Toward effective use of REACH data for science and policy

Fantke, Peter; Aurisano, Nicolo; Provoost, Jeroen; Karamertzanis, Panagiotis G.; Hauschild, Michael Zwicky

Published in:
Environment International

Link to article, DOI:
10.1016/j.envint.2019.105336

Publication date:
2020

Document Version
Publisher's PDF, also known as Version of record

Environment International 135 (2020) 105336

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Toward effective use of REACH data for science and policy

Peter Fantke[a,*], Nicolò Aurisano[a], Jeroen Provoost[b], Panagiotis G. Karamertzanis[b], Michael Hauschild[a]

[a] Quantitative Sustainability Assessment, Department of Technology, Management and Economics, Technical University of Denmark, Produktionstorvet 424, 2800 Kgs. Lyngby, Denmark
[b] Computational Assessment Unit, Directorate of Prioritisation and Integration, European Chemicals Agency, Annankatu 18, 00121 Helsinki, Finland

ARTICLE INFO

Handling Editor: Adrian Covaci

Keywords:
REACH regulation
Data curation
Substance prioritisation
Chemical substitution
Chemical safety assessment
Life cycle impact assessment

1. Introduction

With the implementation of the European Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), a unique and valuable body of physicochemical, environmental fate and (eco)toxicity data has been collected. These data are relevant for decision makers to ensure regulatory compliance and to close data gaps as well as for researchers to study substances and develop assessment methods and models for various contexts, including risk and sustainability assessment, chemical substitution, substance prioritisation, and eco-labelling (Dearden et al., 2013; Gilbert, 2016; Luechtefeld et al., 2016; Arp et al., 2017; Müller et al., 2017; Fantke and Illner, 2019; Kirchhübel and Fantke, 2019). However, using REACH data is challenging due to the inherent complexity of the data and the underlying data model implemented in the International Uniform Chemical Information Database (IUCLID) maintained by the European Chemicals Agency (ECHA). Despite earlier data format harmonization efforts (Sobanska and Le Goff, 2014), the current REACH submission system allows for a considerable amount of critical information to be submitted via free text fields. Extracting data from such free text fields is difficult, since data structure, units, and boundary conditions are often unclear, which introduces additional sources of error (Krallinger et al., 2017). Furthermore, several fields in the Endpoint Study Records (ESR), which contain a summary of the study for a specific endpoint (e.g. partition coefficient or long-term toxicity to fish), need to be processed to evaluate information type and reliability. Finally, the IUCLID database is constantly evolving as industry keeps submitting new (and to a limited extent also updated) registration dossiers, while the database itself and related OECD harmonized templates (oecd.org/ehs/templates) are also evolving, requiring periodic data migrations to newer versions in support of scientific and regulatory needs (Heidorn et al., 2003; Sobanska and Le Goff, 2014).

Primarily, data submitted under REACH are used as input for chemical safety assessment to “ensure a high level of protection of human health and the environment” (EC, 2006, p. 2), referring to the production and use of substances in Europe. In addition to chemical safety assessment, there are other science and policy fields, that is other environmental and health assessment contexts and related regulations in Europe and elsewhere, which require different kinds and extents of substance data to address distinct questions and purposes (see Fig. 1) – some of these science and policy fields and their data needs are discussed further below. However, publicly available REACH-related substance information can currently not be used as originally collected to provide relevant, quality-assured data for the various purposes. Instead, the collected information will first have to be meaningfully transformed and curated, which is to find, pre-process, re-structure, and annotate relevant data and their presentation, in order to enhance their usability for any given purpose. Further, integrating REACH data with other sources to close data gaps faces additional challenges due to

* Corresponding author.
E-mail address: pefan@dtu.dk (P. Fantke).

https://doi.org/10.1016/j.envint.2019.105336
Received 18 June 2019; Received in revised form 15 November 2019; Accepted 15 November 2019
Available online 26 December 2019

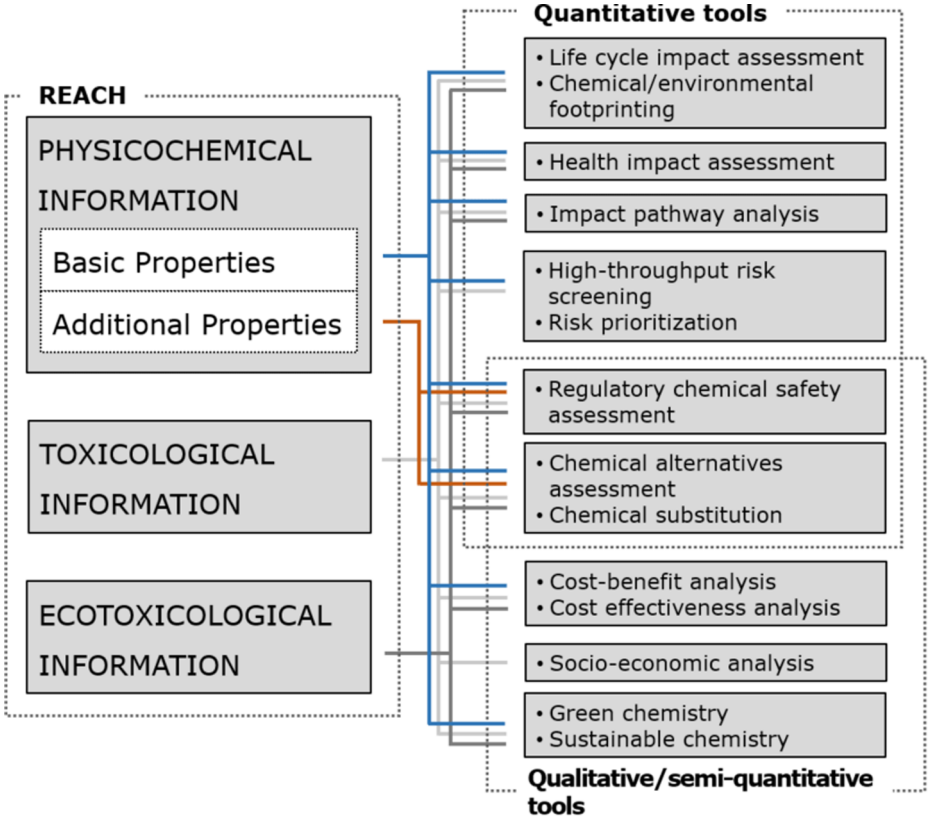

Fig. 1. General overview of potential uses of substance data submitted under the European REACH regulation in different regulatory and non-regulatory science and policy fields.

differences in data quality and underlying assumptions for e.g. deriving relevant values from several raw data. Any data transformation and curation mechanism will moreover have to be adapted to potential IUCLID data format changes. Such processing of the data submitted under REACH will require a technological and scientific investment into a single, generic and automated transformation and curation procedure that will produce data that can be tailored toward different needs by the user. This can be achieved via annotations and systematic rules, based on which users can select those data that are applicable to their given context (Karapetyan et al., 2015; Mansouri et al., 2016). In response, ECHA intends to execute such curation rules in its infrastructure to ensure that data remain available and up-to-date with regard to both newly received information and IUCLID updates.

Different uses require the data to be filtered and aggregated in different ways and levels, depending on the purpose, reliability tolerance, and data quality. Ideally, any automated pre-processing should hence be done via clearly defined annotations that can be applied by end users to filter data according to their specific needs. As industry has put considerable effort into data gathering and generation, and ECHA into data processing, there is an urgent need to strengthen and extend the use of available REACH data, while ensuring high data quality, transparency, and scientific integrity. This is particularly difficult as information submitted under REACH is not always compliant with information requirements (UBA, 2015). Moreover, with the continuously growing worldwide public concerns about the potential impacts of substances on human and environmental health (OECD, 2008; Stehle and Schulz, 2015; UNEP, 2016; Landrigan et al., 2018) and the paucity of substance-related data (Scheringer, 2017), there is a global call for better access to data that can be made publicly available to support improved chemicals assessment and management (Gilbert, 2016; Saouter et al., 2018).

In the present study, we provide an overview of substance data required in different science and policy fields related to chemicals assessment and management, and discuss information submitted under REACH as possible source for addressing these data requirements, aiming at increasing the dissemination and effective use of the large amount of data collected under REACH.

2. Data needs in different science and policy fields

Different types of substance data are required in regulatory chemical safety assessment, but also in various other environmental and health assessments and related policy fields (Fig. 1). Basic physicochemical property data have the widest application domain, ranging from design and high-throughput testing of new substances and drugs, chemical and material engineering, product and environmental quality management, to all fields related to environmental chemistry including the prediction of properties of substances that cannot be directly measured, such as overall environmental persistence. Many property data in IUCLID can also be obtained from other publicly available databases, such as ChemSpider (chemspider.com) (Williams, 2011) or the CompTox Chemicals Dashboard (comptox.epa.gov/dashboard) (Williams et al., 2017).

In addition to physicochemical property data, IUCLID contains selected human toxicological and ecotoxicological information (e.g. data on skin sensitization, see also Fig. 2), which is a crucial component in various qualitative and quantitative frameworks, where human or environmental health quality in relation to chemical exposure is assessed (Fantke et al., 2019). Examples, where such data might be needed are for the evaluation of human and ecological exposure and toxicity in (a) health/ecological impact assessment and impact pathway analysis for assessing e.g. policy interventions, (b) life cycle impact assessment and chemical and environmental footprints for assessing the environmental performance of products and services, or (c) high-throughput risk screening for substance prioritisation. Each of these fields requires its specific assessment endpoints to consider, along with specific levels of

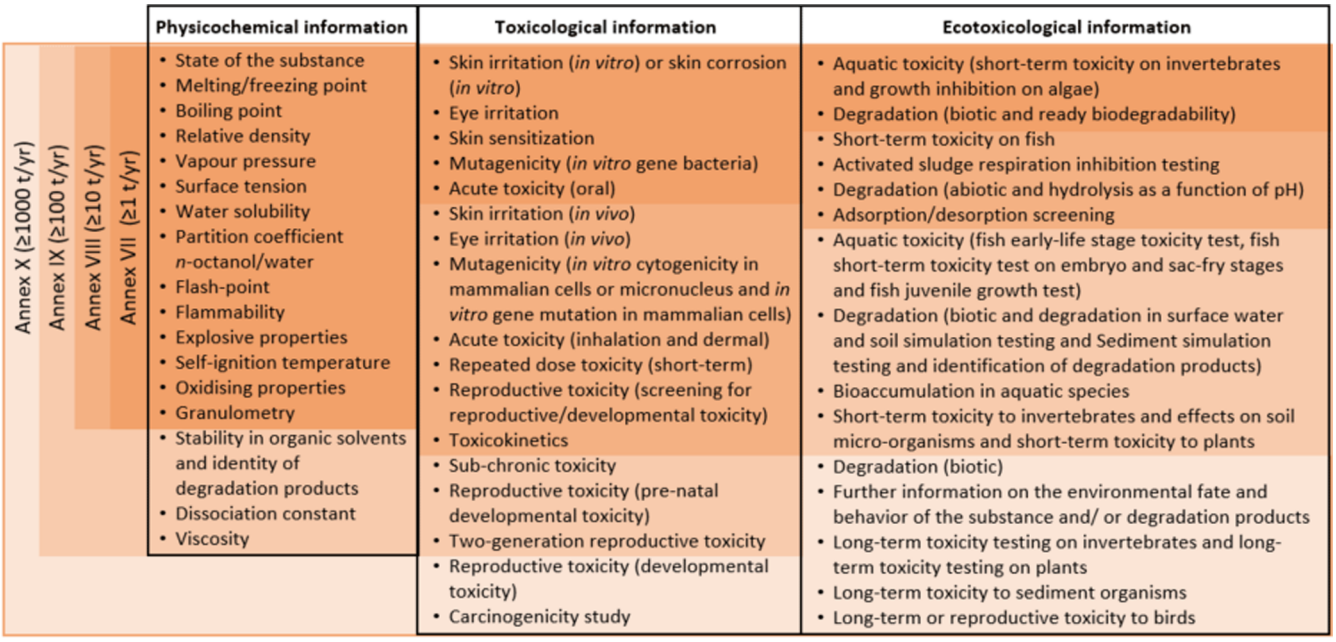

Fig. 2. Substance information required as function of annual production/import volume into the European Economic Area (EEA) according to the Annexes of the European REACH Regulation.

data aggregation and quality. (Eco)toxicological data are furthermore relevant for designing new substances or drugs (green and sustainable chemistry), new products and technologies (life cycle engineering), and identifying and evaluating viable alternatives to hazardous substances in specific applications (chemical alternatives assessment).

REACH-related data could finally be useful as a source for developing read-across approaches and category arguments as input for filling data gaps for a substance by using information from one or more similar substances, which might be required in fate, exposure and toxicity effect estimation approaches, and for validating *in vitro* (high-throughput) techniques where needed (Berggren et al., 2015; Müller et al., 2017; Patlewicz et al., 2017). To give a specific example, the life cycle assessment community has developed various emission inventory databases and impact characterisation methods including the widely applied scientific consensus model USEtox for characterising toxicity-related impacts on humans and ecosystems (Rosenbaum et al., 2008; Westh et al., 2015). Yet, no consistent data source for substance information in USEtox is available. This situation has been criticised, and information submitted under REACH has been proposed as potential starting point for a harmonised data source, which however requires further adaptation of the data for effective use in life cycle toxicity characterization (Müller et al., 2017; Saouter et al., 2017a,b; Fantke et al., 2018a).

3. Overview of data submitted under REACH

REACH entered into force on 1-Jun-2007 and as of 15-Jun-2019, 19,067[1] unique substances are registered (70% mono-constituent substances, 9% multi-constituent substances, and the rest being substances of unknown or variable composition, complex reaction products or of biological materials, UVCB) based on more than 96,000 submitted dossiers, consisting of 8% individual and 92% joint submissions (echa.europa.eu/information-on-chemicals/registered-substances). Study results are usually summarized in Endpoint Study Records per listed endpoint (ECHA, 2018c).

REACH registered data are nested in the IULID system and their curation requires knowledge from different scientific disciplines including chemistry, environmental chemistry, exposure science, (eco) toxicology as well as computational data analysis, statistics, data mining, automation, and cheminformatics. If such knowledge is omitted, data misinterpretation will occur, such as misclassification of ecological species if species names are misspelled or multiple names are used per species (de Zwart, 2002; Müller et al., 2017). Additionally, extracted data need to be processed in line with the given boundary conditions of any assessment context, for example averaging ecotoxicity data across species versus using data from a particular (e.g. the most sensitive) species.

On the technical side, ECHA maintains the data structure for intrinsic and hazard properties of substances via IUCLID (ECHA, 2018b). The following substance information can be recorded: identity, composition, and supporting analytical data of the substance; classification and labelling; physical/chemical and fate properties; and (eco)toxicological hazard properties. An overview of REACH information requirements as function of annual European production/import volume is provided in Fig. 2.

Guidance documents (ECHA, 2012) facilitate the implementation of REACH by describing good practice on how to fulfil the information requirements, and how to report data in IUCLID.

In accordance with REACH Articles 119(1) and (2), ECHA is required to publish information it holds on all registered substances. Information is published from all registrants; joint submission leads, joint submission members, and individual registrants (ECHA, 2018a). The published data contain information on, amongst others, substance identity (name, EC/List number or CAS number), administrative data (registration type, registrant name, publication date, country, etc.), substance data (total tonnage band, outcome of persistence, bioaccumulation and toxicity (PBT), etc.), and uses and exposure. IUCLID study results (iuclid6.echa.europa.eu/reach-study-results), such as indication of endpoint addressed, year and report date, and test material, are made publicly available as a collection of non-confidential substance data submitted to ECHA under REACH, derived from data that are already accessible on the ECHA website. However, study results datasets only contain results and in reduced form, while details about, for example, followed test methods are reported elsewhere or not reported at all. Results for approximately 15,000 unique substances are available for

[1] As of 17-Oct-2019 (latest update), ECHA has received registrations for 22,468 unique substances containing information from 96,761 dossiers.

download in a single IUCLID 6 database. These study results are provided for research, education, safety data sheet compilation, and classification and labelling of chemicals, while the data may not be used for other purposes (ECHA, 2018a).

Despite managing its own database, ECHA is a key collaborator in developing software and hosting the eChemPortal (echemportal.org) (de Marcellus, 2014), in cooperation with the OECD and other international regulatory institutions. The eChemPortal provides free access to information on substance properties, allowing simultaneous searching of reports and datasets by substance name, identifier or property. Links to collections of hazard and risk information prepared for regulatory substance review programs at national, regional and international levels are available. Classification results according to national/regional hazard classification schemes or the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) are also provided where available. In addition, eChemPortal provides use and exposure information, and the published detailed information on substances from REACH registration dossiers, as part of ECHA's collaboration.

Despite the available information, several aspects relevant for evaluating chemical safety, but also for other science and policy contexts are currently missing or not disseminated via REACH. This includes, for example, human exposure and toxicity impact estimates from substances in the various product applications and via environmental emissions, which is important in chemical risk assessment, life cycle impact assessment, chemical substitution, substance prioritisation, and other fields (Fantke et al., 2016; Suciu et al., 2016; Fantke et al., 2018b).

4. Harvesting REACH data as input for various assessment frameworks

The REACH registration process has resulted in a wealth of substance data. However, the data submitted under REACH show great variation in terms of study design and reliability, which hampers ready use of these data in different contexts. As demonstrative example of the information complexity in REACH, we use data on 'repeated dose toxicity via the oral route'. Short-term repeated dose toxicity data (28 day) and sub-chronic toxicity data (90 day) are respectively required for substances manufactured/imported at $\geq$10 tonnes/year and $\geq$100 tonnes/year. For both requirements, data can be combined with reproduction/developmental toxicity screening (OECD, 2016), creating several possibilities to fulfil the information requirements. To characterise the type of repeated dose toxicity studies received under REACH (ECHA, 2017), we extracted all corresponding endpoint study records from IUCLID (iuclid6.echa.europa.eu) on 18-Dec-2018. Duplicates were identified and removed using study period, guideline, reference, and test material to create a finger print of the study. This is challenging, primarily because of the extensive use of read-across and category arguments in REACH registrations, leading to the same experimental study being reported in more than one registration dossier. We then removed studies that were not experimental or read-across (itself based on an experimental result, although the test material does not match the substance being registered), and kept only endpoint study records reported to be reliable, i.e. studies conducted according to internationally accepted testing guidelines or well documented and scientifically acceptable (Klimisch et al., 1997). By using their finger prints, studies were made unique after which they were binned. The binning for the study period is based on the reported date, namely older than 31-Dec-1959, 1-Jan-1990 to 31-Dec-1999, 1-Jan-2000 to 31-Dec-2007, 1-Jan-2008 to 31-Dec-2014, and 1-Jan-2015 and newer. Study duration was binned according to required days set by the test (e.g. a 28 or 90 days rodents test). The derived effect levels were then binned as effect level not determined, $\leq$10, $\leq$100, $\leq$300, $\leq$1000 or $\leq$2000 mg per kg body-weight per day.

The number of unique repeated dose toxicity studies via the oral route (n = 16,633) are shown in Fig. 3, displaying the relationship between the study period (left hand bar), study duration (middle bar) and derived effect level (right hand bar) for the data requirement 'repeated dose toxicity'. This figure indicates that approximately one third of the experimental studies was carried out after REACH entered into force. In terms of study types, approximately one quarter are sub-acute studies of 28 days duration, while an equal proportion is sub-chronic studies of 90 days duration. For a large number of studies, the study type could not be automatically assigned by processing the guideline, which points to possible study quality or study reporting issues, which were not investigated further for the purposes of our analysis. With regard to effect levels, for approximately one third of the studies, (no/low) effect levels below 100 mg/kg/d have been reported, whereas for the remaining studies, toxicity was lower or the effect levels were not reported in a way that could be automatically retrieved and processed.

This example illustrates that a careful and systematic data transformation and curation approach for making substance data submitted under REACH accessible and suitable as input for different science and policy application fields is required, which needs to be transparent, reproducible and practical (Mesirov, 2010). Moreover, there is a need to clarify the level of aggregation and quality for each application of the data. One example is to use REACH-related data for creating datasets in support of extrapolations, for example, across ecotoxicological effect endpoints (Aurisano et al., 2019), and facilitating quantitative comparisons at the level of substance class, exposed population or species group, as component of consumer or ecological exposure assessments. In this example, most restrictive data selection criteria apply to arrive at highest possible data quality at the expense of disregarding available data of lower quality. Another example is to use REACH-related data as input for rapid-screening level evaluations that are found in high-throughput risk screening or chemical alternatives assessment (Tickner et al., 2019). For these purposes, more inclusive data selection methods apply to yield a high data coverage but with reduced overall data quality. Both approaches are meaningful in their specific contexts. However, to identify which data aggregation and quality level is relevant for a given context, the question or assessment frame must first be analysed. Relevant data should then be selected in a way to generally be as inclusive as possible and as restrictive as necessary according to the prescribed frame. This will yield data with different recommended levels-of-detail specific to each application context, in line with the data quality requirements of different science and policy fields.

Furthermore, any context-specific requirements for harvesting and using data from a live data source like the IUCLID database need to be clarified. Such requirements include relevant curation criteria, data for which substance information can be curated using automated methods (e.g. checking assessment criteria classes) and which information needs to be curated at least to some extent manually (e.g. extracting certain data from free text fields), both requiring respective algorithms for data selection and annotation. In support of addressing such requirements, recommendations for improving the structuring of data should be developed to facilitate maximum automation in the data transformation and curation process. Such recommendations should clarify the required information to allow for automated curation of all relevant data endpoints in REACH. For example, information about the dissociation of a substance is needed to determine quality and uncertainty of reported n-octanol/water partition coefficients as function of test method and conditions, or any substance property that varies with temperature (ECHA, 2014).

Finally, in addition to substance-specific data, average default background information might be obtained from all substances with available data to fill data gaps for substances with insufficient or missing reported data. In such cases, it should be clarified if any other data source has been considered, such as risk assessment reports from the European Food Safety Authority or databases from the U.S. Environmental Protection Agency, including related data quality and reliability information.

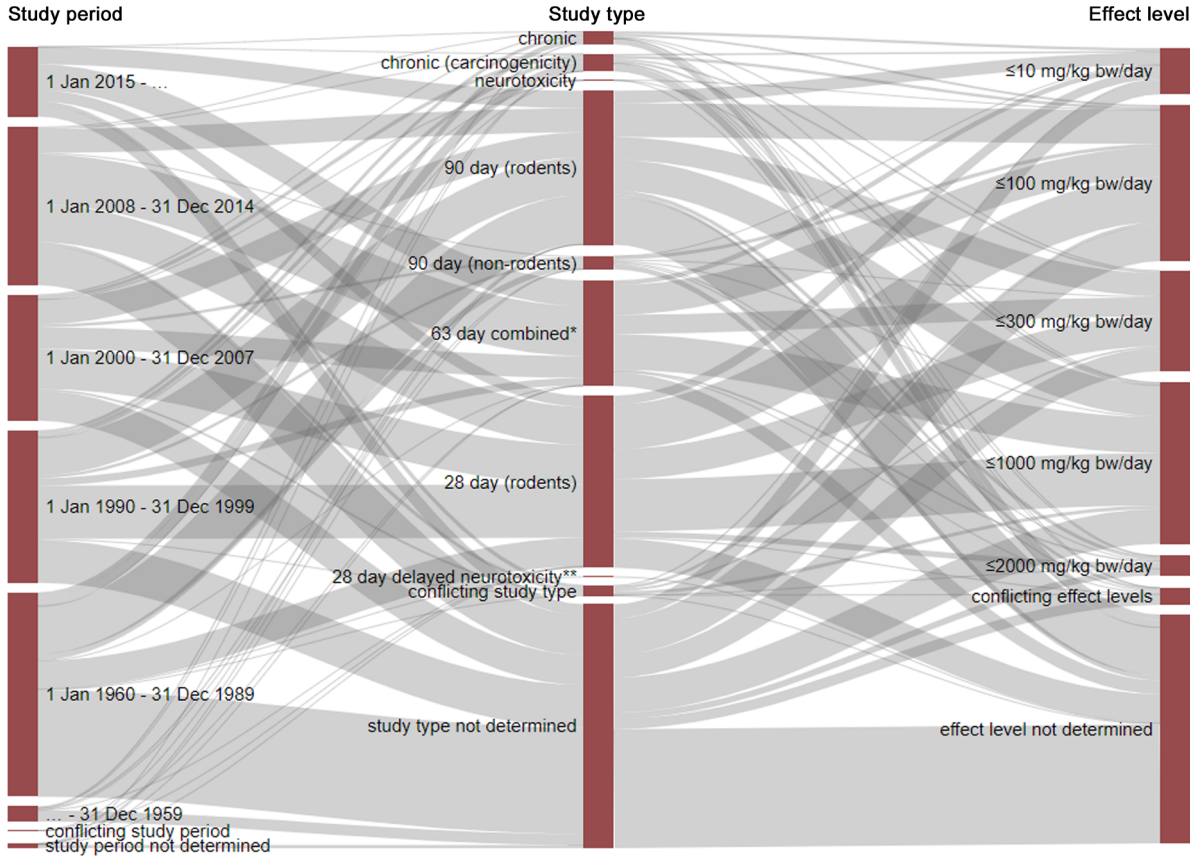

Fig. 3. Partitioning of 16,633 repeated dose toxicity studies via the oral route in terms of study period, guideline and effect levels observed, demonstrating the complexity of REACH data requiring systematic data selection and curation before use in various contexts. *63 day combined repeated dose toxicity with reproduction/developmental toxicity screening; **28 day delayed neurotoxicity of organophosphates/organophosphorous substances.

5. Conclusions and way forward

REACH is a valuable substance data source that finds applications well beyond regulatory safety assessment. Simply extracting and directly applying data submitted under REACH as input for models and approaches applied in the various chemicals assessment and management contexts, however, is not advocated due to challenges in data quality, complexity and presentation. Instead, systematic and flexible data transformation and curation approaches based on multidisciplinary knowledge are required, which can, for example, build on initial work by Arp et al. (2017), Schulze et al. (2018), and Zahn et al. (2019). Automated methods should be included in these developments wherever possible to minimize human mistakes, and complementary manual methods where automation is difficult (e.g. mining text from variable free text fields in IUCLID). Such approaches need to be adaptive to the ever-growing pool of additional and updated data submissions and potential format changes, while respecting the different boundary conditions of the various chemicals assessment and management frameworks. With such data curation approaches at hand, data submitted under REACH can be disseminated to a wider range of chemical assessment and management frameworks in Europe and elsewhere.

At the same time, efforts should be pursued to complement existing data available under REACH with metrics and data from other fields, such as consumer and population exposure estimates. This would facilitate a broader consideration of REACH related data as input complementary for assessing consumer and public health and for chemical substitution across various consumer product categories.

Both the development of an approach for REACH data curation and the integration of complementary metrics and data requires a strong collaboration with ECHA to exchange structural, technical, and data requirement considerations to build a long-term platform for 'good use of available data' across relevant science and policy fields worldwide.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

Acknowledgements

This work was financially supported by a collaborative project between the European Chemicals Agency and the USEtox International Centre hosted at DTU Management, Technical University of Denmark (grant agreement no. ECHA/2017/445).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.105336.

References

Arp, H.P.H., Brown, T.N., Berger, U., Hale, S.E., 2017. Ranking REACH registered neutral, ionizable and ionic organic chemicals based on their aquatic persistency and mobility. Environ. Sci. Proc. Imp. 19, 939–955. https://doi.org/10.1039/C7EM00158D.

Aurisano, N., Albizzati, P.F., Hauschild, M., Fantke, P., 2019. Extrapolation factors for characterizing freshwater ecotoxicity effects. Environ. Toxicol. Chem. 38, 2568–2582. https://doi.org/10.1002/etc.4564.

Berggren, E., Amcoff, P., Benigni, R., Blackburn, K., Carney, E., Cronin, M., Deluyker, H., Gautier, F., Judson, R.S., Kass, G.E.N., et al., 2015. Chemical safety assessment using read-across: assessing the use of novel testing methods to strengthen the evidence base for decision making. Environ. Health Perspect. 123, 1232–1240. https://doi.org/10.1289/ehp.1409342.

de Marcellus, S., 2014. eChemPortal - The global portal to information on chemical substances. In: Wexler, P. (Ed.), Encyclopedia of Toxicology, third ed. Academic Press, Oxford, pp. 655–662. https://doi.org/10.1016/B978-0-12-386454-3.00570-4.
de Zwart, D., 2002. Observed regularities in species sensitivity distributions for aquatic species. In: Posthuma, L., Suter, G.W., Traas, T.P. (Eds.), Species Sensitivity Distributions in Ecotoxicology. CRC Press, Boca Raton, pp. 133–154. https://doi.org/10.1201/9781420032314.ch8.
Dearden, J.C., Rotureau, P., Fayet, G., 2013. QSPR prediction of physico-chemical properties for REACH. SAR QSAR Environ. Res. 24, 279–318. https://doi.org/10.1080/1062936X.2013.773372.
EC, 2006. Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Commission of the European Communities, Brussels p. 849.
ECHA, 2012. Guidance on Registration. European Chemicals Agency, Helsinki p. 126.
ECHA, 2014. Guidance on Information Requirements and Chemical Safety Assessment Chapter R. 7b: Endpoint Specific Guidance. European Chemicals Agency, Helsinki p. 257.
ECHA, 2017. Guidance on Information Requirements and Chemical Safety Assessment Chapter R. 7a: Endpoint Specific Guidance. European Chemicals Agency, Helsinki p. 610.
ECHA, 2018a. Dissemination and Confidentiality under the REACH Regulation. European Chemicals Agency, Helsinki p. 77.
ECHA, 2018b. Functionalities of IUCLID 6. European Chemicals Agency, Helsinki p. 212.
ECHA, 2018c. What is a Registered Substance Factsheet? European Chemicals Agency, Helsinki p. 21.
Fantke, P., Aurisano, N., Backhaus, T., Bulle, C., Chapman, P.M., Cooper, C.A., De Zwart, D., Dwyer, R., Ernstoff, A., Golsteijn, L., et al., 2018a. Toward harmonizing ecotoxicity characterization in life cycle impact assessment. Environ. Toxicol. Chem. 37, 2955–2971. https://doi.org/10.1002/etc.4261.
Fantke, P., Aylward, L., Bare, J., Chiu, W.A., Dodson, R., Dwyer, R., Ernstoff, A., Howard, B., Jantunen, M., Jolliet, O., et al., 2018b. Advancements in life cycle human exposure and toxicity characterization. Environ. Health Perspect. 126, 125001. https://doi.org/10.1289/EHP3871.
Fantke, P., Ernstoff, A.S., Huang, L., Csiszar, S.A., Jolliet, O., 2016. Coupled near-field and far-field exposure assessment framework for chemicals in consumer products. Environ. Int. 94, 508–518. https://doi.org/10.1016/j.envint.2016.06.010.
Fantke, P., Illner, N., 2019. Goods that are good enough: Introducing an absolute sustainability perspective for managing chemicals in consumer products. Curr. Opin. Green Sustain. Chem. 15, 91–97. https://doi.org/10.1016/j.cogsc.2018.12.001.
Fantke, P., von Goetz, N., Schlüter, U., Bessems, J., Connolly, A., Dudzina, T., Ahrens, A., Bridges, J., Coggins, M.A., Conrad, A., et al., 2019. Building a European exposure science strategy. J. Expo. Sci. Environ. Epidemiol. https://doi.org/10.1038/s41370-019-0193-7.
Gilbert, N., 2016. Legal tussle delays launch of huge toxicity database. Nature News. https://doi.org/10.1038/nature.2016.19365.
Heidorn, C.J.A., Rasmussen, K., Hansen, B.G., Nørager, O., Allanou, R., Seynaeve, R., Scheer, S., Kappes, D., Bernasconi, R., 2003. IUCLID: An information management tool for existing chemicals and biocides. J. Chem. Inf. Comp. Sci. 43, 779–786. https://doi.org/10.1021/ci0202786.
Karapetyan, K., Batchelor, C., Sharpe, D., Tkachenko, V., Williams, A.J., 2015. The Chemical Validation and Standardization Platform (CVSP): Large-scale automated validation of chemical structure datasets. J. Cheminf. 7, 30. https://doi.org/10.1186/s13321-015-0072-8.
Kirchhübel, N., Fantke, P., 2019. Getting the chemicals right: Toward characterizing toxicity and ecotoxicity impacts of inorganic substances. J. Cleaner Prod. 227, 554–565. https://doi.org/10.1016/j.jclepro.2019.04.204.
Klimisch, H.-J., Andreae, M., Tillmann, U., 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regul. Toxicol. Pharm. 25, 1–5. https://doi.org/10.1006/rtph.1996.1076.
Krallinger, M., Rabal, O., Lourenço, A., Oyarzabal, J., Valencia, A., 2017. Information retrieval and text mining technologies for chemistry. Chem. Rev. 117, 7673–7761. https://doi.org/10.1021/acs.chemrev.6b00851.
Landrigan, P.J., Fuller, R., Acosta, N.J.R., Adeyi, O., Arnold, R., Basu, N., Baldé, A.B., Bertollini, R., Bose-O'Reilly, S., Boufford, J.I., et al., 2018. The Lancet Commission on pollution and health. Lancet 391, 462–512. https://doi.org/10.1016/S0140-6736(17)32345-0.
Luechtefeld, T., Maertens, A., Russo, D.P., Rovida, C., Zhu, H., Hartung, T., 2016. Global analysis of publicly available safety data for 9,801 substances registered under REACH from 2008–2014. Altern. Anim. Exp. 33, 95–109. https://doi.org/10.14573/altex.1510052.
Mansouri, K., Grulke, C.M., Richard, A.M., Judson, R.S., Williams, A.J., 2016. An automated curation procedure for addressing chemical errors and inconsistencies in public datasets used in QSAR modelling. SAR QSAR Environ. Res. 27, 911–937. https://doi.org/10.1080/1062936X.2016.1253611.
Mesirov, J.P., 2010. Accessible reproducible research. Science 327, 415–416. https://doi.org/10.1126/science.1179653.
Müller, N., de Zwart, D., Hauschild, M., Kijko, G., Fantke, P., 2017. Exploring REACH as potential data source for characterizing ecotoxicity in life cycle assessment. Environ. Toxicol. Chem. 36, 492–500. https://doi.org/10.1002/etc.3542.
OECD, 2008. OECD Environmental Outlook to 2030. Organisation for Economic Co-operation and Development, Paris, France, pp. 523.
OECD, 2016. OECD Guidelines for the Testing of Chemicals, Section 5 Other Test Guidelines, Test No. 422: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test. Organisation for Economic Co-operation and Development, Paris p. 19.
Patlewicz, G., Helman, G., Pradeep, P., Shah, I., 2017. Navigating through the minefield of read-across tools: a review of in silico tools for grouping. Comput. Toxicol. 3, 1–18. https://doi.org/10.1016/j.comtox.2017.05.003.
Rosenbaum, R.K., Bachmann, T.M., Gold, L.S., Huijbregts, M.A.J., Jolliet, O., Juraske, R., Koehler, A., Larsen, H.F., MacLeod, M., Margni, M.D., McKone, T.E., Payet, J., Schuhmacher, M., van de Meent, D., Hauschild, M.Z., 2008. USEtox - The UNEP-SETAC toxicity model: recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment. Int. J. Life Cycle Assess. 13, 532–546. https://doi.org/10.1007/s11367-008-0038-4.
Saouter, E., Aschberger, K., Fantke, P., Hauschild, M.Z., Bopp, S.K., Kienzler, A., Paini, A., Pant, R., Secchi, M., Sala, S., 2017a. Improving substance information in USEtox®, Part 1: Discussion on data and approaches for estimating freshwater ecotoxicity effect factors. Environ. Toxicol. Chem. 36, 3450–3462. https://doi.org/10.1002/etc.3889.
Saouter, E., Aschberger, K., Fantke, P., Hauschild, M.Z., Kienzler, A., Paini, A., Pant, R., Radovnikovic, A., Secchi, M., Sala, S., 2017b. Improving substance information in USEtox®, Part 2: Data for estimating fate and ecosystem exposure factors. Environ. Toxicol. Chem. 36, 3463–3470. https://doi.org/10.1002/etc.3903.
Saouter, E., Biganzioli, F., Ceriani, L., Sala, S., Versteeg, D., 2018. Using REACH and EFSA database to derive input data for Environmental Footprint chemical toxicity impact categories. In: Draft Report Prepared for the Environmental Footprint Stakeholder Workshop of February 14th 2018 JRC Publication. N° JRC110659. European Commission, Joint Research Centre, Ispra, Italy, pp. 184.
Scheringer, M., 2017. Environmental chemistry and ecotoxicology: in greater demand than ever. Environ. Sci. Eur. 29, 3. https://doi.org/10.1186/s12302-016-0101-x.
Schulze, S., Sättler, D., Neumann, M., Arp, H.P.H., Reemtsma, T., Berger, U., 2018. Using REACH registration data to rank the environmental emission potential of persistent and mobile organic chemicals. Sci. Total Environ. 625, 1122–1128. https://doi.org/10.1016/j.scitotenv.2017.12.305.
Sobanska, M., Le Goff, F., 2014. IUCLID (International Uniform Chemical Information Database). In: Wexler, P. (Ed.), Encyclopedia of Toxicology, third ed. Academic Press, Oxford, pp. 3–5. https://doi.org/10.1016/B978-0-12-386454-3.00567-4.
Stehle, S., Schulz, R., 2015. Agricultural insecticides threaten surface waters at the global scale. Proc. Natl. Acad. Sci. 112, 5750–5755. https://doi.org/10.1073/pnas.1500232112.
Suciu, N., Tediosi, A., Ciffroy, P., Altenpohl, A., Brochot, C., Verdonck, F., Ferrari, F., Giubilato, E., Capri, E., Fait, G., 2016. Potential for MERLIN-Expo, an advanced tool for higher tier exposure assessment, within the EU chemical legislative frameworks. Sci. Total Environ. 562, 474–479. https://doi.org/10.1016/j.scitotenv.2016.04.072.
Tickner, J., Simon, R., Jacobs, M., Rudisill, C., Tanir, J., Heine, L., Spencer, P., Fantke, P., Malloy, T., Edwards, S., Zhou, X., 2019. Lessons from the 2018 International Symposium on Alternatives Assessment: Advances and reflections on practice and ongoing needs to build the field. Integr. Environ. Assess. Manage. 15, 909–916. https://doi.org/10.1002/ieam.4213.
UBA, 2015. REACH Compliance: Data Availibility of REACH Registration. Part 1: Screening of Chemicals > 1000 tpa. German Federal Environment Agency, Dessau-Roßlau, pp. 185.
UNEP, 2016. Global Environmental Outlook – GEO 6: Assessment for the Pan European Region. United Nations Environment Programme, Nairobi, Kenya p. 376.
Westh, T.B., Hauschild, M.Z., Birkved, M., Jørgensen, M.S., Rosenbaum, R.K., Fantke, P., 2015. The USEtox story: a survey of model developer visions and user requirements. Int. J. Life Cycle Assess. 20, 299–310. https://doi.org/10.1007/s11367-014-0829-8.
Williams, A.J., 2011. Chemspider: a platform for crowdsourced collaboration to curate data derived from public compound databases. In: Ekins, S., Hupcey, M.A.Z., Williams, A.J. (Eds.), Collaborative Computational Technologies for Biomedical Research. John Wiley and Sons, Hoboken, New Jersey, pp. 363–386. https://doi.org/10.1002/9781118026038.ch22.
Williams, A.J., Grulke, C.M., Edwards, J., McEachran, A.D., Mansouri, K., Baker, N.C., Patlewicz, G., Shah, I., Wambaugh, J.F., Judson, R.S., Richard, A.M., 2017. The CompTox chemistry dashboard: a community data resource for environmental chemistry. J. Cheminf. 9, 61. https://doi.org/10.1186/s13321-017-0247-6.
Zahn, D., Mucha, P., Zilles, V., Touffet, A., Gallard, H., Knepper, T.P., Frömel, T., 2019. Identification of potentially mobile and persistent transformation products of REACH-registered chemicals and their occurrence in surface waters. Water Res. 150, 86–96. https://doi.org/10.1016/j.watres.2018.11.042.