Integrated Environmental Assessment and Management — Volume 17, Number 3—pp. 498–506
Received: 4 June 2020 | Returned for Revision: 7 August 2020 | Accepted: 5 January 2021

Brief Communication

Environmental Risk Assessment of Technical Mixtures Under the European Registration, Evaluation, Authorisation and Restriction of Chemicals—A Regulatory Perspective

*Wiebke Galert**† and Enken Hassold†*
†German Environment Agency (UBA), Section IV 2.3 Chemicals, Dessau Roßlau, Germany

ABSTRACT

The European Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation has been in force since 2007 and is intended to ensure a high level of protection for human health and the environment. The REACH regulation is based on the principle that manufacturers, importers, and downstream users take responsibility for their chemicals. Currently about 23 000 single chemicals are registered within the REACH legislation. A large proportion of substances registered under REACH end up in technical mixtures, intentionally manufactured as such, or generated mixtures containing byproducts of processes. Such mixtures that contain a number of different components are, for example, ink, paint, lacquer, mortar, or cleaning agents. However, REACH focuses on single substances and addresses the safe use of substances as such (e.g., bisphenol A) or substances in mixtures (e.g., bisphenol A used as an antioxidant in mixtures) and in articles (e.g., bisphenol A used as a monomer for polycarbonate production from which greenhouse sheets may be made). In contrast to other substance regulations, under REACH the registrants and downstream users of chemicals are responsible for the risk assessment. According to the REACH regulation, they also have the obligation to derive and communicate safe use conditions for their technical mixtures. Currently, no guidance document and no distinct obligations for an assessment of technical mixtures exist. In light of the available evidence for the joint exposures and effects of chemicals due to co-exposures, the need for approaches for a mixture assessment and improved data communications were highlighted by various stakeholders from industry, European member states, and the European Chemicals Agency (ECHA). The lead component identification (LCID) methodology and the safe use of mixtures information (SUMI) tool were proposed by the European Chemical Industry Council (Cefic) as working tools for the evaluation of the hazard potential, derivation of safe use conditions, and data communication for mixtures along the supply chain. The present paper analyzes the workability and pitfalls of these proposed methodologies from a regulatory perspective, aiming at a safe use of technical mixtures which considers the joint effects and exposures of its components. *Integr Environ Assess Manag* 2021;17:498–506. © 2021 Umweltbundesamt. *Integrated Environmental Assessment and Management* published by Wiley Periodicals LLC on behalf of Society of Environmental Toxicology & Chemistry (SETAC)

Keywords: REACH Technical mixture Lead component identification (LCID) methodology Extended safety data sheets Supply-chain communication

INTRODUCTION: MIXTURES OF CHEMICALS AND THEIR ENVIRONMENTAL RISKS

As consumers we regularly encounter technical mixtures in our daily lives, that is, formulations of different chemicals such as inks, paints, lacquers, or cleaning agents. Such mixtures usually contain a number of different chemicals, which are intentionally manufactured, or generated mixtures that contain byproducts from production processes. In contrast to pharmaceuticals, biocides, or plant protection products, industrial chemicals are not designed and intended to be biologically active. Yet, a chemical by itself or chemicals blended together can have harmful effects and pose risks to man and the environment, depending on their concentrations and exposures throughout their life cycle. Chemical substances are usually formulated together like a cocktail, some in several steps and with many different substances. These substances are used together and end up in the same environmental compartment. Therefore, knowledge about the composition of mixtures and potential hazardous effects of the chemical substances are necessary for their assessment.

Data generated by monitoring studies show the occurrence of various mixtures in the environment and therefore their environmental relevance, entering into various

* Address correspondence to wiebke.galert@uba.de
Published 15 January 2021 on wileyonlinelibrary.com/journal/ieam.

environmental compartments (air, water, sediment, soil, and groundwater), leading to a possible substance cocktail (Bunke et al. 2013).

In the European Union, the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation (EC 2006) governs the assessment of potential risks from industrial chemicals and their safe use. Currently, about 23 000 single chemicals are registered within the REACH legislation. A large proportion of these substances end up in a variety of mixtures, which again may be reformulated to further mixtures. Hence, the explicit number of possible mixtures is unknown and complex.

In contrast to other substance regulations, under REACH the registrants and downstream users of chemicals are responsible for the risk assessment with the obligation to derive and communicate safe use conditions for their technical mixtures. Currently, no guidance document and no distinct obligations for an environmental assessment of technical mixtures exist.

BACKGROUND: RESPONSIBILITIES AND STEPS DURING ENVIRONMENTAL RISK ASSESSMENT OF CHEMICALS UNDER REACH

In order to understand how REACH works, how environmental risks of chemicals are assessed by different actors, and how environmental risks of technical mixtures can be better addressed under REACH, some background is provided in the following sections. A quick overview on the availability of necessary information under REACH for an environmental assessment and tasks of the different actors in the supply chain is given in Table 1.

The different actors under REACH

The abbreviation "REACH" refers to the registration, evaluation, authorization, and restriction of chemicals, which are the main tasks during risk assessment and regulatory measures. The REACH regulation (EC 2006) has been in force since 2007 and is considered one of the strictest chemical laws in the world. It aims to ensure a highly protective level for human health and the environment. At the same time, it is intended to ensure the free movement of chemicals within the EU internal market, where REACH needs to be applied, and to promote competitiveness and innovation. The REACH regulation is based on the principle that manufacturers, importers, and downstream users take responsibility for their chemicals. They must ensure that the chemicals they produce and place on the market are used safely.

The REACH regulation requires that chemicals have to be registered by manufacturers or importers at the European Chemicals Agency (ECHA) before entering the European market. The registration dossiers contain a required standard data set of information on the chemicals. For chemicals with a production or import quantity greater than 10 tons per annum (tpa), the registrants of chemicals, as the manufacturer and/or importer of the chemicals, prepare chemical safety reports. Together with the downstream users, registrants have to generate safety data sheets to ensure the safe use and the communication of safe use conditions along the supply chain.

The regulatory authorities under REACH evaluate approximately 20% of the registration dossiers, provided by the registrants, on a random basis during so-called "compliance checks." In the case of a justified concern, authorities perform more detailed substance evaluations. They can propose further regulatory management options. The regulatory managment option can be a restriction and inclusion in Annex XVII of REACH, where all restricted chemical substances are listed. Regulatory authorities also identify substances of very high concern (SVHC) on the basis of specific concerns. This identification results in inclusion in the candidate list, possibly followed by inclusion in Annex XIV of REACH listing the substances that require an authorization. Further measures may include a harmonized classification and labeling, or handling under other regulatory frameworks. Different from other substance-oriented regulations, REACH chemicals acquire their marketability with registration and are not per se authorized and approved by authorities before being placed on the market. This is called the "shifting of proof" under REACH. The authorities have to rely on the safety assessments of the responsible registrants and downstream users for single substances and in particular for the formulated mixtures. The availability of mixtures information to authorities is especially scarce.

Environmental risk assessment, calculation of safe use amounts, and communication

Registrants are obligated to provide information on intrinsic physical and chemical properties, fate and behavior, hazards, exposures, and risks for their substance. The details for these data requirements are described in Annexes VII to XI of the REACH regulation. In order to describe the hazards, a predicted no-effect concentration (PNEC) is derived (as described in ECHA [2017a]). The predicted exposures are described with a predicted environmental concentration (PEC), calculated as described in ECHA (2016). For single substances, the predicted effects are compared with the predicted exposures for specific uses in "risk characterization ratios (PEC-to-PNEC ratio). For a safe use of substances, the risk characterization ratio needs to be below 1. In case of an unacceptable risk, PEC/PNEC > 1, a substance may not be used under the current conditions, and operational conditions or risk mitigation measures have to be defined and applied.

The assessment by the registrant shall also cover all relevant uses in the subsequent steps of the supply chain, such as formulations or further processing downstream. For this purpose, the registrant receives generalized information, for example, downstream on the uses. But the registrant has no obligation to have complete knowledge about the specific uses and the operational conditions for a substance or technical mixture containing the substance during the entire life cycle. Subsequently, the registrant has little knowledge

 DOI: 10.1002/ieam.4393

Table 1. Information availability for an environmental assessment and tasks of the different actors in supply chain under REACH

Tasks and data	Registrant	1st downstream user	Further downstream users, end user	Regulatory authority
Tasks and documents to be provided	Dossier Chemical safety report >10 tpa Safety data sheet >1 tpa for hazardous chemicals Extended safety data sheet >10 tpa for hazardous chemicals, including exposure scenarios	Adaptation or derivation of M_{safe}, safe use conditions (operational conditions or risk mitigation measures) for their respective application types	Adaptation or derivation of M_{safe}, safe use conditions (operational conditions or risk mitigation measures) for their respective application types	Evaluation and derivation of risk mitigation measures possible if unacceptable risks or hazards are indicated or justified
Effect data	Basic requirements depending on tonnage: 1–10 tpa: physical and chemical data 10–100 tpa: *Daphnia* acute testing (EC 2006, Annex VIII, nr 9.1.1) 100–1000 tpa: long-term testing fish or *Daphnia* (EC 2006, Annex IX, nr 9.1.5) >1000 tpa: long-term toxicity soil (invertebrates, plants), sediment, birds (EC 2006, Annex X, nr 9.4) (QSAR or waiving possible)	(Extended) safety data sheet: most sensitive values for CLP substances, PBT status[a]	(Extended) safety data sheet Other publicly available data	Gain insight into chemical safety report on random basis or on request
Exposure data	Use descriptor system, life cycle assessed PECs, yearly or daily processed tonnage for several application types, operational conditions, risk mitigation measures, M_{safe}	Relevant life cycle assessed PECs, yearly or daily processed tonnage for his or her application type, operational conditions, risk mitigation measures, M_{safe}	M_{safe} if given from extended safety data sheets; concentration used for application type to derive own M_{safe} or safe use conditions	Use descriptor system, life cycle assessed PECs, yearly or daily processed tonnage for several application types, operational conditions, risk mitigation measures, M_{safe}, might get monitoring data (prospective, retrospective)
Composition of technical mixture	Information from industry and associations for specific use groups, but regularly not for specific mixture	Knowledge of own confidential recipe	Knowledge of own confidential recipe	Databases, communication with industries und associations

CLP = European Classification, Labelling and Packaging regulation; M_{safe} = safe use amount; PEC = predicted environmental concentration; PBT = persistent, bioaccumulative, toxic; QSAR = quantitative structure–activity relationship; REACH = European Registration, Evaluation, Authorisation and Restriction of Chemicals regulation; tpa = tons per annum.
[a]ECHA (2017b).

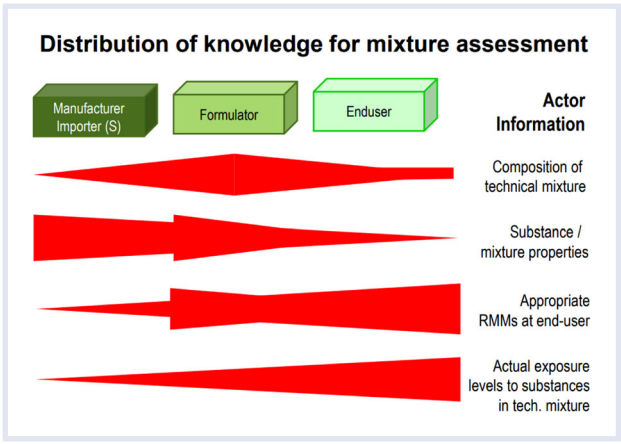

Figure 1. Information availability for different actors under REACH (Reprinted with permission from Bunke et al. 2013, p 165). RMM = risk mitigation measure.

of whether his or her substance is contained in a mixture or article that is produced downstream.

In contrast to the registrant, the downstream users do have knowledge about the substances they use together for formulating and further processing their mixtures. The downstream users receive a basic data set on intrinsic substance properties, hazards, and risks via an extended safety data sheet from the registrants, which they may adapt to guarantee safe use conditions for their specific uses. It is not intended that the registrant communicates complete substance records. Hence, depending on the assessment method used, occurrence and concentration of relevant hazardous ingredients will remain unknown to the downstream users if these are not communicated via the extended safety data sheet. Figure 1 shows the distribution knowledge for the mixtures assessment relevant for the actor to derive safe use conditions for the mixtures.

The safety data sheet is used for downstream communication and has to be created for substances registered with a production or import volume >1 tpa. For substances registered with >10 tpa, the extended safety data sheet includes an exposure scenario. The extended safety data sheet also applies if a substance is classified as persistent, bioaccumulative, or toxic (PBT) or very persistent very bioaccumulative (vPvB), if aquatic effects below 100 mg/L are demonstrated or indications of other hazards (e.g., hazards to bees) are given. The downstream user in the first instance receives the basic information from the registrant via the extended safety data sheet and has to ensure that his or her uses are covered by the exposure scenario and that the risk characterization ratio remains <1.

In order to define the amounts of a chemical that may be produced per day without posing risks, "safe use amounts" (M_{safe}) are derived. The M_{safe} represents the "amounts used (kg/y or kg/d)" rated as "safe" by the registrant on the basis of PNEC and PEC calculations. These are also used by the downstream users in order to adjust the use of substances that show unacceptable risks. A detailed document on how to calculate the safe use amounts does not exist, even for single substances. A PEC/PNEC summation at the level of the registrant for mixtures is rather impractical because the registrant is not yet familiar with the mixture and there is usually a wide variety of applications or mixtures in the downstream application. Due to differences in data availability, downstream users do not always receive the necessary PEC/PNEC relevant to their application or scenario. The M_{safe} is thus a tangible value that is used for tools in the mixture evaluation. Because these derived values obviously have such a high value, their derivation should also be comprehensible and equal for all actors.

Communication tasks and tools of the registrant. For each substance, the registrant has to perform a life cycle assessment for the registered uses. Therefore, the registrant needs information from downstream users along the supply chain, which is usually achieved via industry associations. However, the registrant has no obligation for complete life cycle knowledge and no obligation to cover every single application (EC 2006, Art. 14). To fulfill the requirements, the registrant provides information for single scenarios covering the life cycle steps: manufacturing (if not imported) and formulation or processing and service life (and waste). Several documents have to be prepared for the registration process by the registrant if a substance is found to be hazardous or an SVHC:

- Documentation of the chemical safety assessment for the substance
- Exposure scenarios as part of the registration dossier for all identified uses of the substance (EC 2006, Art. 14.4)
- Extended safety data sheet with relevant exposure scenarios as annexes (EC 2006, Art. 14.4 and 37.4) if the substance is placed on the European market (M_{safe}, risk mitigation measure, operational conditions).

Communication tasks and tools of downstream user. Every supplier or formulator of a registered substance has to verify whether their foreseen application is covered by the registration dossier and whether safe use conditions, which where communicated by the registrant via an extended safety data sheet, are met. Downstream users of chemicals are required to check whether the conditions of use apply to them or whether they can adapt them under consideration of known conditions of use. If this is not the case, the downstream users can inform the registrant to implement the downstream use conditions in the registrants dossier. It is also possible for the downstream user to adapt the information for the use conditions according to the registrants dossier. Therefore, it is recommended that the downstream user develop a chemical safety report. Likewise, there is an obligation for the downstream user to prepare or forward to the registrant REACH documents related to a mixture that is classified as hazardous (EC 2006):

 DOI: 10.1002/ieam.4393

- Safety data sheet for the mixture containing safe use information (M_{safe}, risk mitigation measure, operational conditions) for intended downstream uses
- Exposure scenarios for substances in the mixture (EC 2006, Art. 31.7)
- Safe use conditions for the mixture
  - Own assessment
  - Safety data sheet (EC 2006, Art. 31.2)

- Downstream user notification to ECHA of uses not covered by the exposure scenario received from suppliers (EC 2006, Art. 38)
- Downstream user chemical safety report for substances in the mixture (EC 2006, Art. 37.4) if uses are not covered
- Optional chemical safety report for mixture (EC 2006, Art. 31.2).

PREREQUISITES FOR AN ENVIRONMENTAL RISK ASSESSMENT OF TECHNICAL MIXTURES UNDER REACH

Obligations under REACH with respect to mixtures

If a substance shows an unacceptable risk (risk characterization ratio >1) during the life cycle steps, risk mitigation measures have to be applied to derive safe use conditions. Data from the registrant's exposure and hazard assessment are fundamental for the derivation of safe use by the downstream users. These safe use conditions have to be communicated completely from registrant to downstream user via the extended safety data sheet (EC 2006, Art. 31). With these data and information, safe use conditions of mixtures containing hazardous or risky substances should be derived by downstream users. And again, the downstream users also have the obligation to forward their information about the safe use conditions of their mixture via the extended safety data sheet (EC 2006, Art. 31), if these mixtures are further processed (EC 2006, Art. 37).

Data quality and availability for an assessment of mixtures

Under the REACH regulation, there are different data requirements depending on the registered substance volumes to assess environmental risks of single substances, ranging from physicochemical properties to effects and exposure data for different environmental compartments. For an assessment of technical mixtures, the data already available for single substances can be used. For a risk assessment, a PNEC value and a PEC value are usually derived for every single substance. On this basis, safe use conditions are derived.

Available options and challenges for a mixture risk assessment

The data available for single chemical substances (i.e., PNECs, PECs, or risk characterization ratios) are sufficient to calculate predicted mixture risks for technical mixtures via a PEC/PNEC summation using component-based approaches according to, for example, the well-established principle of "concentration addition." These concepts are used in other substance-oriented statutes, for example, for pesticides, pharmaceuticals, and biocides, using tiered approaches based on the data availability. The concepts are also established under the European Classification, Labelling and Packaging (CLP) regulation (ECHA 2017b) ("additivity" and "summation method") as well as under REACH in the context of assessment of multicomponent substances and substances of unknown or variable composition (UVCBs), complex reaction products, or biological materials. Despite this quite simple approach, the main challenge under REACH is the data availability to the respective assessor. The single-substance PNECs, PECs, and risk characterization ratios are usually calculated by the registrant, who has no detailed knowledge of the mixtures that will be formulated, whereas the downstream user often does not receive sufficient information and has only limited capacities to do his or her own safety assessment of the mixture under consideration.

In addition, higher-tier risk assessments generated by registrants, for example, monitoring data or adapted release factors from specific environmental release categories, are not available for downstream users and could not be adequately transformed to perform higher-tier hazard assessments for mixtures. For substances with low production volumes, (extended) safety data sheets are missing or rudimentary due to missing ecotoxicity data.

Exposure data are of variable quality and precision because they are often estimated following different approaches and do not reflect actual local concentrations (Bunke et al. 2013).

Hence, an approach is needed that can be applied by the formulating downstream users on the basis of a limited set of data and limited resources to assess the technical mixtures. Because the chemical-specific derived PECs, PNECs, and risk characterization ratios are not always available for all ingredients, an adaptation of the abovementioned M_{safe} to estimate the safe use amounts produced per day is an option to address the co-occurrence of several ingredients in a technical mixture.

Every single actor along the supply chain has its specific communication obligations, according to Title IV, Articles 31(1) and 32 to 36 of the REACH regulation (EC 2006).

THE LEAD COMPONENT IDENTIFICATION APPROACH TO IMPROVE THE DOWNSTREAM ASSESSMENT AND SAFE USE COMMUNICATION FOR MIXTURES

Stakeholders from industry, European Union member states, and ECHA work together for improvements in communication along the supply chain and across actors, addressing specific communication needs and harmonized approaches, that is, via unified templates for sectors. The ECHA provides guidance, checklists, and examples, helping actors along the supply chain to document and

communicate relevant data in the right way (ECHA 2015, 2018b, 2018c). In the context of the exchange network of exposure scenarios (ENES), consisting of industry sectors, organizations, and ECHA, the need for approaches for mixture assessment was highlighted by various participants several years ago. In this context, the working tools for improved data communication of lead component identification (LCID) (Cefic and VCI 2019) and safe use of mixture information (SUMI) (DUCC 2019) were developed.

The format of the SUMI was developed by the Downstream Users of Chemicals Co-ordination Group and several sector associations. The bottom–up approach focuses on understanding the end use of a mixture for a specific industry sector. Currently only a few sectors have developed SUMI. The SUMI works with sector use maps (https://echa.europa.eu/csr-es-roadmap/use-maps/concept). These are standard templates to send information bottom–up from downstream user to registrants. Three exposure description types exist: The exposure description type for the worker (Specific Worker Exposure Description [SWED]), the environment targeting exposure description type (Specific Environmental Release Category [spERC]), and the Specific Consumer Exposure Determinants [SCED]), concerning the consumer exposure.

The SUMIs were developed for unifying the format for the distribution of the obligatory information but currently addresses worker exposure (SWED) only. Environmental exposure information can be transferred with this tool within the supply chain, but as "additional information" only.

The LCID method (Cefic and VCI 2019) was proposed as a practical guide in 2016 by the industry organizations European Chemical Industry Council (Cefic) and German Association of the Chemical Industry (VCI) as a contribution to the chemical safety report–exposure scenarios (CSR/ES) roadmap (http://echa.europa.eu/regulations/reach/registration/information-requirements/chemical-safety-report/csr-es-roadmap), following a drafting, consultation, and testing period. This method aims to generate an M_{safe} for formulations by downstream users with the available data of the registrant's extended safety data sheets.

The LCID tool is an update of the methodology called "DPD+," which is based on the Dangerous Preparations Directive (DPD) (Cefic 2010). The DPD+ method aims to identify the risk-determining components in mixtures. A description of the DPD+ method is provided in Part 3 of the REACH Practical Guide on Exposure Assessment and Communication in the Supply Chains (https://www.vci.de/Themen/Chemikaliensicherheit/REACH/Seiten/REACH-Praxisfuehrer.aspx#). The so-called "lead substance indicators" for mixtures, and thus the primary substance leading to unacceptable risks or showing the highest hazard potential or the main concern of the mixture, will be derived. This derivation is done on the basis of the most sensitive PNEC available for classified substances and their concentration in the mixture. The substance that contributes most to the calculated risk on the basis of the "concentration addition" concept is selected as lead substance. Substances whose lead substance indicator makes up at least 10% of the lead substance are identified as sublead substances. The risk characterization ratio of lead substances and sublead substances are identified for each exposure pathway in order to assess possible additive effects.

The workflow LCID consists of 2 steps: First, identify and select one or more lead substances to prioritize, and derive their conditions of use to adequately control environmental risks. Second, consolidate information on conditions of use and risk mitigation measures (e.g., lower the used amounts) to ensure safe use for all substances in the mixture, derived from the prioritized substances.

LCID: NEEDS FOR IMPROVEMENT FROM A REGULATORY PERSPECTIVE

The DPD+ methodology has already been analyzed with respect to its workability and applicability to a sound environmental risk assessment, and several uncertainties and gaps were concluded by Jepsen and Bunke (2012) and Bunke et al. (2013) on behalf of the German Environment Agency (UBA). The LCID tool was improved on the basis of those conclusions and became more complex and more realistic. It aims at harmonizing exposure scenarios for environmental exposure to identify the most hazardous substance in a mixture and give advice on how to derive a safe use of the whole mixture, without sector-specific requirements. However, the LCID methodology still raises open questions, for example, how to account for hazards from other environmental compartments. Although LCID was certainly improved, several weak points are identified in the assessment approach and need to be urgently improved, in our point of view:

- Lead substances according to release pathway: In general, LCID still aims at a single-substance approach, not a mixture assessment that considers the joint effects and exposure of all the components present in a mixture. It has not been demonstrated that the sole identification of a representative lead substance covers risks for all environmental compartments, that is, that the calculated safe use amounts cover the joint effects and exposures of all ingredients acting jointly together. For environmental exposure assessment, the most practicable risk mitigation measure (RMM) is concentration reduction of the source substance of the risk or the reduction of the safe use amount of the whole mixture. Different lead components can be found for different exposure routes (surface water, marine water, soil, air). Therefore, the derivation of RMMs has to be done for the different exposure routes and needs to be communicated for all types of application for the variance of applicators.
- Data availability and quality: The data availability from the REACH dossiers, data quality, and communication are important issues and influence the result. Data are often still not available to the respective assessor (registrant vs downstream user). To consider the poor data availability, a default generic approach could be applied as a

 DOI: 10.1002/ieam.4393

safeguard to account for mixture effects and exposures and to be refined when possible. The generic approach could be a mixture allocation factor for the technical mixture or the first step of a tiered approach.

- Exclusion of substances: To rely solely on classified substances above a certain threshold seems insufficient. All hazardous substances present in a mixture may contribute to the hazard potential because they may add up even when present in low concentrations and lead to joint effects. It has also been shown that effects can be estimated using concentration addition, regardless of knowledge about their ecotoxicological mode of action.
- Exclusion of environmental compartments: Some hazards are not covered by the classification system, for example, risk to the terrestrial environment is not reflected at all. Only hazards for the aquatic compartment are considered. This gap was already known under the previous method DPD+.
- Substance loss due to cut-off criteria: Referring to the hazard classes that usually have defined cutoff criteria may lead to over- or underestimation of substance risks if aquatic toxicities are just above or below a defined ecotoxicological cutoff value (e.g., effect concentration ≤1 mg/L).
- Classification versus hazard potential: If substances have no harmonized classification according to Annex VI of the CLP regulation (ECHA 2017b), despite showing hazardous properties, they need to be self-classified. Differences in the M_{safe}, risk mitigation measures, and operational conditions derivation of a mixture with the same ingredients from different registrants may result. The reasons may be varying classification and therefore differing lead substances, resulting in divergent M_{safe} for the mixture. This continues with all consequences in the supply chain. Moreover, it is not well-defined in LCID whether selection of substances relies on self-classifications or only on existing legal classifications.
- Dealing with SVHC: The LCID methodology remains unclear as to how to consider SVHC. In addition, the PBT status of substances is often unclear. Persistent, bioaccumulative, toxic substances are only rarely considered by registrants and downstream users, and only if the substance is formally identified as SVHC or fulfills the criteria (in their opinion). In Table 2, a short statistical summary of the substances considered PBT under REACH is given as an example. The same applies for endocrine disrupters, where legally binding criteria are not promulgated and are seldom considered by registrants or downstream users.

In summary, the lead substance, derived with the LCID methodology, does not necessarily reflect the overall risks from the joint exposure and effects of substances in the mixture. Checking all substances in a mixture and the according exposure scenarios is essential. This finally determines whether or not the formulator's recommendations for his or her mixture cover all conditions of use in the received exposure scenarios and are useful, understandable, and implementable. Formulators should ensure that they provide information to the respective downstream users in a compliant, concise, and understandable way regarding their mixtures.

The abovementioned issues cannot be solved only by improvements to the LCID methodology but also rely on overall improvements to the REACH regulation. The LCID method cannot resolve the overarching open questions of the REACH legislation. The possibilities and obligations for a mixture assessment are only vaguely described in REACH and are not yet clearly defined in the practical guide.

Due to the existing ambiguities under REACH, the LCID method remains only partially reliable. If gaps were fully addressed under REACH, LCID would provide more reliable results with respect to, for example, the legal classification status.

When the LCID is used for the evaluation of mixtures, the responsibility lies with the downstream users, including the small and medium-sized enterprises. It may be concluded that the inventors of LCID assumed that these users have sufficient expertise and resources to apply the concept, which seems not to be the case. A case study or survey is needed to evaluate whether a downstream user applies and uses the methodology and whether it leads to reduced environmental risks.

Table 2. Example SVHC and PBT statistics showing unclear status[a]

Substance status	Nr substances	Assessment
PBT assessment does not apply	1712	In consequence of CSA
Substance is not PBT or vPvB	7463	In consequence of CSA
Substance is PBT or vPvB	93	Also caused by impurities
Substance is handled as if it were PBT or vPvB	0	Screening PBT
Further information relevant for PBT assessment is necessary	91	No clear data

CSA = chemical safety assessment; PBT = persistent, bioaccumulative, toxic; REACH = European Registration, Evaluation, Authorisation and Restriction of Chemicals regulation; SVHC = substance of very high concern; vPvB = very persistent, very bioaccumulative.
[a] REACH statistics for PBT (ECHA 2018a): 89 905 dossiers from 21 405 unique substances.

CONCLUSIONS, FURTHER NEEDS, AND WAYS FORWARD

Guidance and a clear legal mandate are needed

The REACH regulation stipulates the obligations for each actor, so that safe use conditions can be derived and communicated between the actors. The communication of data is still quite unstructured and follows diverse approaches. This communication difficulties applies both to the formats and the type of forwarding: via paper, file, or fully automated along the supply chain from the registrant through the formulator to the downstream users. In order to be able to apply the requirements under REACH and get the knowledge he or she needs, every actor along the supply chain needs accompanying guidance. This guidance needs to be tailored to the concerned actor and to cover procedures for data assessment and handling, as well as tiered approaches, depending on data availability.

Anyone with supply chain responsibilities should receive detailed instructions on how to proceed. Therefore, instructions are obligatory on the one hand and the data availability of required data according to REACH on the other. Only those who have all the relevant data at their disposal may derive safe use conditions for mixtures that fully meet this requirement to communicate safe use conditions along the supply chain via extended safety data sheets (EC 2006, Title IV).

There is a need for a clear mandate under REACH to develop these guidances for the different actors along the supply chain.

Efficient communication tools are needed

There has to be a dialogue between stakeholders to strengthen data communication between registrants and downstream users. Reporting templates and coordinated automated data forwarding processes (e.g., program, blockchain technology, database) can help to reach conformity in the processes of mixture assessment and communication.

Tasks for industry could be to support communication requirements with case studies: What are typical mixtures? How many components do they typically contain? How many are classified? Do downstream users use LCID and do they use it appropriately?

Safe use of technical mixtures needs to be ascertained to address combined effects and exposures

From the regulatory point of view, it is important to tackle mixtures at the "source" concerning their uses and possible technical mixtures before contained substances enter environmental compartments, regardless of their common impact. Assessment and regulation of these joint impacts are possible only at this level. The safe use of technical mixtures, soundly and adequately considering their joint effects and exposures, has to be ensured.

The REACH actors have legal obligations (EC 2006) to ensure safe use of articles and substances, but also of substances in mixtures, which implies the safe use of mixtures. Starting points could be voluntary action or product responsibility for a mixture assessment. We see a discrimination in the assessment of technical mixtures in contrast to substances in articles, given that they have their own resources in the legal text concerning the use of hazardous substances (EC 2006, Title VIII, Art. 67–73).

Improve assessment approaches and tools for technical mixtures

Under the CLP, for example, all chemical components of the mixture are taken into account for the hazard classification of a mixture using the summation method. The same should apply for a simple assessment tool like LCID. Even in the case of substances that are not closely related and that have dissimilar modes of action, additive action can be assumed and assessed with "concentration addition." Hence, all substances present in a mixture—even in low concentrations—can contribute to risks and should be considered. Every single derived risk characterization ratio from the ingredients of a mixture could be added up, as is done under other substance-oriented frameworks. The safe use amount can be used due to its obligation to be communicated along the supply chain under REACH. This value will be adapted in a sound way, considering all ingredients. One open question to be discussed is whether a generic mixture allocation factor could be used as default to safeguard for co-occurrence and environmental risks of several components in an intended technical mixture, in particular when data and/or resources are limited for the assessing downstream user.

Outlook

Another future question will be that under REACH we do not solely have to consider intended technical mixtures reaching an environmental compartment. At the same time, due to the same application, co-exposure of coincidental mixtures and in addition environmental background concentrations of various substances in all environmental compartments need to be considered.

Acknowledgment—The authors declare no conflicts of interest. The research project number FKZ 3711 63 429 "4M: Mixtures under REACH. Concepts and options to act," project number FKZ_371063403 "DPD+-an appropriate method to assess the risk for mixtures under REACH?," and project number FKZ 360 01 058 "Basic principles for the development of a concept for environmental exposure assessments of single substances released from multiple uses under REACH" that form a basis for these thoughts were conducted on behalf of UBA and financed in the context of the national environmental research program of the German environment ministry. We received no further financial support from external sources. The authors thank Daniel Sättler, Wiebke Drost, Jona Schulze, and Eva-Maria Burkhardt for constructive review of the manuscript. Open Access funding enabled and organized by Projekt DEAL.

 DOI: 10.1002/ieam.4393

Disclaimer—The views expressed in this manuscript are those of the authors and may not necessarily be regarded as official position of the German Environment Agency (UBA).

Data Availability Statement—Data are available upon request from corresponding author Wiebke Galert (wiebke.galert@uba.de).

REFERENCES

Bunke D, Groß R, Kalberlah F, Reihlen A, Reineke N, Oltmanns J, Schwarz M. 2013. Mixtures in the environment—Development of assessment strategies for the regulation of chemicals under REACH. Dessau-Roßlau (DE): Umweltbundesamt. Nr 3711 63 429. 307 p.

[Cefic] European Chemical Industry Council. 2010. Guidance on ES development and supply chain communication. [accessed 2021 Mar 15]. https://cefic.org/app/uploads/2019/01/Guidance-on-ES-development-and-supply-chain-communication-REACHImpl-ES-CSA-CSR.pdf

[Cefic, VCI] European Chemical Industry Council, Verband der Chemischen Industrie eV (German Association of the Chemical Industry). 2019. REACH practical guide on safe use information for mixtures under REACH—The lead component identification (LCID) methodology. Brussels (BE). [accessed 2021 Mar 15]. https://cefic.org/app/uploads/2019/11/Mixtures-under-REACH-%E2%80%93-Exemplification-of-the-LCID-output-in-the-SDS-REPORT.pdf

[DUCC] Downstream Users of Chemicals Co-ordination Group. 2019. SUMI selection for mixture safety data sheets. [accessed 2021 Mar 15]. https://echa.europa.eu/documents/10162/28589151/enes12-24_sumi_method_cepe_en.pdf/ee8e6df9-59e8-b012-b7ea-e52f87fea27a

[EC] European Commission. 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), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. *OJ* L 396. 2006 Dec 30. p 1–849.

[ECHA] European Chemicals Agency. 2016. Guidance on information requirements and chemical safety assessment, chapter R.16: Environmental exposure assessment. ECHA-16-G-03-EN. [accessed 2021 Mar 15]. https://echa.europa.eu/documents/10162/13632/information_requirements_r16_en.pdf/b9f0f406-ff5f-4315-908e-e5f83115d6af

[ECHA] European Chemicals Agency. 2017a. Guidance on information requirements and chemical safety assessment, chapter R.7b: Endpoint specific guidance. ECHA-17-G-10-EN. [accessed 2021 Mar 15]. https://echa.europa.eu/documents/10162/13632/information_requirements_r7b_en.pdf/1a551efc-bd6a-4d1f-b719-16e0d3a01919

[ECHA] European Chemicals Agency. 2017b. Guidance on the application of the CLP criteria. Guidance to regulation (EC) no 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. [accessed 2021 Mar 15]. https://echa.europa.eu/documents/10162/23036412/clp_en.pdf/58b5dc6d-ac2a-4910-9702-e9e1f5051cc5

[ECHA] European Chemicals Agency. 2018a. PBT asessment list. [accessed 2018 Jun 10]. https://echa.europa.eu/pbt

[ECHA] European Chemicals Agency. 2018b. Extended safety data sheets. [accessed 2020 May 5]. https://echa.europa.eu/safety-data-sheets

[ECHA] European Chemicals Agency. 2018c. Guide on safety data sheets and exposure scenarios. Helsinki (FI). 62 p.

[ECHA] European Chemicals Agency. 2020. Guidance on the compilation of safety data sheets. [accessed 2021 Mar 15]. https://echa.europa.eu/-/guidance-on-the-compilation-of-safety-data-sheets

Jepsen D, Bunke D. 2012. Kommunikation in den Lieferketten, Herausforderung, Umsetzung [Communication in supply chains, the challenge of implementation]. In: Reach in der Praxis III Fachworkshop Nr. 5; 2012/12/13. Berlin (DE): Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit. [accessed 2021 Mar 15]. https://www.umweltbundesamt.de/sites/default/files/medien/362/dokumente/reach_in_der_praxis_ws_iii_5_dokumentation.pdf

