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TITLE

TREXMO: A Translation Tool to Support the Use of Regulatory Occupational Exposure Models

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RUNNING TITLE

TREXMO – Translation tool for Exposure Models

ABSTRACT

Occupational exposure models vary significantly in their complexity, purpose and the level of expertise required from the user. Different parameters in the same model may lead to different exposure estimates for the same exposure situation. This paper presents a tool developed to deal with this concern – **TREXMO** or **Tr**anslation of **Ex**posure **Mo**dels. TREXMO integrates six commonly used occupational exposure models, namely, ART v.1.5, STOFFENMANAGER® v.5.1, ECETOC TRA v.3, MEASE v.1.02.01, EMKG-EXPO-TOOL and EASE v.2.0. By enabling a semi-automatic translation between the parameters of these six models, TREXMO facilitates their simultaneous use. For a given exposure situation, defined by a set of parameters in one of the models, TREXMO provides the user with the most appropriate parameters to use in the other exposure models. Results showed that, once an exposure situation and parameters were set in ART, TREXMO reduced the number of possible outcomes in the other models by 1-4 orders of magnitude. The tool should manage to reduce the uncertain entry or selection of parameters in the six models, improve between-user reliability and reduce the time required for running several models for a given exposure situation. In addition to these advantages, registrants of chemicals and authorities should benefit from more reliable exposure estimates for the risk characterisation of dangerous chemicals under REACH.

KEYWORDS
Occupational exposure models, between-user reliability, Advanced REACH Tool (ART), STOFFENMANAGER®, ECETOC TRA

INTRODUCTION

Occupational exposure models are an indispensable part of scientifically sound evaluations of human exposure to chemicals. Since the Regulation, Evaluation, Authorisation and restriction of CHemicals (REACH) legislation entered into force in 2007, exposure models have been widely used to perform chemical safety assessments and establish exposure scenarios for dangerous substances (ECHA, 2012a). There are several models available with which to assess occupational exposure to chemicals in the workplace (Money, 2003), each different in terms of complexity and conservatism (Tielemans et al., 2007; BAuA, 2015b). In order to cope with the large number of industrial chemicals that require registration, the European CHemicals Agency (ECHA) advocates a Tiered approach. Tier 1 models should be used as screening tools that provide a rough but conservative estimate of exposure. Tier 2 models should be used for an in-depth and more complex exposure assessment requiring more input parameters (ECHA, 2012a). It has been argued, however, that Tier 1 models are preferable to Tier 2 models whenever the relevant model parameters are uncertain or the exposure scenario is difficult to interpret (Riedmann et al., 2015).

Several different Tier 1 models are available, such as STOFFENMANAGER® (Marquart et al., 2008), the European Centre for Ecotoxicology and Toxicology of Chemical Target Risk Assessment (ECETOC TRA) (ECETOC, 2012), Metals' EASE (MEASE) (EBRC, 2010) or the EMKG-EXPO-TOOL (BAuA, 2015a). There are only a small number of complex Tier 2 models, such as the Advanced REACH Tool (ART) (Fransman et al., 2013). These models rely on a combination of different approaches, e.g. mechanistic model prediction and exposure measurement in ART, or a refined initial exposure estimate in ECETOC TRA (see Table 1 for more details). However, for many exposure scenarios, it is not clear which specific model should be used for the exposure assessment or even whether a Tier 1 or 2 approach is more appropriate. In most situations, the user can choose between several suitable models. However, each one will probably result in different exposure estimates for the given exposure scenario (Hofstetter et al., 2012). For Tier 1 and Tier 2 models, no guidance is available to the user on how to interpret different models' results, and little information is available about the levels of uncertainty associated with the exposure scenarios, parameters and the model (ECHA, 2012b; Hesse et al., 2015; Riedmann et al., 2015). The sources of uncertainty related to an exposure scenario may include approximations of workplace floor plans and room volumes or unreported risk management measures (e.g. local exhaust ventilation). The sources of uncertainties related to a models' parameters may include data quality (e.g. measurement errors, the amount of data or bias in expert judgement), but they may also reflect the qualitative or subjective definition of some parameters (e.g. for the dustiness of powders), which may further complicate the correct specification of the parameters (Hesse et al., 2015). Uncertainties related to the model itself – such as its fields of application, simplified hypotheses (e.g. the validity of using the ideal gas state) or correlation between model parameters – will further affect its overall performance.

An extensive Evaluation of the Tier 1 Exposure Assessment Models (the ETEAM project) (BAuA, 2015b) was recently conducted. The authors showed that Tier 1 models appeared to exhibit varying levels of conservatism when compared to a broad set of different Exposure Situations (ESs). For example, STOFFENMANAGER® showed only a low level of conservatism when assessing low-volatile substances (≤ 10 Pa), whereas it estimated levels comparable to the measured data for volatile substances. Furthermore, the ETEAM study on between-user reliability (Lamb et al., 2015) showed extensive variability in users' choices of model parameters (e.g. use description, dustiness of solids or risk management measures) leading to exposure estimates that ranged over several orders of magnitude for the same ES. Two recent publications investigating the between-user reliability of ART (Schinkel et al., 2014a) and STOFFENMANAGER® (Landberg et al., 2015) confirmed the significant variability in exposure estimates by users interpreting the same ESs. Poor between-user reliability could have severe health consequences for workers when exposure estimates are underestimated – they could have financial consequences for companies when overestimated (Schinkel et al., 2014a). Developers of future models will have to factor in concerns about the improved between-user reliability of different tools so that they provide reliable and sufficiently conservative exposure estimates for a wide range of different ESs.

The present paper describes the development, validation and performance of a new tool – Translation of Exposure Models (TREXMO) – that integrates six commonly used exposure models: ART v.1.5, STOFFENMANAGER® v.5.1, ECETOC TRA v.3, MEASE v.1.02.01, EMKG-EXPO-TOOL and EASE v.2.0. The goal was to produce a single user-friendly interface combining all six models that would help the user to enter or select the correct parameters and facilitate the simultaneous use of several models for the same ES. TREXMO assumes that a set of parameters in one model – reflecting the user's knowledge about the ES – can be translated into another model. In order to build this "guided" translation framework, we carried out a systematic comparison of the structures and determinants of the six models and their parameters. The comparison established a single set of translation rules between every pair of the six models. By narrowing down the number of parameters, TREXMO should reduce the number of possible different or false choices a user might make and reduce the time required to implement all the models in comparison using models individually. Ultimately, TREXMO should contribute to improve between-user reliability and more reliable exposure estimations for exposure scenarios of concern.

METHODS

Classification of the determinants of exposure

To facilitate the comparison and interpretation of the results, the determinants of exposure in the six exposure models were classified into five exposure groups: **source**, **activity**, **control**, **time** and **Respiratory Protective Equipment** (**RPE)** (Table 1). The source group includes determinants related to the substance's physical and chemical properties. Typical examples are "dustiness" for powders or vapour pressure for liquids; both describe the substance's potential to become airborne. The activity group describes, in general terms, how the substance is used. These are termed process categories (PROCs) in ECETOC TRA, activity classes and subclasses in ART. The activity group usually combines several approaches by which to categorise an activity or a relevant process, such as type and amount of energy applied to the product, the product surface subjected to exposure, the amount of the product used in the task and, for some, the preventive measures used at the source (e.g. level of containment) (ECHA, 2012a; Marquart et al., 2011). The control group contains the determinants intended to prevent, reduce or limit ambient exposure (e.g. local controls or general ventilation). Task duration and RPE could not be associated with any of the three exposure groups and were therefore classified separately. Depending on the complexity of the models, each group might contain one or several determinants of exposure. It should be pointed out that ART, EASE and EMKG-EXPO-TOOL do not use RPE as part of their model structures. Furthermore, EASE considers neither task nor exposure duration; thus, no time-related parameters are available. It is also unclear whether outputs from EASE are based on full-shift or task-based exposure (Creely et al., 2005).

Each determinant was analysed separately in order to set up a translation pattern for the parameters between the six exposure models considered. The methodology used was similar to that of Riedmann et al. (2015) for ART, STOFFENMANAGER® and ECETOC TRA v.3.

Parameter Translation

Selected publications related to the six models were reviewed – as were technical guidelines if available – in order to collect information about their determinants and parameters. An overview of each determinant's fields of application was prepared, thus identifying overlaps between parameters' ranges or values. This consolidation of information for each models' parameters built a single set of rules for translating each parameter into the corresponding parameters of the other models. Translating a given ES from one model to another is therefore represented by a complete list of parameters from one model and the corresponding parameters of the others (see Supplementary Material 1, Tables S1-S17 available in the online edition).

As an example, Fig. 1 shows how the "Movement and agitation of powders, granules or pellets" activity class from ART, together with other underlying parameters (amount of product and level of agitation), can be translated into the appropriate activity parameters in STOFFENMANAGER®, ECETOC TRA and MEASE. This example shows that ART's activity parameters translate directly into STOFFENMANAGER®. A translation that leads to just one possible outcome is defined here as a "straightforward" translation. However, the user may also have to enter or select additional parameters in order to translate the ES between different models. The example in Fig. 1 shows that there are no straightforward translations for ECETOC TRA v.3 and MEASE because several PROCs can be selected for each activity class in ART.

Development of TREXMO

A simple programming solution, accessible to users with basic software engineering skills, was needed to set the translation of the parameters and the validation tests. In order to do this, a new descriptive programming language was developed in collaboration with the University of Geneva. The "Data Descriptive and Transformation Language" (DDTL) is unique to TREXMO. It is a three-fold language used to generate complex forms containing sets of parameters, the models with which to run them and the algorithms to translate them into other forms. The syntax structure is similar to those used the in Python programming language and YAML code, but the programming itself does not require any specific knowledge. A specific compiler – a program that transforms the descriptive code into another computer language – was incorporated in the DDTL in order to develop a standalone tool. When compiled, DDTL descriptive programming is transformed into Python (v.3) and Javascript code, which together provide the graphical user-interface. The two-layer structure provided by DDTL and its compiler allows the tool to be managed flexibly. The DDTL *layer*, which does not require advanced skills in computer sciences, is freely accessible to exposure modellers to add to or update their models. The compiler *layer*, however, is developed and maintained by computer scientists.

Validation of the TREXMO tool

By systematically changing only one parameter at a time, while keeping the other parameters constant, we generated hundreds of different sets of parameters. Each set of parameters generated for each model was executed and translated to all the other models. The outputs obtained using TREXMO were compared to those from official models (i.e. the original web-based tools of ART and STOFFENMANAGER®, the MS Excel platforms of ECETOC TRA v.3, MEASE and EMKG-EXPO-TOOL or the exposure ranges of the EASE decision-tree). Furthermore, the translations obtained were compared to the list containing all the translations established previously (see Supplementary Material 1, Tables S1-S17 available in the online edition). Any disagreement between TREXMO and the original models was corrected accordingly. Once completed, the validation showed that TREXMO calculates the same outputs as the official models and performs the translations as defined.

A further external validation was conducted by independent experts in the field of exposure sciences. Professionals from BAuA (Federal Institute for Occupational Safety and Health, Germany), NIOSH (National Institute for Occupational Safety and Health, USA), the INRS (National Institute for Research and Safety, France), KIST-Europe (Korea Institute of Science of Technology, Germany) and IOM (Institute of Occupational Medicine, UK), were asked to assess at least four ESs using TREXMO and to carry out the appropriate translations between different models in TREXMO. They were also asked to review the list containing all the established translations and the tool's user-friendliness. The feedback was used to confirm the accuracy of the initial set of rules for translation. Feedback on TREXMO's user-friendliness will be considered in the tool's next version.

Translation efficiency test

As shown in Fig. 1, a given parameter in one model can be translated to one or several parameters in the other models. The more choices a user has, the more likely an error of interpretation is likely to occur and the more time-consuming an exposure assessment might become. TREXMO's translations decreased the number of choices, which should lead to more efficient and less erroneous exposure assessments.

Translation efficiency is defined here as the number of possible translations (*n*) of a parameter or a set of parameters from one model to another. Translation efficiency was calculated for every model in TREXMO, using all the exposure groups and determinants for each exposure type (solids, dusts and liquids). A translation operation is defined as efficient when it decreases the number of choices available to the user. TREXMO's translation efficiency was investigated using ART, STOFFENMANAGER®, ECETOC TRA v.3 and MEASE as starting models. Due to their simplicity, the remaining two models (EASE and EMKG-EXPO-TOOL) were not used to calculate the translation efficiency of the tool. In the present paper, the methodology and the result section are restricted to ART only, while the results for the three additional models are presented in the Supplementary Material 3, available in the online edition.

R software version 3.1.1 (R Development Core Team, 2010) was used to generate different sets of parameters, corresponding to the different ESs for ART. The parameters within every determinant were changed one by one, whereas the parameters for the other determinants were randomly selected with the same probability (e.g. the five parameters of dustiness had a 1 in 5 probability of being selected). Matrices 1 and 2 (shown below) present two example sets of parameters corresponding to two different ESs that differ only in the spraying rate applied. Additionally, each parameter was selected for at least ten sets of parameters. For example, "movable capturing hood"–a parameter of localised exposure control in matrices 1 and 2–was selected for at least eight more sets.

$$\left[E\begin{pmatrix} P = 1150\ Pa & C = 12\% \\ \gamma = 1.5 & T = 25°C \end{pmatrix} \ H\begin{pmatrix} spraying & low\ comp.\ air \\ 0.3\text{-}1\ l/min & downward \end{pmatrix} \ D\begin{pmatrix} & near\text{-}field \\ 300\ m^3 & 3ACH \end{pmatrix} \ LC(movable\ cap.\ hood) \right]$$

Matrix 1

$$\left[E\begin{pmatrix} P = 1150\ Pa & C = 12\% \\ \gamma = 1.5 & T = 25°C \end{pmatrix} \ H\begin{pmatrix} spraying & low\ comp.\ air \\ 1-3\ l/min & downward \end{pmatrix} \ D\begin{pmatrix} & near\text{-}field \\ 300\ m^3 & 3ACH \end{pmatrix} \ LC(movable\ cap.\ hood) \right]$$

Matrix 2

Determinants *E*, *H*, *D* and *LC* are explained in Table 1. The sets of parameters for the different exposure types (solids, dusts and liquids) were generated separately since each exposure type requires different number and types of parameters. In total, 804, 2,214 and 1,414 different sets of parameters were generated to test TREXMO's translation efficiency for solid, dust and liquid ESs, respectively. The number of ESs tested was considered to be representative since the translation efficiency results obtained did not change when the number of sets was increased further.

The sets of parameters generated were used as arguments in a translation function programmed using the same software. This function calculated the probabilities of having *n* outcomes for each determinant and model when translated from ART using the set translation rules. Results are expressed as probability matrices in the following form:

$$n : P_n$$

Where, n represents the number of possible translations for a determinant or a set of parameters for the ESs generated; P_n represents the probability that the user, after translation from one model to another, must choose between n parameters for a specific determinant (see Fig. 1 for example) or can establish n different sets of parameters. P_n was calculated as the ratio between the number of sets which led to n translations for a specific determinant (or n different sets possible in another model, after translation) and the total number of sets generated by the R software. For example, a probability matrix of 1:0.40 and 4:0.60, means that the user will have a straightforward translation in 40% of cases, whereas in 60% of cases he will have to choose between 4 possible translations for a determinant or can establish 4 different sets of parameters. In this example, 4 sets of parameters can be the result of a choice between 4 different parameters for a single determinant (e.g. PROCs) or two choices between 2 parameters for 2 different determinants (e.g. PROCs and GV) leading to 4 different possible combinations of the respective parameters.

The number of theoretically possible sets (combinations) of parameters (N_{sets}) was also calculated for every model in TREXMO. The multiplication of the number of parameters (N_{ip}, e.g. six parameters for dustiness in STOFFENMANAGER®) defined for every determinant of a model (Table 1) gives the total number of possible combinations of parameters for each model. This calculation was done for every exposure type, separately. However, those determinants that use continuous scaling (e.g. vapour pressure) were not used in this calculation. The calculation of N_{sets} for every model considered and every exposure type is briefly shown in Supplementary Material 2. The TREXMO tool's overall performance is obtained by comparing its n possible translation pathways for the generated ESs with N_{sets}.

RESULTS

The results of the translation efficiency test are presented in Tables 2-4 (see also Supplementary Material 3, Tables S1-S9 available in the online edition for the investigated Tier 1 models). TREXMO reduced the overall number of available parameters (N_{ip}) and the total number of combinations of parameters (N_{sets}) possible for the models considered. Since the translations from ART generated different percentages of non-applicable ESs, the results present the translation efficiency only for the applicable fraction in the other five models:

STOFFENMANAGER® (100%) < ECETOC TRA v.3 (75%) < MEASE (37.5%) = EASE (37.5%) < EMKG-EXPO-TOOL (26%)

This means that any ESs established in ART is applicable in STOFFENMANAGER®, while only every fourth randomly generated ESs is applicable in EMKG-EXPO-TOOL.

Almost all the ESs generated for STOFFENMANAGER® were either from straightforward translations or required the selection of one additional parameter (99% for solid and dust ESs, 96% of liquid ESs, Table 2) that could establish 2 or 3 different combinations of parameters, depending on the number of choices available. Only a small number of the ESs generated for ART could be translated into 6 different combinations of parameters (1% of solid and dust ESs, 4% of liquid ESs) by two additional selections.

Additional selections were required for all ES translations from ART to ECETOC TRA v.3 and MEASE. The ESs generated could be translated using one or two additional selections to, at most, 2, 14 and 12 different combinations of parameters for solid, dust and liquid ESs, respectively (Table 3).

For the EMKG-EXPO-TOOL, the dust ESs generated were either straightforward translations (92% of ESs) or required one additional selection (8% of ESs) that could lead to 3 different combinations of parameters (Table 4). For the liquid ESs, only 36% of cases were able to generate a straightforward translation, and in 64% of cases, one or two additional selections lead to 2, 3 or 6 different combinations of parameters. Translations from ART to EASE (Table 4) were straightforward for all the applicable ESs.

The translation efficiency calculated from ART to the other models also varied over the five exposure groups (Table 1) and their respective determinants. A ranking of translation efficiency was established across all models for all exposure types and situations:

Time group > Source group > Control group > Activity group

This ranking means that the time group parameter was most efficiently translated from ART into the other models, whereas additional selections were usually required for the activity group.

Here, we present and explain the translation efficiency results for each exposure group and its determinants, separately.

Source group

For the solid and dust ESs provided in ART, the source group determinants (dustiness, moisture content and weight fraction) defined all the parameters in that group in the other models and could, therefore, be directly translated. Solid ESs are outside the EMKG-EXPO-TOOL's field of application and were therefore not translated (see Table 1).

For liquid ESs, the continuous scaling used for the parameters in that source group in ART (vapour pressure, activity coefficient and weight fraction) allowed straightforward translations to the corresponding determinants of the other models and no additional choices were required.

Activity group

Straightforward translations between ART and STOFFENMANAGER® (Table 2) were possible in 96%, 99% and 83% of cases for solid, dust and liquid ESs, respectively. For all other ESs and exposure types, translation led to two possible outcomes.

For ECETOC TRA v.3 and MEASE, the activity parameters in ART could be translated into 1 to 7 different PROCs for the ESs generated (see Table 3 and Fig.1 for an example). For dust and liquid ESs, an additional choice between two different PROCs was required in 32% and 37% of cases, respectively. However, in 55% and 60% of cases, a choice between 3–7 PROCs was required, whereas only 13% and 3% of cases were straightforward translations for dust and liquid ESs, respectively. The situation was quite different for solid ESs as all 804 in ART led to a single PROC (see Supplementary Material 1, Table S5 available in the online edition). Furthermore, since ART does not consider the Sector of Use (SU3 and SU22), the number of choices doubled in ECETOC TRA v.3 and MEASE.

For the EMKG-EXPO-TOOL, a straightforward translation was possible in 92% and 40% of cases using the scale-of-use determinant for dust or liquid ESs, respectively (Table 4). For dust ESs, three choices were available in 8% of cases, whereas three choices were available in 60% of liquid ESs. Further, in 88% of cases a straightforward translation was possible for liquid applications-on-surface determinant; whereas in 12% of cases translation was possible with two choices.

In the activity group, *straightforward* translations from ART to EASE were possible for all the ESs generated and all the exposure types (Table 4).

Control group

A straightforward translation of the determinants of the control group was applicable from ART to STOFFENMANAGER® for all the indoor and outdoor ESs generated (Table 2). In 25% of cases, however, which included spray rooms/cabins or enclosed spray booths, STOFFENMANAGER® required the specification of the workplace volume.

Parameters of this group generated the high percentages of the non-applicable ESs. Since ECETOC TRA v.3 is not applicable to spray rooms/booths, a quarter of the cases were not translated into this model. Furthermore, MEASE, the EMKG-EXPO-TOOL and EASE were applicable only to ESs representing indoors exposure (not including ESs related to spray rooms/booths).

Time group

Since ART applies continuous scaling for its "duration" determinant, all the translations to the corresponding determinants in other models (excluding the EASE, see also Table 1) were straightforward.

RPE group

The use of RPE is not incorporated into ART's field of application. Translations from ART to the other models were therefore not attempted.

DISCUSSION

The present paper described a new tool – **TREXMO**, or **Tr**anslation of **Ex**posure **Mo**dels – to help users select parameters for six common occupational exposure models and assessed its adequacy. TREXMO's overall structure is illustrated in Fig. 2. and an overview of its user-interface is presented in the Supplementary Material 4, available in the online edition. A single set of translation rules, based on a comparison study, allows parameters from TREXMO models to be translated into its other models. The results of the translation efficiency test showed the tool's significant efficiency. That is, after translation of the parameters from the Advanced REACH Tool (a Tier 2 model) TREXMO showed a strong capacity to narrow down the number of parameters to choose from in the other models – reducing possible different or false choices. It also reduced the time required to implement all the models under comparison. Based on the efficiency results, translations from ART should significantly improve the between-user reliability in the other models included in the tool.

TREXMO is unable to make a straightforward translation to the other five models of every possible ES provided by ART. The translation between models most likely to give the highest percentage of straightforward parameters in different ESs was from ART to STOFFENMANAGER®. When used as the starting model for the efficiency test, ART is the most complex model in TREXMO. However, some of the parameters are used in various models with different definitions or are only described in general terms (e.g. PROCs). Moreover, some of the determinants used in the other five models are not used in ART (e.g. SU). These issues either reduce the efficiency of translation by increasing the number of possible outcomes or preclude the definition of a translation. Consequently, the translation rules put in place cannot provide a straightforward translation from any ES established in ART to any parameter in ECETOC TRA v.3 or MEASE; rather, they decrease the number of parameters available per determinant. For example, in the case of a least efficient translation for a liquid ES provided by ART, TREXMO decreases the number of PROCs available for selection in ECETOC TRA v.3 by a factor of 3.5. This should also result in a lower probability of an erroneous selection of the PROC parameter.

The proportions of different ESs generated for this study – spray rooms/booths (25%), indoor (37.5%) and outdoor exposure (37.5%) – was arbitrary and is probably not a true reflection of reality. The consequences of this distribution were the high percentages of ESs that were not applicable using MEASE, EASE and EMKG-EXPO-TOOL. However, the results do give a general insight into the fields of application defined in these models. Additional knowledge about the distribution of different exposure situations in the field or in industry could be used to re-calculate the present results and calculate a more realistic ratio of the ESs that are applicable or non-applicable in the different models.

TREXMO is also expected to provide more reliable exposure estimates for characterizing risks of dangerous chemicals assessed under REACH (e.g. for chemical safety assessments or for establishing exposure scenarios). Since the models use different weightings for physical phenomena, they present different aspects of the same ES (Riedmann et al. 2015). In TREXMO, if all six models are applicable to a particular ES, then all six estimates can help the user draw a conclusion about it. The more modelled estimations the user has available, the less uncertainty there should be in the Risk Characterization (RC). The more estimates there are below the OEL, the less likely the OEL will be exceeded. In addition, when using this approach, entering or selecting an erroneous parameter in one of the models should not significantly change the conclusion drawn in the RC for that ES. Consequently, TREXMO will improve the RC of dangerous chemicals for a wide range of ES.

Between-user reliability

The observed performances of TREXMO, as investigated starting from ART, could be used to predict the tool's potential impact on between-user reliability in different models. This prediction could be given by comparing N_{sets} (Tables 2–5) for the model considered and its corresponding n translations in TREXMO, with respect to their calculated probabilities (P_n) for k possible translation routes:

$$r = \frac{N_{sets} - N_{n.a.}}{n_1 \times P_{n_1} + n_2 \times P_{n_2} + ... + n_k \times P_{n_k}} \quad (1)$$

Equation 1 only considers the applicable fraction of the ESs generated, i.e. the non-applicable fraction ($N_{n.a.}$) is excluded. The larger the ratio (r-factor in Equation 1), the higher the positive impact on between-user reliability should be. An r-factor was calculated (averaged over the three exposure types) for the translations from ART to the other models and a ranking was established:

STOFFENMANAGER® (r = 1.4 × 10^4) > MEASE (r = 7.2 × 10^3) > ECETOC TRA v.3 (r = 4 × 10^3) > EASE (r = 1.4 × 10^2) > EMKG-EXPO-TOOL (r = 0.29 × 10^2)

According to the r-factors, TREXMO should most improve the consistency in results between the users of ART and STOFFENMANAGER®. The efficiency of translations from ART to MEASE and ECETOC TRA v.3 were almost the same. However, the gain in certainty is bigger for MEASE, which has the greater N_{sets}. An opposite situation was observed for EASE and EMKG-EXPO-TOOL, which both had a moderate r-factor and small N_{sets} values. Only a limited improvement in certainty is to be expected when using TREXMO with these two last models.

Tier 1 models in TREXMO

Among Tier 1 models investigated (see Supplementary Material 3, Tables S1-S9 available in the online edition) STOFFENMANAGER® showed the strongest capacity to narrow down the number of parameters. Comparing with STOFFENMANAGER®, ECETOC TRA v.3 and MEASE showed lower efficiency also for Tier 1 models. Therefore, STOFFENMANAGER® is recommended to be used as a starting model for a Tier 1 approach.

The results for ART from ECETOC TRA v.3 and MEASE were not calculated due to the fact that these models can lead to a high number of translation pathways which makes the calculation complex.

Conclusion and recommendations

With regard to the number of ESs and parameters that TREXMO allowed us to evaluate, and the results presented here, we believe that it could represent a tool of choice in occupational exposure assessment when the entry parameters are uncertain. The reduction in the number of choices which the user faces should provide fewer opportunities for erroneous parameter selection or entry and increase between-user reliability, as expected. Registrants of chemicals and authorities working with REACH legislation might especially benefit from using TREXMO. For example, chemical safety assessments and the evaluation of ESs under REACH might be improved significantly by the use of TREXMO as it provides more reliable exposure estimates that consider different models for the risk characterization of dangerous chemicals.

However, further evaluations of TREXMO should be conducted alongside users in order to assess the tool's real impact on between-user reliability. One obvious benefit of TREXMO, however, is that it provides outputs from several models with a limited set of parameters. As all these models have their limitations and strengths, comparing results from different sources is of utmost interest.

Using ART as the initial model for this study was logical – ART includes more information in its activity description than the other models – but TREXMO's interface does not limit users to this model. The other five models can also be selected as the initial model, but the translations would be less efficient and, therefore, more choices would have to be made by the user. STOFFENMANAGER® should be selected as the initial model if only a Tier 1 exposure assessment is required. For some ES, in our experience, more than one handling (in STOFFENMANAGER®) or PROC (in ECETOC TRA v.3 and MEASE) parameter might seem suitable. In order to reduce such uncertainty, translations from ART can clearly highlight more suitable parameter in these models. We therefore recommend using translations from ART at least for parameters related to the activity group, since their selection can be more uncertain.

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TABLES AND FIGURES

Table 1. Review of the models included and the classification of their determinants.

Model	Description	Determinants					References
		Source	Activity	Control	Time	RPE	
EASE v.2.0	The model is based on three determinants: the tendency of a substance to become airborne, the way in which a substance is used and the means of control. A decision-tree implements these determinants as selection categories that lead the user to the corresponding exposure range. **Applicability:** *fibrous and non-fibrous dusts (both non-abrasive and abrasive), liquids, gases and vapours*	-Type and size of particles -Vapour pressure -Aggregation of particles	-Pattern of use -Aerosol formation	-Pattern of control	/	/	Devillers et al. (1997) Tickner et al. (2005) Cherrie et al. (2003) Creely et al. (2005)
EMKG-EXPO-TOOL	An MS Excel- based tool. The EMKG-EXPO-TOOL is based on COSHH Essentials and was developed to estimate inhalation exposure in workplaces. It assumes that exposure is determined by the exposure potential of the substance and its control strategy. **Applicability:** *non-abrasive dusts and liquids (not used for spraying)*	-Volatility -Dustiness	-Scale of use -Application on surfaces > 1 m^2	-Control strategy	-Short- or long-term exposure	/	HSE (2012) BAuA (2015a) Kindler and Winteler (2010)
ECETOC TRA v.3	An MS Excel-based tool. ECETOC TRA first estimates an initial exposure based on the PROC, the Fugacity band (fug), Local Exhaust Ventilation efficiency (LEV) and Sector of Use (SU). Then a dimensionless score is applied to the initial exposure estimate by entering or selecting the appropriate fraction of the contaminant (χ), General Ventilation (GV) and Respiratory Protective Equipment (RPE). The estimates of ECETOC TRA are considered to represent the 90th percentile of the full-shift exposure distribution. **Applicability:** *dusts (both non-abrasive and abrasive) and liquids*	-Vapour pressure -Dustiness -Weight fraction	-PROC -Type of settings (SU3 and SU22)	-Control strategy	-Exposure duration	-RPE	ECETOC (2012) ECHA (2012a)
MEASE v.1.02.01	An MS Excel-based tool developed to address the specific needs of the metal industry. Similar to ECETOC TRA, exposure is calculated by the initial exposure estimate modified by a dimensionless score. However, it goes beyond ECETOC TRA, by including three additional PROCs: 26, 27a and 27b. Furthermore, the model uses additional fugacity ranges for metal objects and aqueous solutions, and Risk Management Measures (RMM) with a corresponding set of efficiency values. **Applicability:** *dusts, liquids, aqueous solutions, gases and fumes*	-Vapour pressure -Dustiness -Weight fraction	-PROC -Scale of operation	-RMM	-Exposure duration	-RPE	EBRC (2010) EUROMETAUX (2012) HERAG (2011)

Table 1. Continued.

Model	Description	Determinants					References
		Source	Activity	Control	Time	RPE	
STOFFEN-MANAGER® v.5.1	STOFFENMANAGER® is a web-based source-receptor model and, similarly to ART, it calculates exposure based on a combination of mechanistic scores and measurement data. It includes exposure determinants for the intrinsic Emission (E) (dustiness for solid particles and vapour pressure and weight fraction for liquids), Handling (H), Local Control (LC), Dispersion (D), Background sources (a), Separation (Sep), RPE and the exposure duration (t). STOFFENMANAGER® also provides exposure estimations at different percentiles. **Applicability:** *dust (both non-abrasive and abrasive) and liquids (both low- and high-volatile)*	-Vapour pressure -Dustiness -Weight fraction -Background sources	-Handling	-LC -GV -Emission	-Exposure duration	-RPE	Marquart et al. (2008) Tielemans et al. (2008) Schinkel et al. (2010) Koppisch et al. (2012) Landberg et al. (2015)
ART v.1.5	ART is a web-based source-receptor Tier 2 model. It defines nine, independent, principal modifying factors (MF) associated with its components (e.g. source or Near-Field (NF) zone): Substance emission potential (E), Activity emission potential (H), Local Control (LC), Segregation (Seg), Dilution (D), Separation (Sep), Surface contamination (Su), Personal behaviour (P) and RPE. ART calculates exposure (distribution) for multi-task activities for an 8 h work shift based on mechanistically modelled (dimensionless) exposure and measurement data. Further, a Bayesian update for model predictions can be performed by analogous exposure data. **Applicability:** *dust (both non-abrasive and abrasive) and liquids (both low- and high-volatile)*	-Vapour pressure -Dustiness -Weight fraction -Activity coefficient, (γ) -Viscosity -Moisture content -Surface contamination	-Activity classes and subclasses	-LC -GV -Seg -Sep	-Exposure duration	/	Fransman et al. (2011) Schinkel et al. (2011) Schinkel et al. (2013) McNally et al. (2014) Schinkel et al. (2014a) Schinkel et al. (2014b)

Table 2. Probability distribution of the translation efficiency for the determinants covered in STOFFENMANAGER®. ART is used as the starting tool for the probability calculation.

Exposure group	Determinant	N_{ip}	n:P_n
Source	Kind of dust (wood or stone)	2	1:1
	Dustiness	6	1:1
	Vapour pressure	(0-30,000 Pa)[a]	1:1
	Concentration	(0-100%)[a]	1:1
	Background sources	4	1:1
Activity	Handling (solid ESs)	4[b]-6[c]	1:0.96 2:0.04
	Handling (dust ESs)	8	1:0.99 2:0.01
	Handling (liquid ESs)	8	1:0.83 2:0.17
Control	Room size	4	1:0.75 3:0.25
	General ventilation	4	1:1
	Localized controls	5	1:1
	Immission	3	1:1
Time	Time	(1-480 min)[a]	1:1
RPE	RPE	The translations from ART are not applied	

Exposure type	N_{sets}	n:P_n	
Solid	10,400	1:0.72 2:0.03	3:0.24 6:0.01
Dust	49,920	1:0.74 2:< 0.01	3:0.25 6:0.01
Liquid	8,320	1:0.62 2:0.13	3:0.21 6:0.04

[a]Continuous scaling
[b]Exposure to stone dust
[c]Exposure to wood dust

Table 3. Probability distribution of the translation efficiency for the determinants covered in ECETOC TRA v.3 and MEASE. ART is used as the starting tool for the probability calculation.

Exposure group	Determinant	Model	N_{ip}	$n:P_n$
Source	Dustiness	ECETOC	3	1:1
		MEASE	4	1:1
	Vapour pressure	ECETOC	4	1:1
		MEASE	3	1:1
	Concentration	ECETOC/MEASE	4	1:1
Activity	PROC (solid ESs)	ECETOC	25	1:1
		MEASE	28	1:1
	PROC (dust ESs)	ECETOC	25	1:0.13 5:0.10 2:0.32 6:0.04 3:0.14 $7:10^{-4}$ 4:0.27
		MEASE	28	1:0.13 5:0.16 2:0.32 6:0.04 3:0.11 7:< 0.01 4:0.24
	PROC (liquid ESs)	ECETOC	21	1:0.03 4:0.08 2:0.37 6:0.20 3:0.32
		MEASE	22	1:0.03 4:0.08 2:0.37 6:0.20 3:0.32
	Sector of use	ECETOC/MEASE	2	2:1.0
Control	Control approach	ECETOC	7	1:1
	Risk management measures	MEASE	9	1:1
Time	Time	ECETOC/MEASE	4	1:1
RPE	RPE	ECETOC/MEASE	The translations from ART are not applied	

Table 3. Continued.

Exposure type	Model	N_{sets}	$n:P_n$	
Solid	ECETOC	14,325	2:1	
	MEASE	28,800	2:1	
Dust	ECETOC	14,325	2:0.13 4:0.32 6:0.14 8:0.27	10:0.10 12:0.04 14:< 10^{-4}
	MEASE	28,800	2:0.13 4:0.32 6:0.11 8:0.24	10:0.16 12:0.04 14:< 0.01
Liquid	ECETOC	16,192	2:0.03 4:0.37 6:0.32	8:0.08 12:0.20
	MEASE	15,984	2:0.03 4:0.37 6:0.32	8:0.08 12:0.20

Table 4. Probability distribution of the translation efficiency for the determinants covered in EMKG-EXPO-TOOL and EASE. ART is used as the starting tool for the probability calculation.

Exposure group	Model	Determinant	N_{ip}	$n:P_n$
Source	EMKG-EXPO-TOOL	Dustiness	3	1:1
		Vapour pressure	3	1:1
	EASE	Type and size of particles	3	1:1
		Aggregation	2	1:1
		Vapour pressure	6	1:1
Activity	EMKG-EXPO-TOOL	Scale (dust ESs)	3	1:0.92 3:0.08
		Scale (liquid ESs)	3	1:0.40 3:0.60
		Surface of application	2	1:0.88 2:0.12
	EASE	Pattern of use (solid/dust ESs)	3	1:1
		Pattern of use (liquid ESs)	4	1:1
		Aerosol formation	2	1:1
Control	EMKG-EXPO-TOOL	Risk management measures	3	1:1
	EASE	Pattern of control (solid/dust ESs)	2	1:1
		Pattern of control (liquid ESs)	5	1:1
Time	EMKG-EXPO-TOOL	Task duration	2	1:1
	EASE	No relevant determinant for this group		
RPE	EMKG-EXPO-TOOL / EASE	No relevant determinant for this group		
Exposure type		**Model**	N_{sets}	$n:P_n$
Dust		EMKG-EXPO-TOOL	54	1:0.92 3:0.08
		EASE	36	1:1
Liquid		EMKG-EXPO-TOOL	108	1:0.36 2:0.04 3:0.50 6:0.10
		EASE	240	1:1

Figure 1. An example of possible translation routes from an activity class in ART (Moving and agitation of powders, granules or pellets) to STOFFENMANAGER®, ECETOC TRA and MEASE.

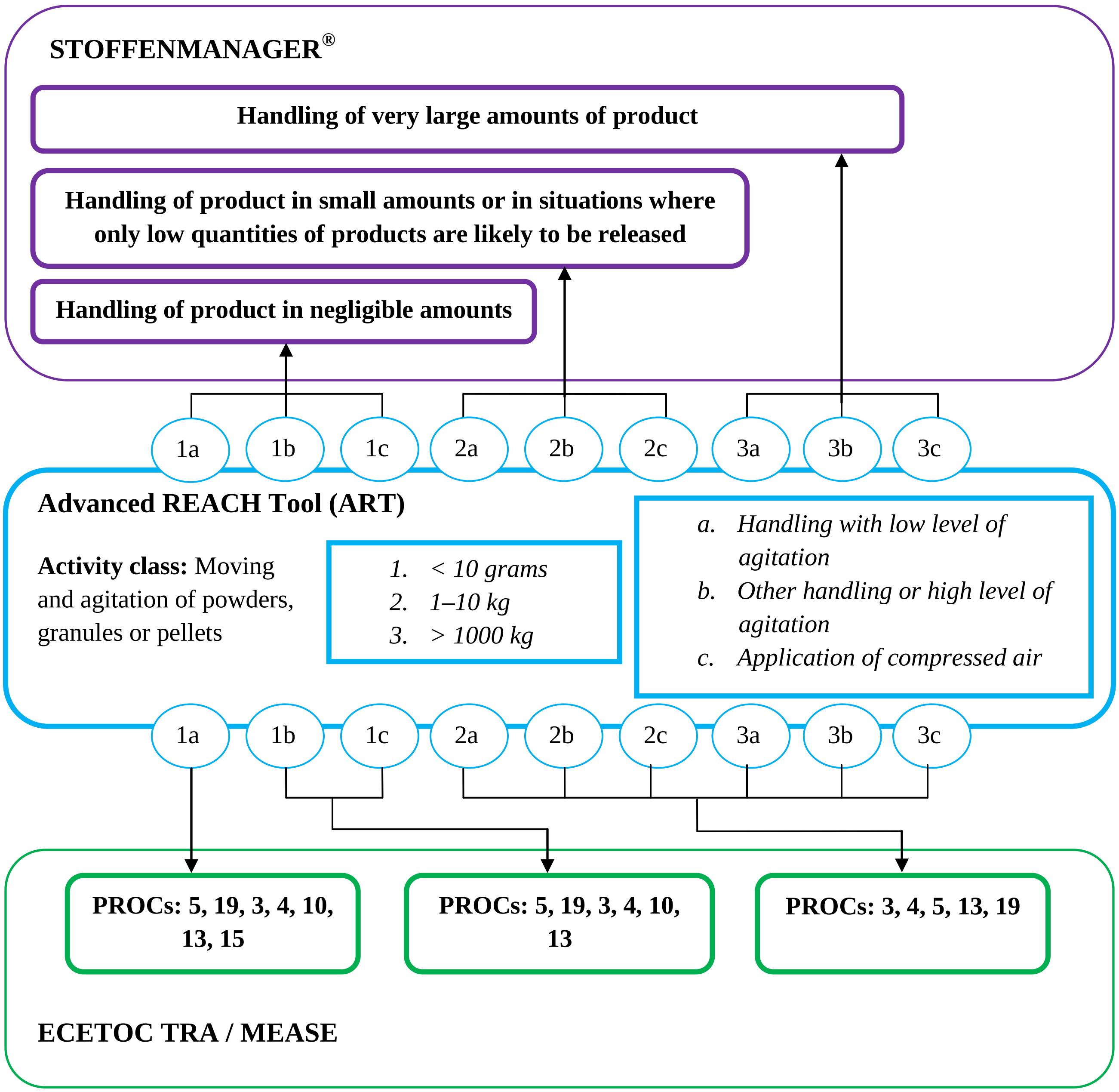

Figure 2. TREXMO workflow. 1) Interpretation of the ES; 2) additional choices due to non-*straightforward* translations; and 3) *direct* exposure calculation after a *straightforward* translation.