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Exploring REACH as potential data source for characterizing ecotoxicity in life cycle assessment

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Abstract

Toxicity models in life cycle impact assessment (LCIA) currently only characterize a small fraction of marketed substances. This is mainly due to limitations in the underlying ecotoxicity data. One approach to improve the current data situation in LCIA is to explore new data sources, such as the European database of the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). We explored REACH as potential data source for LCIA based on matching reported ecotoxicity data for substances that are currently also included in the UNEP/SETAC scientific consensus model USEtox for characterizing human toxicity and ecotoxicity impacts in LCIA. Data are evaluated with respect to number of data points, reported reliability and test duration, and are compared with data listed in USEtox at the level of hazardous concentrations per substance. Our results emphasize deviations between data available in REACH and USEtox. The comparison of ecotoxicity data in REACH and USEtox shows the general potential of REACH ecotoxicity data to be used in LCIA toxicity characterization, but also highlights issues related to compliance with REACH reporting requirements and different assumptions underlying REACH as regulatory risk assessment support database and LCIA. We recommend to systematically investigate current quality-, extrapolation-, and applicability-related issues, before considering REACH as data source for use in LCIA and to also look at additionally available databases, published studies and reports.

Keywords: Life Cycle Impact Assessment, ecotoxicity data, EC50, HC50, USEtox

INTRODUCTION

More than 100,000 substances are awaiting evaluation in the European Union (EU) for their safe use in various technological products and systems [1]. Life cycle assessment (LCA) is widely applied as a methodology to quantitatively compare the overall environmental performance of products and systems over their full life cycle looking at various impacts related to chemical emissions and resource use [2]. To ensure comparability across impact categories, average or representative values are used in the life cycle impact assessment (LCIA) phase of LCA as “best estimates” to characterize potential impacts on humans and ecosystems associated with chemical emissions occurring over a product life cycle [3]. Aquatic ecotoxicity is one of the impact categories in LCIA with high associated variability in characterization results and limitations mainly related to data availability and extrapolation from acute to chronic effects. Several tools have been developed over the last 2 decades to characterize and compare aquatic ecotoxicity impacts of chemical emissions in LCA, but all rely on different assessment models, assumptions, and data, which is one of the main reasons for high variability and inconsistency in assessment results across tools [4]. Variability across tools has been addressed in a multi-year consensus building effort to harmonize existing models under the auspices of the United Nations Environment Programme (UNEP)/Society of Environmental Toxicology and Chemistry (SETAC) Life Cycle Initiative. This effort resulted in the development of the scientific consensus model USEtox for characterizing human toxicity and freshwater ecotoxicity impacts of chemical emissions for use in LCA and other comparative assessments [5]. The consensus building process is described elsewhere [6, 7]. However, variability and uncertainty related to underlying aquatic ecotoxicity data in USEtox and other LCIA models as well as low substance coverage compared to marketed and potentially harmful chemicals remain critical issues that need to be addressed to improve ecotoxicity characterization in LCA.

The starting point for characterizing ecotoxicological effects in LCA is the chemical concentration in freshwater at which 50% of the tested aquatic organisms are affected, EC50. EC50 for organic substances in USEtox are currently taken from 2 scrutinized and quality-assured data sources as part of the consensus-building process [5]. One source is based on data from the RIVM's E-toxBase [8], while the other source is mainly based on data from ECOTOX [9] and IULCID [10]. Preference is given to chronic data [5] as long as they represent measured EC50 values. If chronic data are not available, acute data are used applying a fixed acute-to chronic extrapolation ratio (ACR) of 2 [11]. Extrapolating from acute to chronic data certainly requires additional research, but is not further discussed in the present study. Freshwater ecotoxicity effect factors based on EC50 are available in USEtox for approximately 2500 substances, while other LCIA characterization models typically provide ecotoxicity effect factors for less than 1000 substances [12]. Hence, most commercially used chemicals remain to be characterized, mainly due to the limited availability or use of underlying EC50 data. More specifically, reported chronic EC50 values are in general relatively rare and the lack of data and the increased uncertainty by extrapolating from acute data constitute unsolved issues for a reliable ecotoxicity characterization in LCIA [13]. Thus, exploring new sources for freshwater ecotoxicity data for use in LCIA is required to improve current ecotoxicity characterization. One potential source for ecotoxicity information is the database of the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) established by the European Chemicals Agency (ECHA) under Regulation (EC) No 1907/2006 that became effective in June 2007 in consequence of the new EU chemicals legislation [14].

Very few studies already considered REACH as potential data source for use in LCIA. Askham (2012) [15] compared ecotoxicity data from REACH registration dossiers with data used in USEtox for benzene and found that REACH provides more data than are currently used in USEtox and that REACH may be useful to fill existing data gaps. The study by

Askham recommended using REACH and USEtox exploiting concurrence and synergies to identify potential conflicts, while a qualitative assessment of the REACH data, i.e. the evaluation of the data with respect to their reliability and quality for inclusion into the scientific consensus model USEtox was not performed. Igos et al. (2014) [16] developed characterization factors using REACH ecotoxicological data for 9 dishwasher detergents, which are currently not characterized in USEtox. Despite general agreement with results from other studies, Igos and coauthors doubt the reliability of the underlying REACH data, since underlying data requirements were not completely met or testing studies were poorly documented. As a result, further investigation of the qualitative assessment of REACH data was recommended. A systematic analysis of appropriateness and applicability of REACH data for use in LCIA toxicity models is, however, still missing. In response to this need, we investigate in the present study the agreement between aquatic ecotoxicological data submitted under REACH and data used in the life cycle toxicity assessment model USEtox. The main aim is thereby to identify the potential for improving LCIA toxicity characterization by incorporating REACH effect data and related feasibility requirements. To address this aim, we focus on 4 objectives: (i) to identify a set of chemicals that are on the one hand registered under REACH and on the other hand included in USEtox; (ii) to analyze for these chemicals the aquatic ecotoxicity information reported in REACH with respect to their variability and stated data reporting quality; (iii) to calculate the average toxicity for each chemical from REACH data and compare it with the average toxicity currently used in USEtox; and (iv) discuss options and provide preliminary recommendations for improving aquatic ecotoxicity assessment in LCA based on REACH.

MATERIALS AND METHODS

The main steps involved in selecting, preprocessing, and analyzing freshwater ecotoxicity data are shown in Figure 1.

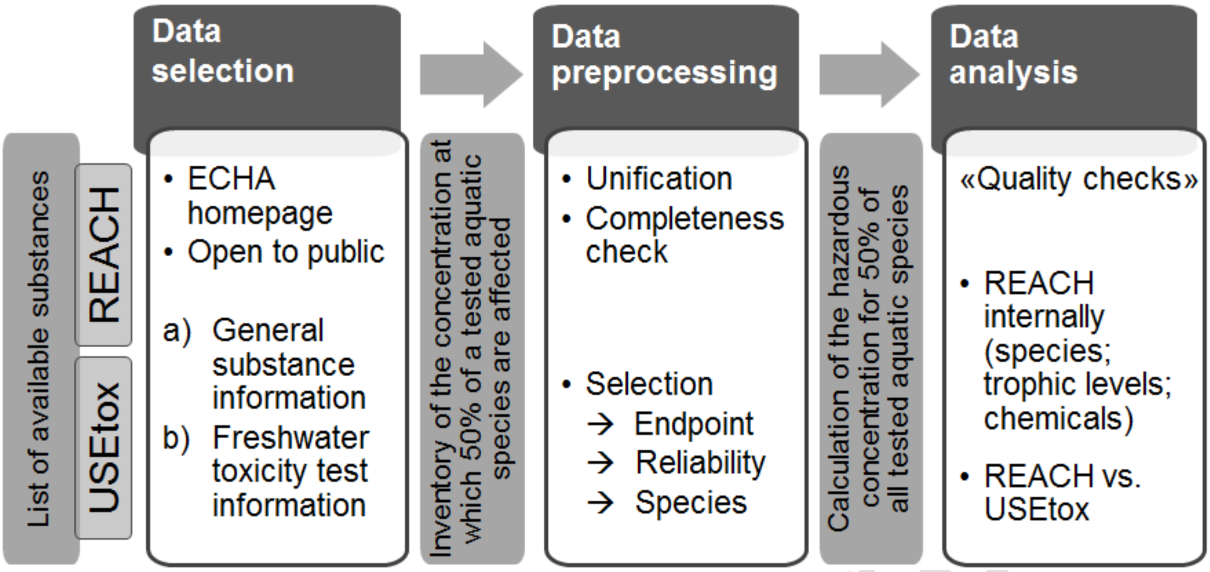

Figure 1. Main steps involved in REACH freshwater ecotoxicity data selection, preprocessing, and analysis for potential use in life cycle toxicity characterization models

Data selection

For comparing freshwater ecotoxicity data available in REACH with data currently used in LCIA characterization models, the starting point is to look at those substances for which a submitted dossier under REACH is available and which are also included in USEtox. We hence compiled a database containing all individual aquatic ecotoxicological effect data reported under REACH for the full set of substances for which also ecotoxicity effect factors exist in USEtox. Relevant information for tested substances is taken from REACH registration dossiers which have been assigned a registration number and are accessible on the ECHA homepage (echa.europa.eu/information-on-chemicals/registered-substances). All information collected from REACH is provided in the present study (Supplemental Data, Table S1) and was systematically included to identify and evaluate data for different substances and to assess data source, toxicity testing method and resulting ecotoxicity data. The information used for EC50 data evaluation includes for the substance identification the

CAS registration number and the IUPAC name. Study result type, reliability score, tested species, exposure duration, endpoint type, and effect concentration are included as aquatic toxicity test information.

Data preprocessing

Extracted data for the selected substances were harmonized and scrutinized in a preprocessing step to prepare a consistent inventory set of EC50 values based on REACH. Preprocessing included harmonization of differently spelled test species names, reported exposure duration units (e.g. converting 48 h into 2 d) and effect concentration units (e.g. converting 1 g/L into 1000 mg/L or removing data points with ambiguous units like ppm that can be based on mass or molarity, which is typically not indicated). Furthermore, effect concentration endpoints other than EC50 or equivalent endpoints IC50 (inhibitory concentration) and LC50 (lethal concentration) were removed from the data set. EC50, LC50, and IC50 were selected as endpoints, because EC50 values are mostly from acute tests, where the endpoint is usually lethality (LC50) or in the case of *Daphnia* immobilization (IC50). Finally, data were removed for test species 'activated sludge' and data that were not measured but estimated (e.g. study result type 'read-across data', 'QSAR', or 'estimated by calculation'), and data entries were then checked for completeness of test details necessary to subsequently calculate substance-specific average toxicity including reliability score, test organism (species), test category assigned by ECHA containing the tested trophic level, exposure duration, and type of endpoint. As the information requirements for ecotoxicological data in REACH depend on the chemical tonnage, either referring to produced or imported substance volume (Table 1) [14], more data are typically available for substances with higher production or import volumes.

Table 1. Aquatic ecotoxicological information required for substance registration under REACH depending on the annual quantity manufactured or imported according to Annexes VII to X of Regulation (EC) No 1907/2006 [14]

Aquatic Ecotoxicological Information*	≥1 t/yr Annex VII	≥10 t/yr Annex VIII	≥100 t/yr Annex IV	≥1000 t/yr Annex X
Short-term toxicity testing on invertebrates (preferred species *Daphnia*)	X	X	X	X
Growth inhibition study aquatic plants (*algae* preferred**)**	X	X	X	X
Short-term toxicity testing on fish (long-term toxicity testing instead of short-term may be considered)		X	X	X
Activated sludge respiration inhibition testing		X	X	X
Long-term toxicity testing on invertebrates (preferred species *Daphnia*)			X	X
Long-term toxicity testing on fish			X	X

*Except for the long-term testing, the studies do not need to be conducted if there are factors indicating that aquatic toxicity is unlikely to occur. This could for instance be the case for substances that have a high insolubility in water or are unlikely to cross biological membranes. In this case long-term testing is advised, but not compulsory

Reliability scores in REACH are based on the Klimisch scoring system [17] that allows the experimental study information to be ranked and organized for focusing on the most relevant data for toxicity assessment [18]. Main focus of this scoring system is on the data reporting requirements, especially regarding the use of standard test guidelines and within the REACH registration process, each registrant submitting data needs to assign the appropriate score [19]. Through an evaluation process ECHA checks the compliance with reporting requirements of at least 5% of the registration dossiers received for each tonnage band [14]. For the present study, only data points with assigned Klimisch scores 1 ('reliable without restriction') and 2 ('reliable with restrictions') are used, whereas all other (i.e. considered non-reliable) data points were ignored.

Data analysis

Freshwater aquatic ecotoxicity effect factors, applied in the calculation of freshwater ecotoxicity characterization factors, are defined in USEtox as the change in the potentially affected fraction (PAF) of exposed freshwater species per change in concentration of truly dissolved chemical in freshwater. The chosen working point on the PAF curve corresponds to a 50% fraction of species that is potentially affected [12] and is referred to as hazardous concentration, HC50 (mg/L), at which 50% of exposed aquatic ecosystem species are showing effects above their species-specific EC50 (mg/L). In the USEtox substance data files chemical-specific HC50 are available in log scale. Hence, to compare and assess ecotoxicity data provided in REACH directly with data reported in USEtox, the HC50 for a chemical has to be calculated in 5 steps from the selected REACH EC50 data. First, a set of ecotoxicological effect data $\mathrm{EC50}_{i,j} \triangleq \{\mathrm{EC50}_{i,j}^{\mathrm{REACH}}, \mathrm{IC50}_{i,j}^{\mathrm{REACH}}, \mathrm{LC50}_{i,j}^{\mathrm{REACH}}\}$, is built composed of all reported species-specific data points *i* for all aquatic test species *j* per substance from the full list of extracted REACH data including effect (EC50), inhibitory (IC50) and lethal (LC50) concentration endpoints. Second, data are structured into chronic or acute exposure duration by means of a taxonomy data set (Supplemental Data, Table S2). In case the test species were not stated or are not available in the taxonomy, test durations were extrapolated based on stated trophic level and acute test durations for different trophic levels (≤1 d for microorganisms, ≤4 d for algae, cyanobacteria and crustaceans, and ≤7 d for invertebrates, fishes and aquatic plants other than algae) [20] based on various sources [11, 21, 22] and additional expert judgement. Third, all data points with assigned ‘acute’ exposure duration are used to estimate the preferred ‘chronic’ data by applying an acute-to-chronic ratio (ACR) of 2 in line with the generic ACR applied in USEtox [12]. With this, the effect data are restructured as $\mathrm{EC50}_{i,j} \triangleq \{\mathrm{EC50}_{i,j}^{\mathrm{chronic}}, \mathrm{EC50}_{i,j}^{\mathrm{acute}}/\mathrm{ACR}\}$. Although ACR may vary considerably between chemicals and test species as shown for selected cationic metals [23], we apply the generic ACR of USEtox for consistency, thereby acknowledging that further research is required to refine this assumption in future exercises. Fourth, an average value is calculated across all data points per test species in log scale, building a set of species-specific $\log \mathrm{EC50}_j$ for each chemical. Fifth, the average of all $\log \mathrm{EC50}_j$ per chemical is calculated and denoted as $\log \mathrm{HC50}$ – this metric finally matches the log of the hazardous concentration for 50% of the included test species that is reported in USEtox substances data files. The last 2 steps are performed separately for the data set of reported chronic data alone and for the combined set of reported chronic data and chronic data converted from reported acute data, where the latter set is referred to as 'combined acute and chronic' for simplicity.

RESULTS

Selected freshwater ecotoxicity data from REACH

REACH includes ecotoxicity information from more than 50000 dossiers for approximately 15000 registered substances in total, of which more than 9000 registered with a CAS number. Around 75% of the substances without CAS number are registered as Notification of New Substances (NONS) that will be updated gradually by ECHA [24]. The remaining substances without a CAS number are incompletely registered or mixtures, reaction products, distillate fractions, etc. Out of substances with CAS, approximately 7500 unique chemicals are represented with the rest being multiple registrations per substance having different registration or submission types. USEtox 2.0 provides ecotoxicity data for 2498 out of 3076 organic substances and for all of the 27 included cationic metals. Matching REACH with USEtox for registered substances for which $\log \mathrm{HC50}$ can be determined based on the REACH data yields a list of 819 unique chemicals that are included in our data set. For these chemicals, a total of 22834 individual ecotoxicity data points was found in REACH as of April 2015. The distribution of the data on different reliability scores and types of ecotoxicity endpoints is summarized for the 819 selected substances in Table 2.

Table 2. Statistics on the distribution across reliability scores and ecotoxicity endpoints of the REACH data for 819 selected substances. Numbers highlighted in grey are data points considered for further analysis in the present study

Reliability	1			2			3			4			n.d.			
Endpoint*	acute	chronic	n.d.	acute	chronic	n.d.	acute	chronic	n.d.	acute	chronic	n.d.	acute	chronic	n.d.	Total
EC50	1435	170	-	2746	231	13	494	77	1	465	38	-	29	1	-	5700
IC50	16	3	-	232	39	-	33	13	-	23	8	-	2	4	-	373
LC50	724	73	1	3686	213	2	618	63	-	566	29	-	13	2	1	5991
ECxx	866	106	-	2134	262	3	360	96	-	302	21	1	7	2	-	4160
LOEC	145	241	-	133	234	3	33	57	-	14	30	-	2	1	-	893
NOEC	1090	588	3	965	1191	15	138	210	-	132	89	-	3	9	-	4433
Other	88	46	-	603	213	-	128	97	1	81	21	-	6	-	-	1284
Total	4364	1227	4	10499	2383	36	1804	613	2	1583	236	1	62	19	1	22834

*EC50: Effect Concentration (50% of test organisms affected); IC50: Inhibitory Concentration (50% of test organisms affected); LC50: Lethal Concentration (50% of test organisms affected); ECxx: Effect Concentration (xx% of test organisms affected); LOEC: Lowest Observed Effect Concentration; NOEC: No Observed Effect Concentration.

Of 22834 available ecotoxicity data points from REACH we selected 9584 data points as starting point for our data analysis corresponding to EC50, IC50 or LC50 (the endpoints prescribed and used for calculation of effect factors in USEtox) with reliability 1 or 2 (highlighted data in Table 2). Preprocessing (harmonizing and scrutinizing) these data finally yielded a data set of 787 unique substances with 7723 measured ecotoxicity data points, of which 7.4% are based on chronic and 92.6% on acute tests. In our final data set, the number of data points per substance varies between 1 (e.g. 2,5-dichloroaniline, CAS: 95-82-9 or 2,5-dimethylphenol, CAS: 95-87-4) and 171 (silver, CAS: 7440-22-4) with an average of 9.8 data points per substance. Many substances with only few data points remaining in our final data set have more reported data in REACH, but these did not pass our selection criteria (i.e. not considered reliable in REACH or endpoints currently not included in USEtox). The average number of data points per substance for chronic tests is 0.72 and data covering 3 trophic levels are reported on average per substance (data not shown).

REACH ecotoxicity data analysis

Our final set of scrutinized REACH ecotoxicity data is analyzed (i) at the level of species-specific $\log \mathrm{EC50}_j$ values that are compared with regard to different test durations (assigned ‘chronic’ vs. assigned ‘acute’) and reliability scores (reported reliability 1 vs. 2), and (ii) at the level of species-specific chronic $\log \mathrm{EC50}_j$ values that are compared with regard to different trophic levels.

(i) Influence of test duration and reliability score is investigated plotting species-specific acute $\log \mathrm{EC50}_j$ values against chronic $\log \mathrm{EC50}_j$ values per substance (average per substance across all species-specific ‘acute’ respectively chronic, ‘reliability 1’ and ‘reliability 2’ EC50 data points) for 251 different combinations of substance and species (Figure 2A) and plotting REACH reliability score 1 versus reliability score 2 $\log \mathrm{EC50}_j$ values (chronic and acute) for 252 different combinations of substance and species (Figure 2B).

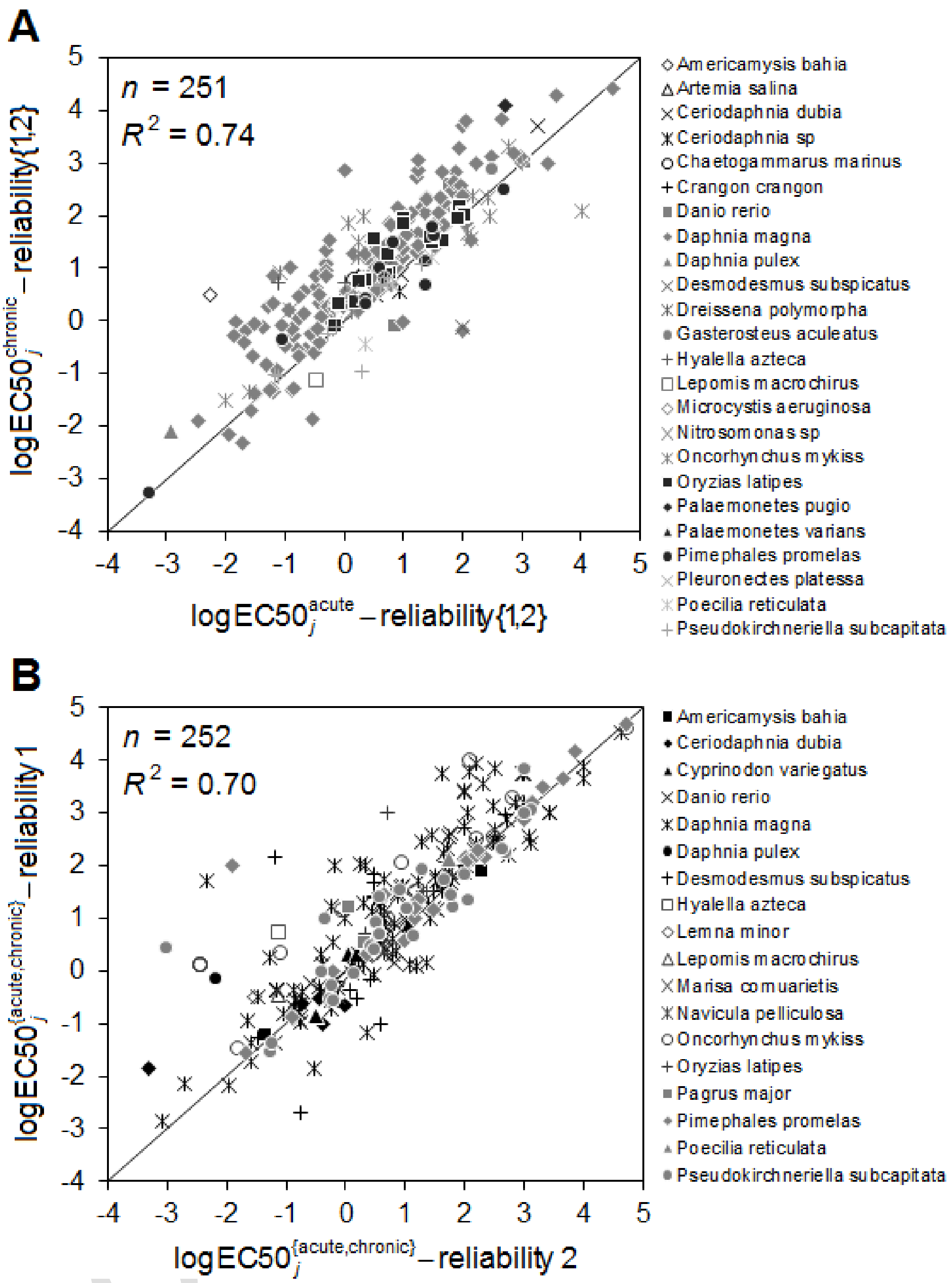

Figure 2. Comparing log $\mathrm{EC50}_j$ values for (**A**) chronic vs. acute data with reliability scores 1 and 2, and for (**B**) acute and chronic data with reliability score 1 vs. reliability score 2. All axes are on a $\log_{10}$ scale. Diagonal solid line indicates the hypothetically ideal 1:1 confirmation relationship between data on y-axis and x-axis

For comparing test durations, data with reported reliabilities 1 and 2 were combined, while for comparing reliability scores, acute and chronic data were combined to maximize the number of data points that can be considered. Chronic and acute $\log \mathrm{EC50}_j$ values in Figure 2A generally fall in the same range with an average deviation of a factor 2.9 (calculated from an average difference of 0.46 log units) and with 90% of chronic versus acute $\log \mathrm{EC50}_j$ values falling within a difference of a factor 23 (1.37 log units). Some species, however, show differences in chronic versus acute $\log \mathrm{EC50}_j$ values that vary up to more than 2 orders of magnitude, such as chronic versus acute $\log \mathrm{EC50}_j$ for *Americamysis bahia* varying by up to a factor 613 (2.8 log units) after exposure to zinc pyrithione (CAS: 13463-41-7) and $\log \mathrm{EC50}_j$ of *Daphnia magna* varying by up to a factor 159 (2.2 log units) after exposure to isopropyl myristate (CAS: 110-27-0). A similar picture is obtained when comparing combined acute and chronic $\log \mathrm{EC50}_j$ data with reported reliability score 1 versus data with reported reliability score 2. Good agreement is shown between most combined $\log \mathrm{EC50}_j$ data with reliability score1 versus combined $\log \mathrm{EC50}_j$ data with reliability 2. These data show an average deviation of a factor 2.1 (0.32 log units), and 90% of reliability 1 versus reliability 2 $\log \mathrm{EC50}_j$ values fall within a difference of a factor 30 (1.48 log units). Largest deviations in data with different reliability scores per species-substance combination are found for *Daphnia magna* with $\log \mathrm{EC50}_j$ varying by more than 5 orders of magnitude (4.1 log units) after exposure to octabenzone (CAS: 1843-05-6) and for *Pimephales promelas* with $\log \mathrm{EC50}_j$ varying by up to a factor 8000 (3.9 log units) after exposure to tin (CAS: 7440-31-5). Thereby, no consistent variation in the sensitivity of $\log \mathrm{EC50}_j$ values to reliability scores was observed across test species.

(ii) Comparing different trophic levels: To evaluate our data set with respect to the long-term sensitivity of test species from different trophic levels in the freshwater ecosystem all chronic $\log \mathrm{EC50}_j$ values per trophic level are plotted in Figure 3 as average per substance across all species-specific 'chronic' EC50 data points. Chemicals with data from chronic tests available for only one trophic level are not included.

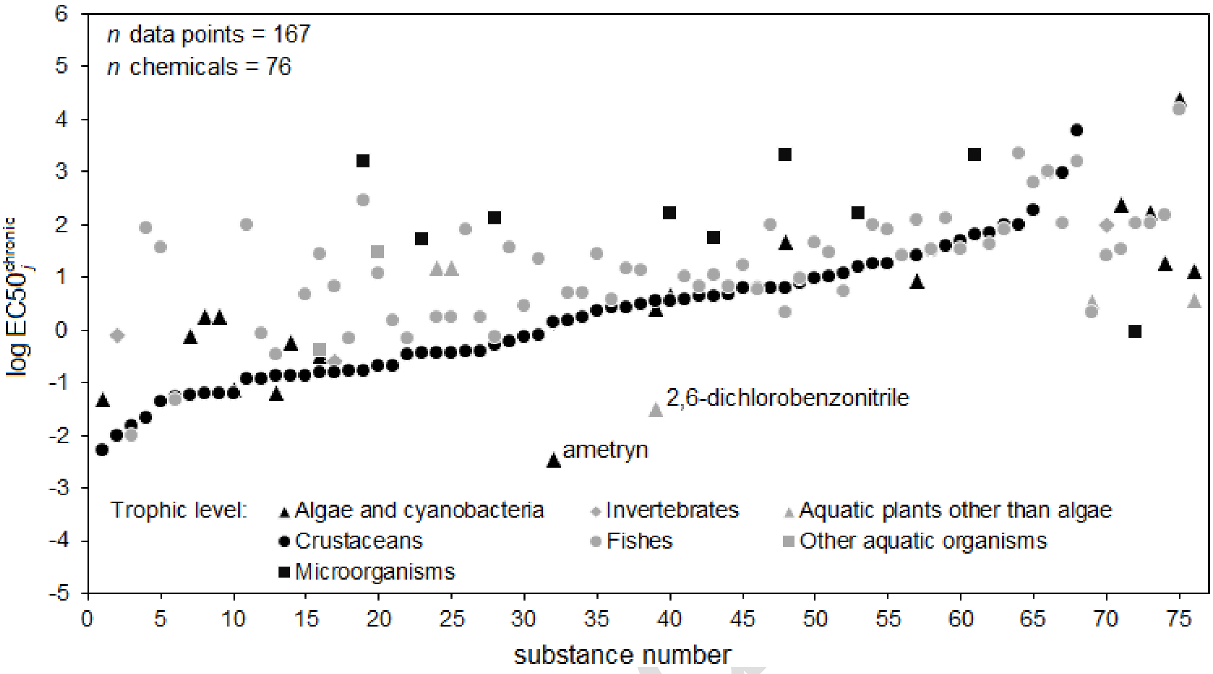

Figure 3. Chronic log EC50$_j$ (mg/L) values per trophic level, i.e. average values per substance across 'chronic' EC50 data points for all species belonging to that trophic level. Data are ranked according to crustaceans as trophic level with the largest number of data points

Out of 167 averaged chronic log EC50$_j$ values, 68 values were determined for crustaceans with *Daphnia magna* as most frequent species and 62 values for fishes, whereas only 3 and 2 values could be calculated for invertebrates and other aquatic organisms, respectively. Figure 3 indicates that species of different trophic levels do not strictly follow the same sensitivity patterns towards chemical exposure. More specifically, crustacean species show consistently a higher sensitivity than fish, algae and other aquatic plants and organisms for exposure to many substances. In contrast, for a limited number of the analyzed substances for which crustacean data exist, other trophic levels are found to be more sensitive, potentially because these substances have specific effect mechanisms towards the species of these trophic levels (like e.g. herbicides acting on algae and macrophytes). However, there are not enough data points and chemicals included to generalize this deviation from the general trend. Exceptions from this general trend are moreover ametryn (CAS: 834-12-8), to which algae and cyanobacteria on average show a factor 380 higher sensitivity than crustaceans, and dichlorobenzonitrile (CAS: 1194-65-6), to which aquatic plants (other than algae) on average show a factor 100 higher sensitivity than crustacean species. For the different trophic levels, the highest sensitivity is shown for algae and cyanobacteria to ametryn (CAS: 834-12-8) with an average $\log \mathrm{EC50}_j = -2.4$ (corresponding to an average $\mathrm{EC50} = 0.004$ mg/L), for crustaceans to zinc pyrithione (CAS: 13463-41-7) with an average $\log \mathrm{EC50}_j = -2.3$ (average $\mathrm{EC50} = 0.005$ mg/L), and for fishes to octamethylcyclotetrasiloxane (CAS: 556-67-2) with an average $\log \mathrm{EC50}_j = -2$ (average $\mathrm{EC50} = 0.01$ mg/L), with crustaceans showing a very similar sensitivity to this substance.

Comparing ecotoxicity data from REACH and USEtox

Finally, $\log \mathrm{HC50}$ were calculated combining reported chronic data and chronic data estimated from reported acute data with REACH reliability scores 1 and 2 to compare use of ecotoxicity information from REACH with use of data listed in USEtox (Figure 4). Data for organic substances and for cationic metals are taken from USEtox 2.0.

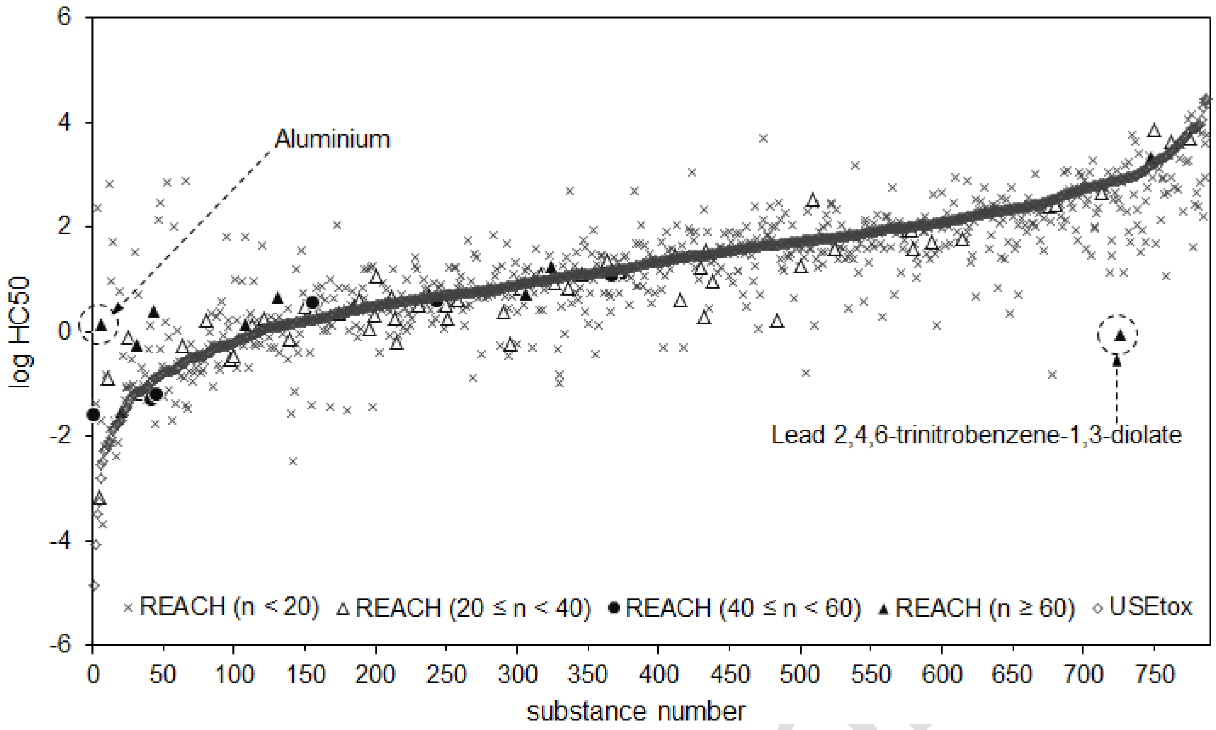

Figure 4. Comparison of substance-specific log HC50 values of combined acute and chronic data with reliability scores 1 and 2 from REACH and USEtox. REACH-based values are classified according to the underlying number of reported individual data points per substance

Out of 787 considered substances with ecotoxicity data both in the USEtox database and in REACH, log HC50 values were calculated from REACH for substances with less than 20 reported data points ($n = 714$), which is considered a desirable minimum for variety in species and trophic levels with respect to the effect of sample size on accuracy of species distribution models as applied in LCIA [25]. These REACH data deviate from the corresponding log HC50 given in USEtox on average by a factor 2 (0.31 log units) with 95% of all deviations falling within a factor 44 (1.65 log units). Similarly, log HC50 values calculated from REACH for substances with more than 20 data points ($n = 73$) deviate on average from the corresponding USEtox values by a factor 1.7 (0.23 log units) with 95% of deviations falling within a factor 23 (1.35 log units). For 30% of all considered substances ($n = 237$) less than 5 data points were available in REACH. In contrast, for 16 substances more than 40 data points were available in REACH and for 3 cationic metals, namely for aluminium, silver and nickel, more than 100 data points were available. Surprisingly, the $\log \mathrm{HC50} = 0.14$ for aluminium (CAS RN: 7429-90-5) with 107 data points available in REACH, comprising 17 chronic and 90 acute data points representing species from 3 trophic levels, deviates by a factor 500 (2.7 log units) from the $\log \mathrm{HC50} = -2.56$ listed in USEtox 2.0 based on data also from species from 3 trophic levels provided in Dong et al. (2014) [23]. However, both $\log \mathrm{HC50} = 0.14$ values fall within the range of sensitivities of species from the different trophic levels covering more than 4 orders of magnitude for this substance (Figure 5A). This indicates that the calculated $\log \mathrm{HC50}$ heavily depends on the considered species and trophic levels. A similar deviation is found for exposure to lead 2,4,6-trinitrobenzene-1,3-diolate (CAS RN: 15245-44-0) with 92 evaluable EC50 data points available in REACH. The calculated $\log \mathrm{HC50} = -0.04$ deviates from the corresponding value in USEtox of $\log \mathrm{HC50} = 2.9$ by a factor 870 (2.95 log units). The underlying REACH data consist of tests from 3 different trophic levels (Figure 5B), all based on acute tests. The value listed in USEtox is based on a single acute test data point [10] that is not included in REACH.

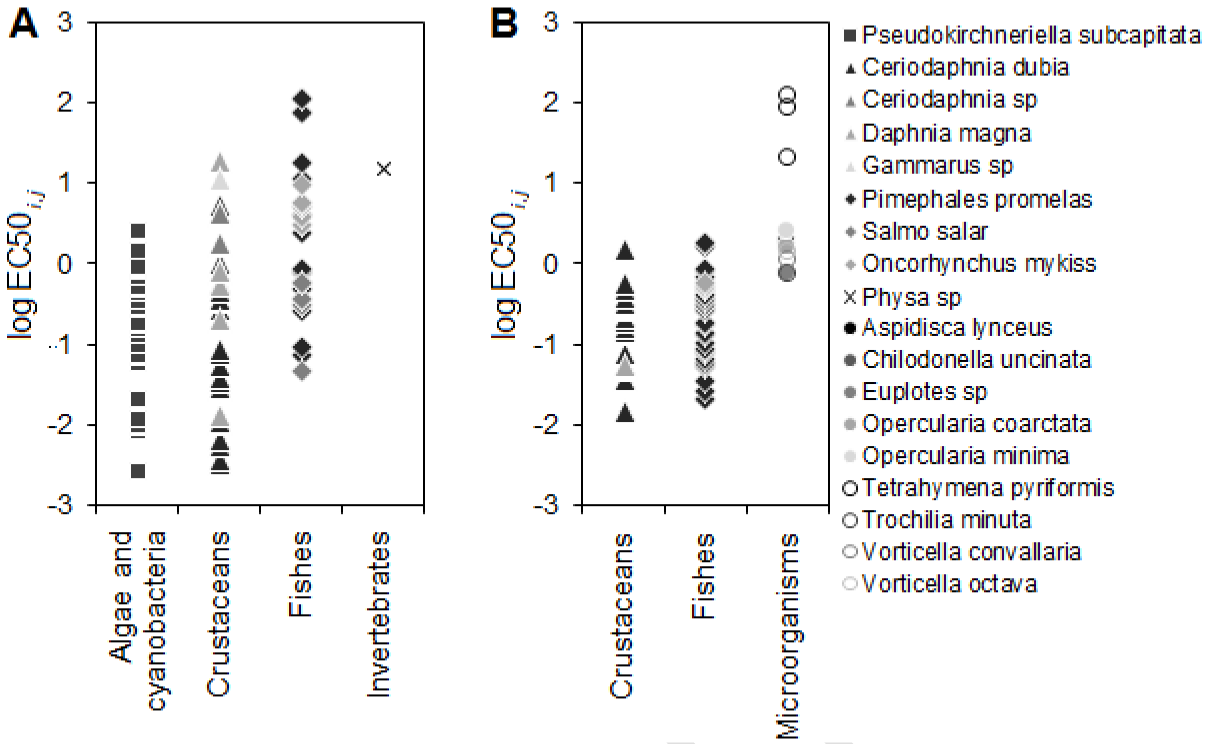

Figure 5. Sensitivity distribution of different species within distinct trophic levels to exposure of (**A**) aluminium and (**B**) lead 2,4,6-trinitrobenzene-1,3-diolate expressed by individual reported log EC50$_{i,j}$ acute and chronic data points in REACH

DISCUSSION

REACH internal data evaluation

It is a requirement in REACH that tests have to be carried out in compliance with the principles of Good Laboratory Practice (GLP) described in Directive 2004/10/EC [26]. In addition, in Annexes VII to X on standard information requirements, the use of various OECD test guidelines is required in cases where no EU test method exists [14]. Deviations from the standard guidelines need to be explicitly indicated in line with the endpoint-specific testing strategies for aquatic toxicity testing [19] and reflected in the reliability score of the reported data. However, issues in complying with data reporting requirements including reliability have recently been identified in several studies [27-29]. This means for the potential use of REACH data in LCIA that compliance with reporting requirements might need to be double checked.

The average of 9.8 data points available in REACH per substance included in the present study for freshwater ecotoxicological information seems generally sufficient for comparative assessment purposes, but a fraction of only 7.5% of the data being based on chronic tests demonstrates a strong dependency on predominantly acute test data. Extrapolation from acute to chronic exposure data remains a topic for future research. This might also include to look at data reported for additional effect endpoints, such as no-observed effect concentrations (NOEC) to increase available data for comparative toxicity characterization [30], although EC50 data are generally considered more suitable for relative comparison applications [31].

Sensitivities to some substances vary strongly between the tested species whether they belong to the same or to different trophic levels. This is the case when the chemical has a specific mode of action towards some species and a perhaps more general narcotic mode of action against all other species. This means that high deviations between the log HC50 values calculated for the same substance from data of different data sources do not necessarily indicate a poor quality of the underlying data of any particular data source. This leads to the conclusion that the quality and representativeness of the calculated log HC50 values from REACH data can be improved by including toxicity test data for as many different species and trophic levels as possible, thereby also exploring additional data sources than those currently included in REACH.

REACH and USEtox data comparison

Only 5% of the approximately 15000 substances registered under REACH are included in the present study, i.e. those that also have ecotoxicity effect data listed in USEtox. REACH data that are not associable with a unique substance via a CAS registration number as substance identifier – in our test set of selected substances approximately 50% of the data – are not useful for LCA, where emissions and impacts are calculated at the level of individual substances. The use of relevant data from REACH is further limited by the fact that around 25% of the data have a reported reliability score higher than 2 (i.e. data not considered reliable) and many reported ecotoxicity data are based on endpoints currently not considered in LCIA – in our test set these together eliminate approximately 53% of all data points. While we only used the remaining 47% of data from REACH in our comparison with USEtox to gain deeper insight into data considered reliable and matching effect endpoints currently used in LCIA, the data source situation could be generally improved by further scrutinizing data not considered reliable in REACH and by developing methods to include additional effect endpoints available in REACH.

For USEtox, it is recommended to characterize freshwater aquatic ecotoxicity based on data of at least 3 different species covering at least 3 different trophic levels to ensure a minimum variability of sensitivities towards the substance [5]. Freshwater ecotoxicological effect data are predominantly available for species belonging to algae (phytoplankton; primary producers), crustaceans (zooplankton; primary consumers), fish (secondary/tertiary consumers), and bacteria (microorganisms; reducers) [13]. However, in our test set of considered substances, we found for 181 substances (23%) that data from only 1 or 2 trophic levels were reported in REACH and for 147 substances (19%) less than 3 species were reported, while for 606 substances (77%) data corresponding to the suggested minimum of 3 species from 3 trophic levels were available, and for 39 substances (5%), even data for 7 or more species from 5 to 7 different trophic levels were available. In contrast, from the ecotoxicity data points listed in USEtox for 2262 organic substances with available information on number of test species and trophic level, for 1659 substances (73%) data for species from only 1 or 2 trophic levels are listed and for 1187 substances (52%) less than 3 species are listed, while for 604 substances (27%) the suggested minimum of at least 3 species from 3 different trophic levels are listed. The problem with this situation is reflected in our results, where the majority of substances for which log HC50 from REACH and USEtox show large deviations of more than a factor 10 typically either has only very few underlying data points in REACH, USEtox, or even both. Consequently, different scrutinized data sources should be consistently combined building a stronger ecotoxicity characterization data basis in order to accommodate the desired stability when using average values across all available data, species and trophic levels for LCIA purposes.

Finally, chronic effect endpoints are strongly suggested as preference over acute endpoints as it has been shown that single-species chronic tests are the most suitable in many cases to reflect whole ecosystem sensitivity to chemical exposure [32].

The assumption of a generic conversion factor from acute to chronic effects currently implemented in USEtox may explain some of the significant differences between log HC50 calculated from REACH versus USEtox. First estimates for cationic metals indicate a high variation in the acute-to-chronic relationship for different trophic levels in tests with the same substance, where it was shown that for aluminium, fishes show in general more than 6 times higher acute-to-chronic ratios than crustaceans [23]. For a wide range of organic substances, however, it was shown that there is no systematic deviation between chronic and acute endpoints for most considered substances [33]. Therefore, we recommend focusing future research efforts on assessing the feasibility of defining acute-to-chronic ratios at the level of test species or trophic levels and chemical classes or toxic mode of action.

Options for improving LCIA ecotoxicity characterization

Using REACH ecotoxicity information as one potential input data source for freshwater ecotoxicity characterization in LCIA requires addressing several aspects. Data from study types such as read-across, QSAR or grouped data should be excluded. Further, data with reported reliability scores other than 1 and 2 in REACH should currently not be considered without further scrutinizing. Activated sludge and other potentially inadequate test ‘organisms’ should be excluded as long as they do not reflect a species of freshwater aquatic ecosystems. Substances in REACH need to have a CAS number to be considered in LCIA to be able to quantify substance-specific fate, exposure and effect factors as well as to match impact characterization results with chemical-specific emission flows. According to Article 111 of the REACH regulation [14], registration dossiers have to be submitted with a software tool through the ECHA-internal IT system. Nevertheless, information is at times entered in a wrong format, category or not entered at all. In fact, ECHA evaluates the general completeness of the registration documents, whereas any statement about the evaluation of the submitted data by ECHA is not part of the regulation. This does not allow for identifying which submitted data effectively comply with the data reporting requirements [27].

The present study is primarily limited with respect to comparing REACH and USEtox at the level of aggregated log HC50 per substance. It would be more appropriate to compare directly individual EC50 data points from REACH with underlying individual EC50 data points used in USEtox. Since the original EC50 data used to compile HC50 values for USEtox are not freely accessible, the comparison has been performed based on aggregated data. However, we recommend that all underlying data used to compile input and output data from USEtox are available on request via the USEtox team to ensure reproducibility and transparency. We recommend directly comparing EC50 values per species and substance in future research to contrast different data sources. Additionally, we recommend collecting and analyzing data from different existing ecotoxicity databases like REACH, OECD SIDS, and ECOTOX to aim for completeness and identify and avoid potential cross-referencing to the same underlying original studies.

CONCLUSION

Currently, LCIA characterization models do not use all ecotoxicological data available from regulatory databases, published studies and other data sources. Several chemicals are characterized based on only a single tested species and trophic level and often only acute data. Hence, using REACH as a continuously updated and extended data source could be a starting point to improve the current data situation in LCIA with several tens of thousands of available ecotoxicity data for approximately 15000 registered chemicals as of 2015. To use this potential, however, it is a prerequisite to further assess the reported data in terms of reliability and applicability for LCIA as we found several aspects that require further research before considering REACH as a viable data source in the consensus model USEtox. REACH-internal quality control of approximately 5% of the submitted data might be sufficient for the actual purpose of this database to support regulatory risk assessment if these 5% mainly focus on the most sensitive species. For the purpose of being applied in LCIA, however, the most sensitive species is not considered as good a representative of the sensitivity of the exposed ecosystem as the average across all sensitivities of all available (tested) species and trophic levels. When considering all data from REACH that are labeled reliable (with and without restrictions), it would hence be necessary to scrutinize all data (including the 95% of data that are currently not checked by ECHA). Focus in future research efforts should be put on systematically analyzing differences between data with reliability scores 1 and 2 and between acute and chronic data as these are currently also the main limitations in LCIA models with respect to ecotoxicity characterization. As REACH contains a very limited amount of reported chronic EC50 (or equivalent) data, extrapolations are necessary from acute to chronic effects, which also requires further research and improvement. Finally, it remains unclear how well REACH covers existing and available ecotoxicity data for characterizing ecotoxicity in LCIA. In conclusion, we recommend to systematically investigating quality-, extrapolation-, and applicability-related issues, before considering REACH and also other available databases as potential basis for the characterization of ecotoxicity in LCIA. For USEtox as consensus-based model, we recommend to explicitly differentiate between substances with sufficient and reliable ecotoxicity information and substances with insufficient or missing ecotoxicity information to pinpoint current data gaps and to avoid underestimating potential effects from substances with missing or insufficient data.

SUPPLEMENTAL DATA

Tables S1−S2. (30 KB XLSX).

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