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TREXMO - Technical Report

Translation tool for exposure models

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A large, abstract geometric shape composed of several overlapping, semi-transparent polygons in shades of blue and grey, creating a 3D effect. The shape is positioned at the bottom of the page, spanning most of the width.

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SUMMARY

Occupation exposure models are widely used in the European Union for regulatory and workplace exposure assessments. These models vary in their complexity, level of conservatism and the accuracy of calculated estimates. The correct use of these models has been a subject of concern addressed in many studies. The studies have shown that different users modelling the same exposure situations can set different input parameters in the model and therefore get different conclusions about the exposure safety.

This technical report describes backgrounds and user-handling for TREXMO-web – version 1.5. TREXMO-web is an updated version of the first TREXMO – version 1.0 – released in 2015 as a standalone tool. TREXMO-web is an online tool available on URL: <http://trexmo.unige.ch>.

TREXMO-web is a single interface for six most used exposure models, namely: Advanced REACH Tool (ART version 1.5), STOFFENMANGER® (version 5.1), European Centre of Eco-toxicology and Toxicology of Chemicals (ECETOC) Target Risk Assessment (TRA version 3), Metals' EASE (MEASE version 1.02.01), EASE (version 2.0) and EMKG-EXPO-TOOL. The interface enables semi-automatic translations between different models. These translations are intended to guide the users to more appropriate parameter sets and more valid exposure calculations for a given exposure situation (ES). Ultimately, the tool should contribute to improve between-user reliability and provide the users with more reliable exposure estimates for risk characterization of dangerous chemicals.

Why online tool?

Version 1.0 of TREXMO was a standalone version which required several pre-installations to be done prior to the installation of TREXMO. Since it was a time-consuming process that could include the administrative restrictions for the installation or even the software itself could be recognized as a virus and blocked by the antivirus system. In addition, any new update to the standalone version would require re-installation of the tool. These obstacles were an initiation sparkle to develop the online version in parallel with the standalone tool. With online version, the users avoid the installation and have always the newest version of the software updated.

What's new?

Version 1.5 of TREXMO-web has introduced several new features:

1. **Save as** button (see the photo bellow) – avoids losing of a parameter set established in the starting model after translation. This option allows the users to save the translated set as a new ES and still keep the original one.



2. **Save as PDF** button – after the exposure calculation it is now possible to save the list containing selected parameters as a PDF. This option can enable easier data exchanges between the users or institutions.
3. Better graphical-user interface (GUI) – the fields (exposure determinants) have been split into two columns if the display size it allows.
4. Rapid calculation of exposure – comparing with the standalone tool, the time required to perform an exposure calculation has been reduced.
5. Exposure calculations in the Advanced REACH Tool and STOFFENMANGER[®] generate exposure prediction at several percentiles through a single step.
6. Rounding of exposure outputs as in the official platforms.

GENERAL

In 2007 REACH (Registration, Evaluation, Authorization and restriction of Chemicals) regulations entered into force in the European Union (Europa 2013). The purpose of the regulation is to ensure a high level of protection of human health and the environment. In order to derive specific recommendations on how a substance or preparation is used and controlled during its life cycle, REACH recommends use of exposure assessment tools – models (ECHA 2012).

A variety of models have already been developed and the tiered approach is suggested during model selection (Keil 2000, Money 2003). Tier 1 models are simple screening tools (Tielemans, Warren et al. 2007) which require a small number of parameters for exposure calculation. Because of their simplicity, Tier 1 models must include more conservatism in order to not underestimate exposure. Unlike these models, Tier 2 models require more exposure parameters to set and therefore it is expected to be more accurate.

Beside the model selection, misinterpretation of parameters presents one more obstacle for a correct use of the models. Two users (having different expertise) may differently interpret the same exposure situation and therefore get different conclusions. This might be a consequence of insufficient training and experience of workers for the models' use in chemical exposure assessments. Furthermore, the variability can be expected to be even larger if more than one model is used. This variability, when combined together with fact that these models are wrong, might make assessment pointless. Finally, this can result in wrong conclusions about safety (e.g. an “unsafe” diagnosed as a “safe”) or could lead to costly over-engineering. Nevertheless, different decisions in models can have different degree of impact on the final output in different models.

This report is intended to explain basic backgrounds of TREXMO-web and its use for exposure calculations. The tool includes the six, commonly used, exposure models in a unique interface. The models, namely: ART v. 1.5, STOFFENMANAGER v. 5.1, ECETOC TRA v. 3, EASE v. 2, MEASE v. 1.02.01 and EMKG-EXPO-TOOL, were re-programmed and connected. A systematic comparison of the definitions used in the six models allowed establishing of a translation system between them. This translation system narrows down the total number of parameter entry and selections required from the user and therefore should lead to less erroneous estimates.

The six models that have been included in TREXMO are briefly described in this chapter. This chapter introduces the reader to the different models' structures which have been connected with the translations of parameters.

Background to Advanced REACH Tool

ART is a higher tiered exposure assessment tool that combines mechanistically modeled inhalation exposure predictions with available exposure data using the Bayesian approach (McNally, Warren et al. 2014). The mechanistic model is based on a conceptual framework that adopts a source-receptor approach (Cherrie and Schneider 1999), with movement of contamination affected by nine principal modifying factors (Fransman, Van Tongeren et al. 2011).

ART (current version 1.5) differentiates between three different exposure types: vapours, mists, and dust. Exposure types: fumes, fibers and gases are not included in the current version of the model. Equations 1 and 2 present algorithms for near- and far-field exposure assessment in the ART, respectively.

$$B_{nf} = (E \times H \times LC)_{nf} \times D_{nf} \quad (1)$$

$$B_{ff} = (E \times H \times LC \times D \times Seg \times Sep)_{ff} \times D_{ff} \quad (2)$$

Subsequently, the overall exposure is estimated by summation of both estimates (near- and far-field) and surface contamination factor (Su). ART can be used for multiple activities (up to four) within an 8-h work shift (t_{total}). The total exposure (B_t) is estimated by algorithm in equation 3 (Fransman, Van Tongeren et al. 2011).

$$B_t = \frac{1}{t_{total}} \sum_{tasks} \{t_{exposure} \cdot (B_{nf} + B_{ff} + Su)\} \quad (3)$$

The output of the algorithm (equation x) is a dimensionless score. Calibration of the ART's score has been done by Schinkel, Warren et al. (2011). Unlike tier 1 models, the ART gives confidence intervals (CI) around different percentiles (variability). Different percentiles in the ART are calculated by taking into account three sources of the variability: between company, between worker and within worker. The parameters used for this computation are given in McNally, Warren et al. (2014).

Background to STOFFENMANAGER

Stoffenmanger is a web-based platform that was developed at the initiative of the Dutch Ministry of Social Affairs and Employment (Marquart, Heussen et al. 2008). STOFFENMANAGER follows the source-receptor conceptual approach described by Cherrie and Schneider (1999). The web-based platform offers two modules of assessment: the generic Stoffenmanger and Nano module (Van Duuren-Stuurman, Vink et al. 2012).

Mechanistic model of STOFFENMANAGER tool, and its determining factors (version 3.5), are described by Marquart, Heussen et al. (2008). A quantitative exposure algorithm together with required parameters of the model were published by Tielemans, Noy et al. (2008). Experimentally, a cross-validation and refinement were done by Schinkel, Fransman et al. (2010) and resulted in an updated version 4.5.

The dimensionless total exposure score B in STOFFENMANAGER is calculated according to Marquart, Heussen et al. (2008). Equation 4 presents STOFFENMANAGER algorithm with its exposure determinants.

$$B = [E \times H \times LC \times (D_{nf} + D_{ff} \times Sep) + (E \times a)] \times RPE \quad (4)$$

The final exposure is expressed as a product of several scores: fugacity (E), type of handling (H), level of applied localized control (LC), dispersion for near- and far-field (D_{nf} , D_{ff}), separation of worker from the source (Sep) and background sources of emission (a). It should be emphasized that RPE score is applied as multiplier after the score quantification.

Background to ECETOC TRA

The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) developed the first version of a Targeted Risk Assessment (TRA) in 2004. The current, third version of the assessment tool was released in 2012.

ECETOC developed the approach to assess the health and environmental risk from the supply and use of chemicals. The tool uses established exposure predictions from EASE, but modified by industrial experts in order to obtain a more precise, structured and simplified approach (ECHA 2012a).

The starting point for exposure estimation is defined the so-called “process category (PROC)” determinant, which describes the type of activity. For each of the PROCs, the exposure estimates are made using the modified EASE model (ECHA 2012a). PROC together with fugacity (fug), Sector of Use (SU) and presence of Local Exhaust Ventilation (LEV) defines the initial exposure estimation (E_{ini}). The initial exposure values can be found in (ECHA 2012b).

$$E_{ini} = f(PROC, SU, LEV, fug) \quad (5)$$

The estimated exposure (E , equation x) in ECETOC TRA is determined using initial exposure (E_{ini}) modified by dimensionless parameters: mole fraction of contaminant in the mixture (χ), general ventilation (GV), duration (t) and respiratory protective equipment (RPE).

$$E = E_{ini} \times \chi \times GV \times t \times RPE \quad (6)$$

Comparing work of EASE outputs with known values of exposure for a variety of current workplace activities showed over- and under-prediction of exposures in many cases. For this reason the values of EASE estimates were reviewed and modified within the ECETOC TRA tool (ECHA 2012a).

Background to EASE

The estimation and assessment of the substance exposure (EASE) model was developed by the Health and Safety Executive laboratory (HSE, UK), in conjunction with the Artificial Intelligence Institute (AIAI, UK) (Devillers, Domine et al. 1997). EASE is a general model that was under development since the early 1990s (Tickner, Friar et al. 2005).

The basis for development of EASE was the conceptual model described by Devine (1993). The model is based on three parameters: the tendency of a substance to become airborne, the way in which a substance is used and the means of control (Tickner, Friar et al. 2005). The exposure parameters used in EASE are incorporated into a decision-tree that constitutes model’s workflow. The workflow decision-tree is a guide which leads the assessor to final exposure output, an exposure range. The inhalation exposure ranges were constructed from occupational exposure measurements of the National Exposure Data Base in the UK (Devillers, Domine et al. 1997).

Background to MEASE

So far, there are no publications explaining the basic principles of the MEASE exposure model. The parameters are explained in the MEASE glossary, which is provided along with the tool on an MS Excel platform.

MEASE is designed to assess both inhalation and dermal exposure to metals and inorganic compounds. The inhalation part is based on the ECETOC TRA tool. Similarly to ECETOC TRA, MEASE uses the "PROC" determinant to describe the activity, although three experimental PROCS are available in MEASE: 26, 27a, 27b.

Like ECETOC TRA, the tool also calculates PROC initial value by using: fugacity (fug), process category (PROC), presence of Local Exhaust Ventilation (LEV) and Sector of Use (SU).

$$E_{ini} = f(PROC, SU, LEV, fug) \quad (7)$$

The determinants used to estimate fugacity are: dustiness for solids, volatility for liquids, and melting point for substances used in hot work processes. Solid particles dissolved in liquid are assimilated to aqueous solution within MEASE.

Once obtained, the “initial” exposure value is modified by several determinants: content of contaminant in preparation (χ), applied Risk Management Measures (RMM), duration of the task (t) and Respiratory Protective Equipment (RPE).

$$E = E_{ini} \times \chi \times RMM \times t \times RPE \quad (8)$$

The final exposure prediction, unlike TRA, is further modified by Molecular weight of the substance. This is the case only with liquids and gaseous physical states.

Background to EMKG-EXPO-TOOL

The EMKG-EXPO-TOOL (MS Excel tool) is part of “Easy-to-use workplace control scheme for hazardous substances” of the German Federal Institute for Occupational Safety and Health (BAuA 2008). The tool uses banding approaches based on COSHH Essentials (Control of Substances Hazardous to Health Regulations) (HSE 1999).

EMKG uses three determinants, namely: fugacity (dustiness of solids or volatility of liquids), scale (amount of substance used in the task) and control approach (used to reduce obtained exposure level). Combining the fugacity and the amount of substance, the tool gives the exposure potential, which is ranked according to four exposure bands.

Depending on the exposure potential band of the substance and the applied control strategy, the exposure assessment leads to six possible predicted exposure ranges.

Inter-model translations

Different models include different number and types of parameters for exposure calculation. ART, as Tier 2 model, defines the most determinants and their parameters. The approach in TREXMO uses already entered parameter data in one of the models to derive the corresponding parameters in the others. These derivations of parameters from another model are defined as parameter “translations”.

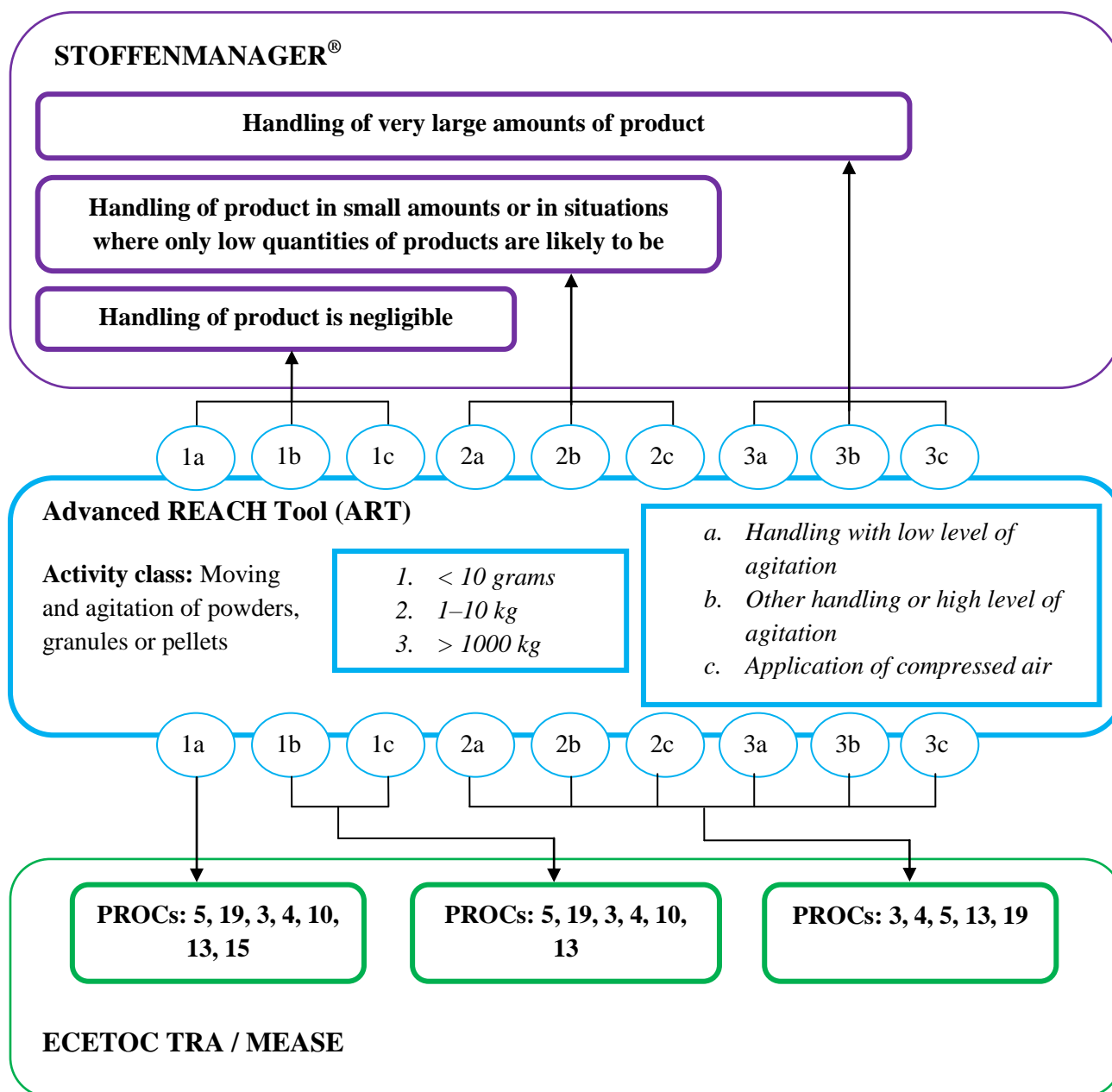
For every pair of the six models included, a single set of translation rules has been defined. The translation rules, however, include different amount of uncertainty. Two different translation types are differentiated:

1. **Recommended** and
2. **Uncertain**

After a *recommended* translation, given parameters can be used for exposure calculation with a small amount of uncertainty about its validity. A parameter given by an *uncertain* translation should be, however, taken into consideration, but with some uncertainty about its validity.

An example of translation is illustrated in the Figure 1. In this example, an activity class in ART is translated to STOFFENMANGER, ECETOC TRA and MEASE. As Figure 1 shows, activity class “moving and agitation of powders, granules or pellets” can be translated strictly to a single handling parameter in STOFFENMANGER. However, the definition of this activity class covers several “Process Categories – PROCs” in ECETOC TRA and MEASE. When more than one outcome is obtained, an additional choice is required from the user.

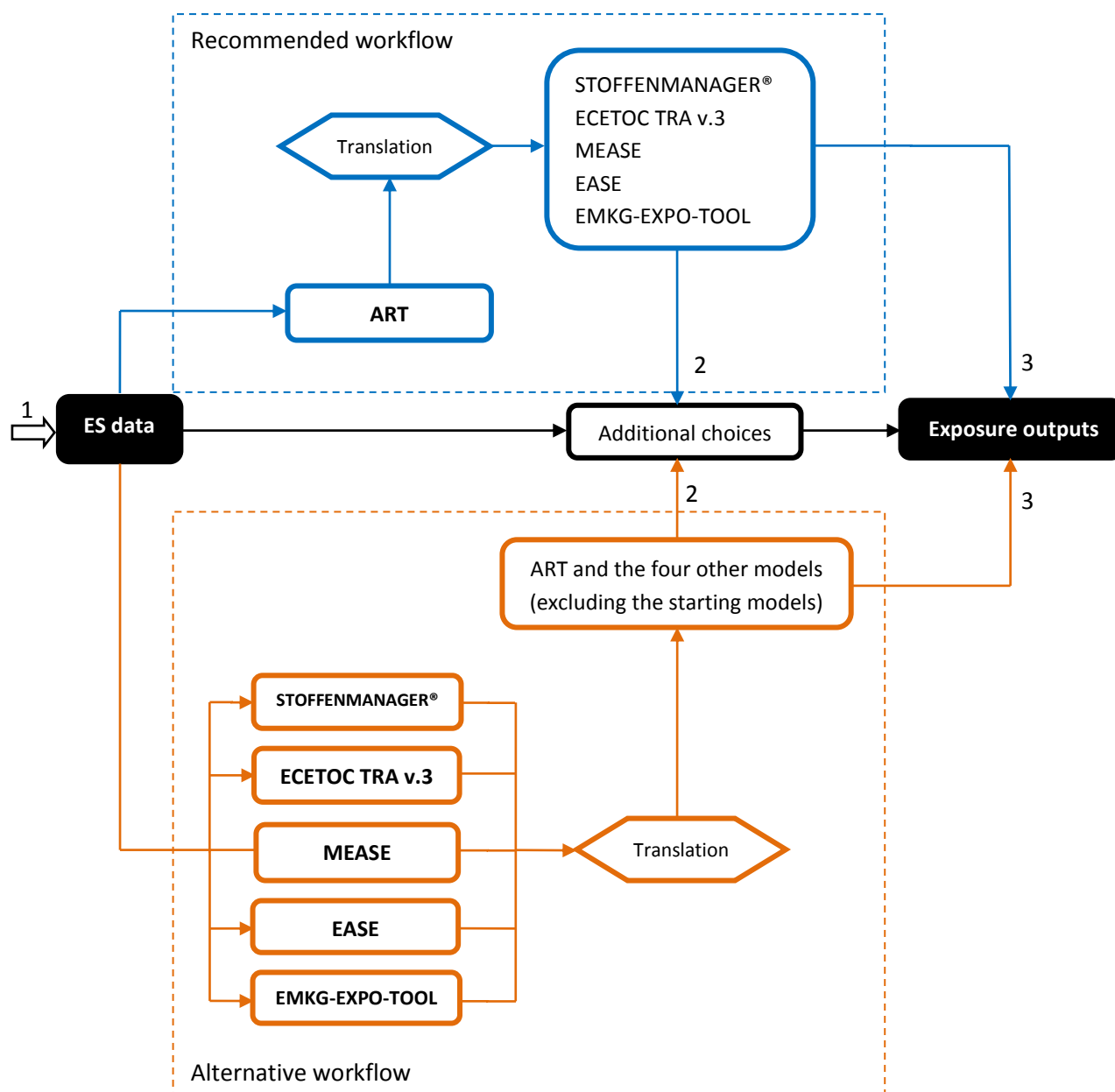
Figure 1. An example of possible translation routes from an activity class in ART (Moving and agitation of powders, granules or pellets) to STOFFENMANAGER, ECETOC TRA and MEASE.



User-interface interaction in TREXMO

The general structure of TREXMO is shown in figure 2. Six of the most common used exposure models, are included in TREXMO. In accordance with the published data, the six models were programmed in the tool.

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.



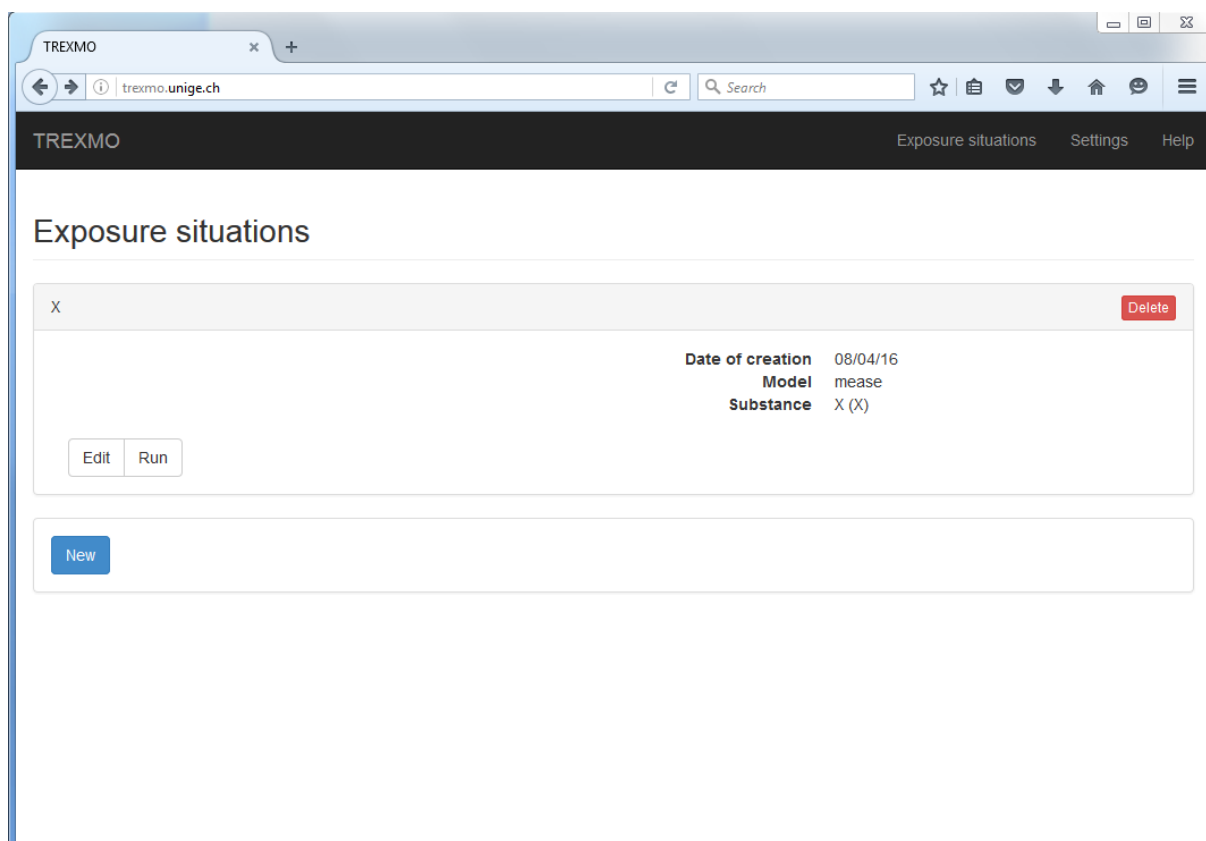
As shown in Figure 2, TREXMO interface includes two optional workflows: recommended and alternative. The recommended workflow suggests selection of ART as the **starting model**, while alternative uses one of the other five models included for the starting selection of relevant parameters. Once the parameters are entered and selected in one of the models, a translation of the parameters to

the others can be performed. The translation can lead to straightforward outcome – only one parameter recommended per determinant (field) – or to the additional parameter selection required.

Exposure assessment in TREXMO

Home page of the tool is shown in figure 3. As it can be seen, it contains a list of already established ESs and an option to generate a new ES.

Figure 3.Home page available at URL: <http://trexmo.unige.ch>



When the **New** button is applied, a new window opens (figure 4), where the general information are required from the users, namely:

1. Name of the ES,
2. Name of the substance,
3. CAS-number (not mandatory),
4. The starting model.

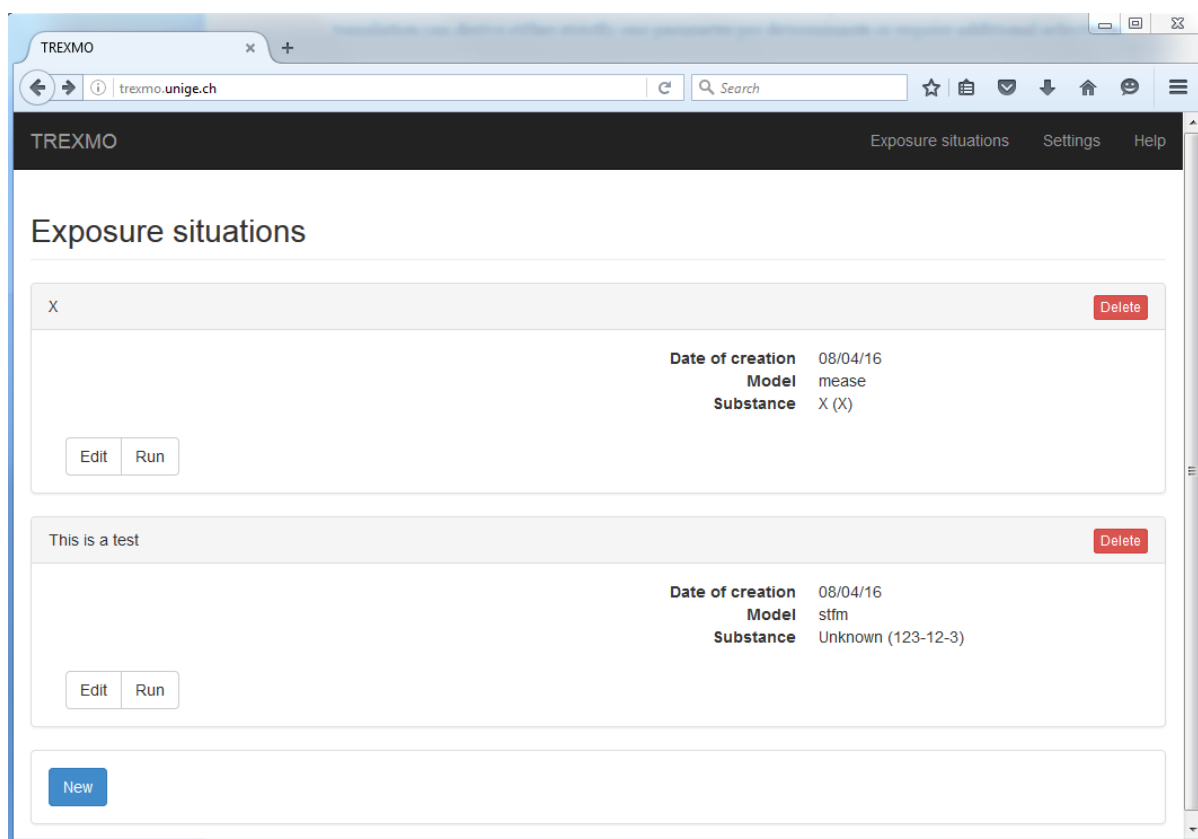
Figure 4.General information entry.

The screenshot shows a web browser window with the URL `trexmo.unige.ch`. The page title is 'TREXMO'. A modal dialog box titled 'Create new exposure situation' is open in the center. The dialog contains four input fields: 'Name' with the value 'This is a test', 'Substance' with the value 'Unknown', 'CAS' with the value '123-12-3', and 'Model' with a dropdown menu showing 'STOFFENMANAGER 5.1'. A blue 'Create' button is at the bottom right of the dialog. In the background, the 'Exposure situations' page is visible, showing a table with one entry: 'This is a test'. The table has columns for 'Date of creation' (08/04/16), 'Model' (stfm), and 'Substance' (Unknown (123-12-3)). There are 'Edit' and 'Run' buttons for each entry, and a 'Delete' button for each entry. A 'New' button is at the bottom left of the page.

Name	Substance	CAS	Model
This is a test	Unknown	123-12-3	STOFFENMANAGER 5.1

These inputs are mandatory (except CAS – number) to be able to proceed to the form containing list with all model's determinants. Once they are entered, the user has to apply the **Create** button. When the ES is created it appears in the home page (figure 5).

Figure 5.Home page of the TREXMO with new ES added



Exposure parameters are required in order to calculate exposure estimate. Before the calculation, the user must fulfill the list containing all required parameters. The selected model (Figure 4) dictates which set of exposure determinants appears in the forthcoming form.

Figure 6 shows the form used to set the parameters for STOFFENMANAGER. The user is required to go through the whole list of the STOFFENMANAGER determinants and to assign appropriate parameters for every determinant that is shown. At any time the user can **save** the scenario or **reset** to the previously saved version. The calculation is enabled only if the established situation was saved.

Figure 6.Interface containing a list with the determinants for the relevant model.

The screenshot shows the TREXMO web application interface. At the top, there is a browser window with the URL `trexmo.unige.ch/scenario/90e21b30fd6611e582045254006939c2`. The application header includes the TREXMO logo and navigation links for 'Exposure situations', 'Settings', and 'Help'. Below the header, the main content area displays 'This is a test (modified)' with buttons for 'Save', 'Save as ...', 'Reset', and 'Run'. The form is divided into two columns. The left column contains a 'Description' field with the placeholder text 'type a description of the scenario here'. The right column contains fields for 'Date of creation' (08/04/16), 'Model' (STOFFENMANAGER 5.1), 'Substance' (Unknown), and 'CAS' (123-12-3). Below these fields, there are tabs for 'Determinants' and 'Report'. The 'Determinants' tab is active, showing a section titled 'Determinants for STOFFENMANAGER 5.1'. This section contains several dropdown menus for configuring the scenario: 'Is the product a solid or a liquid?' (solid), 'Type of task:' (manual sanding of wood), 'Is the task being carried out in the breathing zone of an employee (distance head-product < 1 metre)?' (yes), 'Does your situation concern shaping by removing or cutting of material? If yes, what kind of dust is released?' (wood), 'Select available control measures:' (use of the product that limits the emission), 'Is the task followed by a period of evaporation, drying or curing?' (no), and 'Is there more than one employee carrying out the same task simultaneously?' (yes).

TREXMO

Exposure situations Settings Help

This is a test (modified) Save Save as ... Reset Run

Description

type a description of the scenario here

Date of creation

08/04/16

Model

STOFFENMANAGER 5.1

Modifying the model may require the translation of the determinants.

Substance

Unknown

CAS

123-12-3

Determinants Report

Determinants for STOFFENMANAGER 5.1

Is the product a solid or a liquid?

solid

Type of task:

manual sanding of wood

Is the task being carried out in the breathing zone of an employee (distance head-product < 1 metre)?

yes

Does your situation concern shaping by removing or cutting of material? If yes, what kind of dust is released?

wood

Select available control measures:

use of the product that limits the emission

Is the task followed by a period of evaporation, drying or curing?

no

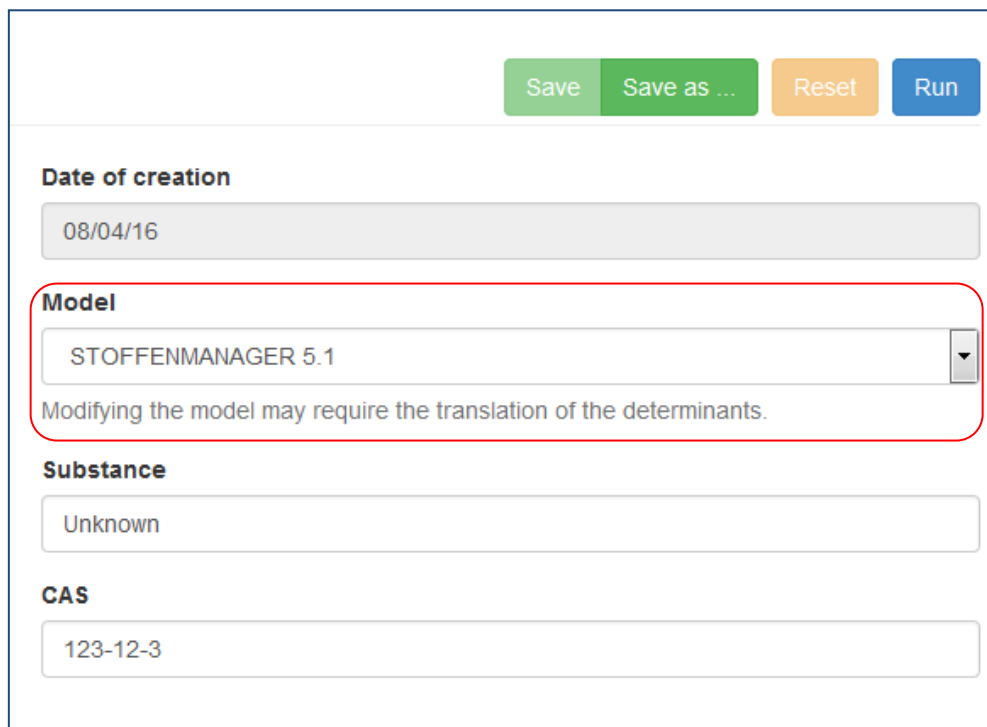
Is there more than one employee carrying out the same task simultaneously?

yes

Performing the translations in TREXMO

As it is shown in figure 7, translations to the other models are possible by changing the selected model in the **Model** field.

Figure 7.Applying the translation function in the tool.



The screenshot displays the TREXMO interface with the following elements:

- Buttons: Save, Save as ..., Reset, Run
- Date of creation: 08/04/16
- Model: STOFFENMANAGER 5.1 (highlighted with a red box)
- Substance: Unknown
- CAS: 123-12-3
- Message: Modifying the model may require the translation of the determinants.

Different types of translation, which can be obtained in the analogue exposure set, are clearly labeled (figure 8). In this way the user can differentiate between those translations which are strongly suggested, or *recommended*, from those which are not.

The user of TREXMO is not limited to the only pre-selected parameters after the translation. After performed translation, every determinant keeps an entire list of parameters with *recommended* and *experimental* parameters labeled. **In addition, the authors suggest the users to open every field after translation and check if there are two or more parameters recommended and make a decision before saving the ES. The users are also obliged to enter or select parameters where missing (no translation rule defined).**

The set of parameters obtained through a translation, describes the same ES in different model (as one established in the starting one). **In order to not lose the ES established in the starting model, after the translation, the users should differentiate three buttons in TREXMO interface: *Save*, *Save as* and *Reset*.** The *Save* button will paste the new set over the set of parameters established in the starting model. If the users want to keep both, the starting ES and the one obtained through the translation, the *Save as* button must be applied. The third, *Reset* button, or undo button, returns the ES established in the starting model if neither *Save* and *Save as* button were not applied. In other words, this function annuls the most recent translation performed.

Figure 8. List of the parameters obtained through a translation from STOFFENMANAGER to ECETOC TRA v.3

The screenshot displays the TREXMO web application interface. The browser address bar shows the URL: `trexmo.unige.ch/scenario/90e21b30fd6611e582045254006939c2`. The application header includes the TREXMO logo and navigation links for "Exposure situations", "Settings", and "Help".

The main content area is titled "This is a test (modified)" and includes action buttons: "Save", "Save as ...", "Reset", and "Run".

The form is organized into several sections:

- Description:** A text area with the placeholder "type a description of the scenario here".
- Date of creation:** A date field set to "08/04/16".
- Model:** A dropdown menu set to "ECETOC TRA 3". Below it, a note states: "Modifying the model may require the translation of the determinants."
- Substance:** A text field set to "Unknown".
- CAS:** A text field set to "123-12-3".

Below these fields are two tabs: "Determinants" (selected) and "Report".

The "Determinants" section contains several dropdown menus for configuration:

- Physical state:** (recommended) solid
- Process category (PROC):** (experimental) PROC 21
- Substance in preparation?:** (empty)
- Use of respiratory protection (if so, minimal efficiency?):** (recommended) no
- Dustiness of solids:** (recommended) high
- Type of settings:** (empty)
- Use of ventilation:** (recommended) indoors with good general ventilation
- Duration of activity:** (recommended) > 4 h

Limitations of TREXMO-web (version 1.5)

The current version, both standalone and online, include some limitations which should be eliminated in a next version. User-management system is one very important feature, especially for the online version, which must be added to the tool. This will make ESs established confidential and only seen by their creators. Unfortunately, the current version do not includes these restrictions and therefore the user's ESs can be seen and changed by other assessors or visitors to this web page. For the current version, we suggest the users to use TREXMO as a calculator of exposure – after the performed calculation the user should export the execution report and delete his ES.

After a translation performed, a determinant (field) may contain two or more translations, both *recommended* and *experimental*. If the user does not make a decision between these several recommended translations, an erroneous parameter might be selected. This can be avoided by labeling determinants which include: only one recommended, only one experimental and two or more translations. For the users would therefore be clear which determinants must be re-evaluated and which not.

In addition, neither TREXMO online nor the standalone version includes the calculation of confidence intervals for the ART. Some of these calculations will be provided already in the next version.

The authors of TREXMO would be grateful and appreciate very much any suggestion, comment or criticism for the current version. You can send your suggestions/comments/criticisms to:

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References

- BAuA (2008). "Bundesanstalt für Arbeitsschutz und Arbeitsmedizin." from <http://www.baua.de/emkg>.
- Cherrie, J. W. and T. Schneider (1999). "Validation of a New Method for Structured Subjective Assessment of Past Concentrations." Annals of Occupational Hygiene **43**(4): 235-245.
- Devillers, J., et al. (1997). "Occupational Exposure Modelling With EASE." SAR and QSAR in Environmental Research **6**(1-2): 121-134.
- Devine, J. (1993). "The estimation of occupational exposure to chemicals." Occupational and Consumer Assessments (OCDE/GD(93)128) OECD Paris Annex II - The Estimation of Occupational Exposure to Chemicals: 35-50.
- ECHA (2012). Guidance on information requirements and chemical safety assessment Chapter R.14: Occupational exposure estimation. **2.1**.
- ECHA (2012a). "Guidance on information requirements and chemical safety assessment." **Chapter R.14. Occupational exposure estimation**.
- ECHA (2012b). "Guidance on information requirements and chemical safety assessment." **Chapter R.12: Use of descriptor system**.
- Europa (2013). "REACH - Registration, Evaluation, Authorisation and Restriction of Chemicals." Retrieved September 17, 2014, from http://ec.europa.eu/enterprise/sectors/chemicals/reach/index_en.htm.
- Fransman, W., et al. (2011). "Advanced Reach Tool (ART): Development of the Mechanistic Model." Annals of Occupational Hygiene **55**(9): 957-979.
- HSE (1999). "COSHH Essentials, Health and Safety Executive."
- Keil, C. B. (2000). "A Tiered Approach to Deterministic Models for Indoor Air Exposures." Applied Occupational and Environmental Hygiene **15**(1): 145-151.
- Marquart, H., et al. (2008). "'STOFFENMANAGER', a Web-Based Control Banding Tool Using an Exposure Process Model." Annals of Occupational Hygiene **52**(6): 429-441.
- McNally, K., et al. (2014). "Advanced REACH Tool: A Bayesian Model for Occupational Exposure Assessment." Annals of Occupational Hygiene **58**(5): 551-565.
- Money, C. D. (2003). "European Experiences in the Development of Approaches for the Successful Control of Workplace Health Risks." Annals of Occupational Hygiene **47**(7): 533-540.
- Schinkel, J., et al. (2010). "Cross-validation and refinement of the STOFFENMANAGER as a first tier exposure assessment tool for REACH." Occup Environ Med **67**(2): 125-132.
- Schinkel, J., et al. (2011). "Advanced REACH Tool (ART): calibration of the mechanistic model." J Environ Monit **13**(5): 1374-1382.
- Tickner, J., et al. (2005). "The Development of the EASE Model." Annals of Occupational Hygiene **49**(2): 103-110.
- Tielemans, E., et al. (2008). "STOFFENMANAGER Exposure Model: Development of a Quantitative Algorithm." Annals of Occupational Hygiene **52**(6): 443-454.

Tielemans, E., et al. (2007). "Tools for regulatory assessment of occupational exposure: development and challenges." J Expos Sci Environ Epidemiol **17**(S1): S72-S80.

Van Duuren-Stuurman, B., et al. (2012). "STOFFENMANAGER Nano Version 1.0: A Web-Based Tool for Risk Prioritization of Airborne Manufactured Nano Objects." Annals of Occupational Hygiene **56**(5): 525-541.