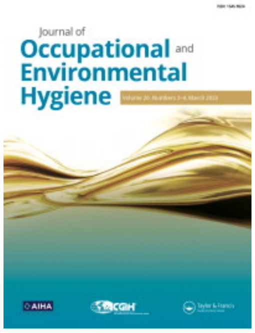

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Understanding the limitations and application of occupational exposure models in a REACH context

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ABSTRACT

Exposure modeling plays a significant role for regulatory organizations, companies, and professionals involved in assessing and managing occupational health risks in workplaces. One context in which occupational exposure models are particularly relevant is the REACH Regulation in the European Union (Regulation (EC) No 1907/2006). This commentary describes the models for the occupational inhalation exposure assessment of chemicals within the REACH framework, their theoretical background, applications, and limitations, as well as the latest developments and priorities for model improvement. Summing up the debate, despite its relevance and importance in the context of REACH not being in question, occupational exposure modeling needs to be improved in many respects. There is a need to reach a wide consensus on several key issues (e.g., the theoretical background and the reliability of modeling tools), to consolidate and monitor model performance and regulatory acceptance, and to align practices and policies regarding exposure modeling.

KEYWORDS

Chemical risk assessment; chemical safety assessment; exposure science; regulatory assessment; regulatory exposure modeling; occupational exposure assessment

Introduction

Despite classical occupational hygiene paradigms stressing the importance of high-quality exposure measurements (Kromhout 2016), there remains an important role for occupational exposure modeling for regulatory organizations, companies, and professionals involved in assessing and managing occupational health risks in workplaces (Fransman 2017; Jones 2022). There are several definitions of models (IPCS 2004, 2005; Council NR 2007; US EPA 2009; Heinemeyer et al. 2022) that are not always consistent with each other, especially when different types of models need to be classified (Jones 2022; Koivisto et al. 2022). As defined by Heinemeyer et al. (2022), an exposure model is adopted here as a conceptual or mathematical representation of one or more exposure processes. Since the introduction of the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation in the European Union (EU) (Regulation (EC) No 1907/2006) (Council Epa 2006), considerable efforts have been directed toward developing and testing models to support companies and regulators in complying with these regulations. This commentary describes the models for the occupational inhalation exposure assessment of chemicals and their applications and limitations within the REACH framework (dermal exposure models and consumer exposure models were not considered, although many are available). Following an introduction to the requirements and systems used under REACH, the available models used in REACH will be introduced, as well as evidence regarding their performance. Key issues related to the models' theoretical backgrounds, the latest developments, and the identified priorities for model improvement are also presented.

Occupational exposure modeling in reach

Introduction to requirements under REACH

REACH, or the Registration, Evaluation, Authorisation and Restriction of Chemicals, is a regulation of the EU that was adopted to improve the protection of human

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health and the environment from the risks that can be posed by chemicals (substances on their own, in mixtures, or articles) while enhancing the competitiveness of the EU chemicals industry (ECHA 2022e). REACH is based on the principle that it is the responsibility of manufacturers, importers, and downstream users to ensure that they manufacture, place on the market, or use (in the context of their professional activities) chemicals that do not adversely affect human health or the environment. The responsibility for the risk management of these chemicals is also borne by these subjects. It is worth noting that two key concepts in REACH go beyond former chemical control schemes: (i) industries are responsible for the safe use of chemicals, with the European Chemicals Agency (ECHA) and the other regulators playing a supervisory and control role; and (ii) risk assessment is central to the REACH processes (ECHA 2017a). Briefly, manufacturers and importers are required to obtain information on the chemicals they manufacture or import and to use this information to assess the risks related to these chemicals to develop and recommend appropriate risk management measures to control these risks. This process is documented in the chemical registration dossiers, which must be submitted to the ECHA. In more detail, the registration information requirements are intended: (i) to define and characterize the identity of the chemical; (ii) to identify the hazardous properties for hazard communication; (iii) to quantify the hazardous properties for risk assessment; and (iv) to obtain the parameters necessary for exposure assessment and risk characterization. This information is then used by industries to assess the hazards and risks to human health and the environment and to determine how to control them by applying suitable risk management measures using the chemical safety assessment (CSA) procedure (ECHA 2017a). In practice, the very first step of the CSA is the hazard assessment: if the results indicate that the substance meets the criteria for any of the hazard classes or categories set out in REACH, the CSA must conduct an exposure assessment (i.e., generation of exposure scenario(s) and exposure estimation) and risk characterization. For occupational scenarios, an exposure assessment consists of determining, quantitatively or qualitatively, the concentrations of the substance to which humans may be exposed; it includes as a first step the generation of exposure scenarios (ES) for all the identified uses and stages in the life cycle and secondly their use as a basis to estimate exposure. An exposure scenario (ES) is a set of conditions that describe how a substance (whether on its own, as a component of a formulated mixture, or in an article) is manufactured or used during its lifecycle in the EU and how the manufacturer or importer or downstream user controls or recommends controlling its exposure to humans and the environment. It must include appropriate risk management measures and operational conditions that, when properly implemented, ensure that the risks from the use of the substance are controlled. Risk characterization is the final step in the chemical safety assessment where it should be determined whether risks arising from the manufacture/import and use of the substance are controlled; it is carried out for each ES, and it involves comparing the estimated exposure concentrations with threshold values that are defined ad hoc for this purpose (derived, no-effect levels (DNELs)) (ECHA 2012a, 2019). Risk assessment for hazardous physicochemical properties consists also of the assessment of the likelihood and severity of an adverse effect. If the estimated exposure levels are below the DNELs, risks are under control. If not, iteration of the CSA should be carried out until risks can be demonstrated to be under control (the CSA is an iterative process: if the initial assessment demonstrates that risks to human health and/or the environment are not controlled, the assessment can be refined by obtaining more information on the properties of the substance or improving the exposure assessment or the risk management measures. There may have to be several cycles of successive refinement of the assessment before risks can be demonstrated to be under control). The CSA is documented in the chemical safety report (CSR), which is submitted, together with the chemical's technical dossier, to the ECHA as part of the registration process. The registrant transmits the relevant information—including risk management measures to be adopted in the exposure scenarios—documented in the CSR to the actors further down the supply chain using an extended safety data sheet (extended SDS) (ECHA 2012–2016). Practical examples of the chemical registration process (ECHA 2018b), exposure scenarios (ECHA 2017c), and CSR procedures (ECHA 2017b), as well as other guides (ECHA 2022b) providing practical information on requirements under REACH, are available at the ECHA website.

Exposure description in the REACH guidance

In practice, within the REACH context, companies need to identify all relevant ES for hazardous chemicals, assess the occupational exposure levels, and, if necessary, provide information on risk management measures so that the risk can be managed and the chemicals can be used safely. This places a large burden on manufacturers and importers to carry out risk assessments, many of which will require the assessment of exposures for a wide range of chemical agents and a wide range of exposure situations. The REACH descriptor system aims to facilitate this supply chain communication. REACH uses five descriptors—sector of use (SU), process category (PROC), product category (PC), article category (AC), and environmental release category (ERC)—to describe identified uses. Table S1 (supplementary material—Text S1) describes the use of descriptors with some examples. Measurement data are not available in sufficient quantity and quality to provide exposure estimates for all the exposure situations that need to be addressed and to estimate the impact of making changes to the risk management measures within the REACH context. Hence, REACH risk assessment relies to a large extent on exposure models implemented with a "tiered approach" to obtain quantitative estimates of occupational exposure to chemicals in specific ES (ECHA 2016). For a better understanding of the limitations and the application of occupational exposure models in the REACH context, it is pivotal to understand the system of exposure and risk assessment under REACH, the different processes of REACH for which exposure assessment is necessary, and the logic of the REACH guidance documents. All REACH guidance documents are available on the website of the ECHA (ECHA 2012–2016). A brief list of the most relevant guidance documents to be considered for this publication is reported in the supplementary material (Text S2) (ECHA 2012b, 2015, 2016, 2017d), but a discussion of the fundamentals is given below.

Tiered approach for exposure assessment in REACH

The R14 REACH guidance "Occupational Exposure Assessment" (ECHA 2016) introduced a tiered approach for exposure assessment at workplaces. According to the R14 Guidance, "a pragmatic workflow is to start with Tier-1 modeling and, based on the results, to identify a limited number of (contributing) scenarios for which either higher Tier modeling or a measurement campaign is needed" (ECHA 2016). In the first step of the tiered approach (Tier 1), exposure situations are assessed using relatively crude—with a relatively high level of uncertainty—and conservative—thus less accurate—exposure tools. If safe use cannot be demonstrated, the user then has the option of introducing further risk management measures or applying a more accurate and less conservative higher-tier tool to assess the exposure (Figure 1). The Tier 1 tools, such as the European Center for Ecotoxicology and Toxicology of Chemicals - Targeted Risk Assessment (ECETOC TRA), MEASE, and EMKG-Expo-Tool (Table 1), are generally very easy to use and have a broad application range based on a small number of input parameters. Higher tier models (Tier 2), such as Stoffenmanager and ART (The Advanced Reach Tool) (Table 1), use a greater number of more detailed input parameters to produce estimates of higher accuracy and confidence, but still for a wide range of applications. Tier 3 assessments are intended to provide high-quality, high-accuracy, representative, and realistic results for specific scenarios. Such exposure assessments require either models that have been developed specifically for an exposure situation or the use of exposure measurement data that are representative of an exposure scenario. Higher-tier mass-balance-based models could also provide a refined quantitative estimate (i.e., Tier 3 estimate) of exposure, but require a nontrivial investment in quantifying the model inputs and are often complex, requiring a level of expertise beyond novice to identify or generate the required input data and appropriately interpret their output (Schlüter et al. 2022a).

Exposure models listed in the REACH guidance: "R14-modeling-tools"

The R14 guidance (ECHA 2016) mentions and describes in detail only a limited number of exposure assessment tools for workplaces, which will be referred to as "R14-modelling-tools" in this paper (Table 1). A conceptual evaluation of the Tier 1 models recommended for use under REACH was provided by Hesse et al. (2015a). Briefly, the ECETOC TRA tool is based on the PROCs used under REACH. Initial exposure

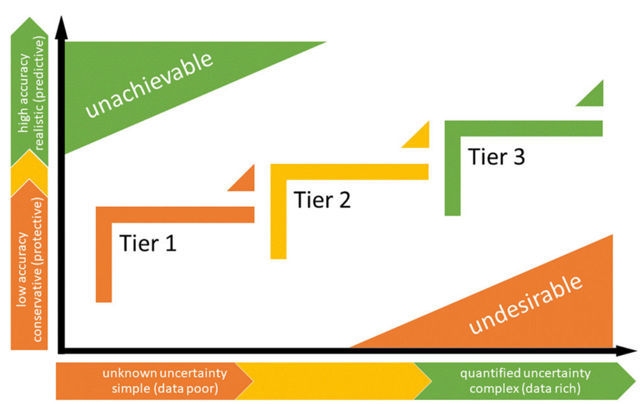

Figure 1. Tiered approach: principles. Relationships between tiers, uncertainty and accuracy of outcome in exposure assessment studies (following Solomon et al. (2008)).

Table 1. Occupational/Worker Exposure Assessment Tools modified from (ISES Europe 2022).

Tool	Description	Link
Tier 1		
ECETOC TRA	**Screening** tool to predict **inhalation** and **dermal** exposure. For details on the applicability domain for the quantitative inhalation exposure model see model website and the ECHA R.14 guidance (Table R.14- 8) Availability: Free (registration is needed). Platform: Excel spreadsheet. Level of maintenance: Active (v3.1).	https://www.ecetoc.org/glossary/tra/
MEASE	**Screening** tool to estimate **inhalation of** and **dermal** exposure to **metals and inorganic substances.** For details on the applicability domain for the quantitative inhalation exposure model see model website and the ECHA R.14 guidance (Table R.14- 10) Availability: Free (registration is needed). Platform: Windows 10/Java 8. Level of maintenance: Active, continuous updates available.	https://www.ebrc.de/tools/downloads.php
EMKG-Expo-Tool	**Screening** tool to derive **inhalation** exposure values for workplaces only. The EMKG-Expo-Tool is currently not appropriate for special situations, including activities where dusts are formed through abrasive techniques, open spray applications, gases, and pesticides. Operations that give rise to the generation of fumes (soldering, welding) and wood dusts are exempted as well. The tool is also not suited for CMR substances. For details on the applicability domain for the quantitative inhalation exposure model see the model website and ECHA R.14 guidance (Table R.14-12) Availability: Free. Platform: Java (TM) Desktop Application (MS Windows, Mac OS X, Linux); a Java Runtime Engine (JRE) must be installed. Level of maintenance: Active.	https://www.baua.de/EN/Topics/Work-design/Hazardous-substances/REACH-assessment-unit/EMKG-Expo-Tool.html
Higher Tier		
Stoffenmanager	**Higher tier** tool to estimate **inhalation** exposure to vapors, aerosols of low volatility liquids, and inhalable dusts. For details on the applicability domain for the quantitative inhalation exposure model see the model website and ECHA R.14 guidance (Table R.14-13) Availability: Free (registration is needed; paid versions are also available). Platform: Web-based. Level of maintenance: Active (v8), continuous updates available.	https://stoffenmanager.com/
Advanced REACH Tool (ART)	**Higher-tier** tool used for the whole distribution of inhalation exposure variability and uncertainty. ART is currently only calibrated to assess exposure to inhalable dust, vapors, and mists. For details on the applicability domain for the quantitative inhalation exposure model see the model website and ECHA R.14 guidance (Table R.14-15) Availability: Free. Platform: Web-based. Level of maintenance: Active (v1.5).	https://www.advancedreachtool.com/

estimates are derived from the Estimation and Assessment of Substance Exposure (EASE) model (Bredendiek-Kämper 2001) adapted to more recent exposure experiences (ECETOC 2012). The initial exposure estimates are subsequently modified based on some exposure modifiers (e.g., operational conditions, risk measurement measures, and personal protective equipment). MEASE is based on a modified version of the ECETOC TRA (version 2) tool and was developed to specifically address exposure to metals and other inorganic substances (Urbanus et al. 2020). The EMKG-Expo-Tool was developed based on COSHH Essentials (Control of Substances Hazardous to Health), which are based on expert assessments by occupational hygienists (Maidment 1998). Stoffenmanager is a mechanistic, source-receptor model based on algorithms that were originally developed by Cherrie et al. (1996) and Cherrie and Schneider (1999). The algorithms incorporate information on the process, physical chemical information, and mass balance to produce a semi-quantitative exposure estimate (Tielemans et al. 2008). These semi-quantitative estimates are subsequently used to derive quantitative exposure estimates based on calibration with measurement data (Schinkel et al. 2010). ART is a similar model to Stoffenmanager but with some additional parameters; ART is based on a mechanistic model combined with an empirical component related to exposure databases (Fransman et al. 2011). Furthermore, ART provides an opportunity to update the exposure estimates by including exposure measurements through a Bayesian module (McNally et al. 2014). Among all the R14-modeling tools, the ECETOC TRA model is the most frequently used tool for REACH registrations. This Tier 1 tool was specifically designed for REACH registration purposes and has been included in the CHEmical Safety Assessment and Reporting tool (CHESAR) (ECHA 2021), which is an application developed by the ECHA to help companies carry out chemical safety assessments and prepare chemical safety reports and exposure scenarios for communication in the supply chain (Urbanus et al. 2020).

The applicability domains of each of the above-mentioned model for the quantitative inhalation exposure are reported in The R14 guidance (ECHA 2016), but some insights are reported in Table 1. Other tools that are not included and described in the R14 guidance can be used if appropriate. A more comprehensive list of the available tools and models (including models for occupational exposure, general population exposure, environmental exposure, dosimetry, and PBPK) is available in the International Society of Exposure Science (ISES) Europe Exposure Model Inventory (ISES Europe 2022).

Performance of the R14-modeling tools

Only a few basic pieces of information on the R14-modeling tools' strengths and weaknesses are provided in the REACH guidance (ECHA 2016) (i.e., Table R.14-2 on page 39 and Appendix R.14-1 of the cited document) and in the "Mapping of the Conditions of use (input parameters) of the different tools for workers assessment" document that was developed by the Exchange Network on Exposure Scenarios (ENES) (ENES 2020). Only a few comprehensive studies have been carried out to test the performance of the R14-modeling tools (e.g., model reliability, robustness, uncertainties, between-user reliability, etc.). Probably the most complete source of information about this issue is the results from the ETEAM project (Crawford et al. 2015; Hesse et al. 2015a, 2015b; Jung et al. 2016; Lamb et al. 2017; Tischer et al. 2017; van Tongeren et al. 2017; Schlüter and Tischer 2020) and the results obtained by Lee and coworkers (Lee et al. 2019a, 2019b). In addition, a systematic review of the performance of R14-modeling-tools was published recently (Spinazze et al. 2019). In summary, the results of the systematic review showed that most studies testing the performance of the models were small-scale studies with heterogeneous experimental designs. Most studies focused on the lower-tier tools, with fewer evaluating the available higher-tier tools (Landberg et al. 2017; Savic et al. 2017a, 2018; Lee et al. 2019b). Overall, the evidence suggests that ECETOC TRA is not sufficiently conservative in some exposure scenarios (e.g., for volatile chemicals, high-dustiness chemicals, etc.). Two other Tier 1 models (i.e., MEASE and EMKG-Expo-Tool) were generally considered to be sufficiently conservative but showed poor performance when predicting exposure levels (van Tongeren et al. 2017). The evidence suggests that Stoffenmanager (often ranked midway between Tier 1 and Tier 2) is the most balanced and robust model, although, like most other models, it tends to overestimate low exposure and underestimate higher exposure levels (Schinkel et al. 2010; Vink et al. 2010; Koppisch et al. 2012; Jankowska et al. 2015; Landberg et al. 2015; Riedmann et al. 2015; Terwoert et al. 2016; Lamb et al. 2017; Landberg et al. 2017; Savic et al. 2017a; 2018; Spinazze et al. 2017; Tischer et al. 2017; van Tongeren et al. 2017; Koivisto et al. 2018; Landberg H. E. et al. 2018; Landberg et al. 2019; Lee et al. 2019a, 2019b; Savic et al. 2019; Ribalta et al. 2019a, 2019b). The Advanced REACH Tool (ART) was generally found to be accurate, although ART also appears to overestimate low exposures and underestimate higher exposures (Fransman et al. 2011; Mc Donnell et al. 2011; Schinkel et al. 2011; van Tongeren et al. 2011; Hofstetter et al. 2013; Schinkel et al. 2013; McNally et al. 2014; Schinkel et al. 2014; Riedmann et al. 2015; Bekker et al. 2016; Terwoert et al. 2016; Landberg et al. 2017; Savic et al. 2017b; Spinazze et al. 2017; Koivisto et al. 2018; LeBlanc et al. 2018; Sailabaht et al. 2018; Landberg et al. 2019; Lee et al. 2019b; Ribalta et al. 2019b; Lee et al. 2019c). Another important consideration when investigating the performance of the models is the between-user reliability. The available evidence demonstrates that different assessors can generate very different exposure estimates, even when using the same information and models. These differences could be very large and potentially lead to false-safe or false-unsafe scenario assessments (Schinkel et al. 2014; Landberg et al. 2015; Lamb et al. 2017; Tischer et al. 2017; Savict al. 2019).

Since the publication of the review by Spinazzè et al. (2019), only a few studies concerning the performance of R14-modeling tools have been published. Franken et al. (2020a) described a study where inhalation exposure data were collected under defined exposure conditions and scenarios, including tasks that have not been investigated in previous validation studies (i.e., PROC 4, PROC 5, PROC 10, PROC 13, PROC 19). The results of the exposure measurements were compared with those of ECETOC TRA model version 3.1 predictions. The results suggested that ECETOC TRA overestimated inhalation exposure for closed and partially closed processes but underestimated inhalation exposure for PROC 10 (rolling) and PROC 13 (handling of immersed objects). Urbanus et al. (2020) described the path that led to the creation of a review concerning studies published since 2010 in which the exposure estimates of ECETOC TRA are compared with workplace exposure measurement results; The review was subsequently published in 2022 (ECETOC 2022) and, later, Savic et al. (2023), utilizing this curated data set as the reference, was investigated the overall performance of the ECETOC TRA (version 3) to analyze which input parameters contributed most to the model's identified over- and underestimations. The results indicated that the ECETOC TRA v3 overestimated 80% of the measured data sets and that both over- and underestimations were mostly by factors 1–5. On average, the difference between the 75th percentile of exposure data and the TRAv3 estimate was less than one order of magnitude. A multiple linear regression showed that some input parameters such as medium volatility, certain PROC, industrial settings, and the presence of local exhaust ventilation are associated with under-estimations. Interestingly, the results of the study could be applied by ECETOC TRA users to review the degree of over- or underestimation in their exposure assessments and by the model developers to further develop the tool as a conservative screening tool for chemical safety assessment of occupational exposure to chemicals used in the REACH context. Another study (Lee 2023) evaluated the performance of Stoffenmanager and ART (this last with and without the Bayesian approach) by comparing estimates with measured full-shift exposures to volatile liquids (in terms of accuracy, precision, and conservatism) in forty-two exposure situation scenarios (251 exposures). Overall, Stoffenmanager appeared to be the most accurate among the testing tools, while ART (with the Bayesian approach) was the most precise. Interestingly, the author recommended that users should select a tool based on the performance results of three components (i.e., accuracy, precision, and conservatism), not depending on one or two components, since the results of this study indicate that no single tool would work for all ESs.

It is important to realize that most of the R14-modeling tools have been modified since the publication of the various studies described above, often to improve their performance. For Stoffenmanager, most evaluations were performed with version 3.0, 3.5 (Tielemans et al. 2008), and 4.0 (Schinkel et al. 2010), but subsequent versions (Stoffenmanager is now available as version 8) have been developed and tested by the model developers (Stoffenmanager. 2022). In addition, user support has been improved (i.e., using a helpdesk, training, a downloadable manual, YouTube instruction movies, peer review user sessions, webinars, crash courses, etc.) (Heussen et al. 2020). The EMKG-Expo-Tool is now available as a beta version 2 on the BAuA (i.e., the German Federal Institute of Occupational Safety and Health) homepage. The evaluation studies for this tool were carried out with version 1. As reported above, the ECETOC TRA tool is under evaluation for updates by the tool developers (Urbanus et al. 2020; ECETOC 2022; Savic et al. 2023) right now. However, some of the other tools (e.g., ART) have not been updated in recent years (except for some extensions, as in the case of the application for welding fumes (Sailabaht et al. 2018).

Discussions on the theoretical background of occupational exposure models

The theoretical framework for two of the higher tier models (ART and Stoffenmanager) is debated among experts (Cherrie 1999; Cherrie et al. 2011; Koivisto et al. 2018, 2019; Cherrie et al. 2020) (some references to that discussion are given in the supplementary material—Text S3). For this reason, the ISES Europe Exposure Models Working Group (ISES Europe 2021) organized a workshop to discuss the theoretical background, application domain, and limitations of "modifying-factor" (such as R14-modeling-tools) and "mass-balance-based" (i.e., those that rely on physico-chemical relationships and the conservation of mass (Keil 2000)) modeling approaches. A background document and supporting information are available on the ISES Europe website (ISES Europe 2021), and a summary of the extensive and thorough experts' and participants' discussions has been published (Schlüter et al. 2022a). In brief, the workshop participants identified challenges, ways forward, and necessary actions for model developers to improve model performance in the context of regulatory risk assessments. On other issues (e.g., theoretical background and validation of models), no consensus was reached among experts, and ultimately "it was not possible to define if one modelling approach is superior to other approaches." Nevertheless, experts agreed that the superior model may be the one that can provide the best estimate, given the nature of the source, the environment, and what is known about them. In many cases, the combined use of different types of models (i.e., "modifying-factor" and "mass-balance-based") to obtain an exposure estimate might be better than relying on a single (type of) model (Schlüter et al. 2022a). In this regard, it should be noted that the combined use of models and measurements, such as is facilitated in the ART, is likely to provide better estimates than relying purely on predictive models. Since the workshop, some further commentaries and editorials have appeared discussing the relative merits of modifying factor and mass-balance models (Fransman et al. 2022; Jones 2022; Koivisto et al. 2022). It is clear from this debate that there is a scope for different types of models with their respective advantages and disadvantages (Jones 2022).

Newer developments

Among the most interesting developments, a recent study (Goede et al. 2021) explored the possibilities of pairing modeling with miniaturized sensor data, to enrich existing models and develop new ones. Further, in recent studies, the application of machine-learning techniques was used to develop a new modeling approach (Savic et al. 2020). The new "meta" exposure model, called TREXMO+, applies the concept of the multi-model approach of TREXMO (Savic et al. 2016). By using between-model translations, TREXMO + calculates exposure estimates for three REACH models: ART, Stoffenmanager, and ECETOC TRA (it should be noted that updated tools' algorithms are not applied in TREXMO, anyway). Furthermore, the model incorporates a regression tree algorithm to account for the different performances of these individual models for different exposure conditions. In the validation study, TREXMO + led to improved results over the three REACH models considered. In another study, cluster analysis and Bayesian modeling were applied to improve methods for predicting exposure modeling estimates based on available data (Huang et al. 2021) in a similar way to what is already implemented in ART (McNally et al. 2014). Some industry sectors have also developed their own exposure models for REACH exposure assessment. The European Solvents Industry Group (ESIG) developed the Generic Exposure Scenario (GES) Risk and Exposure Tool (EGRET) (Zaleski et al. 2014). The MEASE tool was developed for the estimation of occupational inhalation and dermal exposure to metals and inorganic substances on behalf of Eurometaux.

Authorities using models for regulatory assessments

Occupational exposure tools are mostly used in REACH registrations but also in the other REACH processes such as the identification of substances of very high concern (SVHC) (ECHA 2022d), proposals for restrictions (ECHA 2022c), and substance evaluation and authorization (ECHA 2022a). In these processes, REACH authorities have different roles, which include exposure assessments in some cases. When exposure assessments are performed or evaluated, the ECHA and Member State Competent Authorities predominantly take on this responsibility in the different REACH processes.

Recently, the ECHA changed the process of compliance checks in dossier evaluations. For some so-called "full compliance checks," exposure- and use-related evaluations are also performed by the ECHA and challenge the use of occupational exposure tools in specific cases. The ECHA decided that exposure assessments were performed outside the boundaries of the used tool and needed updates. The ECHA's R14 guidance was updated in 2016 (ECHA 2016) and now has integrated validation information. For each of the tools evaluated in the ETEAM project, a sub-chapter was added that describes the status of validation. This enables tool users, to some extent, to make informed decisions about this aspect of tool performance. However, the R14 guidance has not been updated since 2016. Therefore, some of the validation exercises performed in more recent years are not considered, and the latest versions of some of the tools are not described in the guidance.

During substance evaluation, one of the important tasks for Member State Competent Authorities in the framework of REACH is exposure- and use-related information that also needs to be evaluated. The registration dossiers are also important for this evaluation as a source of information. Therefore, the correct use of exposure assessment tools can be relevant in substance evaluation. In the case that the evaluating Member State Competent Authority cannot find exposure- and use-related information of high quality, modeling is used and the validity of exposure assessment tools can be important for regulatory decisions. Bearing in mind the limitations of Tier 1 worker exposure tools (as described above), the authorities should use these tools with caution before preparing regulatory activities. When preparing regulatory activities based on modeled exposure estimates, those PROCs or activities that were identified as critical should be thoroughly evaluated. Additionally, scenarios associated with greater between-user variability and the effectiveness of risk management at workplaces (e.g., LEV, general ventilation) should be evaluated cautiously.

It should be noted that, in addition to REACH, exposure models could also, in principle, be applied within the Occupational Safety and Health framework, for the assessment of occupational exposure to chemicals. According to the current technical standards (i.e., DIN (2020)), basic exposure characterization is required to decide if personal exposure measurements are needed to evaluate compliance with occupational exposure limit values. This preliminary characterization can also be carried out—among the other methods indicated—using adequate exposure models. However, it should be noted that some of the tools used and developed for REACH are intended to model an idealized situation where control measures are implemented and used properly; this may be appropriate for regulatory purposes in REACH but not for the modeling of actual exposures in workplaces, so these models should probably not be used to replace exposure measurements. Regardless, the discussion of the applicability of OSH exposure estimation models to the world is a broader topic that goes beyond the objectives of the present study. It should be noted that REACH does not require that registrants use measured data for CSA, and thus measured data are often generated for other purposes (i.e., exposure assessment in the practice of occupational hygiene). If relevant, representative, high-quality, and reliable exposure data exist, these should be interpreted as part of the exposure assessment reported within the CSR. Where no specific data exist, appropriate analogous data (viz, measured data for analogous substances that are used in the same way as the assessed substance or from the assessed substance that is used in analogous situations) can be used (ECHA 2016). Analogous monitoring data are rarely used in REACH assessments; however, Franken et al. (2020b) recently proposed an approach involving using a model to extrapolate monitoring data on worker inhalation exposure to chemicals. Finally, one important parameter for workplace exposure assessment is the use and effectiveness of risk management measures (RMMs). RMMs documented in the CSR are reflected in the safety data sheet and by that communicated along the supply chain. By these RMMs, in principle, the occupational risk assessment and management can be improved in each affected workplace. So far, experience shows that this supply chain communication needs to be improved. Some information is already available in the R13 guidance “Risk management measures and operational conditions” (ECHA 2012b) that provides some information about the effectiveness of RMMs. Fransman et al. (2008) and others (CEFIC-LRI 2022) developed an exposure control efficacy library (ECEL) as a database based on the available evidence from the scientific literature. Unfortunately, real-world evidence on the effectiveness of RMMs is generally poor, and the reported effectiveness of RMMs can vary widely between studies. Hence, it is recommended to use conservative estimates of the effectiveness of the RMMs.

Consequences drawn by industry

Stakeholders from industry play different roles in worker exposure assessments. Individual companies submit registrations to the ECHA and use Tier 1 tools for this purpose. The European Commission, ECHA, Member State Competent Authorities, and industries have started to engage in several activities to evaluate the status of REACH registrations. Only a limited number of dossiers have been updated so far, and industry is not very proactive in this regard. Few, if any, REACH registrations have been improved based on emerging knowledge of the performance of exposure assessment tools. This observation seems to hold in all REACH processes. However, the issue of data quality and dossier improvement has recently received some attention from industry (BAuA 2016). REACH obliges registrants to update the registration dossier “without undue delay” for several reasons. One reason is that new information about risks caused by the use of a substance lead to changes in the chemical safety report or the safety data sheet. Therefore, registrants should evaluate whether the assessments in their chemical safety reports are still valid in light of the validation studies regarding exposure assessment tools. Registrants should pay special attention to uncertain assessments.

Two important projects aim to improve the supply chain communication and how modeling results in REACH registrations can be used for workplace risk assessment. The German Federal Institute of Occupational Safety and Health (BAuA) project From registration dossier via safety data sheet to workplace risk assessment - data availability and quality between REACH and occupational safety (REACH2SDS) (BAuA 2016) aims to analyze the quality of the information flow from the registration dossiers to the safety data sheets and subsequently evaluate the usability for the workplace risk assessment. The results of this ongoing project will be used to develop approaches for further improvements to the communication of risks and measures in the supply chain. The ongoing CEFIC LRI B23 project on Optimizing the benefit of REACH worker exposure assessments: ensuring meaningful health risk communication (CEFIC-LRI 2019) seeks to ensure that the information from exposure assessments (exposure modeling) communicated to downstream users is relevant and understandable and supports existing OSH regulations. These projects do not directly aim to improve modeling but will have an indirect influence on how modeling results are communicated and used for workplace safety.

The industry also plays a role in associations for sectors of manufacturers and users of chemicals. These associations try to bundle information and provide sector-specific guidance and information. Different industry associations, together with the ECHA, have started the Exchange Network on Exposure Scenarios (ENES) (ECHA 2018a). ENES aims to identify good practices for preparing and implementing exposure scenarios and to develop effective communication between actors in the supply chain. Within the ENES Work Program, the action consolidate the different worker exposure tools into a common framework was also included. However, this ENES action is not yet finished, and therefore it remains to be evaluated in the future how successful this activity will be and how the expected results can be implemented, e.g., in guidance documents, in exposure assessment tools, and finally in regulatory exposure assessments. The second activity mainly driven by industry associations that is presented here is use maps. See Supplementary Materials Text S1 and Table S2.

Conclusion and recommendations

There are several deficiencies regarding the application of occupational exposure models in the REACH context. Some of these are described above. To address these deficiencies, different stakeholders should take action. Some ideas were recently developed by Schlüter and Tischer (2020). Following this proposal: (1) model/tool developers/owners should publish information for revisions and advances; (2) authorities (i.e., the European Commission, the ECHA, and Member State Competent Authorities) should consider the information when basing regulatory decisions on modeled exposure values; (3) REACH registrants should identify which registrations and uses are affected by the information from validation studies and react accordingly; and (4) industry associations should identify areas and industry sectors where the development of use maps or other means of harmonization of exposure- and use-related information would be beneficial. Further, a strategy was recently proposed for the priority area of exposure modeling in Europe with four strategic objectives and an associated action plan and roadmap for the implementation of exposure modeling in the context of the European Exposure Science Strategy 2020–2030 (Fantke et al. 2022; Schlüter et al. 2022b). These strategic objectives are: (1) improvement of existing models and tools; (2) development of new methodologies and support for the understudied field; (3) improvement of model use; and (4) regulatory needs for modeling (ISES Europe 2022) (Schlüter et al. 2022b).

The need for harmonized evaluation criteria of occupational exposure modeling tools and comprehensive validation studies, as well as good-quality exposure data to properly define the actual state of model performance, are priority issues. Furthermore, the continuous development, adjustment, and recalibration of modeling tools are essential to improve the reliability of REACH models, expanding these models' domains (Spinazze et al. 2019; Schlüter et al. 2022a). With regard to the improvement and harmonization of the existing exposure models/tools, the ECHA recently started the CHESAR-Platform (ECHA 2021). This platform is meant to be for exchange in the stakeholder community that will play a key role in collecting and discussing a wide range of scientific proposals, from assessment methodologies and approaches to the usability of the tool. This platform just launched, and no results have been published so far. However, it aims to support users of CHESAR in their assessments (e.g., improved support in the software), improve the tools (e.g., by adding additional models to the CHESAR tool), and generally improve the communication between different stakeholders to develop a common understanding of regulatory needs for exposure modeling.

In conclusion, some insights can be drawn from this discussion. Despite exposure models being essential for exposure assessment for risk assessment purposes in the REACH framework (as well as in other contexts), exposure modeling needs to be improved in many respects. Model development and improvement require further research to meet the global needs of chemical safety assessments and to reach a wide consensus on several key issues (including the theoretical background and the reliability of some modeling tools). The performance and regulatory acceptance of exposure models need to be consolidated and monitored continuously by regulatory decision-makers and independent scientists. Current official documents (e.g., the R14 REACH guidance document (ECHA 2016) reflects the state of knowledge of 2016) and procedures show a lack of awareness of the importance and needs of exposure modeling. Regulatory decision-makers must cooperate and align practices and policies (e.g. within the revision and update of European chemical legislation) regarding exposure modeling across different legislation (Schlüter et al. 2022a).

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Conflicts of interest

The authors report that there are no conflicts of interest to declare.

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Data availability statement

This article has generated no new data to share.

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