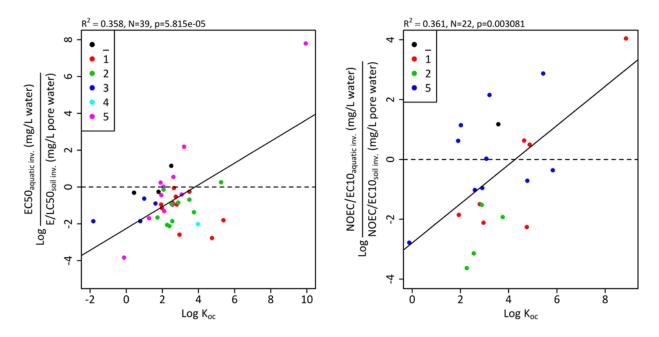


Figure 11. Ratio of aquatic and terrestrial invertebrate toxicity data against substance log K_{oc} <u>prior to</u> application of the data screening steps outlined in Section 2.5. Verhaar class indicated by colour (see legend). Left: acute toxicity data. Right: chronic toxicity data.

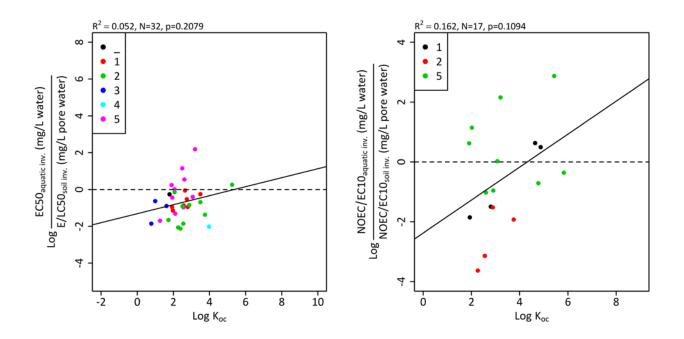


Figure 12. Ratio of aquatic and terrestrial invertebrate toxicity data against substance Log K_{oc} <u>after</u> application of the data screening steps outlined in Section 2.5. Verhaar class indicated by colour (see legend). Left: acute toxicity data. Right: chronic toxicity data.

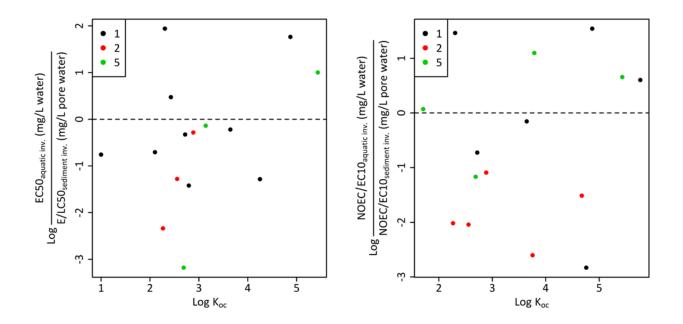


Figure 13. Ratio of aquatic and sediment invertebrate toxicity data against substance Log K_{oc} <u>after</u> application of the data screening steps outlined in Section 2.5. Verhaar class indicated by colour (see legend). Left: acute toxicity data, N = 17. Right: chronic toxicity data, N = 17.

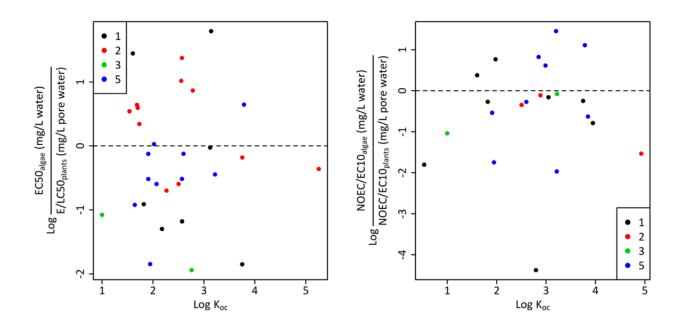


Figure 14. Ratio of algal and terrestrial plant toxicity data against substance Log K_{oc} <u>after</u> application of the data screening steps outlined in Section 2.5. Verhaar class indicated by colour (see legend). Left: acute toxicity data, N = 30. Right: chronic toxicity data, N = 23.

Correlation with physico-chemical and environmental fate properties has also been investigated for PNECs for soil/sediment by plotting the ratio between PNEC.AF and PNEC.EPM against Log K_{oc} and other parameters. This exercise aimed to determine whether the log K_{oc} (or other parameters) has a bearing on the relationship between PNEC.AF and PNEC.EPM. In other words, this illustrates whether an increase in the log K_{oc} results in one PNEC becoming more or less protective than the other. For example, if the log ratio between PNEC.AF and PNEC.EPM decreases when the Log K_{oc} increases, this means that the PNEC.EPM becomes higher, and thus less protective, than the PNEC.AF. As for the ecotoxicity data, initially a strong correlation with Log K_{oc} was observed. This correlation was greatly weakened after application of the data screening described in Section 2.5 (see Figure 15). A great amount of scatter remains in these data as well, perhaps not surprisingly given that the aquatic and soil/sediment toxicity data are at the basis of the calculation of these PNEC values. As noted in Section 3.2, there is uncertainty around derivation of the PNEC values, and thus caution should be applied in making conclusions in relation to this comparison.

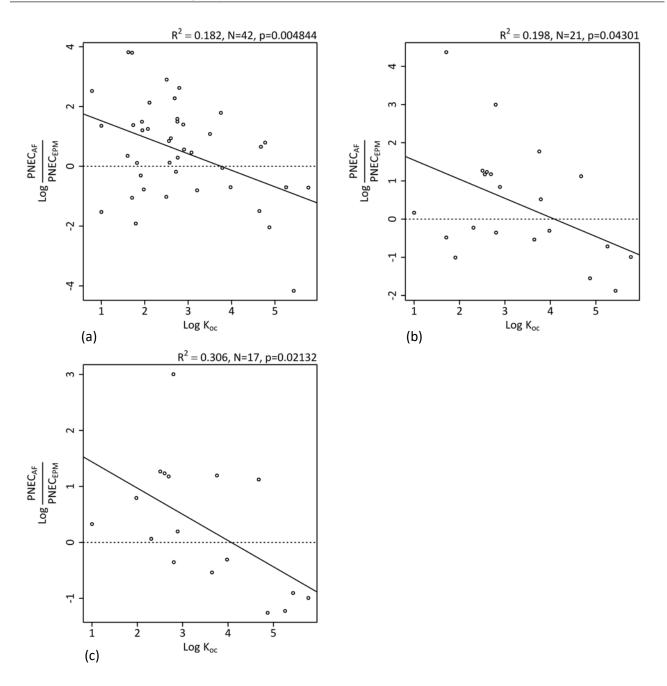


Figure 15. Correlation of the log ratio between PNEC.AF and PNEC.EPM with the log K_{oc} <u>after</u> application of the data screening steps outlined in Section 2.5. (a), (b), (c) represent this correlation for soil, freshwater and marine sediment, respectively.

4. **DISCUSSION**

The findings of the direct comparison of acute and chronic levels of toxicity shown by a chemical in water and soil/sediment (Section 3.2) are that toxicity in one compartment is generally indicative of toxicity in other compartments. However, the spread of the data makes it difficult to be conclusive about the relationship between aquatic and terrestrial/sediment toxicity data.

Direct comparisons were also made between soil/sediment PNECs derived from soil/sediment toxicity data using the assessment factor method (PNEC.AF) and calculated PNECs derived by application of the EPM to the PNEC_{aquatic} (PNEC.EPM) (Section 3.2). It was difficult to establish the significance of this comparison, however, in view of the uncertainties surrounding PNEC derivation. It was concluded that conclusions from this PNEC comparison should be considered with caution.

To investigate further the relationship between acute and chronic levels of toxicity shown by a chemical in water and soil/sediment, an investigation into the influence of various physico-chemical and environmental fate properties on the ratio between aquatic and terrestrial/sediment toxicity was conducted (Section 3.3).

Though prior to the data screening steps described in Section 2.5 a correlation between the ratio of aquatic to terrestrial/sediment toxicity and log K_{oc} was observed, the correlation became statistically insignificant after the data screening steps were applied. Correlation between the ratio of PNEC.AF: PNEC.EPM and Log K_{oc} was also investigated. As for the toxicity data comparisons, initially a strong correlation with Log K_{oc} was observed. This correlation was greatly weakened after application of the data screening steps, and, as indicated above, conclusions from this PNEC comparison should be considered with caution.

After the data screening steps, a significant amount of scatter remains in the data and the ratio between aquatic and soil/sediment toxicity data spans several orders of magnitude.

It is likely that variation in the data is explained by experimental artefacts and other data issues relating to reliability/applicability including the differential application of assessment factors to derive the individual PNECs.

As discussed in Section 2.7, the data presented in the ECHA database were assumed to be accurate and reliable. In an ideal situation, it would have been possible to assess the reliability of each result in the database before including it in the analysis, but this was not possible under the timeframe and resourcing of the work set out in the present report. Additionally, whilst it was intended to only include Klimisch 1 (reliable without restrictions) and 2 (reliable with restrictions) data in the database, eventually all available data on a substance was included in the final data pull, i.e. including Klimisch 3 (not reliable) and 4 (not assignable) data. This includes both toxicity data and physico-chemical and environmental fate data from the ECHA database that were included in the EPM calculation. As a result, it is reasonable to expect that some of the data included in the database are in fact unreliable and would contribute to noise or outliers in any subsequent analysis.

In relation to the physico-chemical and environmental fate data, where physico-chemical properties were not available in the ECHA database these were predicted by QSAR. However, as noted in Section 2.7, it was assumed that all substances fell within the applicability domain of the QSAR applied (though some obvious

outliers were identified and investigated on a case-by-case basis). In reality, certain types of substances are likely to fall outside these applicability domains.

Another important consideration in addition to whether data are reliable, is whether the data are suitable to be used in such quantitative analysis as has been applied in this report. In order to compare toxicity results, it is important that exposure concentrations are as accurately defined as possible to be used as point estimates. This may not have always been the case.

Considerations regarding reliability and suitability of the data are discussed further in the below two subsections.

It is also worth considering briefly the presence of dissolved organic carbon (DOC) in aquatic toxicity test systems. DOC represents particulate organic matter that is too small to be removed by conventional filtration or centrifugation methods (DiToro et al., 1991). Hence, aquatic concentrations determined through the use of conventional chemical analytical techniques include the fraction of a chemical sorbed to DOC. However, as this fraction is not deemed to be bioavailable, this causes an overestimation of the true exposure concentration. This in turn leads to an underestimation of the actual aquatic toxicity, which is carried forward when an aquatic toxicity value is extrapolated to soil or sediment toxicity through the use of EPM. For higher log K_{oc} substances, the impact of DOC in underestimating the actual aquatic toxicity would be most pronounced, and this could have explained the initially observed correlations between the ratio of aquatic to terrestrial/sediment toxicity and log K_{oc}.

4.1 Reliability/suitability of soil (and sediment) data

It is worth looking in more detail at the issues inherent to experimental soil toxicity data, as there are a number of potential factors which make precise estimates of exposure concentrations uncertain. Many of these discussions are relevant to sediment toxicity data also.

Firstly, considering the test system itself, soil substrates are far more complex and variable than aqueous test media, consisting largely of solid phase material with varying composition, pH and degrees of particle size and organic carbon content. This can lead to difficulties in dosing the material consistently throughout, as well as presenting a number of variable additional fate processes (e.g. adsorption, degradation processes, equilibration between organic carbon and pore water) that could lead to uncertainty around exposure. It is acknowledged that the result of any terrestrial toxicity test will incorporate both the intrinsic toxicity and the bioavailability of a substance according to the conditions in that particular system (ECETOC, 2002). This makes comparison of results from one test method to another difficult, and the need for standardisation of methodologies is recognised, particularly in relation to soil organic matter content and equilibration time (aging) after addition of the test compound, as these can have a major influence on bioavailability.

Analysis of test concentrations is also often not a guideline requirement in soil studies and is therefore frequently omitted, which means that results are often expressed as nominal concentrations. This could lead to a significant overestimation of test substance exposure concentrations if fate processes such as biodegradation, volatilisation and hydrolysis, in addition to those described above, are expected to play a significant contribution over the duration of the test. Even if analysis of test substance concentrations is

incorporated into the methodology, there can still be significant uncertainty as to the true exposure concentration due to the difference between what is extractable and what is bioavailable (Ortega-Calvo et al., 2015), potential uneven distribution of test substance throughout the substrate, plus the fact that concentration may not be stable over time and that renewal of test concentrations is typically not performed in terrestrial tests.

It could also be the case that an inappropriately high dose was used (if the material was poorly soluble), and that a significant amount of the test material remained undissolved and unbound in the test system, possibly leading to physical effects being observed and inappropriately attributed to chemical toxicity (Redman et al., 2014). In aquatic toxicity tests, rigorous steps are taken to prevent the inclusion of undissolved material in test solutions, but this is not feasible in soil toxicity studies and therefore much of the reported test concentrations may in fact be test material in the free-phase, rather than that which is in equilibrium with the substrate i.e. either dissolved in pore water or bound to organic carbon. Even if the test material has not been 'overdosed' in the system, equilibration between pore water and organic carbon can be a slow process, particularly for highly hydrophobic substances, and this may not have been achieved within the timeframe of the test (EPA, 2000).

All of these issues in combination amount potentially to a high degree of uncertainty surrounding the effect concentrations resulting from soil toxicity tests, meaning that using these data as point estimates in a quantitative analysis could be problematic. The use of these data to calculate pore water concentrations using EPM will also carry forward any error inherent in the data. Additionally, as the EPM calculation assumes a standard amount of organic carbon in the test system, any deviation from this amount in the actual test system will have a corresponding over/underestimation of the partitioning to pore water. Furthermore, the potential lack of equilibration is important as EPM assumes that a system is in equilibrium. Therefore, if a concentration in mg kg⁻¹ representing a significant proportion of free-phase material is converted to mg L⁻¹ pore water, this free-phase material will be erroneously assumed to instead be in equilibrium between the pore water and organic carbon and subsequent pore water concentrations will be overestimated.

Consideration should also be given to the overall availability and sources of data on terrestrial and sediment toxicity. A recent poster produced by ECHA performed an analysis of the terrestrial toxicity studies submitted under REACH for both the 2010 and 2013 registration deadlines (Rodriguez-Ruiz et al., 2016). This assessment found that more than 60% of studies submitted under REACH were from publicly available sources, rather than studies conducted by the registrants, and that these were mainly from publications in scientific journals. In addition, the assessment found that a large number of study records did not report any test guideline (33 – 74% across the four terrestrial endpoints). Overall this is not really surprising as it is more common for industrial chemicals to undergo aquatic toxicity testing than terrestrial testing. However, it does perhaps suggest a reliance on publicly available information and a lack of consistent methodology in the available data. Sediment data are by far the scarcest type of toxicity data in the ECHA database, but no analysis has yet been published as to the most common guideline or source.

In light of the considerations discussed above, it can perhaps be considered that effect concentrations in aquatic toxicity tests will generally (though not always) be more reliably determined than those in soil toxicity test systems. By comparison to terrestrial toxicity tests, aquatic toxicity tests are more likely to have followed a standardised methodology, maintained consistent exposure of the test substance (i.e. by using renewal or

flow-through systems), verified exposure by chemical analysis, and have been performed by the registrants in GLP accredited laboratories. In addition, the issue and uncertainty surrounding partitioning between the aqueous and particulate organic carbon phases of a heterogeneous system is eliminated. Furthermore, a greater degree of established guidance is available to support aquatic toxicity testing of particular families of chemicals and difficult test substances (OECD (2019), US EPA (1996), ECETOC (1996), Concawe (1992)). This is not to say that aquatic toxicity test systems are perfect, only that they are less complex and difficult to test and interpret than terrestrial or sediment systems.

The fact that aquatic toxicity data are likely to be more reliable suggests that they are more suitable to be used in quantitative analysis, and are also better as inputs to the EPM calculation. The latter, in particular, is true because they are more likely to represent equilibrium concentrations and not include undissolved test material. Concerning soil toxicity data, on reflection there are many reasons why an experimental result may not reflect the effect concentration (mg kg⁻¹ dw) that would have been derived on a theoretical basis from an accurate determination of the pore water concentration. It might therefore have been more logical to have converted aquatic toxicity data into mg kg⁻¹ dw, rather than soil toxicity data into mg L⁻¹ pore water, however it's important to note that the correlations would have been exactly the same irrespective of which way the calculation was performed.

4.2 Reliability of physico-chemical and environmental fate data

Another important consideration is the data gap filling exercise that was performed for physico-chemical and environmental fate properties that did not have data available in the ECHA database. The QSAR models within the EPI Suite[™] software package were used to generate physico-chemical and environmental fate data on all substances that were missing these data. This exercise was conducted as a high throughput exercise without assessing whether individual substances were within the applicability domains of the models. In an ideal situation, each substance will have been assessed individually as to whether it fitted within the applicability domains of the models. This must therefore be regarded as a potentially significant source of uncertainty and inaccuracy in the data used for the analysis.

This uncertainty is difficult to quantify and requires more investigation on a substance-by-substance and model-by-model basis. However, an insight can be gained by referring to the types of substances present in the database (Section 2.4.4), which indicates that a broad range of organic compounds are present, with a number of ECOSAR classes represented. Interestingly, many of the substances in the database could not be assigned to an ECOSAR class, suggesting that they are unusual or at least not organic compounds. This indicates that a variety of different types of compounds are present in the database and it is reasonable to assume that some will be outside the applicability domain of the models, particularly those that could not be assigned to an ECOSAR class.

The uncertainty around physico-chemical and environmental fate properties is of particular importance for the K_{oc} parameter, because this is an input to the EPM equation to convert soil and sediment toxicity values in mg kg⁻¹ dw to mg L⁻¹ pore water. This means that any error in this value will be directly translated into the calculated pore water effect concentration. Furthermore, where the ratio of aquatic to soil/sediment toxicity is compared to K_{oc} , this error will be replicated in both axes and therefore magnified significantly. This has

been suggested as one of the reasons that such a strong correlation was initially observed between the ratio of toxicity values and K_{oc} , because any error in the value would cause the datapoint to move along a diagonal line of gradient 1, in effect leading to an 'autocorrelation'. There were initially also some extreme calculated log K_{oc} values (>>6) included in the correlations (a tell-tale sign that some predictions are erroneous), which had the effect of pulling the overall correlation toward the diagonal and increasing the apparent strength of any correlation. Such observations were at the basis of the decision to apply the additional data screening steps described in Section 2.5.

The uncertainty around the accuracy of the predicted K_{oc} values is clearly of critical importance to the pore water effect concentrations calculated and the correlations produced. Similarly, to the discussion around soil toxicity data, in order to draw further conclusions around the observed data scatter, it is important to first validate the data that have been used in the analysis. It is therefore recommended that a refined analysis is performed using K_{oc} data that are confirmed to be based on either reliable experimental data, or calculated using QSARs that have been appropriately validated as applicable to the substances in question.

5. CONCLUSIONS AND RECOMMENDATIONS

The main objectives of this report were to:

- a) Compile the available aquatic, soil and sediment toxicity data publicly available via the European Chemical Agency REACH registration database into a single dataset.
- b) Determine if the larger amount of aquatic toxicity data were indicative of effects in soil and/or sediment-dwelling organisms for both acute and chronic endpoints.
- c) Evaluate whether equilibrium partitioning methodology (EPM) was sufficient for extrapolation of aquatic hazard data to the soil and/or sediment compartments.

There was a large array of data available, representing several trophic levels, organisms, endpoints and duration. As well as the data preparation steps described in Section 2.4, some screening steps were applied to the dataset (Section 2.5), particularly to exclude data where the reported effect concentration was above the chemical's solubility in the respective matrix based on chemical activity.

A high throughput approach has been applied in the current work. High throughput analyses are opportunistic and make use of available data. However, since data quality can vary in such analyses, it can provide inconsistent results. Therefore, some screening of data (e.g., chemical activity in this current case) are generally required to avoid misleading trends and results. A thorough data quality/reliability analysis would have been optimal, but was outside of the scope of the current report. Investigators from all areas, including industry, government and academia are encouraged to consult literature regarding data quality such as that of Klimisch et al. (1997) during experimental design and reporting.

The variability in the underlying data limit definitive conclusions, and for any future assessment a more refined data analysis would need to be performed. In particular, test concentrations should be verified by analysis and be representative of the entire duration of the test, there should be reasonable confidence that the system has equilibrated and free-phase material is not present, and the organic carbon content of the substrate should be known so that partitioning behaviour of the test substance can be reasonably estimated.

Furthermore, the REACH database used in the present work, after screening, is relatively small and contains many different types of chemical classes, which may not be appropriately combined in this analysis due to potential different mechanisms for binding to soil and sediment, or perhaps due to differential mode of action in aquatic vs soil, or sediment, compartments. Thus, the limitation and uncertainties discussed above reduce the ability to draw meaningful conclusions on the mechanistic validity of the EPM from this work. However, while inconsistencies in the data availability/quality for this exercise affect the ability to draw firm conclusions, previous EPM studies performed with more appropriate datasets demonstrate that EPM is fit for purpose to support environmental risk assessments (Redman et al. (2014), Golsteijn et al. (2013), EPA (2012), Verbruggen (2012), Fuchsman et al. (2006), Nowell et al. (2016), Burgess et al. (2013)).

Literature examples of studies into equilibrium partitioning are discussed in more detail in Section 2.2. These studies have shown that in general EPM is appropriate, but that deviations can be expected for sediments that contain specific sorption phases such as soot. The EPM may also not be applicable to predict toxicity of

organisms that live on top of the sediment or the soil and thus for sediment or soil risk assessment this could be a factor to take into account in the selection of test species.

The observed biases inherent to regulatory risk assessment practices (i.e. using the most conservative values) as well as data collection practices designed to include as much data as possible, contrast greatly with the methods used in studies strictly designed to investigate the applicability of EPM. As the rigorous exposure characterisation typical for such studies is lacking in many studies used to constitute regulatory dossiers, the work presented in this report should be seen as an illustration of how EPM tends to perform under such less scrutinous circumstances. Therefore, the biases that were discussed may be products of the practices of regulatory dossiers constitution, and the biases and experimental artefacts identified and discussed in this report may help to make improvements in these practices to more efficiently and reliably incorporate the EPM.

Any future studies should ensure rigorously exposure characterisation, including consideration of organic carbon content in the test systems, and thoroughly evaluate the reliability and sufficiency of the dataset overall.

ABBREVIATIONS

а	Chemical activity
AF	Assessment factor
BSAF	Biota sediment accumulation factors
CAS	Chemical abstracts service
DDT	Dichlorodiphenyltrichloroethane
DD	Dichlorodiphenyldichloroethylene
DDD	Dichlorodiphenyldichloroethane
DOC	Dissolved organic carbon
EbC ₅₀	Effective concentration, 50%; b means based on biomass
EC	European Commission
EC ₁₀	Effective concentration, 10%
EC ₅₀	Effective concentration, 50%
ErC ₅₀	Effective concentration, 50%; r means based on growth rate
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECHA	European Chemicals Agency
ECHA CHEM	European Chemicals Agency's dissemination portal
EPM	Equilibrium partitioning methodology
EPI	Exposure/potency index
НС	Hazardous concentration
K _d	Distribution coefficient for adsorption
K _{oc}	Organic carbon-water partition coefficient
K _{ow}	Octanol-water partition coefficient
K _p	Permeability coefficient

LAS	Linear alkylbenzene sulfonate
LC ₅₀	Lethal concentration, 50%;
LC ₁₀₀	Lethal concentration, 100%
LD ₉₅	Lethal dose, 95%
LOEC	Lowest observed effect concentration
MATC	Maximum acceptable toxicant concentration
NOEC	No-observed-effect concentration
NOECr	No-observed-effect concentration; r means based on growth rate
OECD	Organisation for Economic Co-operation and Development
РАН	Polycyclic aromatic hydrocarbon
РСВ	Polychlorinated biphenyl
PNEC	Predicted no effect concentration
PNEC.AF	Predicted no effect concentration derived using the assessment factors (AF) method
PNEC.EPM	Predicted no effect concentration derived using the equilibrium partitioning method (EPM)
QSAR	Quantitative structure-activity relationship
REACH	Registration, evaluation, authorisation and restriction of chemicals
SQG	Sediment quality guidelines
SMILES	Simplified molecular-input line-entry system
TLM	Target lipid model
ToR	Terms of Reference
US EPA	United States Environmental Protection Agency
WS	Water Solubility

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