Evaluation of Tier 1 Exposure Assessment Models under REACH (eteam) Project

Substudy Report on Uncertainty of Tier 1 Models

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Abstract

In this work package of the eteam project different aspects of the tools were evaluated which may lead to an uncertainty of the model estimate, i.e. a deviation of the estimate from the actual exposure value at a workplace. For this purpose a qualitative approach as suggested by the WHO and the corresponding REACH guidance document about uncertainty assessments was used.

In order to assess the overall uncertainty, a matrix was developed for each model, which includes a list of all possible sources of uncertainty and a categorisation of different aspects (e.g. transparency and uncertainty of the knowledge base).
The different aspects were then discussed and compared.

As a result it was shown that for each tool a number of possible sources of uncertainties exists, however, it has to be taken into account that it always depends on the model and the situation itself which sources of uncertainty are dominant and how uncertain the final exposure estimate may be.

In combination with the results of the between user reliability evaluation (BURE) it can be summarised that a clear scenario description including unambiguous parameter definitions is essential for a successfull exposure assessment, since wrong input parameters can easily cause deviations of the result up to three orders of magnitude. Furthermore, indications could be drawn from BURE, which input parameters may have major influence on the overall uncertainty, e.g. dustiness, RMMs and the type of setting, and thus, should probably be improved concerning vagueness and level of detail.
A lower between user variability can be supported by decreasing the vagueness of model input parameters and implemented tool guidance but also has to be accompanied by further measures, e.g. information about the exposure situations, model user trainings.
As a consequence, the results of the model uncertainty described in this work package should not be interpreted isolated but only in combination with the other work packages of the eteam project and within the regulatory context.

Key words:

exposure assessment; exposure modelling; validation; REACH; risk assessment;

Teilbericht zu Unsicherheiten bei Tier 1-Modellen

Kurzreferat

In diesem Arbeitspaket des eteam-Projektes werden Aspekte der Tools beleuchtet, die zu einer Unsicherheit der Expositionsabschätzung führen können, d. h. einer Abweichung des modellierten Ergebnisses von der realen Exposition am Arbeitsplatz. Für die Analyse kam ein qualitativer Evaluierungsansatz zur Anwendung, der von der WHO und in der entsprechenden REACH-Leitlinie für Unsicherheitsanalyse vorgeschlagen wird.

Um die Gesamtunsicherheit zu analysieren, wurde für jedes Modell eine Matrix entwickelt. Diese enthält eine Liste aller möglichen Unsicherheitsquellen sowie verschiedene Aspekte (z. B. Transparenz, Unsicherheit der Wissensbasis) klassifiziert aufführt.
Anschließend werden die Aspekte diskutiert und verglichen. Das Ergebnis zeigt, dass für jedes Tool verschiedene Quellen der Unsicherheit existieren., welche Quellen zur Geltung kommen und wie unsicher das endgültige Modellergebnis sein kann, hängt immer entscheidend vom Modell und der Expositionssituation ab.

In Kombination mit den Resultaten der BURE („Between user reliability“) ist zusammenfassend festzustellen, dass eine klare Beschreibung eines Szenarios einschließlich eindeutiger Parameterdefinitionen essenziell für eine erfolgreiche Expositionsabschätzung ist. Die Eingabe falscher Parameter kann leicht zu Abweichungen von drei Größenordnungen führen. BURE ließ ferner den Schluss zu, dass z. B. die Staubigkeit, Risikominimierungsmaßnahmen und das generelle Setting (professionell (Handwerker) vs. industriell) großen Einfluss auf die Gesamtunsicherheit haben und daher in Bezug auf Vagheit und Detaillevel verbessert werden sollten.
Eine geringere Variabilität (bei verschiedenen Nutzern) lässt sich fördern, indem die Vagheit der Eingabeparameter verringert wird und implementierte Hilfsfunktionen im Tool Verwendung finden. Andere Maßnahmen wie z.B. Informationen über die Arbeitsplatzsituationen und Anwendertraining für Modellbenutzer müssen aber begleitend hinzukommen.

Letztendlich sind die Ergebnisse der Unsicherheitsanalyse daher nicht isoliert zu interpretieren, sondern im Zusammenspiel mit anderen Arbeitspaketen des Projektes und dem regulatorischen Kontext zu betrachten.

Schlagwörter:

Expositionsabschätzung, Expositionsberechnung, Validierung, REACH, Risikobewertung

1 Introduction: Basis of uncertainty assessment

In this report we will qualitatively analyse and describe the uncertainty of the evaluated tier 1 models (ECETOC TRA v.2 and v.3, MEASE version 1.02.01, the EMKG-EXPO-TOOL, STOFFENMANAGER® version 4.5, RISKOFDERM version 2.1), through identification and evaluation of the factors that influence the uncertainty of the modelled exposure estimates. We are aware that all evaluated models are tier 1 models, thus, a comparatively high level of uncertainty due to the conservative nature of exposure estimation can be expected. This fact will of course be reflected in our conclusion.
Some general definitions and suggestions for categorisation of the level of uncertainty and vagueness are presented below, with the main elements of the uncertainty analysis visualised in Figure 1.1.

1.1 General definitions

In the context of uncertainty assessment, for clarity it is helpful to differentiate between variability, uncertainty and vagueness:

Uncertainty:

Lack of or imperfect knowledge concerning the present or future state of an organism, system, or (sub)population under consideration, which may affect its accuracy or relevance. Uncertainty can be reduced, at least in principle, by improving the quality and/or amount of information (WHO, 2008).
In case of WPII.1 the word "uncertainty" refers both to the uncertainty of the final exposure estimate of a model (i.e. the possibility that the result does not represent the true exposure present at the assessed workplace) and also to the uncertainty of model parameters, the underlying equations etc. (see below and Figure 1.1). These in turn represent sources of the uncertainty of the overall exposure estimate.
In this project we will evaluate the uncertainty of the model result, i.e. it will be discussed in which way the separate parameters and other sources of uncertainty will influence the exposure estimate and how their influences will be combined in the final exposure estimate.
Examples for sources of uncertainty related to tier 1 models and a categorisation of these sources into three groups are given later in this text (see also Figure 1.1).

Variability:

Heterogeneity of values over time, space or different members of a population, including stochastic variability[1] and controllable variability[2]. Variability is a true or an

[1] Stochastic variability: "Sources of heterogeneity of values associated with members of a population that are a fundamental property of a natural system and that as a practical matter cannot be modified, stratified or reduced by any intervention: for example, variation in human susceptibility to illness for a given dose for which there is no predictive capability to distinguish the response of a specific individual from that of another" (WHO 2008).
[2] Controllable variability: "Sources of heterogeneity of values of time, space or different members of a population that can be modified in principle, at least in part, by intervention, such as a control strategy.

inherent property of the system or population being evaluated and cannot be reduced by collection of additional information (WHO, 2008).
Variability can also influence the uncertainty of an exposure estimate. If a deterministic model is fitted to a set of measured exposure values, the result will not reflect all possible workplaces within one scenario equally well, as even within this one scenario (e.g. mixing operations, LEV present, professional type of setting) there is still a specific range of possible exposure values reflecting differences that are not captured by respective model parameters.
Thus, the result of an exposure estimation for a specific workplace will have a component of uncertainty that is caused by the variability of the underlying measurements on which it is based.

Vagueness:

Something that is (due to a lack of sharp boundaries) not clearly defined, grasped or understood. A term is vague to the extent that it has borderline cases.[3]

In case of an exposure assessment, vagueness can appear at different points:

- a vague description of the exposure situation;
- a vague, i.e. qualitative and/or subjective definition of input parameters. An example is dustiness, which is often defined by comparison with other substances ("like flour", "like sugar" etc.) in contrast to the vapour pressure, which is mostly defined in a clear quantitative way; and
- vagueness can also occur in the description of the tool development process which can hinder delineation of the scope of application or prevent reproduction of the origin of the model algorithm and implemented default values.

Vagueness during scenario documentation and vagueness of the definition of input parameters both lead to an increased uncertainty of the model estimate as they may prevent correct use of the tool.
A high level of vagueness relating to the model background also represents a source of uncertainty for the exposure estimate (e.g. if the boundaries (i.e. the scope) of the model are defined in an insufficient way due to vagueness in the documentation or missing information, this may lead to usage beyond the scope). It may also prevent an estimation of the influence of a specific source of uncertainty due to a lack of information.

1.2 Sources of uncertainty

According to available literature the sources of uncertainty influencing an exposure assessment can be divided into three groups representing the various steps of an estimation (ECHA, 2008a; WHO, 2008): Sources of uncertainty related to the scenario, sources related to the parameters and sources related to the model.

For example, variability in emissions of a chemical to the atmosphere could be modified via a control strategy" (WHO 2008)
[3]http://plato.stanford.edu/entries/vagueness/

In WPII.1 we will analyse the model uncertainty and – if appropriate - the parameter uncertainty, i.e. the origin of default values implemented into the models and the model inherent definition of input parameters, in a qualitative way. Scenario uncertainty and the uncertainty of specific input values (e.g. uncertainty of the measured vapour pressure, information gaps) will not be evaluated, as in most cases there will not be enough information available to do so and moreover the uncertainty of the exposure situations used for the validation process is not a part of the uncertainty of the models but will be addressed in WPI.4.
How the various sources of uncertainty affect the exposure estimate of a model depends on the specific exposure situation and the model that is used to describe this situation.

Sources of uncertainty related to the scenario (out of scope of WPII.1):

Uncertainty in specifying the exposure scenario that is consistent with the scope and purpose of the assessment. Examples of this type of uncertainty are exposure pathways and routes (e.g. dermal exposure via body contamination or a certain type of food for oral exposure) that have not been taken into account due to a lack of knowledge about their importance, or risk management measures that have not been reported.

Sources of uncertainty related to parameters:

Uncertainty involved in the specification of numerical values (be they point values or distributions of values) for the factors that determine the exposure, for example the data type (expert judgment, measured data, surrogate data etc.) or statistical or sampling errors within a set of measured data.

This type of uncertainty relates to both the input parameters of a model (e.g. vapour pressure, dustiness) and model inherent values, i.e. how the model actually reflects the user input within its algorithm (e.g. the initial exposure estimates that are assigned to a certain combination of input parameters like volatility, type of setting and PROC number; RMM efficiencies).

Sources of uncertainty related to the model:

Uncertainty caused by gaps in scientific knowledge that hamper an adequate capture of the correct causal relationships between exposure factors.

Examples for this type of uncertainty are underlying assumptions (e.g. applicability of ideal gas law; independency of efficiencies for different, simultaneously used RMMs), usage beyond the scope (e.g. use in large industries if only small and medium enterprises (SMEs) have been used for calibration), dependencies within the algorithm (e.g. duration modifiers for dermal exposure only being applicable for certain fugacity classes) or missing determinants (e.g. droplet spectrum in case of spray applications or concentration modifiers).

The boundaries between these three types of uncertainty are not always clearly defined, however this approach provides a useful method of categorising sources of uncertainty, and so develop a clear overview of the uncertainty assessment process.

1.3 Categorisation of vagueness and uncertainty

The evaluation of model uncertainty will include the following aspects:

A list of possible sources of uncertainty, i.e. elements which will influence the uncertainty of the exposure estimate

This includes a list of all model parameters (user input and/or implemented values) and/or assumptions as well as a collection of missing determinants.
As far as possible missing determinants will be identified based on the conceptual evaluation (WPI.1), the results of the external validation (deliverables D15 and D16; draft and final report on external validation) and a relative comparison between the different models.
Depending on the type of uncertainty source additional categorisations and analyses as explained in the following paragraphs will be performed

For **model inherent values, missing determinants and/or assumptions** the transparency and the uncertainty of the knowledge base from which the model was developed will be evaluated:

An evaluation of the transparency (vagueness and completeness of documentation):

This point has already been addressed in WPI.1, which will form the basis for categorising the potential sources of uncertainty into one of three groups:

- high transparency: sufficient, clearly defined information about the derivation of the specific parameter/assumption is available; no contradictions in available information.
- medium transparency: information is available but there are gaps, things that are unclear, doubts about the reliability of the information and/or contradictions.
- low transparency: no information is available.

An evaluation of the **uncertainty of the knowledge base** of the model:
The following questions will be addressed:

- Are the parameters based on measured values and is their derivation documented?
- Is the influence of the parameters proven by measurements or observations?
- How is the measured influence of the parameters incorporated in the algorithm?

The following categories for the uncertainty of the knowledge base will be applied:

- high certainty, i.e. low level of uncertainty.: a sufficient and reliable set of experimental experience is available that supports the value of a parameter and/or an assumption
- medium level of (un)certainty: information of limited quality is available (e.g. small sample size, known bias in the sampling method)
- low certainty, i.e. high level of uncertainty: pure “expert judgement”, no experimental background available, based on a hypothesis

This categorisation is n.a. to input parameters, as we will not analyse the experimental and/or scientific background in these cases (e.g. the appropriateness of sampling methods in case of vapour pressure). Furthermore, depending on the specific level of transparency this categorisation may also not be applicable to some of the different sources of uncertainty due to a lack of information, i.e. if the basis of a modifier or initial exposure estimate is not documented it cannot be judged if the value relies on expert judgement or measured values or if the quality of the measured samples is sufficient. On the other hand a value for which it is clearly documented that it was derived by expert judgement will have a high transparency (i.e. a low level of vagueness related to the model development) but a high level of uncertainty in terms of the knowledge base.
In order to increase the readability of the evaluation matrices by using homogeneous categories (i.e. “high” is always the “best” category) this aspect has been categorised as “certainty” and not as “uncertainty”.
This categorisation only applies to datasets that have been used during model development. The influence and/or level of relevance of validation studies is cannot be evaluated with the available information (see also Chapters 2.2.1 and 2.2.2).

For **model inherent values and defaults** a categorisation of the origin of uncertainty will be done:

- Will the uncertainty in the exposure estimate be caused by variability and/or uncertainty of the parameter/assumption?

For each **input parameter** we will evaluate the quality of the parameter definition and its potential to lead to a wrong assignment of the parameter categories:

We propose the following categories:

- high quality: the parameter is defined in a quantitative way (low vagueness) or it is defined in a qualitative way but described with a high level of detail (e.g. control guidance sheets, vapour pressure).
- medium quality: the parameter is defined in a quantitative way with some missing information (e.g. missing definition of units; medium vagueness) or it is defined qualitatively with a medium level of detail (e.g. PROC codes)
- low quality: the parameter is defined qualitatively (high vagueness, e.g. comparative dustiness categories) or with a low level of detail.

For **each source of uncertainty** an evaluation of the magnitude and direction of uncertainty:
Will the source of uncertainty lead to over- or underestimations of exposure and how large will this deviation probably be? In principle this will be done for each source of uncertainty, however, depending on the level of transparency this part of the evaluation may not be possible for all parameters/assumptions. We propose the following categories for the magnitude of uncertainty with corresponding abbreviations given in brackets:

- low magnitude: deviations of the exposure estimate up to a factor of 10 can be expected (“+/-“)
- medium magnitude: the source of uncertainty may cause a deviations of more than a factor of 10 and up to a factor of 100 (“++/--“)
- high magnitude: the expected deviation exceeds a factor of 100 (“+++/---“)

An evaluation of the expected magnitude of uncertainty, which would represent, in a more sophisticated form, a quantitative uncertainty analysis, may also give important information about the influence of scenario uncertainty and/or the quality of the input parameters (→ sensitivity): If an input parameter has a low quality, e.g. because of a high vagueness, or if its true value is not known, but it does not influence the exposure estimate within the model, it will not cause deviations of the exposure estimate (magnitude of uncertainty: “0”). An example is the definition of the dustiness categories in case of ECETOC TRA v.2, which does influence the inhalation exposure but not the dermal exposure and thus, only represents a potential source of uncertainty for the inhalation exposure estimate.
A general overview of the different aspects influencing uncertainty is given in Figure 1.1, whereas every aspect is marked by a light blue box and small explaining remarks are given in grey areas. The figure aims to visualise the different steps of an exposure assessment, starting with the exposure situation, passing through different steps of the modelling process (medium blue area: input of parameters by user, translation of input into model inherent parameter (e.g. efficiency), implementation into model algorithm) and arriving at the uncertainty of the exposure estimate.
Aspects which are within the scope of this work package are marked by a light red area. The remaining aspects are assigned to scenario uncertainty and therefore not relevant for model uncertainty (transparency and knowledge base of scenario documentation, e.g. sampling errors during vapour pressure determination, errors/gaps in the documentation of a situation).
Some aspects can be part of scenario- as well as model uncertainty. This applies to the general terms uncertainty and variability (i.e. fluctuation within a population, always present if a set of situations/measurements may have been summarised) as well as to vagueness (unclear definition in model or scenario documentation) and knowledge base and transparency (documentation and scientific basis of model vs. documentation and basis of scenario including measured values).
The model user represents a borderline case between scenario and model uncertainty which may be connected to the scenario uncertainty but will also be influenced by characteristics of the model, e.g. the definition of the input parameters.

For this reason we will also refer to the **operational analysis:**
Analysis of the variability related to the usage of the different tools will be addressed in WPI.6 and we will refer to the corresponding reports (deliverables D21 and D22, draft and final report on workshop outcomes).
The variability concerning the tool usage is a reflection of the quality of the documentation of the exposure situation (which is a source of uncertainty related to the scenario), the general transparency of tool usage including the vagueness of input parameters, and to a certain extent the expertise of the tool user.
It is often not possible to separate out the extent of these influences within this project, however we will give a general overview of aspects and/or parts of the models where variations are most likely to occur and where therefore improvements either on the scenario description and/or the model side may be advisable.

1.4 Report Outline

All aspects mentioned above will be described and discussed in a narrative way and an evaluation matrix for each of the models will be developed (Appendix A and short versions in Chapter 2).

For each tool some general considerations about the uncertainty will be described. This includes categorisations of transparency, uncertainty of the knowledge base and the quality of parameter definition (including vagueness and level of detail) as far as possible. Concerning the direction and magnitude of uncertainty it will be discussed which would be the maximum impact of the uncertainty source on the exposure estimate.

This general section will be amended by a set of example situations chosen from the exposure situations used for the external validation of the tier 1 tools (WP I.4) which gives an impression of commonly used processes, conditions and protective measures.

The discussion of separate models as well as the example situations is described in detail in Appendix A.

In the overall discussion and summary (see Chapter 2) we will summarise and compare the uncertainty and its sources of the different models on the basis of the previously developed evaluation matrices. Possible dependencies, correlations between sources of uncertainty and their influence on the final exposure estimate will be discussed here in a qualitative way.

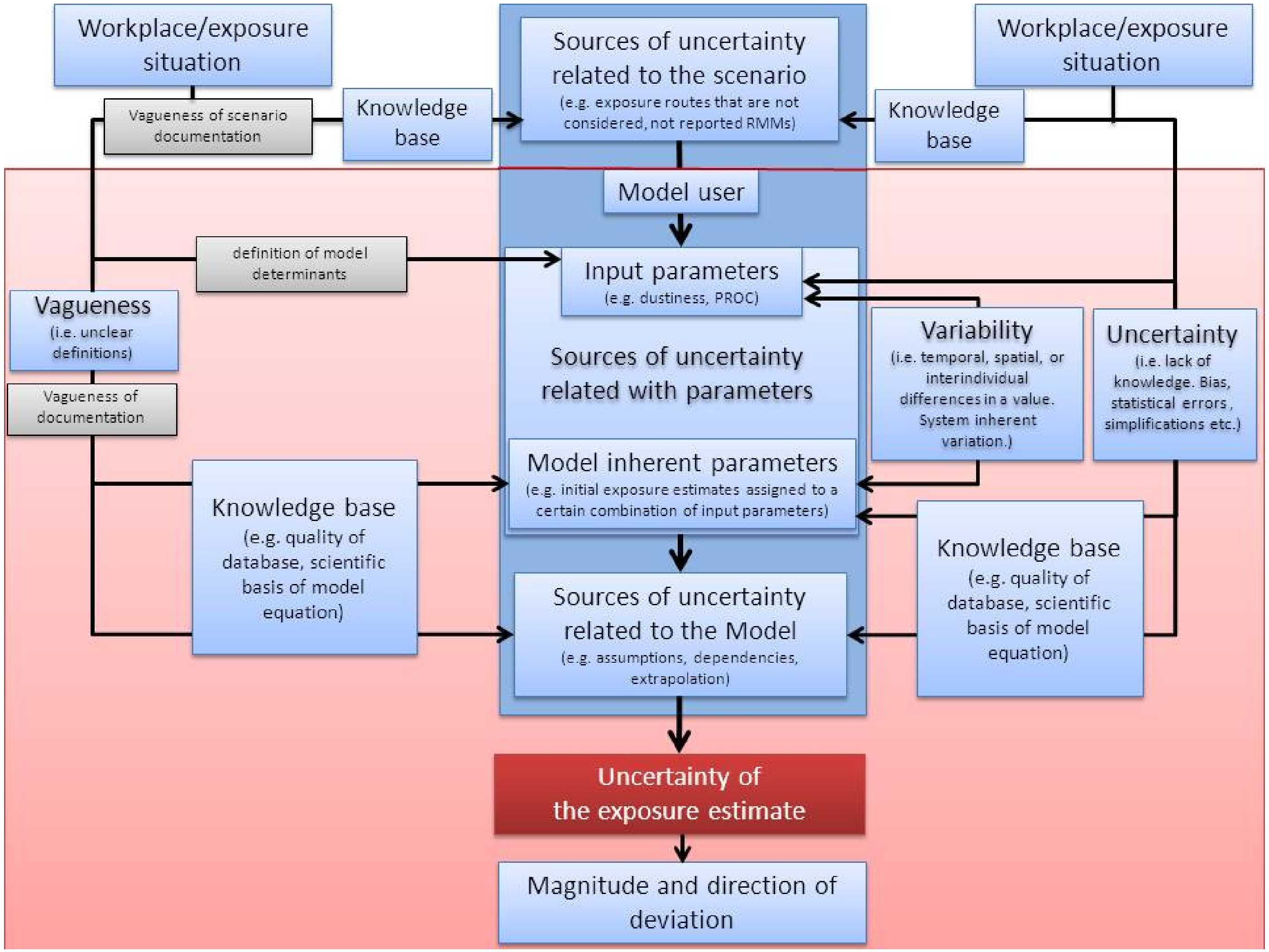

Figure 1.1 Aspects of uncertainty. Concepts outside of the light red area lie beyond the scope of WPII.1.

2 Discussion

In this section the models evaluated in this project will be compared concerning the uncertainty of the exposure estimate due to uncertainties of the general model knowledge base as well as the influence of common and/or missing parameters and aspects. Some background information found in literature about the different sources of uncertainty will be summarised to facilitate the discussion.

2.1 Evaluation matrices (short versions)[4]

In this chapter short versions of the evaluation matrices detailed in Appendix 1 will be given, including all identified potential sources of uncertainty (input parameters, model inherent parameters, assumptions etc.) and the corresponding maximum magnitude and direction of uncertainty.
A comparison and general discussion of the various sources of uncertainty will be given in Chapters 2.2, 2.3 and 2.4.

[4] For details on categorisation approach see Chapter 0.

2.1.1 ECETOC TRA

Table 2.1 Evaluation matrix: ECETOC TRA v.2

Source of uncertainty	**Type of uncertainty source**	**Variability/ uncertainty**	**transparency of documentation**	**Certainty of knowledge base**	**Quality of parameter definition (vagueness/ level of detail)**	**Direction and magnitude of the caused uncertainty**	
Input parameters							
physical state (volatile/solid)	Input parameter/intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high	Inhalation	n. a. p.
						Dermal	0
dustiness (high/medium/low)	Input parameter/intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	medium	Inhalation	**++/--**
						Dermal	**0**
vapour pressure (high/medium/ low/very low)	Input parameter/intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high	Inhalation	++/--
						Dermal	0
Process temperature for PROCs 21-25 (Tproc<Tmelt; Tproc≈Tmelt; Tproc>Tmelt)	Input parameter/process description + operational conditions	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	medium	Inhalation	+/-
						Dermal	0
PROC number (PROC 1-25)	Input parameter/process description + operational conditions	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	medium	Inhalation and dermal	+++/---
type of setting (industrial/ professional)	Input parameter/process description + operational conditions	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	low	Inhalation	+/-
						Dermal	0
Molecular weight (only for unit conversion in case of liquids)	*Input parameter/intrinsic substance property*	*not relevant for model uncertainty*	*not relevant for model uncertainty*	*not relevant for model uncertainty*	*high*	*Inhalation*	*n.a.p.*
						Dermal	*0*
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction)	Input parameter and model inherent reflection/use description and operational condition	n. a. p.	medium:	n.a.p.	medium/high	Inhalation/liquids	+++/-

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/ level of detail)	Direction and magnitude of the caused uncertainty	
						Inhalation/solids	0
						Dermal	0
duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% exposure reduction), maximum 8h	Input parameter and model inherent reflection/Use description and operational condition	n. a. p.	medium	n.a.p.	high	Inhalation	+++/-
						Dermal	0
LEV for inhalation exposure, PROCs 1-20 (present or not)/ efficiency defined by physical state, process description, type of setting	Input parameter and model inherent reflection/localised controls	n. a. p.	low	n.a.p.	medium	Inhalation	n.a.p.
LEV for dermal exposure, PROCs 1-20 (present or not) / efficiency defined by process description	Input parameter and model inherent reflection/localised controls	n. a. p.	low	n.a.p.	medium	Dermal	n.a.p.
Outdoors (30% efficiency)	Input parameter and model inherent reflection/localised controls	n. a. p.	low	n.a.p.	medium/high	Inhalation	n.a.p.
							0
LEV for inhalation, PROCs 21-25 (present or not)/efficiency defined by physical state, process description, type of setting	Input parameter and model inherent reflection/localised controls	n. a. p.	low	n.a.p.	medium	Inhalation	n.a.p.
LEV for dermal, PROCs 21-25 (present or not)/efficiency defined by process description	Input parameter and model inherent reflection/localised controls	n. a. p.	low	n.a.p.,	medium	Dermal	n.a.p.
Respiratory protection equipment (90%, 95% efficiency according to APFs 10 and 20)	Input parameter (and model inherent reflection)/personal protective equipment	n. a. p.	high	n.a.	high	Inhalation	+/-
						Dermal	0
Model inherent parameters							
Breathing rate (10 m^3 per 8h shift) (only used for overall exposure per kg and day)	Model inherent parameter/ process description + operational condition	n. a. p.	low	n.a.p.	n.a.	Inhalation	++/--
							0

Source of uncertainty	**Type of uncertainty source**	**Variability/ uncertainty**	**transparency of documentation**	**Certainty of knowledge base**	**Quality of parameter definition (vagueness/ level of detail)**	**Direction and magnitude of the caused uncertainty**	
70 kg body weight worker	Model inherent parameter/ process description + operational condition	n. a. p.	low	n.a.p.	n.a.	Inhalation	+/-
Initial exposure estimate (PROC1-20 for inhalation and dermal exposure)/defined by fugacity, physical state, process description, type of setting for inhalation; defined by PROC for dermal)	Model inherent parameter/ process description + operational condition	n. a. p.	medium	n.a.p.	n.a.	Inhalation	n.a.p.
Initial exposure estimate (PROC21-25 for dermal and inhalation exposure): defined by fugacity, physical state, process description, type of setting for inhalation; defined by PROC for dermal	Model inherent parameter/ process description + operational condition	n. a. p.	medium	medium	n.a.	Dermal	n.a.p.
Skin areas, Exposed body parts (defined by PROC; palm(s), fingers, hand(s), hands and forearm(s))	Model inherent parameter/ process description + operational condition	n. a. p.	medium	n.a.p.	n.a.	Dermal	+++/--
						Inhalation	0
Presentation of results	Model inherent parameter/ Model assumption	variability / uncertainty	low	n.a.p.	medium/low	Inhalation and dermal	n.a.p.
Model equation, assumptions							
Ideal gas law and approximately 298 K (i.e. molar volume of 24 l/mole) assumed for conversion of units in case of liquids	Model/assumption	uncertainty.	high	n.a.p.	n.a.	Inhalation	n.a.p.
						Dermal	0
GOHP	Model/assumption	uncertainty	Medium	n.a.p.	n.a.	Inhalation and dermal	n.a.p.

Table 2.2 Evaluation matrix: ECETOC TRA v.3

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty	
Input parameters							
Process temperature for PROCs 1-20 (not explicitly implemented, however vapour pressure at process temperature can be entered)	Input parameter/process description + operational conditions	not relevant for model uncertainty	see transparency of the initial exposure estimates	n.a.	high	Inhalation	n.a.p.
						dermal	0
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction) for dermal exposure and solids in general.	Input parameter and model inherent reflection/Use description and operational condition	n.a.p.	medium	n.a.p.	medium/high	dermal and inhalation (solids)	+++/-
duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% efficiency), maximum 8h; for dermal exposure	Input parameter and model inherent reflection/Use description and operational condition	n.a.p.	medium	n.a.p.	high	dermal	+++/-
short term duration for inhalation (peak exposure for duration <15min = 4 x 8h average)	Input parameter and model inherent reflection/Use description and operational condition	both possible	high	medium:	medium	inhalation	n.a.p.
						dermal	0
LEV for inhalation, PROCs 1-20 (present or not)/defined by physical state, process description, type of setting	Input parameter and model inherent reflection/localised controls	both possible	low	n.a.p.	medium	inhalation	n.a.p.
LEV for dermal, PROCs 1-20 (present or not)/defined by process description	Input parameter and model inherent reflection/localised controls	both possible	low	n.a.p.	medium	dermal	n.a.p.
General ventilation (good general vent. 30%, enhanced 70%, good or enhanced + LEV)	Input parameter and model inherent reflection/localised controls	both possible	medium	Medium	high	inhalation	n.a.p.
						dermal	0
Gloves (95, 90, 85, 80 % efficiency, corresponding to different levels of personal behaviour/level of supervision)	Input parameter and model inherent reflection/personal protective equipment	both possible	Low	n.a.p.	low	dermal	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty	
						inhalation	0
Model inherent parameters							
Initial exposure estimates (all PROCs, dermal and inhalation)	Model inherent parameter/ process description + operational condition	both possible	see ECETOC v.2	see ECETOC v.2	n.a.	dermal and inhalation	n.a.p.
Presentation of results	Model inherent parameter/ Model assumption	variability/ uncertainty	medium/high	n.a.p.	medium/high	Inhalation and dermal:	n.a.p.
Model							
Connection/dependency between dustiness/volatility and the implementation of duration in combination with dermal exposure:	Model/assumption	both possible	Low	n.a.p.	n.a.	dermal	+/-
						inhalation	0

2.1.2 MEASE v. 1.02.0

Table 2.3 Evaluation matrix: MEASE v. 1.01.0

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency of documentation	Certainty of knowledge base	Parameter quality (vagueness and level of detail)	Direction and magnitude of the caused uncertainty	
Input parameters and model inherent parameters							
physical form (liquid/solid/aqueous solution/ gas)	Input parameter/ intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high	inhalation	n.a.p.
						Dermal	n.a.p.
molecular weight (free number, default of 24.45 g/mol)	Input parameter and model inherent reflection/intrinsic substance property	not relevant for model uncertainty	not relevant for model uncertainty	not relevant for model uncertainty	high	inhalation	n.a.p.
						Dermal	0
dustiness (high/medium/low/massive object (i.e. very low))	Input parameter/ intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high	Inhalation	++/--
						dermal	0
vapour pressure (high/medium/low)	Input parameter/ intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high	Inhalation	++/--
						Dermal	0
Process temperature for PROCs 21-25, 27a (Tproc<Tmelt; Tproc≈Tmelt; Tproc>Tmelt)	Input parameter and model inherent reflection/process description + operational conditions	n.a.p. both possible	see initial exposure estimate	see initial exposure estimates	high	Inhalation	+/-
						Dermal	0
PROC number (PROC 1-27b)	Input parameter/ process description + operational conditions	see initial exposure estimates	see initial exposure estimates	see initial exposure estimates	medium/high	inhalation	+++/---
						Dermal	+/-

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency of documentation	Certainty of knowledge base	Parameter quality (vagueness and level of detail)	Direction and magnitude of the caused uncertainty	
scale of operation (industrial/professional)	Input parameter/ process description + operational conditions	see initial exposure estimates	see initial exposure estimates	see initial exposure estimates	low	Inhalation	+/-
						Dermal	0
Pattern of use	Input parameter/Use description and operational conditions	see initial exposure estimate	See initial exposure estimate	See initial exposure estimate	Low	Dermal	++/--
						Inhalation	0
Contact level (extensive, intermittent, incidental, none	Input parameter/Use description and operational conditions	see initial exposure estimate	See initial exposure estimate	See initial exposure estimate	High	Dermal	+++/---
						Inhalation	0
Pattern of control (direct/non-direct handling)	Input parameter/Use description and operational conditions	see initial exposure estimate	See initial exposure estimate	See initial exposure estimate	Medium	Dermal	+++/---
						Inhalation	0
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction)	Input parameter and model inherent reflection/Use description and operational condition	n.a.p. both possible	medium	N.a.p.	medium	Inhalation	+++/-
						Dermal	+++/-
duration (<15 min, 15-60 min, 1-4 h, >4 h; 90, 80, 40, 0% exposure reduction), maximum 8 h	Input parameter and model inherent reflection/Use description and operational condition	n.a.p. both possible	medium	N.a.p.	high	Inhalation	+++/-
		n.a.p. both possible	low/medium	N.a.p.	high	Dermal	+++/-
LEV (ECETOC values)	See section 1 in Appendix A (ECETOC TRA) for details						

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency of documentation	Certainty of knowledge base	Parameter quality (vagueness and level of detail)	Direction and magnitude of the caused uncertainty	
Localised control measures for inhalation exposure: LEV (generic, exterior, interior), enclosure, containment, General ventilation, Suppression techniques: generic suppression, capture sprays (wetting system at point release), wet suppression of contaminant (after emission), Separation of workers	Input parameter and model inherent reflection/localised controls	n.a.p. both possible	Medium	(medium/low)	medium	Inhalation	n.a.p..
						Dermal: No influence	0
Average with median confidence or upper or lower confidence limits may be chosen for the inhalation risk management measures	Input parameter/ localised controls	n.a.p. both possible	Medium	medium	Medium/high	Inhalation	+/-
						Dermal	0
Respiratory protection equipment (75%, 80%, 90%, 95%, 97.5% efficiency according to APFs 4, 5, 10, 20 and 40)	Input parameter and model inherent reflection/personal protective equipment	n.a.p. both possible	high	n.a.:	high	Inhalation	++/--
						Dermal	0
Gloves (90%)	Input parameter and model inherent reflection/personal protective equipment	n.a.p. both possible	Low	n.a.p.	low	Dermal	n.a.p.
						Inhalation	0
Model inherent parameters							
Initial inhalation exposure estimate (Inhalation, PROC1-20)/defined by fugacity, physical state, process description, type of setting. Values are mostly identical to ECETOC TRA	Model inherent parameter	n.a.p. both possible	medium	n.a.p.	n.a.	Inhalation	n.a.p.
Initial exposure estimate (Inhalation, PROC21-27a)/defined by fugacity, physical state, process description, type of setting	Model inherent parameter	N.a.p. both possible	medium	high	n.a.	Inhalation	n.a.p..
Initial inhalation exposure estimate (Inhalation, PROC27b)/defined by fugacity, physical state, process description, type of setting	Model inherent parameter	N.a.p. both possible	high	low	n.a.	Inhalation	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency of documentation	Certainty of knowledge base	Parameter quality (vagueness and level of detail)	Direction and magnitude of the caused uncertainty	
Initial exposure estimate (dermal, defined by pattern of use, pattern of control, contact level)	Model inherent paramter / Use description and operational conditions	N.a.p. both possible	Medium/high	Medium	n.a.	Dermal	n.a.p.
						Inhalation	0
Skin area, exposed body parts (defined by PROC; palm(s), fingers, hand(s), hands and forearm(s))	Model inherent parameter/Use description and operational conditions	n.a.p. both possible	medium	n.a.p. due to lack of information.	n.a.	Dermal	+++/- (--)
						Inhalation	0
Presentation of results	Model inherent parameter / Model assumption	variability / uncertainty	high	n.a.p.	high	Inhalation (PROCs21-27) and dermal	n.a.p.
			low	n.a.p.	medium/low	Inhalation (PROCs1-21)	n.a.p.
Model equation, assumptions							
Ideal gas law and approximately 298 K (i.e. molar volume of 24 l/mole) assumed for conversion of units	Model	uncertainty	high	n.a.p.	n.a.	inhalation	n.a.p.
						dermal	0
exposure estimates for aqueous solutions of inorganic substances are based on the same values as assigned to very low dustiness (massive objects) for all PROCs except 7 and 11 (spray processes)	Model / assumptions	n.a.p. both possible	low	n.a.p.	n.a.	Inhalation and dermal	n.a.p.
exposure estimates for aqueous solutions of inorganic substances are based on the same values as assigned to substances of medium dustiness for PROCs 7 and 11 (spray processes)	Model / assumptions	n.a.p. both possible	low	n.a.p.	n.a.	see above.	n.a.p.

2.1.3 EMKG-EXPO-TOOL

Table 2.4 Evaluation matrix: EMKG-EXPO-TOOL

Source of uncertainty	**Type of uncertainty source**	**Variability / uncertainty**	**transparency of documentation**	**Certainty of knowledge base**	**quality of parameter definition (vagueness/level of detail)**	**Direction and magnitude of the caused uncertainty**
physical state (Solid/ liquid)	Input parameter / intrinsic substance properties	See exposure outcomes.	n.a.p.	n.a.p.	High	N.a.p
Vapour pressure at process temperature or boiling point and process temperature (low, medium, high)	Input parameter / intrinsic substance properties	See exposure outcomes.	High	high	High	+/-
dustiness (low, medium, high)	Input parameter / intrinsic substance properties	See exposure outcomes.	n.a.p.	n.a.p.	medium	+/-
application on surfaces (for liquids)	Input parameter / Use description and operational conditions	See exposure outcomes.	medium	high	high	N.a.p.
Scale of use (g, kg, t, solid and liquid)	Input parameter / Use description and operational conditions	See exposure outcomes.	n.a.p.	n.a.p.	medium/high	+/-
Short term application (<15 minutes; liquid and solid)	Input parameter / Use description and operational conditions	See exposure outcomes.	n.a.p.	n.a.p.	high	+/-
Control strategy (general ventilaion, LEV, closed system; liquid and solid) - **Model parameter**	Input parameter / localised controls	See exposure outcomes.	n.a.p.	n.a.p.	low	+/-
Control guidance sheets	Input parameter / localised controls / Use description and operational condications	see above.	see above.	see above.	high/medium	+/-
Resulting exposure ranges	Model inherent parameter / exposure result	Uncertainty	Low	low/medium	N.a.	n.a.p.
Presentation of results	Model inherent parameter / Model assumption	variability / uncertainty	low	n.a.p.	low:	n.a.p.
Most modifiers are independent of each other	Model: assumption	uncertainty	Low:	n.a.p.	n.a.	n.a.p..
GOHP	Model / assumption	uncertainty	High	n.a.p.	n.a.	n.a.p.

2.1.4 STOFFENMANAGER® v. 4.5

Table 2.5 Evaluation matrix: STOFFENMANAGER® v. 4.5

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
Model parameters						
vapour pressure of component (Pa), model internal reflection (intrinsic emission score ei for liquids)	Input parameter and model inherent reflection/ intrinsic substance property	n.a.p. both possible	high	high/medium	high	n.a.p.
concentration of a component within a product	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	high	Medium	n.a.p.
dustiness of product	Input parameter and model inherent reflection/ intrinsic substance property	n.a.p. both possible	medium/high	n.a.p.	medium	+/-
handling categories (7 for liquids, 7 for solids, 6 for wood, 4 for stone)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	Low/medium	n.a.p.
room size (4 categories including outdoor use)	Input parameter and model inherent reflection/ Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	High	n.a.p.
General ventilation (4 categories)	Input parameter parameter and model inherent reflection / localised controls	n.a.p. both possible	medium/high	n.a.p.	Low	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
situation of worker (cabin, no cabin, other room)	Input parameter parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	high	n.a.p.
RMMs (LEV, product that reduces emission, containment, containment and LEV, no RMM)	Input parameter parameter and model inherent reflection / localised controls	n.a.p. both possible	medium/high	n.a.p.	low/medium	n.a.p.
Respiratory protection (6 categories)	Input parameter parameter and model inherent reflection / personal protective equipment	n.a.p. both possible	medium/high	n.a.p.	high	+/-
Is the working room being cleaned daily?	Input parameter parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	Medium	n.a.p.
Take inspections or maintenance of machines place once monthly?	Input parameter parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	High	n.a.p.
Is the task carried out in the breathing zone of an employee? (if “no” is chosen, the next two options (more than one employee is carrying out the task, period of evaporation) are n.a. anymore. If ‘yes’ is chosen, the option ‘the employee does not work in a cabin’ is chosen automatically	Input parameter parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	High	n.a.p.
Is more than one employee carrying out the task?	Input parameter parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	High	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
Is the task followed by a period of evaporation, drying or curing?	Input parameter / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	High	n.a.p.
Is the product diluted with water? (free text field)	Input parameter parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	medium/high	n.a.p.	Medium	n.a.p.
Presentation of results	Model inherent parameter / Model assumption	n.a.p. both possible	high	n.a.p.	high	n.a.p.
Model equation / assumptions						
It is assumed that the exposure score is linearly dependent on the mass fraction of substance in a mixture (and not the mole fraction)	Model/ assumption	uncertainty	medium/high	n.a.p.	n.a.	n.a.p.
Exposure estimates for solutions of solids in liquids are based on the solids' vapour pressure (such as for liquid/liquid mixtures)	Model/ assumption[33]	uncertainty	medium/high	n.a.p.	n.a.	n.a.p.

2.1.5 RISKOFDERM v. 2.1

Table 2.6 Evaluation matrix: RISKOFDERM v. 2.1

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
DEO 1 (mixing, filling, loading)						
Intercept (includes: more than light contact, frequent contact, good ventilation, low/moderately dusty, solid, no aerosol generation, manual task)	Model inherent parameter	n.a.p. both possible	high	n.a.p.	N.a.	n.a.p.
Kind of skin contact (more than light or. light)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	Low	n.a.p.
Contact frequency (rare or more than rare)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	high	n.a.p.
Ventilation (normal or good ventilation / poor or no ventilation)	Input parameter and model inherent reflection / localised controls	n.a.p. both possible	high	n.a.p.	Low	n.a.p.
Dustiness (highly dusty, low or moderately dusty)	Input parameter and model inherent reflection / Intrinsic substance property	n.a.p. both possible	high	n.a.p.	Low/medium	n.a.p.
Physical state (solid/liquid)	Input parameter and model inherent reflection / Intrinsic substance property	n.a.p. both possible	high	n.a.p.	High	n.a.p.
Aerosol generation	Input parameter and model inherent reflection /Use description and operational conditions	n.a.p. both possible	high	n.a.p.	Medium	n.a.p.
Application/use rate (free number)[2]	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	high	n.a.p.
Level of automation (automated or semiautomated / manual)	Input parameter and model inherent reflection / Use description and operational	n.a.p. both possible	high	n.a.p.	Medium	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
	conditions					
only hand exposure is estimated for this DEO unit	Model	uncertainty	high	n.a.p.	N.a.	n.a.p.
DEO2 (wiping)						
Intercept (hands, no extensive body contact)	Model inherent parameter	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p.
Body exposure	Model inherent parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	n.a..	n.a.p.
Extensive Body contact	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	low	n.a.p.
Application/use rate (free number)[4]	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	high	Not relevant for model uncertainty
DEO 2: Wiping						
Intercept (hands, viscosity like honey, overhead orientation, more than 30 cm handle)	Model inherent parameter	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p.
Body exposure	Model inherent parameter / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p.
viscosity (like water, like honey, like oil)	Input parameter and model inherent reflection / Intrinsic substance property	n.a.p. both possible	high	n.a.p.	low	n.a.p.
Orientation (overhead/level or downwards)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	medium-high	n.a.p.
Distance to source (tools with handles more or less than 30 cm)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	Medium	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
Application/use rate (free number)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	high:	n.a.p.
DEO4 (Spray dispersion)						
Intercept (work indoors, not highly volatile substance, no segregation, level orientation, no airflow or LEV)	Model inherent parameter	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p.
Work environment (Outdoors/indoors)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	medium – high	n.a.p.
Volatility (highly volatile, not highly volatile)	Input parameter and model inherent reflection / Intrinsic substance property	n.a.p. both possible	high	n.a.p.	Medium	n.a.p.
Segregation (physical barrier, no physical barrier)	Input parameter and model inherent reflection / localised controls	n.a.p. both possible	high	n.a.p.	Low	n.a.p.
Body exposure	Model inherent parameter / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	n.a..	n.a.p.
Orientation (overhead, level, downwards)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	low	n.a.p.
Airflow (clearly away from the worker or not clearly away from the worker)	Input parameter and model inherent reflection / localised controls	n.a.p. both possible	high	n.a.p.	low	n.a.p.
Application/use rate (free number)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	high	Not relevant for model uncertainty
DEO5 (immersion)						
Intercept (represents the following scenario: hands, no LEV, distance between 30 and 100 cm)	Model inherent parameter	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
adequate LEV used or not	Input parameter and model inherent reflection / localised controls	n.a.p. both possible	high	n.a.p.	low	n.a.p.
body exposure	Model inherent parameter / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p
Distance to source (more than 100 cm, less than 100 cm, less than 30 cm)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	High	n.a.p.
DEO6 (mechanical treatment)						
Intercept (represents the following scenario: less than 100 cm distance, infrequent contact, liquid formulation)	Model inherent parameter	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p.
Distance to source (more than 100 cm, less than 100)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	low	n.a.p.
Contact frequency (infrequent or frequent)	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	low	n.a.p.
Physical state (solid/liquid)	Input parameter and model inherent reflection / Intrinsic substance property	n.a.p. both possible	high	n.a.p.	high	n.a.p.
Only body exposure can be estimated for DEO 6, only hand exposure can be estimated for DEO 1.	Model equation / scope	n.a.p. both possible	high	n.a.p.	n.a.	n.a.p.
Duration (free text, linear dependency assumed);	Input parameter and model inherent reflection / Use description and operational conditions	n.a.p. both possible	high	n.a.p.	High	n.a.p
only body exposure is estimated for this DEO unit	Model	uncertainty	high	n.a.p.	N.a.	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Magnitude and direction of uncertainty
General sources of uncertainty for all DEO units						
Linear dependency between exposure and weight fraction of a substance in the formulation	Input parameter and model inherent reflection / prossess description and operational condition	uncertainty	high	n.a.p.	N.a. (not implemented in tool)	n.a.p
DEO unit	Input parameter and model inherent reflection / Use description and operational condition	n.a.p. both possible	high	n.a.p.	medium	n.a.p.
The density of liquid substances is assumed to be 1 mg/ml	Parameter / intrinsic substance properties	uncertainty	high	n.a.p.	N.a.	n.a.p.
Presentation of results	Model inherent parameter / Model assumption	uncertainty	high	n.a.p.	high	n.a.p.

2.2 General knowledge base

2.2.1 Datasets used during model development

The quality or uncertainty of measured data that have been used to develop an exposure model directly influences the accuracy and uncertainty of this exposure model. Due to the natural variability of underlying datasets that have been summarised into one more or less broad exposure scenario, the exposure corresponding to specific situations, which do not correspond to the "scenario average" (or a certain percentile) or are not represented within the underlying dataset, may deviate from the model estimate. On the other hand systematic sampling errors or other errors during the sampling and/or collection of measured data may also contribute to the model uncertainty.

Not all models within the eteam project are based on reported data, i.e. it is considered to be likely that some kind of experimental experience will stand behind all of the models but neither all datasets nor all procedures that stand between data and model estimate are known and/or published. This fact prevents a complete evaluation of the uncertainty of the knowledge base.

Some publications are available which provide information on quality categorisation of measured data (MONEY AND MARGARY, 2002; TIELEMANS, 2002). However, the amount of information about the underlying datasets which would be necessary for this evaluation process is not available for any of the included models in a condensed form and the time needed for a detailed assessment of secondary literature (e.g. EU RARs) would be beyond the timeframe of this project. Thus, only a rough and general assessment of uncertainties related to the underlying database can be done for some of the tools, where basic information about the model basis is publicly available or has been made available in the course of this project.

Another important parameter in this context is the variability within this setting which also influences the size of the confidence interval (higher variability will lead to larger confidence intervals and higher uncertainty) but will however not be evaluated in detail in this section.

A summary of the datasets used for model development is given in Table 2.7. As a first and very rough indication of a comparably low uncertainty related to the underlying datasets is a high number of samples. It is one parameter that affects the size of a confidence interval, i.e. a range around the derived exposure value for the evaluated exposure setting in which the actual exposure value will lie with e.g. 90 per cent probability (which would correspond to 90% confidence level).

In other words, a large number of samples decreases the interval around the derived value, within which the actual value will probably lie and thus, it decreases the uncertainty.

Thus, the number of datasets per model may provide a general impression about the uncertainty of this aspect concerning the model while the number of datasets per model-implemented use category[5] may give information about the uncertainty for this category.

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[5] In the context of this report the following definitions are used:
task: a certain activity, e.g. spray application. *process*: something that may include several sub-activities, e.g. closed process including sampling procedures. Use description / categorisation: general way a model categorises the use of a substance. It may be task- or process based refers to one sample as published in the available references (see also Chapter 2.3.3).

However, the influence of the uncertainty of the underlying datasets is also related to the exact use description (broad categorisation that covers many different areas per category vs. specific process or task), the sample quality and the way of implementing these datasets into the model.

Inhalation models

In case of the EMKG-EXPO-TOOL, which is based on COSHH Essentials, the derivation of exposure estimates is based on expert discussion. It is not known if and/or which specific datasets have been used for the derivation of the original exposure ranges, however, some comparison with measured data during the finalisation of the COSHH Essentials model is described by Maidment et al. (MAIDMENT, 1998) (see also Chapter 2.2.2).
In case of ECETOC TRA (both versions) the final exposure estimates and all implemented modifiers are not completely based on published data. However, some datasets concerning exposure to metals are described in TR 109 (ECETOC, 2009). Moreover, it is known that a certain amount of scientific judgement of the model developers has been involved in the creation of this model.
In case of MEASE several approaches have been combined: Large parts of the inhalation algorithm including exposure modifiers are based on ECETOC TRA v.2, i.e. a combination of not reported datasets and scientific judgement. Inhalation RMM efficiencies are based on the work of Fransman et al. (FRANSMAN ET AL., 2008) who summarise a collection of measured efficiencies.
STOFFENMANAGER® is completely based on fitting procedures that were applied to sets of measured data (MARQUART ET AL., 2008; TIELEMANS ET AL., 2008a; TIELEMANS ET AL., 2008b).
The overall number of underlying datasets[8] as well as the maximum number of datasets per use description is highest for MEASE. ECETOC TRA v.2/v.3 offers the same maximum number of datasets per use description (overlap of datasets).
Concerning the data quality in case of STOFFENMANAGER® the documented selection of datasets is reported to have followed strict quality criteria (TIELEMANS ET AL., 2008a). The datasets used in ECETOC TRA v.2/v.3 (metal processes PROC 21-25) and MEASE (PROC21-27a for inhalation; all use categories except closed processes for dermal) have already been described in EU Risk Assessment Reports[6]. Thus, the quality of the measured samples is regarded to be reasonably high for those inhalation models where information has been published although often not all details about sampling strategies have been evaluated in this work package. The datasets used for the derivation of RMM efficiencies are described in (FRANSMAN ET AL., 2008). Their transparency can only be considered as medium as only summarising parameters and not a full list of corresponding secondary literature is given. A final assessment of the uncertainty of underlying datasets is therefore not possible, but medium or low uncertainty is expected as the values are not based on expert judgement.
However, a detailed evaluation of these reports and therefore a detailed evaluation of their uncertainty lies beyond the scope of this report.

[6] EU RARs for Zn, Sb. Pb (+Ni; (only for dermal exposure)), see HERAG fact sheet, ECETOC documentation TR 107 and chapter 0. Some statistical information about the used datasets is given but not all steps that led to the final model estimate are published.

In case of MEASE not enough information is available for an assessment of the quality of data related to RMM efficiencies for inhalation (no secondary literature cited by Fransman et al. (FRANSMAN ET AL., 2008)).

Dermal models

Dermal datasets concerning exposure to metals for ECETOC TRA (both versions) are described in TR 107 (ECETOC, 2009).
The dermal initial exposure estimates (in mg/cm^2) of MEASE are based on published datasets (see MEASE glossary and (HERAG, 2007)) which have been complemented by some scientific judgement in cases where no measured data was available.[7]
RISKOFDERM is completely based on a collection of measured data (WARREN ET AL., 2006).
The overall number of underlying datasets is highest for MEASE and RISKOFDERM, while the highest number of datasets per main activity is reached by MEASE.
For dermal exposure often higher differences between different sampling methods and thus, higher uncertainties have been reported than for inhalation exposure measurements. However, for MEASE it has been stated (Vetter (2012); personal communication), that the two used sampling methods led to comparable results in this case The datasets used in ECETOC TRA v.2/v.3 (metal processes PROC 21-25) and MEASE have already been described in EU Risk Assessment Reports[6].
A general source of uncertainty for the final model estimate is, that in many cases not all body areas (hands and body) could be sampled (see e.g. (WARREN ET AL., 2006)) or were not included into the model algorithm due to other reasons (HERAG, 2007).

Table 2.7 Approximate numbers of measured datasets used for model development.[8]

Number of datasets	MEASE (EBRC, 2008)	ECETOC TRA v.2 and v.3 (ECETOC, 2009)	EMKG-EXPO-TOOL	STOFFENMANAGER® (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a)	RISKOFDERM (WARREN ET AL., 2006)
Inhalation					
Number of datasets for inhalation exposure	> ~6500[9]	> 4000	not published	> 1000 (+146 respirable stone dust) (520 solids and 432 liquids)	n.a. / outside scope
Number of datasets for inhalation exposure, per use category[10]	0-2544[9]	146-2544	not published	not published	n.a. / outside scope

[7] Estimate for lowest exposure category based on scientific judgement; Combination incidental contact + non-dispersive use is estimated to be equal to the next highest exposure range.
[8] One dataset refers to one datapoint as published in the available references: MEASE: number of values (inhalation data); number of counts (HERAG, 2007); efficacy values (Fransman et al., 2008); ECETOC TRA: number of values (inhalation + dermal data); STOFFENMANAGER® number of samples, RISKOFDERM: number of data.
[9] Approximate number. Number of underlying datasets has been increased since development of draft report EBRC, 2008. There is a certain overlap with the ECETOC datasets for metal processes.
[10] use category = one process/task/use description within the models.

Number of datasets	MEASE (EBRC, 2008)	ECETOC TRA v.2 and v.3 (ECETOC, 2009)	EMKG-EXPO-TOOL	STOFFENMANAGER® (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a)	RISKOFDERM (WARREN ET AL., 2006)
Reflected model parts	Datasets represent PROCs 21-27b. Only solids included.	Datasets represent PROCs 21-25	not published	Datasets represent all implemented process descriptions (26 handling categories including wood/stone categories). Solids and liquids.	n.a. / outside scope
Years covered by datasets	RARs from 2003-2008[9]	RARs from 2003-2008	not published	1994-? (not all years published)	n.a. / outside scope
Dermal					
Number of datasets for dermal exposure / Hands	> 500	>250	n.a. / outside scope	n.a. / outside scope	> 500
Number of datasets for dermal exposure / Hands, per use category	0-285	0-125	n.a. / outside scope	n.a. / outside scope	13-195 (no separation into solid and liquid published)
Reflected model parts (hands)	Datasets represent three of four exposure ranges assigned to the EASE use description. Only solids.	Datasets represent PROCs 21-25. Only solids	n.a. / outside scope	n.a. / outside scope	Datasets represent DEO units 1-5 (DEO unit 1 and 4 solids, DEO units 1-5 liquids)
Years covered by datasets	1999-2005	1999-2005	n.a. / outside scope	n.a. / outside scope	1996-2004
Dermal exposure / Body	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	> 650
Dermal exposure / Body, per use category	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	57-331 (no separation into solid and liquid published)
Reflected model parts (body)	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	Datasets represent DEO units 2-6 (DEO unit 4 and 6 solids, DEO units 2-6 liquids)
Years covered by datasets	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	n.a. / outside scope	1996-2005
RMM efficiencies					
datasets for RMM efficiencies	> 400	> 4000 (inhalation) > 250 (dermal)	not published	> 1000 (+146 respirable stone dust) (520 solids and 432 liquids) RMM efficiencies are a result	> 500 (hands) > 650 (body) RMM efficiencies are a result of the

For ECETOC TRA and the inhalation part of MEASE this categorisation is the PROC system, for the dermal MEASE part it is the categorisation into EASE use patterns, for RISKOFDERM it is the DEO unit categorisation, for STOFFENMANAGER® it is the differentiation into tasks.

Number of datasets	MEASE (EBRC, 2008)	ECETOC TRA v.2 and v.3 (ECETOC, 2009)	EMKG-EXPO-TOOL	STOFFENMANAGER® (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a)	RISKOFDERM (WARREN ET AL., 2006)
				of the fitting procedure using all datasets available for inhalation exposure (including scenarios with and without RMMs)	fitting procedure using all datasets available for dermal exposure (including scenarios with and without RMMs)
datasets for RMM efficiencies per control measure	12-280	146-2544 (inhalation) 0-125 (dermal)	not published	not published	Hands: 13-195 (no separation into solid and liquid published) Body: 68 per RMM and 331 per 2 RMMs (no separation into solid and liquid published)
Reflected model parts	Physical state for underlying datasets is not known.	LEV efficiencies for PROCs 21-25. For other PROCs and further RMMs/PPE no sets of measured data are published, however rationales for efficiencies are given in ECETOC TRA documentations TR 93, 107, 114.	not published	Datasets represent all implemented RMMs (6 RPE types, 3 different worker situations, 7 categories describing the application of LEV, ventilation and containment). Solids and liquids.	All implemented RMMs: DEO unit 1: Ventilation DEO unit 4: Directed airflow and segregation DEO unit 5: LEV
Years covered by datasets	2000-2007	2003-2008 (inhalation) 1999-2005 (dermal)	not published	1994-? (not all years published)	1996-2005

2.2.2 Previous model validations

There are two types of validation studies: validations which have been used to improve the model performance (often an iterative process during model development or refinement, see also Chapter 2.2.1) and validations which have been done after model development. The former process will certainly decrease the uncertainty of the later model as it will lead to lower magnitudes of uncertainty concerning the model estimates, but is often not fully published. The latter on the other hand will increase the general knowledge about the model and its possible weaknesses, therefore it will not change model performance or magnitudes of uncertainty for the exposure estimate for a given scenario but it may increase the available information about the model scope and accuracy. As a consequence, some situations may be excluded from the model's applicability domain and the interpretation of the model estimate (level of conservativeness for a given scenario)

may be improved. Thus, the general level of uncertainty (according to the definition in Chapter 1.1 “lack of knowledge”) is decreased.
In the following paragraphs a short summary of a selection of published validation studies will be given.

ECECTOC TRA

- ECETOC, 2004 (ECETOC, 2004): Some comparisons between the ECETOC TRA v.1 with EU risk assessment results were performed by ECETOC but no evaluation against actual measured data took place (see also ECHA, 2010b). The extraction of information from the comparison is hindered by the lack of a standard procedure for exposure estimation within the EU risk assessment process.
- Dobecka et al, 2011 (KUPCZEWSKA-DOBECKA ET AL., 2011): An evaluation study for inhalation workplace exposure to organic solvents (toluene, ethyl acetate, acetone, o-xylene) was carried out in Poland. A paints and lacquers factory (section filtration and decanting room), a shoe factory (sole manipulation, sewing section, assembling), and a refinery (supervisor, process controller, operator and mechanic work tasks) were tested. The processes codes (PROCs) 1 (Use in closed process, no likelihood of exposure), 2 (Use in closed, continuous process with occasional controlled exposure) and 10 (Roller application or brushing) were assigned to these workplaces, although the selected PROCs did not precisely describe the studied applications. The outcome of this comparison ranges from underestimation (shoe factory) to correct results (i.e. measurements lying within the interval between exposure with and without LEV).
- Vink et al, 2010 (VINK ET AL., 2010): The outputs from the ECETOC TRA v.2 were compared with other models (STOFFENMANAGER® and RISKOFDERM). The inhalation exposure estimates (full shift) were also compared with the 90th percentile of 745 datasets on propylene glycol monomethyl ether (1-methoxypropan-2-ol, PGME) measurements selected from the MEGA database (1996-2000). Model estimates obtained without LEV and the assumption that the product contains 30% PGME led to a substantial overestimation of the real workplace exposure in case of ECETOC TRA. The PROCs 8a, 11, 13 were assigned to homogenizing and filling, spraying and cleaning respectively.
- Hofstetter et al., 2012 (HOFSTETTER ET AL., 2013): Measured toluene concentrations due to use of spray paint are compared to modelling results including ECETOC TRA v.2. TRA showed overestimations if compared with the 8h time weighted average measurements about a factor of 3.61.

Validation studies of ECETOC TRA v.1 (not part of this project) and v.2 are available, however, the results vary. Outcomes range from underestimations of exposure to overestimations.

MEASE

No validation studies are published so far.

EMKG-EXPO-TOOL

- ❖ Maidment et al.,1998 (MAIDMENT, 1998): Some testing (mostly comparison with measurements relating to large scale closed systems) of the COSHH essentials core model via comparison with measured data or by wider peer reveiw within the British Occupational Hygiene Society and the Brithish Institute of Occupational Hygienists has been documented in this publication. Results suggest mostly conservative results with however some underestimations being present.
- ❖ Lee et al., 2011 (LEE ET AL., 2011): The COSHH essentials model was evaluated using full-shift exposure measurements of five chemicals in a mixture (i.e. acetone, ethyl-benzene, methyl ethyl ketone, toluene and xylene) at a plant producing paint materials. The tasks "batch-making" and "bucket-washing" were evaluated for all three control levels and indicated a significant amount of underestimations for bucket washing in case of acetone (control level 2 and 3), methyl ethyl ketone and Xylenes (both control level 3).
- ❖ Kindler et al., 2010 (KINDLER, 2010): 42 scenarios are evaluated within the EMKG-EXPO-TOOL and EASE. Result: Exposure to substances of low vapour pressure is overestimated. The efficiency of LEV is overestimated (which means that exposure may be underestimated). The model development is not well documented. No chemicals in mixtures are addressed. Only minimal information is required for using the tool. Exposure predictions for substances with high vapour pressure appear to be fine.
- ❖ Lee et al., 2009 (LEE ET AL., 2009): The COSHH essentials model was evaluated for short-term and full shift exposures in a printing plant. 188 measurements of isopropanol and 187 measurements of acetone (each ~60 min) were collected and time-weighted average concentrations were evaluated for methylene chloride. Overall the study suggests the COSHH essentials provides reasonable results, however there are some cases (cleaning with acetone or isopropanol, print preparation with isopropanol, full shift exposure to acetone) where the probability of underestimations is larger than 10%.
- ❖ Tischer et al., 2007 and Tischer et al., 2009 (TISCHER ET AL., 2009; TISCHER AND POPPEK, 2007): It is evaluated by probabilistic modelling if the activity concepts of EMKG provide a sufficient level of safety. A Monte-Carlo simulation of the BWI ("Bewertungsindex"; ratio of measured exposure value and occupational exposure limits (OEL)) distribution is performed. Overall 732 measurements with data for two control banding scenarios were used. It was found that control banding does not guarantee a safe use. However the generic simulation showed that compliance for volatile liquids in closed systems and solids in presence of LEV was high.

  It has to be stated that OELs could vary between different countries. This represents a potential source of error within the study as it also influences the BWI.

  In this publication several earlier evaluations of COSHH and the EMKG concept are cited which show different results but did not lead to an update of exposure ranges or the EMKG scheme.
- ❖ Hashimoto et al., 2007 (HASHIMOTO ET AL., 2007): COSHH essentials was applied to 12 petroleum company workplaces and its results were compared with comprehensive risk assessments. These risk assessments were based on exposure estimations which were created by measurements or expert judgement (depending on the workplace) and their comparison with OELs. For seven of the

workplaces an over-controlled situation was predicted. No under-controlled situations were identified.

- Jones et al., 2006a (Jones and Nicas, 2006): Evaluation of COSHH essentials for vapour degreasing and bag filling operations. 78% of the exposure situations in case of vapour degreasing and 48% in case of bag filling operations are “under-controlled”, i.e. the actual concentration exceeded the predicted upper limit within COSHH.
- Tischer et al., 2003a and Tischer et al., 2003b (Tischer et al., 2003; Tischer and Poppek, 2003): Evaluation of a small subset of the possible scenarios within COSHH essentials. 18 different branch specific situations. Most of the exposure situations are at least represented in a safe way, as the error is on the side of caution. The external evaluation showed good agreements for solids/dusts. For liquids (larger amounts/litres) agreement is good, for millilitre quantities of liquids and dispersive processes (e.g. painting or applying adhesives), the exposure levels may exceed the predicted range.
  “Application on large surfaces” is included in the EMKG-EXPO-TOOL as additional option, but only for quantities larger than 1 l, so this problem (i.e. underestimations in case of dispersive processes with liquids) may remain. There is a lack of exposure data for higher levels of control in the evaluation set.

A comparably large number of validation studies is available for COSHH essentials and the EMKG-EXPO-TOOL which include also some testing procedures during the finalisation of COSHH essentials (Maidment, 1998).
For the EMKG-EXPO-TOOL no underestimations of exposure are published so far.
As some validation studies of COSHH Essentials have been performed before the finalisation of the EMKG-EXPO-TOOL in 2008 and thus, could be taken into account, they can be considered to be a part of the model development process. As an example, analyses of COSHH essentials showed possible underestimations e.g. for application of small quantities of liquids, vapour degreasing and bag filling which led together with some external modelling results (Tischer, 2011) to the implementation of the “application on large surfaces” option in the tool.

STOFFENMANAGER®

- Koppisch et al., 2012 (Koppisch et al., 2012): Validation of STOFFENMANAGER® with data from the MEGA exposure database (1984-2007). Evaluation of two model equations: handling of powders/granules (n=390 data points, 15 scenarios) and machining (n=1133 data points, 22 scenarios) for exposure to inhalable dust. Tasks: grinding, sanding, milling, sawing or cutting of wood, stone or asphalt for machining; filling/dumping, mixing, sweeping, chimney cleaning, plastering for the handling of powders/granules. Result: 11% and 7% of the MEGA data were above the estimated 90th percentile of STOFFENMANAGER®, respectively.
- Schinkel et al., 2010 (Schinkel et al., 2010): Correlations between measured and predicted values, bias and precision were calculated for a set of measurements. The scenarios “handling of powders and granules” (n=82 data points), “handling solids resulting in comminuting” (n=60), “handling of low-volatile liquids” (n=40), “handling of volatile liquids” (n=72) were evaluated separately. The predicted 90th percentile exposure for “handling of powders and granules” was not sufficiently conservative.

- Vink et al., 2010 (VINK ET AL., 2010): This publication includes a comparison of STOFFENMANAGER® and ECETOC TRA predictions for inhalation exposure with full-shift exposure values derived from the MEGA database on PGME (1-methoxypropan-2-ol, 90th percentile of 745 datasets (1990 - 2000)[11]. STOFFENMANAGER® results (75th percentile) were about half of the reasonable worst case derived from the measured values. According to Vink et al. this discrepancy may be caused either by the fact that measured values do not properly fit the assessed exposure scenario, or by STOFFENMANAGER® estimates not being sufficiently conservative.
- Arnone et al., 2013 (ARNONE, 2013): Comparison of GESTIS-Stoffmanager with measured values for coating with Methyl-methacrylate resins and mixing of dry plaster. Overall good agreement between measurements and estimation was shown; slight overestimations were observed but estimates were not excessively conservative.

Some validation studies are available which partly also represent a step within the development process of STOFFENMANAGER® (Schinkel et al.). Underestimations were reported, but were at least partly within the expected number of underestimates suggested by the chosen percentile.

RISKOFDERM

- Vink et al., 2010 (VINK ET AL., 2010): The publication contains a comparison of results from STOFFENMANAGER®, ECETOC TRA and RISKOFDERM with full-shift exposure values derived from MEGA on PGME (1-methoxypropan-2-ol, 90th percentile of 745 datasets). As no dermal exposure data are stored in MEGA the results of RISKOFDERM were only compared with results of ECETOC TRA. It was shown that RISKOFDERM results are higher than ECETOC results, in both cases with and without the exposure reducing factor applied for the risk management measure “LEV” in ECETOC.
- Boogaard et al, 2008 (BOOGAARD, 2008): The publication summarises a comparison of bio monitoring data with dermal exposure estimations of EASE and RISKOFDERM taken from EU risk assessments. The investigated substances were Styrene, 2-Butoxyethanol and 1-methoxy-2-propanol. It was concluded that overall RISKOFDERM tends to overestimate exposure.
- TNO, 2006; Warren et al., 2006 (TNO, 2006; WARREN ET AL., 2006): A benchmark study with a small set of data was performed during the process of tool development, which resulted in quite reasonable results. The underlying data were later integrated into the tool. More detailed information about these benchmark data and the corresponding validation results are not available.

No comparison of RISKOFDERM results with measured exposure values is available, however, the available information suggests no tendency to underestimate exposure.
Overall most of the available external validation studies represent a comparison of the completed model with exposure values.
Only limited information about testing routines or validations during the model development process (e.g. Warren et al. (WARREN ET AL., 2006), Schinkel et al.

[11] Summary of datasets provided by Vink et al. (2010):
http://www.dguv.de/ifa/de/pub/rep/pdf/rep01/bgar0199/mega.zip

(SCHINKEL ET AL., 2010), Tischer et al. (TISCHER ET AL., 2003)), however, it is considered to be likely that for all models such a procedure will have been part of it.

2.2.3 Model approach

The model approach, i.e. the basis of an exposure model may also influence the uncertainty of its result. This does not only refer to single parameters and their implementation, which will be discussed in Chapter 2.3, but also to the general approach (logic tree, linear mixed effect models, initial exposure estimate + modifier) which may to varying extent be able to reflect dependencies and/or variability in an exposure scenario.

Different algorithms have been used within the five models evaluated in this work package which are mostly based on combinations of the three general approaches listed above. Considering the dominating aspects of each model, a combination of initial exposure estimate and modifiers has been used for ECETOC TRA and MEASE, a decision tree in case of the EMKG-EXPO-TOOL and linear mixed effect models in case of RISKOFDERM and STOFFENMANAGER®.

However, this categorisation is quite coarse and does not apply to all parts of the different models, as there are some decision-tree aspects in all of the evaluated models (e.g. the choice of PROC, type of setting and type of substance lead to the correct LEV modifier in case of ECETOC TRA; RISKOFDERM requires to choose a DEO unit which leads to the relevant model equation). Moreover, partly laws of nature have been used to complete the model algorithms, e.g. in case of the EMKG-EXPO-TOOL the Clausius Clapeyron and the Trouton rule (TISCHER AND POPPEK, 2003) for the influence of temperature on volatility.

General advantages of some model approaches, e.g. linear mixed effect models, have been described in (BURDORF, 2005) (e.g. description of between and within worker variability). These advantages are able to lead to a more accurate reflection of an exposure scenario.

However, as of course the uncertainty of a model estimate is also influenced by other aspects, a conclusion from the choice of the basic algorithm to the overall model uncertainty is considered to be too simplistic.

Some model parameters (e.g. RMM efficiencies, other modifiers) may be influenced by each other or substance properties (MARQUART, 2003). If a model does not take into account these dependencies this contributes to the uncertainty of the exposure estimate while on the other hand many dependencies in a model may decrease usability and/or may induce problems concerning the communication of exposure scenarios under REACH.

In some models fixed modifiers for control measures and operational conditions can be found, i.e. modifiers which do not depend on the use description, other parameters or substance properties (e.g. concentration in case of ECETOC TRA v.3; duration in case of RISKOFDERM). However, there are also counter-examples, e.g. MEASE does not allow for a combination of several local controls and ECETOC TRA v.3 connects the influence of duration on dermal exposure with information about volatility and dustiness and the LEV efficiency with the choice of PROC and type of setting.

Limited information is published about dependencies between exposure parameters: According to Marquart et al. (MARQUART, 2003) there is a possible dependency between the amount of substance, the duration of task and the surface area on which a substance is applied. Moreover, a connection is considered to be possible between

the type of setting (professional and industrial) and the amount of substance and surface areas as smaller companies will work with smaller tonnages/amounts. Substance dependant connections between the concentration of a substance in a solid and its dustiness have been reported (e.g. via moistness (MARQUART, 2003)) as well as between concentration and viscosity (may apply only to RISKOFDERM, see e.g. (HIDAYANTO, 2010)). In addition, a connection between spray pressure, release rate and viscosity of a product on the exposure estimate has been observed and thus may be important (WARREN ET AL., 2006).
However, as no studies are available which may quantify these dependencies, their relevance for model uncertainty cannot be evaluated in detail.

2.2.4 Summary

Overall it can be summarised that the uncertainty of the knowledge base (underlying datasets, model approach) shows a high variability concerning the exposure situation. As an example, due to the higher number of published measurements the uncertainty of the knowledge base concerning metal specific tasks is considered to be lower than for other substances. Further differences, which may be quite specific for only some situations are certainly present, as different parts of a model (e.g. certain process types (DEO units, PROCs etc.) or certain substance types (solids, liquids, different dust fractions etc.) may be represented in varying levels of completeness and data quality. Even within one use description there may be some sub-tasks/processes which are not supported by measured data although the corresponding use category would include these.
Thus, the resulting model uncertainty depends on the exposure situation. It cannot be generally evaluated in detail.
If it is assumed that all model parts for which no measured data has been published or at least mentioned are based on scientific judgement and therefore of high uncertainty, a coarse, average categorisation into low/medium uncertainty of the knowledge base in case of the EMKG-EXPO-TOOL, medium uncertainty in case of ECETOC TRA v.2/v.3 and MEASE and low uncertainty in case of STOFFENMANAGER® and RISKOFDERM can be made. Nevertheless it is recognised that a high amount of scientific knowledge does not necessarily lead to a less accurate or less conservative model estimate. This aspect will be evaluated in work package I.4 (external validation).
The magnitude and direction of the uncertainty introduced by the models' knowledge base cannot be assessed for any of the models. However, for ECETOC TRA, the EMKG-EXPO-TOOL, RISKOFDERM and STOFFENMANAGER® varying numbers of external validation exercises are available which may give insight into expected deviations and thus, the probably estimates' level of the conservativeness for some specific workplaces.

2.3 Comparison of common parameters

In addition to the knowledge base, input parameters of the models can represent a source of uncertainty.
There are some parameters which apply to several models and are – at least in some cases – implemented in these models in a different way. Thus, they may introduce different levels of uncertainty via their definition (quality of input parameter) and/or their implementation into the model algorithm (e.g. efficiency). These parameters will be summarised and discussed in the following paragraphs.

2.3.1 Dustiness/Volatility

The volatility or dustiness of a substance/product may directly influence the exposure value, and therefore can be a source of uncertainty. In case of inhalation the exposure is connected to the possible vapour pressure (or dust particle emission) above the area where an activity takes place.
For dermal exposure the connection is less easy, as it is not always known which pathway or influence (vapour exposure vs. drops/splashes, deposition and adsorption of dust particles on skin) is the one with the highest relevance. However, to a certain extent these parameters are also used in dermal models and have therefore an influence on the uncertainty of the exposure estimate.

Inhalation models

Volatility of liquids is implemented in all inhalation models and defined by the vapour pressure in a quantitative and thus, unambiguous way.
While MEASE and ECETOC TRA use categorising approaches that do not for all processes lead to a volatility dependency of the exposure[12], STOFFENMANAGER® uses a linear approach between 10 and 30000 Pa. Although this linear dependency is expected to represent the ideal case it is not known to which extent other parameters like the type of process/task or adsorption behaviour may induce positive or negative deviations from this approach (see Section 2.3.2).
The EMKG-EXPO-TOOL also uses a categorisation approach of vapour pressure implementation, which influences all possible processes/tasks.

An additional source of uncertainty may arise for exposure situations with temperatures other than room temperature, as ECETOC TRA v.2, MEASE and STOFFENMANAGER® do not offer the possibility to alter the vapour pressure or mention this aspect for all use categories (i.e. PROCs, STOFFENMANAGER task descriptions).
However, in case of the EMKG-EXPO-TOOL the user has the possibility to choose the volatility category of a liquid on the basis of the operating temperature in relation to the boiling point or on the basis of the vapour pressure, which is clearly indicated to be the pressure at operating temperature.
In ECETOC TRA v.2 and MEASE the process temperature is implemented for some PROCs which are expected to happen often at high temperatures (see Appendix 1 and report on conceptual evaluation of Tier 1 models for details). Volatility categories

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[12] No dependency for PROC1 in case of MEASE, no dependency for PROC1 and PROC25 for ECETOC TRA v.2 and 3.

are then assigned in relation to the melting point. This is done in a more ambiguous way in case of ECETOC TRA than in MEASE, as the categories are not described quantitatively ("approximately equal to the melting point"). MEASE on the other hand requires the direct input of the process temperature and uses an implemented algorithm if temperature is considered to be relevant for the process category / PROC (only implemented for some PROCs).

ECETOC TRA v.3 offers the possibility to enter a refined vapour pressure for each single exposure scenario in addition, which is then used for the exposure assessment. As this parameter is quantitative, its main uncertainty is considered to lie outside of the model (→ scenario uncertainty).

The dustiness of a solid substance or mixture on the other hand is also implemented for all models but only MEASE gives quantitative descriptions that may be used for the categorisation of this parameter, if an appropriate measurement is available. There is some experience available suggesting that there is not necessarily a relationship between quantitative scoring of dustiness and variability or quality of the associated exposure estimates (Chris Money, personal communication; August 2013).

The BURE exercise showed that many model users see problems with this parameter, feel unsure about a correct assignment of categories or use other PC properties as a help which have not been approved by the model developers, i.e. at some point of the risk assessment improvements could be appropriate (e.g. by a change of the parameter definition, by provision of measured data, substance samples etc.). BURE does not allow for further conclusions concerning the influence of quantitative dustiness values, as no dustiness measurements where available for this exercise.

Dermal models

Volatility and dustiness directly influence dermal exposure estimates only in RISKOFDERM. While the dermal part of ECETOC TRA v.3 uses information about volatility or dustiness in combination with duration modifiers (duration modifiers are applied only for high and moderate volatility liquids and non-dusty solid substances), the vapour pressure or dustiness does not directly influence the dermal exposure estimate in case of MEASE and ECETOC TRA v.2.

Summary/Discussion

The magnitudes of uncertainty due to the model inherent reflection of volatility or dustiness in the different models cannot be assessed quantitatively. Partly this is caused by a missing standard definition of certain dustiness categories and partly because of the unknown influence of other parameters (e.g. adsorption properties). As a consequence, it is also not possible to assess the level of conservativeness of the various model approaches.

Volatility categories are implemented via the initial exposure estimate in case of MEASE and ECETOC TRA whose derivation is stated to be conservative in nature but is only partially documented. In case of STOFFENMANAGER® it follows a linear approach (see Appendix, Chapter "STOFFENMANAGER® version 4.5") between 10 and 30000 Pa vapour pressure whose precision cannot be assessed but which is offers a higher resolution (free number/ continuous implementation instead of categorisation).

In RISKOFDERM the volatility and also the dustiness are (if available for the corresponding DEO unit) part of the complete fitting procedure.
Dustiness is implemented as a set of qualitative, descriptive categories for all models except MEASE.
The magnitudes of uncertainty related to the assignment of a wrong dustiness category can go up to two orders of magnitude for MEASE and ECETOC TRA and up to one order of magnitude in case of STOFFENMANAGER®, RISKOFDERM and the EMKG-EXPO-TOOL (over- and underestimations possible).
Similar results are found for wrong assignment of the vapour pressure (linear correlation for STOFFENMANAGER®, one order of magnitude for EMKG-EXPO-TOOL and RISKOFDERM, up to two orders of magnitude for ECETOC TRA v.2 and v.3, MEASE). However, as the vapour pressure is a quantitative parameter, assignment of a wrong value or category should usually not be related to model uncertainty
BURE results support the relevance of volatility and dustiness input as a source of general uncertainty during exposure assessment. Considerable variability was identified especially concerning the choice of dustiness category which is probably related to the comparably high vagueness of this parameter but may also be influenced by lack of contextual information (e.g. dustiness measurements or at least pictures) within BURE.

2.3.2 Exposure to substances in mixtures

Inhalation models

Different approaches are used to take into account the reduced exposure that may arise due to a dilution of the substance of concern: MEASE and ECETOC TRA use a set of modifiers which result in a non-linear relationship between exposure and fraction in the mixture (>25%, 5-25%, 1-5%, <1% mass fraction are represented by 0, 40, 80, 90% exposure reduction). As these modifiers result in exposure reductions above the linear, ideal approach, they are expected to lead to overestimations for the majority of possible mixtures and thus, considered to be conservative. However, there may exist some examples (see below) for which this approach may not lead to overestimations or even to underestimations of exposure. STOFFENMANAGER® uses a linear approach. However, the parameter which is assumed to be linearly dependant of the concentration is the exposure score which is fitted to measured exposure in its logarithmised form. Overall this leads to a connection between exposure and concentration above the linear approach (e.g. an exposure reduction of ~30% if the concentration is reduced about 50%), i.e. the result is slightly more conservative than the ideal, linear approach but less conservative than the approach used by MEASE and ECETOC TRA.
All these models use the mass fraction as an indicator for concentration, although the molar fraction may be more appropriate in some cases.
Furthermore, the approaches described above only apply to liquid substances in some cases. Solutions of solids in liquids are considered to be beyond the scope in case of ECETOC TRA (v.2 and v.3). In case of MEASE solutions of solids in water are within the scope and give exposure estimates according to materials of very low dustiness. STOFFENMANAGER® does not discriminate between liquids and solids in solution but estimates only overall dust concentrations for solid products in case of version 4.5.

The EMKG-EXPO-TOOL does not use the concentration in a mixture for exposure estimations which may lead to overestimations of exposure in cases of mixtures.
The realistic connection between exposure and concentration of a substance is difficult to describe in a general way, as it depends to a high extent on substance and product characteristics. Especially in case of inhalation exposure the vapour pressure of the substance and its interaction with other components of the mixture are of high relevance. The vapour pressure above the product is directly related to the exposure estimate and thus, its implementation into the models influences the uncertainty of the model result.

Some general facts can be discussed: Inhalation exposure is determined by the vapour pressure of a substance. The vapour pressure of a substance in mixture can be described by Raoult's Law:

$p_i = x_i \cdot p_i^*$

p_i = partial vapour pressure of i above the mixture,
p_i^* = vapour pressure of pure i;
x_i = mole fraction of the component in the mixture

This law fits best for ideal solutions without much interaction between the molecules and in general it applies better to a component with a high concentration.
For substances with low concentrations Henry's Law may be better to describe the partial pressure above aqueous solutions:

$p_i = x_i \cdot H$

H = Henry constant
p_i = vapour pressure of i in mixture,
x_i = mole fraction of the component in the mixture

There are positive and negative deviations from Raoult's Law whose magnitude depends on mixture and concentration and can theoretically go up to three orders of magnitude. Positive deviations show mixtures, for which the attractive forces between molecules of the same kind (i.e. cohesion) are larger than between molecules of different kind (i.e. adhesion) – the molecules break free more easily from the mixture than they would do from the pure substance and the vapour pressure is higher than predicted by Raoult's Law. Examples are benzene/ethanol or water/ethanol[13].
Also negative deviations (e.g. chloroform/acetone[14]) and ideal cases (e.g. hexane/heptane, benzene/methylbenzene[15]) are possible – in these cases there will be an overestimation of the vapour pressure with the proposed modifiers.
Complex mixtures are possible, where no simple equation applies and it cannot be predicted how good reality is represented by the any of the used modifiers.

Dermal models

MEASE and ECETOC TRA v.3 use the same set of modifiers which is also implemented for inhalation exposure.

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[13] http://jcsu.jesus.cam.ac.uk/~rpc25/notes/chemistry/phase_equillibria/
[14] http://www.chm.bris.ac.uk/~chdms/Teaching/Chemical_Interactions/page_17.htm
[15] http://www.chemguide.co.uk/physical/phaseeqia/idealpd.html

The ECETOC TRA v.2 dermal algorithm does not include concentration modifiers.
For RISKOFDERM it is stated in the user guidance (TNO, 2006) that a linear dependency between exposure and concentration can be used, however, the parameter is not directly implemented into the tool and the model users have to use it externally, if it is wished.
A neglect of the substance concentration in the model algorithms may lead to a high number of overestimations.
Influence of concentration on dermal exposure is even less easy to describe than on inhalation exposure. Dermal exposure may not only depend on the vapour pressure / gas concentration of a substance but also, or even predominantly, on direct contact via splashes or contaminated surfaces whose behaviour is in turn influenced by adsorption properties of the estimated substance. Although ideal behaviour of all components suggests a linear dependence between concentration and dermal exposure (i.e. conservative modifiers in case of MEASE and ECETOC TRA v.3) no simple law of nature is known which can be used for a general description in this case.

Summary/Discussion

In summary, all models which include this parameter offer a high or high/medium input parameter quality (quantitative parameter), i.e. uncertainties due to assignment of a wrong category will - if they should happen - probably not be caused by model uncertainty.
The general accuracy of any of these approaches (linear vs. non-linear dependency; dustiness vs. vapour pressure for solids in solution) cannot be judged with the available information and is highly dependent on the exact composition of the assessed mixture.
However, it can be summarised that RISKOFDERM and the EMKG-EXPO-TOOL use the most conservative approach (i.e. no implementation of this parameter), which can lead to overestimations up to three orders of magnitude. ECETOC TRA, MEASE and STOFFENMANAGER® use conservative modifiers which are expected to show a higher tendency to overestimate exposure than to produce underestimations. Magnitudes of uncertainty in these cases cannot be finally assessed in these cases. However, overestimations up to three orders of magnitude (very small concentration) and underestimations up to one order of magnitude (if the vapour pressure above mixture equals the vapour pressure of the pure substance) are theoretically possible. Thus, overall the implementation of this parameter in the different models follows the conservative Tier 1 approach.

2.3.3 Use description

Almost all evaluated models include a general description of the activity (or activities) that should be assessed. As the correct assignment of this parameter is a central part of each model which also influences availability and influence of other parameters, it may introduce a high level of uncertainty.
As use descriptions are usually the same for inhalation and dermal parts of a model they will be discussed together.
In general, use categories implemented in STOFFENMANAGER®, RISKOFDERM and the EMKG control guidance sheets used for the EMKG-EXPO-TOOL are task

based, while the PROC codes implemented in ECETOC TRA and MEASE as well as the EASE use descriptions are process based, i.e. may include several sub-activities.

Inhalation and dermal models

The highest level of detail and thus, the highest parameter quality concerning the process description, offers the EMKG-EXPO-TOOL. It is however the only tool within this project that refers to external use categories (→ control guidance sheets) which have to be accessed manually by the user. To which extent this may influence the correct application of the tool is not known. No further information could be extracted from BURE about the usage of the control guidance sheets as they were not provided in the course of this exercise and no further comments concerning this issue were made by participants.
RISKOFDERM DEO units are considered to be of medium quality as well.
STOFFENMANAGER® task categories are considered to be of low(/medium) quality due to their vague definition of product amounts ("handling of large quantities") and a low level of detail. Some short examples are given only given in background literature (MARQUART ET AL., 2008). However, the most recent version of STOFFENMANAGER (version 5.0) in addition uses the PROC system, which is of medium quality, including a suggested link between handling categories and certain PROC codes.
The PROC system that is used by MEASE and ECETOC TRA v.2/v.3 takes a special role as it is a part of REACH and has been published by ECHA (ECHA (EUROPEAN CHEMICALS AGENCY), 2010b). Compared with other sets of task description the quality of the PROCs and their level of detail are at least medium. However, it has been reported by members of the advisory board (BAuA, Bojan, 2012; personal communication) with experience in the REACH process as well as during the BURE exercise that there are often lacks of clarity concerning the assignment of the correct category which sometimes leads to large differences between possible results. However, it is recognised that the PROC system is a quite special case in this context as there is – due to its relevance under REACH - much more knowledge about possible problems with its application than in case of the other handling categories. It cannot be excluded that e.g. STOFFENMANAGER® categories, if they were extensively used under REACH, would lead to similar difficulties.
Some additional information concerning underlying assumptions and necessary determinants are included in the ECHA guidance documents (e.g. the guidance on intermediates which gives more detailed information about PROC 3 (use in closed batch processes) (ECHA, 2010)). This information is however not always known to and/or used by registrants or downstream users during the assignment of descriptors.
The use descriptions of the different models are also one central point that has been identified in the eteam BURE (between user reliability exercise) as a major source of uncertainty. Many users feel unsure about the correct assignment (uncertainty during choice of parameter was reported). Moreover, there is also significant variability in the exposure results produced during BURE resulting from the choice of PROC. However, other types of use categorisation also showed considerable variability, i.e. it cannot be concluded in which way the established PROC system may be improved (less vagueness / higher level of detail) to reduce variation of the exposure estimates for one scenarios.
For RISKOFDERM less differences and difficulties during the choice of the use categories have been reported than for other tools. This may be due to the

comparably low number of categories (6 DEO units, low resolution) or the fact that many of the BURE situations have been assigned to a relatively widely defined DEO unit 1 (“mixing, filling, loading”). As STOFFENMANAGER® on the other hand does not show reduced variability related to the choice of use category it does not seem to be a general influence of task-based or process based use categorisations.
In some cases the observed variability seemed to be related to confusion about the difference between the task and process (situation: change of filters in a spray booth; some users assessed spraying). This again suggests that it is important to give clear advice on how the use categorisations in the different models should be interpreted, i.e. increase input parameter quality.
An additional type of use related parameter is the type of setting or scale of operations, which is implemented in MEASE and ECETOC TRA (both versions), partly implemented in the PROC system (PROC7 vs. PROC11) and allows for a discrimination between industrial or professional setting (i.e. skilled trade). This parameter is considered to be of low parameter quality, as it does not offer clear boundaries between both categories (high vagueness) and a low level of detail. This impression is supported by BURE, which indicates high uncertainty of the model users concerning this parameter and also noticeable variability for a number of situations. Depending on the situation both under- and overestimations can be induced by a wrong assignment of this parameter, which usually lie around one order of magnitude.

Summary/Discussion

There are very different sets of handling categories used in the tools evaluated in this project. Although each of the process/handling category systems bares some uncertainty it may be difficult in reality to decide in some cases if the origin of uncertainty can be found in the scenario, the documentation of the scenario or in the model itself.
The choice of the correct use description (EASE use pattern, PROC, DEO unit, STOFFENMANAGER® task description, external control guidance sheet) is always the centre of an adequate exposure assessment and deviations caused by the wrong assignment of a process or task category can usually be quite high (two or three orders of magnitude, over- and underestimations possible). For all models the choice of the process/task also implies some consequences concerning the applicability of other parameters (e.g. process temperature in case of MEASE). Therefore it is important to use detailed and unambiguous descriptions which minimise the risk of a wrong assignment of this parameter.
As for most model parameters it is essential that model users are familiar with the exposure situation they want to assess and know how to describe the different steps or parts of the important uses (e.g. use of a substance in paint may include application of paint, drying of paint, refilling of paint spray can etc.). Use maps for different industrial areas as they have been developed by sector organisations like AISE or IFRA may be used as a help in this process, i.e. tools which are able to reflect commonly known documents are expected to show lower uncertainties related to the correct assignment of process/task descriptions.
This aspect may have a positive influence on the uncertainty introduce e.g. by the PROC system and its limitations (see above).

Use maps usually also indicate the type of setting for all scenarios. However, no further information is given on what exactly distinguishes, as an example, the industrial scenario for roller application of adhesives from the professional one.
Furthermore, MEASE offers some guidance about metal specific uses and the corresponding PROC codes in its glossary which also is expected to decrease uncertainty related to the choice of use category.
However, corresponding effects could only partly be evaluated during BURE, as no specific comments were made by the participants concerning use maps and variation did not seem to depend on users' experience with the models or in general REACH. Familiarity with specific situations influenced the ease of translation into tool parameters. However, no clear influence on the variability could be determined.
The reflection of the use description within the models (i.e. initial exposure estimates or exposure scores) cannot be assessed within this work package.

2.3.4 Use rate/amount of substance

Another parameter whose applicability for exposure models is sometimes under discussion, and which therefore contributes to the uncertainty, is the amount of handled substance, which is closely connected with the use rate of a substance or product.

Inhalation models

Only the EMKG-EXPO-TOOL uses the amount of substance to describe the situation directly.
STOFFENMANAGER® offers task descriptions which include information about the expected amount of substance. MEASE and ECETOC TRA (v.2 and v.3) do not use this parameter.

Dermal models

Only RISKOFDERM offers the possibility to enter a freely selectable value for the use rate that is connected with the exposure estimate in a linear way. MEASE and ECETOC TRA (v.2 and v.3) do not use this parameter.

Summary/Discussion

General uncertainties that may arise from this parameter are often connected with possible dependencies. Situations which include the use of large substance quantities will require other technical equipment (application of more and other parts of machinery to mix, transport or use the substance) than situations with low substance quantities.
This may lead to an increased exposure due to the simple presence of higher substance amounts or various changes in the exposure situation. On the other hand, this may lead also to a decreased exposure because the distance between worker and source of exposure increases or other risk mitigation measures are present.
From this follows that there is certainly an influence of the amount of substance or the use rate on the exposure estimate but also the possibility to increase the uncertainty if a model is applied outside the boundaries of its database. As an example in case of RISKOFDERM this may lead to large overestimations for high

use rates of exposure as a linear dependency between use rate and exposure estimate is assumed. On the other hand it is indicated within the RISKOFDERM tool if the ranges indicated by the datasets used for model fitting are exceeded, i.e. situations which are outside this range can be avoided.
In case of STOFFENMANAGER® and the EMKG-EXPO-TOOL the evaluation of possible uncertainties is less straightforward and the magnitude of uncertainty due to the model inherent reflection of this parameter cannot be assessed. However, the model user should aim to describe his specific exposure situation as detailed as possible to minimise the risk of neglecting unknown dependencies (e.g. affecting RMMs).
Uncertainty induced by the assignment of a wrong category is around one order of magnitude for the EMGK-EXPO-TOOL and STOFFENMANAGER and can go up to three orders of magnitude for RISKOFDERM due to its linear approach (over- and underestimations possible). However, for the EMGK-EXPO-TOOL and RISKOFDERM the parameter definition is quantitative, i.e. wrong input will probably not be caused by model uncertainty.

2.3.5 Exposure or use duration/frequency

It is often not the common case that at a workplace the same task or process is done by one worker for the whole 8 hour shift. For this reason the exposure or task/process duration are often important exposure parameters. “Exposure duration” on the one hand means that a worker will only be present at a workplace for some time, while “task/process duration” on the other hand means that an employee is present for a limited time although the task/process may be running for the whole day.
While ECETOC TRA refers to “activity durations”, the EMKG-EXPO-TOOL and MEASE use the term “exposure duration”, STOFFENMANAGER® refers to “task duration” and RISKOFDERM to “scenario duration”.
However, in all models within this project the term “task/process/activity/exposure duration” is linked with the assumption that the employee who will be assessed is actually doing this task/ process for the indicated time, i.e. the results in ppm, mg/m^3 (inhalation) or mg/kg/day (dermal) refer to individual, daily average exposure corresponding to the indicated (task/scenario/activity/exposure) duration per day.

Inhalation models

In case of inhalation models the implementation of this parameter still bares some uncertainty. However, the connection between air concentrations and emission time is more intuitive than it is for dermal exposure.
For inhalation duration modifiers have been implemented for ECETOC TRA (v.2. and v.3), MEASE and the EMKG-EXPO-TOOL. While ECETOC TRA and MEASE use the same set of modifiers consisting of four categories (240-480 min, 60-240 min, 15-60 min, <15 min duration correspond to 0, 40, 80, 90% exposure reduction), the EMKG-EXPO-TOOL only offers a refinement of the exposure estimate in case of very short durations (< 15 minutes, resulting in a factor of 10 lower exposure estimates). Both approaches are expected to be conservative, as they suggest exposure reductions below the linear approach, i.e. a slight inhomogeneity of the emission per time should be compensated.

For a complete risk assessment it has to be taken into account that exposure may be fluctuating and peaks of exposure may be possible which are much higher than full-shift average values. This peak exposure is relevant in case of acute effects. However, not for all models it is within the scope to be estimated:
According to its glossary MEASE provides 8h full shift average results, i.e. time weighted average values. The same applies to ECETOC TRA v.2/v.3. ECETOC TRA v.3 also estimates peak exposures which may arise during a 15 minute time interval. The modifier used for this peak value is based on a combination of experimental data and scientific judgement and still includes some uncertainty (ECHA (EUROPEAN CHEMICALS AGENCY), 2010a). However, it offers at least the opportunity to discuss the possibility of acute hazard due to short time exposure peaks. Moreover, the literature cited in ECETOC documentation TR114 on this topic suggests, that this approach is sufficiently conservative (smaller factors suggested for task based uses and exposure estimates based on the saturated vapour pressure).
STOFFENMANAGER® estimates exposure for 8 h task durations, however, as it is a task based model this result is expected to be equal to the desired peak exposure and can be seen as a worst case. Version 5.0 of the model in addition allows for the estimation of a time weighted average using user inputs about the durations of different tasks involving a certain substance. The same applies to the EMKG-EXPO-TOOL, which is also a task based model (see also ECHA guidance R14).
In cases where only the time-weighted average exposure for a full working shift is estimated users may refer to ECHA guidance R14 (ECHA (EUROPEAN CHEMICALS AGENCY), 2010a) which offers some information about possible extrapolation to short-term exposure values on the basis of full-shift values.
The connection between average exposure and peak exposure is also influenced by the task frequency per day, i.e. how many exposure events of which length are responsible for the estimated average. This parameter is not implemented in any of the models. However, the relation between exposure pattern and average or peak estimate is not trivial and the specific connection between exposure pattern and risk is influenced by a number of factors (e.g. concentration vs. dose-dependent toxicity). Therefore this kind of feature is probably not compatible with the Tier 1 approach.

Dermal models

Exposure or task/process duration are parameters, which are sometimes related with the task frequency, i.e. the number of corresponding activities / exposure events per day.and whose usefulness and correct implementation especially into dermal exposure models is often discussed.
In case of RISKOFDERM duration of exposure is implemented via a linear dependency (exposure ~ duration). In case of ECETOC TRA v.3 and MEASE dermal exposure is modified by a set of factors (240-480 min, 60-240 min, 15-60 min, <15 min duration correspond to 0, 40, 80, 90% exposure reduction) which result in exposure estimates above the ideal, linear approach.
Moreover, contact frequency is implemented in the dermal MEASE part (parameter “contact level”; extensive >10 events per day, intermittent 2-10 events/day, incidental < 2 events/day and no dermal contact).
According to Vermeulen et al. (2002) the contact frequency should be used as dermal model parameter when the exposure is event based and the agent penetrates the skin instantly while exposure duration should be used in case of continuous

exposure and slow skin penetration of the substance. An experimental basis for this recommendation is however not described.

Concerning the influence of task duration there exist some studies about metals (HERAG, 2007) which indicate a saturation of the skin already after a short time period in some cases for dermal exposure. However, for most substances and/or exposure situations only limited information about the correct implementation of this parameter is given. This is also recognised by Vermeulen et al. (VERMEULEN ET AL., 2002) who state that the current level of knowledge about the effect of concentration of contaminant on skin, duration and frequency of exposure, variability and uptake is limited in many areas, although these factors are very or even extremely important.

Moreover the understanding of the influence of exposure duration is also crucial for an appropriated design of exposure measurements, which are sometimes the basis of an exposure model.

If a model is based on samples with a short sampling time, which is partly true for RISKOFDERM, this will lead to overestimations of exposure, if the exposure estimate is extrapolated to longer durations, as saturation effects are usually not taken into account for this procedure. However, RISKOFDERM provides clear information about exposure durations of underlying samples, i.e. the user is able to decide himself, if his exposure situation lies within the model's scope.

If a model is based on samples with longer exposure durations the testing strategy will be important: If several samples, which have been collected during a work shift, are added, this may lead to overestimations, as saturation processes are not covered by this approach. If an average of several samples has been used to estimate time weighted 8 h exposures, as it has been made in case of MEASE, this effect should be minimised. However, it still cannot be decided to which extent commonly used modifiers (see MEASE/ECETOC TRA v.3) are able to reflect the decreasing dermal load at shorter durations in the exposure model.

Moreover, saturation processes, the relation between time and dermal load as well as the maximum dermal load, are expected to be substance dependant. One approach to take this into account is used by ECETOC TRA v.3 which only allows for an application of the duration modifiers in case of high and moderate volatility liquids and non-dusty solid substances. Another substance property that may be of importance is the viscosity of liquids, which may influence the removal of substances over time due to hand washing, touching of non-contaminated objects etc. However, this parameter is not used for in combination with duration in any of the models.

Summary/Discussion

Overall it can be summarised that the implementation of duration in dermal exposure models may be applicable in some cases, but users should be aware that the knowledge base for this parameter leaves room for improvement. Especially situations which are not covered by the model approach and/or database may show an increased level of uncertainty including the possibility of over- as well as underestimations of unknown magnitude of actual exposure.

For inhalation the situation is slightly easier. However, there is still some uncertainty involved. The EMKG-EXPO-TOOL, ECETOC TRA v.2/v.3 and MEASE all use a set of modifiers which is expected to produce mostly conservative results with small magnitudes of uncertainty concerning underestimations and overestimations that can go up to large orders of magnitude. The REACH part of STOFFENMANAGER® version 4.5 does not use this parameter, which introduces some uncertainty, but

however will lead to conservative results. In the REACH part of STOFFENMANAGER® version 5.0 the entered information about exposure duration is used to estimate daily average concentrations.
All models include maximum durations of 8 hours (one normal work shift). Lower values lead to 8 hour average exposure estimates for the corresponding duration.
The parameter quality is high (quantitative) for all models which use this parameter. Erroneous duration input, which may lead to small magnitudes of uncertainty for ECETOC TRA, MEASE and the EMKG-EXPO-TOOL and up to large magnitudes in case of RISKOFDERM, will therefore probably not be caused by model uncertainty.

2.3.6 Body areas

Dermal models

Affected skin areas are an important parameter for dermal exposure, at least if the estimate is based on the combination of per area loading and skin surface (MEASE, ECETOC TRA). Most dermal models (MEASE, ECETOC TRA v.2/v.3) only refer to hand exposure. RISKOFDERM, the only model which also estimates body exposure, states that the level of uncertainty is higher for body exposure than for hand exposure, as an extrapolation procedure is often needed to derive a complete dermal loading with the help of various sampling patches (WARREN ET AL., 2006).
Implemented skin areas are listed in Table 2.8.

Table 2.8 Skin areas implemented in different tools (cm^2).

RISKOFDERM	ECETOC TRA	MEASE	EASE	body part
	240	240		one palm of hand
	480	480		both palms of hands
820	960	960*		both hands
	1500	1500*		hands and one forearm
	1980	1980*	2000	hands and both forearms
18720				body except hands
* not implemented for liquids and aqueous solutions				

Unlike the hands the body is usually covered by clothing which is expected to reduce some exposure types (see also Chapter 2.3.8). Moreover, depending on the general use and the exposure situation, the body is often much less involved in exposure generating activities than the hands which are directly used to wipe, spray or handle contaminated objects. Thus, it is sometimes assumed that body exposure can be neglected in comparison to hand exposure.
This assumption is partly supported by literature:

- Creely et al. (CREELY AND CHERRIE, 2001) describe that hands contribute often 50% of the total body exposure in case of pesticides, sometimes their contribution goes up to 90%. If this assumption is correct the neglection of body exposure will only induce exposure underestimations of small magnitude.
- Popendorf et al. (POPENDORF ET AL., 1995; POPENDORF, 1995) describe measurements which show contributions of the hands between ~12 (high pressure spray) and >90% (mop), which would also lead to underestimations up to one order of magnitude.

In case of ECETOC TRA and MEASE it is also differentiated between different parts of the hands (fingers, palms etc.). A homogeneous distribution of exposure on the skin surface is assumed and the affected surface areas are used to estimate the overall dermal load. On which basis parts of the hands are assigned to a certain PROC is not documented. It is expected that this approach also includes some uncertainty. However, an exact estimation of the expected magnitude of uncertainty is not possible.

Summary/Discussion

In summary most dermal models concentrate on hand exposure, which is – as the cited examples above show – only valid for certain processes/tasks and may therefore lead to underestimations in some cases. A general assessment of expected magnitudes of uncertainty is not possible, as it depends on the exposure situation as well as assumptions concerning protective clothing. While according to a comparison of skin areas underestimations may go up to two orders of magnitude the available literature suggests only small magnitudes whose exact dimension depends on the assessed exposure situation.
RISKOFDERM is the only model within this project which takes into account body exposure – which on the other hand may lead to overestimations due to neglected protective clothing (see Chapter 2.3.8). This aspect is therefore reflected in RISKOFDERM in a more conservative way.
To which extent assumptions concerning the relevant body areas (fingers, palms etc.) are correct cannot be assessed.

2.3.7 Localised controls

The localised control measure most commonly used in Tier 1 models is ventilation, i.e. LEV or other modifiers influencing the local air change rate. However, some models also use other measures, e.g. the level of containment or suppression techniques.

Ventilation

Inhalation models

The least detailed description of the LEV is found in ECETOC TRA, where only “LEV” or “no LEV” can be chosen. In the documentation TR107 a reference to a HSE guidance document can be found where more detailed definitions of possible equipment designs are available (HSE, 2011).
ECETOC TRA v.3 offers also the possibility to use some options concerning general ventilation, for which usual air change rates are given in the corresponding documentation TR 114 (ECETOC, 2013).
STOFFENMANAGER® uses general ventilation as well as LEV and the combination of both. However, the quality of the parameter definition is similar to other models without further information on the required design being available in the tool itself or the corresponding publications.
Moreover, STOFFENMANAGER® includes information about the room size, but without further details about the ventilation systems which may facilitate a correct assignment of this parameter.

MEASE uses confidence intervals which are able to reflect the variability of the underlying datasets (three categories for each local control): upper & lower confidence limit, average with median confidence). Subcategories of ventilation systems are also possible (exterior/ integrated LEV) as well as general ventilation. Exact setup and construction details of an appropriate use of the different measures are not provided. However, a short definition of each possible control measure can be found in the MEASE glossary.
The EMKG-EXPO-TOOL in contrast has as well only short descriptions and definitions of LEV and general ventilation implemented but also uses the external control guidance sheets which offer quite detailed descriptions of the expected workplace design.
Outdoor application, which also influences the current air change rate but is even less easier to judge, is an option implemented in ECETOC TRA and STOFFENMANAGER®. It depends on natural conditions like wind strength which cannot be regulated mechanically. Thus, this parameter is expected to show higher uncertainties than application of mechanical ventilation systems.
It cannot be assessed to which extent different local control measures may influence each other. Nevertheless STOFFENMANAGER® and ECETOC TRA v.3 include options which combine LEV and general ventilation, in case of STOFFENMANAGER® on the basis of the fitting procedure, in case of ECETOC TRA by multiplication of efficiencies.

Dermal models

Similar to the inhalation part of ECETOC TRA, only “LEV” or “no LEV” can be chosen for the dermal exposure assessment. In case of ECETOC TRA v.2 LEV can also be read as “containment” for dermal exposure, a parameter that is not directly implemented in any of the ECETOC TRA versions (only indirect via the PROC system; PROC1 = closed process). For ECETOC TRA v.3 this way of interpretation is not mentioned anymore (ECETOC, 2009, 2013). “General ventilation” does not affect the dermal exposure estimate.
RISKFOFDERM offers “good ventilation / LEV” for DEO unit 1 (filing, mixing, loading) and “airflow away from the worker” for DEO unit 4 (spray), i.e. it is not clearly discriminated between LEV and general ventilation. Further localised control measures are not implemented.
The dermal exposure estimate of MEASE is not influenced by separate parameters describing localised control measures, however, some information about the level of control is included in the implemented EASE handling descriptions (e.g. level of containment) and some of the PROCs which define the affected skin area (e.g. PROC1: closed system).

Other localised controls

Inhalation models

The EMKG-EXPO-TOOL and STOFFENMANAGER® offer parameters which describe the level of containment (control approach = “containment” in case of the EMKG-EXPO-TOOL, “containment”/”containment of source and LEV” in case of STOFFENMANAGER®). In addition, for MEASE and ECETOC TRA v.2/3 some information is included in the use description (PROC system).

Furthermore, STOFFENMANAGER® and MEASE include the option “Segregation” (“Separation” in case of MEASE) which represents the possibility to separate the worker from the source of exposure.
Other suppression techniques are implemented in MEASE (wet suppression, capture sprays, generic suppression) and STOFFENMANAGER® (use of product that reduces emission).
MEASE does not allow for a combination of several localised controls.
Short descriptions of the corresponding measures are available in the glossary in case of MEASE and the as far as the PROC system is concerned in the definitions according to REACH guidance R12. Detailed information about setup and construction details for specific situations are only available for the EMKG-EXPO-TOOL in the corresponding, external control guidance sheets and for ECETOC TRA in the HSE guidance on ventilation systems (HSE, 2011).

Dermal models

Information about the level of containment is implemented via the use description in case of ECETOC TRA v.2/3 (see above) and MEASE (via EASE handling categories).
RISKOFDERM also includes the parameter “Segregation” for DEO unit 4 (spraying).
As for the inhalation models, short descriptions of the corresponding measures are available in the glossary in case of MEASE in the definitions according to REACH guidance R12. RISKOFDERM offers a short description via pop-up messages within the tool.

Summary/Discussion

All evaluated models offer to a certain extent the possibility to enter information about the type and strength of ventilation. In addition, some models also include the option to describe other localised controls, e.g. containment or suppression techniques. The overall number of options for control measures varies largely.
The input parameter quality varies as well. However, most models do not offer details concerning appropriate design and set-up of the suggested control measures (exeption: EMKG-EXPO-TOOL offers external cgs).
Most of the models do not give a direct (i.e. implemented) help on the choice of these parameters considering construction details, i.e. how is the ventilation system intended to look like to REACH the assigned efficiency. However, short descriptions and some examples for the measures implemented are given in the MEASE glossary and small pop-up messages used in RISKOFDERM. Detailed information about intended design of ventilation systems is available in case of the EMKG-EXPO-TOOL in the control guidance sheets (see also Chapter 2.5.2) and for ECETOC TRA in the HSE guidance on ventilation systems (HSE, 2011).
In case of ECETOC TRA (v.2 and v.3), STOFFENMANAGER® and RISKOFDERM efficiencies for the implementation of localised control measures depend on the use category while in case of the EMKG-EXPO-TOOL and MEASE identical efficiencies for all use categories are assigned.
Concerning the implementation and background of the various measures for STOFFENMANAGER, RISKOFDERM and MEASE underlying datasets are available, which have been used in the general fitting procedure (STOFFENMANAGER, RISKOFDERM) or to derive confidence intervals reflecting

the efficiency distribution of the available measurements for one control measure (see also above, MEASE (inhalation), for evaluation of datasets see section 2.2.1). The dermal MEASE part is based on 90th percentiles of a collection of measured data, thus, this percentile is considered also to reflect the conservatism of the included control measures (closed system in EASE handling categories).

For ECETOC TRA v.2/3 and EMKG-EXPO-TOOL no specific datasets have been reported, i.e. a higher level of uncertainty concerning the knowledge base is expected to be present.

Efficiencies are presented as single numbers without percentile distribution in case of ECETOC TRA v.2/3 and EMKG-EXPO-TOOL while confidence intervals can be chosen in case of MEASE (inhalation). STOFFENMANAGER® and RISKOFDERM include the option to choose different percentiles for the final exposure estimate which will also reflect the level of conservatism used for RMM efficiencies (see also section 2.3.9, presentation of results).

As an example, efficiency values for a LEV lie between 75 and 95% in case of ECETOC TRA (v.3, PROC dependent), between ~60 and 75% in case of RISKOFDERM (DEO unit 5 vs. DEO unit 4), and between 78 and 84% in case of MEASE (upper and lower confidence level). For the EMKG-EXPO-TOOL no option without any measure is possible, however, the difference between “general ventilation” and “local exhaust ventilation” already refers to 90% exposure reduction. For STOFFENMANAGER®, exact efficiencies or exposure reductions depend on the specific exposure situation, but some test calculations revealed efficiencies around 50%. Thus, for this parameter STOFFENMANAGER®, MEASE and RISKOFDERM tend to give more conservative estimations of the LEV efficiency than ECETOC TRA or the EMKG-EXPO-TOOL. A reason for this may be, that the tools offering lower efficiencies are at least partly based on sets of measured data which may include also workplaces where the GOHP is not taken into account. However, this is only a general tendency and may vary depending on the specific process or task.

“General ventilation” results in efficiencies of 30 and 70% for ECETOC TRA v.3 and 17, 43 or 61% for MEASE. For STOFFENMANAGER®, exact efficiencies or exposure reductions depend again on the specific exposure situation, but some test calculations revealed efficiencies around 50%. For the EMKG-EXPO-TOOL the exposure reduction due to general ventilation cannot be determined as no control level without any control is implemented. Although a clear conclusion about the level of conservatism of the different models is difficult due to the different options within the models, MEASE seems to give more conservative results than ECETOC TRA and even than STOFFENMANAGER®, taking into account that the lower confidence limit is recommended in case of MEASE.

“Wet suppression techniques” are implemented with an exposure reduction of 77, 83 or 88% in case of MEASE and again around 50% in case of STOFFENMANAGER® (use of product which reduced emission) which means that in this case STOFFENMANAGER® gives more conservative results.

For “separation of worker” MEASE offers 71, 87 and 94% efficiency while STOFFENMANAGER® uses 10% or ~80%, depending on the presence of a separate air supply, i.e. overall more conservative exposure reductions than MEASE.

Although it is not possible at this point to evaluate the accuracy of the implemented efficiencies it is recognised that each exposure reduction method which cannot be described within the model algorithm in an appropriate way will lead to an overestimation of exposure. Therefore the uncertainty of these models is increased, but in a conservative way which is consistent with a tier 1 approach.

Risk management measures in general have also been identified as a source of variability in the BURE exercise. However, this is not necessarily related to increased vagueness or a low level of detail. In some cases fluctuation was caused by allocation of RMMs which were not present in the scenario description, i.e. errors or user expert judgement may have been involved. Although in general quantitative parameter definitions, e.g. via ventilation rates, suggest a lower level of uncertainty in the overall exposure estimate it was recognised by participants of BURE that in the absence of measured ventilation rates the correct assignment of RMMs may be difficult, i.e. a decreased vagueness concerning the input parameter may not be able to reduce overall uncertainty in these cases.

2.3.8 Personal protective equipment

This section includes a short summary of available literature on personal protective equipment. Further details can be found in Appendix 3.

Inhalation models – respiratory protection

Respiratory protection as an input parameter is implemented in STOFFENMANAGER®, ECETOC TRA v.2 and v.3 and MEASE. While MEASE and ECETOC TRA use a description based on assigned protection factors (MEASE: APFs 4, 5, 10, 20 or 40 corresponding to efficiencies of 25, 20, 90, 95, 97.5 %; ECETOC TRA v.2/v.3: APFs 10, 20 corresponding to efficiencies of 90 and 95%), Stoffenmanger uses a general description of the different protection types (“filter mask”, “Full face powered air respirator” etc.) whose influence is implemented via the underlying datasets. Efficiencies depend on the substance types (volatile/low volatile; powder/comminuting activities) for which different model equations were derived (SCHINKEL ET AL., 2010) and the type of protective equipment and range from ~40-90% efficiency.

The APF is defined as the level of respiratory protection that can realistically be expected to be achieved in the workplace by 95% of adequately trained and supervised wearers using a properly functioning and correctly fitted RPE and is based on the 5th percentile of the Workplace Protection Factor data (WPF: level of protection actually experienced by an individual while working in a hazardous environment (CLAYTON, 2012)[16]). APFs have been shown sometimes to lead to an underestimation of the risk (BROUWER ET AL., 2001). They are partly based on professional judgement and safety factors which are applied to the measured WPF. Therefore significant differences between countries are possible (CLAYTON, 2012). An example is a full face mask with a P3 filter (FFM, P3) for which in Sweden an APF of 500 is assigned while Germany only uses 400, UK 40 and the United States 50.

Additional information concerning the safety of APFs has been published by various authors (see Appendix 3) who also describe some uncertainties in the approach of APF derivation and in general in the efficiency of respiratory protection (BELL ET AL., 2012; CRUMP, 2007; NELSON ET AL., 2000; NICAS AND NEUHAUS, 2004; PASZKIEWICZ, 2012).

In summary it cannot be assessed which influence the general approaches (fixed vs. situation dependant RPE efficiency) will have on the uncertainty.

[16] http://www.isrp.com/europe/docs/2012_eur_spring_meet_paper_clayton.pdf

The input parameter quality of all models is comparably high, as APFs are usually documented, quantitative parameters and STOFFENMANAGER® uses unambiguous, descriptive input parameters and deviations induced by a wrong assignment of categories are expected to be small.
However, as has been discussed above, APFs are uncertain in themselves.. Based on the examples listed above deviations may REACH two orders of magnitide, depending on country and type of RPE. However, as the basis for APF derivation is conservative (5th percentile of WPF) it is expected that the probability of overestimations of exposure is higher than for underestimations.
Of course the publications listed in Appendix 3 are, strictly speaking, not model related uncertainty. However, it should be taken into account during model development and model use that these values, which are given by the producers and distributors of respiratory protection, are not fixed and bare a certain level of uncertainty which may REACH one or even two orders of magnitude (see publications listed above).

Dermal models – gloves

The efficiency of clothing and gloves as personal protective equipment is an often discussed issue. In the evaluated models the efficiency of clothes and gloves are considered differently. While ECETOC TRA v.2 and RISKORDERM do not offer a parameter related to protective clothing or gloves, MEASE uses 90% for gloves made of chemically resistant material and ECETOC TRA v.3 includes different categories between 80 and 95%, depending on the level of training and supervision a worker equipped with chemically resistant gloves will experience. No detailed description on the correct handling or the requirements for certain training levels are given in the model guidances.
The choice of efficiency of clothes and gloves will influence the exposure estimate, and thus, also the uncertainty of the exposure estimate.
Within the BURE exercise considerable variability was observed concerning the assignment of this parameter where different glove efficiencies are possible depending on the level of training (i.e. ECETOC TRA v.3) while for MEASE, the model offering one glove efficiency, showed low variability related to this parameter. However, a conclusion concerning the parameter quality cannot be drawn from BURE, as no information about the level of training was provided for the examples situations.
There is some information and experimental data published that includes evaluation of the materials (break-through times) and personal behaviour and training. However, the results and their interpretation differ (BROUWER ET AL., 2001; CHANG ET AL., 2004; CHERRIE ET AL., 2004; CREELY AND CHERRIE, 2001; EC (EUROPEAN COMMISSION), 2003; EFSA, 2008; GARROD ET AL., 2001; JRC, 2007, 2010; LECHTENBERG-AUFFARTH AND RUHL, 2007; PACKHAM, 2006).
An evaluation of the available publications shows, that reported efficiencies for gloves but also coveralls are highly variable (38-99% efficiency). The efficiency depends on the substance material combination, the correctness of choice as well as on the personal behaviour of the worker. Values suggested as default in public literature are often not or only partly supported by experimental results. Several authors indicated that the protection factor that may be reached depends to a high extent on the experience and training of the exposed workers. Although theoretically very high protection factors can be reached (up to 99.7 % according to Creely and

Cherrie (Creely and Cherrie, 2001)) misuse may reduce this protection very much (below 40%), which corresponds to possible uncertainties up to three orders of magnitude. Therefore an accurate description of gloves and their efficiency highly depends on a detailed definition not only of the used material but also of the necessary worker behaviour, an aspect which is only taken into account to some extent by ECETOC TRA.

For none of the evaluated models experimental data is cited that has been used for the assignment of default efficiencies. However, a comparison with the publications described above shows, that the efficiencies implemented in the models are expected only to be valid if a certain amount of good occupational praxis is present and the glove material is chemically resistant. It is mentioned for MEASE as well as for ECETOC TRA, that the glove material should always be chosen on the basis of the substance properties, i.e. be chemically resistant. The lowest glove efficiency in case of ECETOC does not mention any necessity to advise workers on the correct use of gloves, which suggests the possibility to underestimate exposure (lowest reported efficiency in literature: 38%, i.e. small magnitude of uncertainty). However, not for all publications information about the appropriateness of the glove material is available, i.e. there is a certain probability that this low value is caused by too low break-through times.

No specific advice is given by any of the model documentations or manuals on the correct use of gloves (what is “basic training”? etc.).

Protection by the use of coveralls is not implemented in any of the models, but this is only relevant in case of RISKOFDERM, as only this model takes into account potential exposure to the whole body. The neglect of coveralls or normal clothing as a protective influence will often lead to an overestimation of exposure. However, only small magnitudes are expected which depend on the exposure distribution between body and hands and the final efficiency of the protective clothing.

Overall it can be summarised that glove efficiency is a parameter with a comparably poor knowledge base for most substances. Although break-through times are often documented this usually cannot be used for the estimation of a protection factor or efficiency. The magnitude of uncertainty of the exposure estimate is expected to be small or medium (95% glove efficiency assumed but 38% could be correct). As most exposure reduction values this parameter is also substance and situation dependant: As an example, in cases where corrosive substances are handled the gloves are usually acid-resistant and skin contamination is – if it is not avoided in the first place - likely to be discovered quickly due to the local effects. This can be used as an indication of the protection level reached by the application of gloves. However, this observation cannot be used to derive a quantitative exposure reduction value. Moreover, it is considered to be likely that exposure to (inorganic) solids is prevented more efficient than exposure to liquid substances or mixtures. However, underestimations of exposure cannot be excluded if no detailed description on the required handling of gloves corresponding to the assigned efficiency is offered.

2.3.9 Presentation of results

Another issue concerning uncertainty is the correct interpretation of the results. Depending on the presentation of the exposure estimate within the tool, its quality and corresponding ambiguousness some uncertainty may appear if the result is interpreted in a way that was not intended by the model developers (e.g. wrong unit, percentile).

There are three different variants found amongst the tools, which will be discussed together for dermal and inhalation models due to large overlaps: Single value exposure estimates, exposure ranges and exposure distributions which offer the option to choose different outputs based on certain percentiles.
The EMKG-EXPO-TOOL offers exposure ranges and expects the user to select the higher border value for a conservative risk characterisation. It is documented in the tool that this border should be chosen, however, there is a certain, not quantifiable possibility that some users may misinterpret the result. It is not documented which percentile the model results are intended to reflect, i.e. with which level of conservativeness the model claims to estimate exposure situations. Thus, the uncertainty, i.e. the probability for misinterpretation of the results, is comparably high.
Exposure estimates of ECETOC TRA v.2 and 3 as well as estimates provided by MEASE are point estimates (deterministic models). They are designed to represent conservative estimations and often leave – as they are given as discrete values – not much room for the choice of result.
The estimates are intended to represent the 75th percentile of the 8h value for ECETOC TRA (see TR114) and approximately the 90th percentile for MEASE (dermal exposure and inhalation exposure for PROCs 21-27a[17]). Inhalation exposure estimates for MEASE in case of PROCs 1-20 are based on ECETOC TRA v.2 results. However, as MEASE and ECETOC TRA have different scopes and different options to refine the exposure estimates no simple statement about these values in MEASE and the point on the exposure distribution they should represent is possible.
In contrast to the other models, RISKOFDERM and STOFFENMANAGER®, which are fitted to a set of measured data, are intended to represent actual workplace exposures and different percentiles which can be assigned to different levels of conservativeness can be estimated. This approach decreases the general uncertainty, as it aims to stay closer to reality and moreover gives clear information about the applicable percentile. However, it also increases the possibility to underestimate exposure due to the choice of a too low percentile.
To ensure a sufficient level of protection, for STOFFENMANAGER© advice is given by Tielemans et al. (TIELEMANS ET AL., 2008a) to choose the 90th percentile as a reasonable worst case estimate if average input parameters are used, which may vary within a broad scenario. For conservative input parameters the 75th percentile as a reasonable worst case is suggested. Moreover, in the STOFFENMANAGER© tool (v.4.5) the conservative 90th percentile is given as the default result of an exposure assessment and only by clicking the distribution-icon beside it the user is able to see and use other percentiles (50th, 75th, 95th percentile results are shown in a pop-up window together with an illustration of the exposure distribution).[18]
However, no similar suggestions or defaults are given for RISKOFDERM.
For all tools information about a certain percentile that should be reflected can only be useful if additional documentation about the underlying data or information is available (90th percentile of which basis?), which is the case for RISKOFDERM, STOFFENMANAGER® and the dermal and partly also the inhalation part of MEASE (PROCs 21-27).
For ECETOC TRA v.2 and 3 some information about metal related exposure data is available, however, no direct connection between the measured samples and the model estimate is given.

[17] PROC 27b derived by scientific judgement, other PROCs adopted from ECETOC TRA v.2
[18] In the REACH part of STOFFENMANAGER© v. 5.0 the user is able to chose also other percentiles than the 90th as default result.

A distinction is often made between task based and process based exposure estimates (see also Chapter 2.3.3). ECETOC TRA and MEASE are intended to provide process based results which may include several sub-activities per process (e.g. sampling and maintenance in case of PROC2 “Use in closed, continuous process with occasional controlled exposure”) while the EMKG-EXPO-TOOL, RISKOFDERM and STOFFENMANAGER® are intended to give task-based exposure estimates. Moreover ECETOC TRA v.3 provides so-called peak exposures which are intended to reflect fluctuations in the emission process as well as the concentration of a substance in the air.
It is usually described in the corresponding model documentations or manuals which of the two options (task vs. process) is applicable for a certain tool.
In this context, some uncertainty may also be caused by a lack of information about the number and types of tasks which define a certain process and the time, certain tasks should need (or should not exceed) in order to ensure that the model estimates are valid. Some information is given in the PROC code definitions in ECHA guidance R12 which refers mostly to the type of tasks included in a certain PROC. Task frequencies or durations are neither offered by this guidance nor by one the models using process based use descriptions and model estimates. However, it is on the other hand also possible, that their introduction would introduce a higher level of uncertainty due to a lack of experience and knowledge of the model users concerning these aspects (see Chapter 2.3.5).
BURE results did not show less variability for task based or process based models. However, some confusion concerning the difference between task (e.g. situation 7: changing filters) and overall workplace (in this case a spraying booth) seemed to be present.
It is not known to which extent the misinterpretation of task or process based use descriptions and thus, exposure estimates, may influence the overall model uncertainty.
All dermal models within this project only estimate external exposure.

Summary/Discussion

In summary there is always a certain possibility that results are misinterpreted in some way. However, for all models it is documented somehow how the user is intended to use the results of an exposure estimation. Thus, the magnitude and relevance of the resulting uncertainty is expected to be only small.
This aspect of uncertainty is also connected to the model input parameters, as those have to be communicated under REACH and have to be interpreted correctly in order to apply the exposure scenario to the corresponding workplace (see also section 2.6).

2.3.10 Resolution and size (level of detail) of exposure models

Resolution of exposure models

In this chapter the resolution of the evaluated exposure models and its impact on model uncertainty will be discussed. Real life exposures are usually continuous data which can be any positive number. In contrast to this exposure models, especially tier 1 approaches, try to simplify this by a categorisation of parameters (e.g. vapour pressure may be categorised into three volatility ranges which result in three different exposure estimates).

The lower the number of categories per parameter, i.e. the resolution (ZEIGLER ET AL., 2000) is, the higher may usually be the uncertainty of the exposure estimate as the assigned exposure ranges are expected to be broader (due to their lower number) and it is more likely that the upper border of this range, which will usually be used for risk assessment, will be far away from the actual exposure level. The magnitude of uncertainty reached due to categorisation approaches is reflected in the relation between two neighbouring categories or their assigned exposure results, respectively (e.g. if a substance has a vapour pressure only slightly above the lower border of a volatility category, the assignment of this category may lead to deviations almost as high as it would be for a substance of lower volatility which would be assigned to the higher category by error, see Chapter 2, short evaluation matrices).[19] If a parameter does not influence the exposure estimate its categorisation/resolution obviously does not increase the uncertainty and is therefore not discussed in this section.

A summary of all input parameters for each tool and the corresponding number of output categories[20] is given in Table 1-6 in Appendix 2.

To enable a comparison of the resolution, parameters present at least in two of the evaluated models have been collected in Table 2.9. Within one parameter, the model (inhalation and dermal) with the highest resolution has been marked green while the model with the lowest number of categories has been marked yellow. If the parameter was not implemented in the corresponding model, the cell was marked light blue.

It can be seen that there are some parameters which show comparably small differences concerning the number of output categories for the different models (e.g. process temperature (3-4 categories)) while on the other hand there are also parameters which span a wider range of category numbers (e.g. process description (3-15 categories).

These differences depend in some cases on the number of different techniques covered (e.g. different types of RPE) and the level of detail used for the definition of the categories, e.g. differentiation of use descriptions.

There is also a number of parameters which are described in a not categorised way in at least one of the models (vapour pressure, duration, concentration, use rate). This approach obviously leads to a very high resolution compared to the categorising models, therefore this contribution to the overall model uncertainty is low. However, there may on the other hand be some uncertainty introduced by the equation used to describe the relationship between the input parameter and the exposure estimate. As an example, a linear dependency between concentration and inhalation exposure

[19] This aspect interacts with the definition of the input parameter: For input parameter definitions with a high vagueness more categories will not necessarily mean a lower overall uncertainty as the assignment of the refined output category may be compromised by a false choice of the input parameter. However, this interaction also depends very specifically on the individual parameter definition (e.g. dustiness categorisation with examples (like fluor/ pellets (two categories) vs. like flour/ like salt/ pellets (three categories) or with vague, undefined descriptions (fine powder / powder / coarse powder)) and will therefore not be evaluated in detail.

[20] Output categories = Number of different exposure estimates which can be calculated if the corresponding parameter is varied and all other model parameters are kept constant. Example: Vapour pressure can be given as a free number within ECETOC TRA (input: no categorisation), but four volatility bands are assigned on its basis (output: 4 categories). Input parameters which do not influence the exposure estimate obviously do not influence the model resolution.

may in some cases be an appropriate approach but for other scenarios it may lead to over- or underestimations.
Some parameters are only relevant for one exposure route (e.g. gloves, RPE) or not used for both routes due to other reasons. For parameters which are used in models for both exposure routes the dermal models offer often lower average numbers of categories (dustiness, vapour pressure, process temperature, LEV), but there are also cases where the number of categories is comparable (concentration) or even higher (use description, duration). However, the specific number of course depends on the model(s) and the considered parameter.
Comparing only the dermal models in relation to parameters implemented in more than one of them it can be summarised that for the use description and the task or contact frequency MEASE offers the highest number of categories, while for the duration and the concentration RISKOFDERM offers linear approaches and therefore the highest resolution. For LEV and overall ventilation all models which use the parameter offer similar numbers of categories while for gloves ECETOC TRA v3 offers the highest number of categories.
Comparing only the inhalation models STOFFENMANAGER® offers the highest resolution for containment, overall ventilation, dustiness, vapour pressure, concentration and general ventilation, while MEASE includes the highest number of categories for the use description, LEV, RPE and suppression techniques. In case of the duration ECETOC TRA v2, TRA v3 and MEASE offer an identical number of categories (4), while the EMKG-EXPO-TOOL includes 2 categories.
Therefore, overall it can be summarised that the dermal models in this project have on average a smaller number of categories than inhalation models. Moreover they show more similar resolutions for one parameter than the inhalation models (e.g. LEV always two categories).

Concerning the dermal models MEASE and RISKOFDERM use often more categories to describe a parameter than the other models. In case of the inhalation models in most cases STOFFENMANAGER® offers the highest number of categories.
However, the resolution – as well as other aspects of uncertainty – depends also on the exposure scenario, which parameters are needed to describe the scenario and which route should be assessed. Moreover other aspects of uncertainty are interacting with the influence resolution, e.g. the quality of the parameter definition (vagueness, level of detail), therefore a simple conclusion about the resulting magnitudes of exposure is not possible.

Size of exposure models

Another aspect that may be of relevance in this context is the size (i.e. number of parameters and therefore the level of detail with which a situation can be described) which leads together with the resolution to the complexity of a model (ZEIGLER ET AL., 2000).
The overall number of parameters per model has already been summarised in earlier parts of this project (see “Conceptual evaluation”, WPI.1) and will therefore not be evaluated in detail at this point.
It has been shown that this number is highest for STOFFENMANAGER® (17 parameters) and the lowest number can be found for ECETOC TRA v.2 (12 parameters) in case of inhalation models. The EMKG-EXPO-TOOL is a special case,

as it refers to external guidance documents which define the assessed task and the applicable control measures, i.e. while the number of implemented parameters is very low (8; each control approach counted as one parameter) the control guidance sheets and/or German “Schutzleitfäden” include a number of details about the scenarios which are not implemented in any of the other models (e.g. design of the ventilation system).

Table 2.9 Comparison of resolution: Number of output categories per parameter. Only parameters present at least in two models which are not categorised in themselves have been included (i.e. physical state, outdoor/indoor are not included). If several possibilities exist (e.g. depending on process/task category or substance), the maximum number of categories was chosen.

	ECETOC TRA v2 inhalation	ECETOC TRA v2 dermal	ECETOC TRA v3 inhalation	ECETOC TRA v3 dermal	MEASE inhalation	MEASE dermal	EMKG-EXPO-TOOL	RISKOFDERM	STOFFENMANAGER
dustiness	3 (included in initial exposure estimate)	x	3 (included in initial exposure estimate)	x	4	x	3	2	6
vapour pressure	4 (included in initial exposure estimate)	x	4 (included in initial exposure estimate)	x	3	x	3	2	linear + “very low” + “very high”
process temperature	3 (process temperature in relation to melting point)	x	4 (included in vapour pressure categorisation)	x	x	3	3	x	x
use description	8 (max. number of initial exposure estimates in microgram/cm^2 in one fugacity category)	8 (max. number of initial exposure estimates in microgram/cm^2 in one fugacity category)	8 (max. number of initial exposure estimates in microgram/cm^2 in one fugacity category)	9 (max. number of initial exposure estimates in microgram/cm^2 in one fugacity category)	10 (max. number of initial exposure estimates in one fugacity category)	3 (pattern of use); 5 skin areas -> 15	3	6	8
task/contact frequency	x	x	x	x	x	4	x	2	x
duration	4	x	4	4 (Depending on fugacity)	4	4	2	linear dependency	x
concentration	4	x	4	4	4	4	x	x	linear dependency (only liquids)
Use rate	x	x	x	x	x	x	3	linear dependency	x
general Ventilation	x	x	3	x	2	x	1*	x	4
LEV	2	2	2	2	4	x	1*	2	3**

	ECETOC TRA v2 inhalation	ECETOC TRA v2 dermal	ECETOC TRA v3 inhalation	ECETOC TRA v3 dermal	MEASE inhalation	MEASE dermal	EMKG-EXPO-TOOL	RISKOFDERM	STOFFENMANAGER
Ventilation overall (LEV+ general)	*2*	*2*	*6*	*2*	*5*	*x*	*2*	*2*	*7*
gloves	x	x	x	4	x	2	x	x	x
RPE	3	x	3	x	6	x	x	x	5
suppression techniques	x	x	x	x	4	x	x	x	2
containment	x (included in PROCs)	x (included in PROCs)	x (included in PROCs)	x (included in PROCs)	2	x (closed system in "dermal" included in pattern of use and pattern of exposure control)	1*	x	3**

*included in control strategy
** LEV and containment combined included

For dermal models the number of parameters is highest for RISKOFDERM (14), but MEASE and ECETOC TRA v.3 (9 and 8 parameter for dermal exposure) are quite close to the maximum number of parameters per DEO unit (maximum 9 per DEO unit (for Spraying, DEO unit 4). The lowest number of parameters is found for ECETOC TRA v. 2 (4 parameters for dermal).
Only parameters which actually influence the exposure estimate within the model approach have been compared in this subsection.

Resolution/Size of exposure models: Summary/Discussion

The results presented in this section indicate that the size of the dermal models are mostly comparable, while in case of inhalation models the size is highest for STOFFENMANAGER®. The resolution depends on the specific parameters taken into account although the discussion in Chapter 2.3.10 indicates that tools, which are considered to be at the border between Tier 1 and Tier 2 level ("Tier 1.5") such as RISKOFDERM, STOFFENMANAGER® and partly MEASE tend to use more categories per parameter. This on the one hand may decrease the uncertainty introduced by the resolution/size of a model, but on the other hand it also may decrease the user friendliness and in turn lead to a higher number of wrong decisions during the exposure assessment process, especially if the parameter quality of a model is not very high (see also BURE report and section 2.3.11). The resolution can also differ between use categories, e.g. in case of RISKOFDERM different selections of parameters are implemented for each DEO unit.
Furthermore these results indicate that dermal models are – due to different reasons – often less complex than inhalation models.
However, the number of parameters or categories does not allow for a final conclusion if the level of detail of a specific model is sufficient or how high the introduced level of uncertainty will be, as the number of necessary parameters also depends on the exposure situation, exposure routes and the parameters that are really needed to define the level of exposure (see section 2.4). Thus, this aspect is only able to give a first and rough impression of the possible level of detail of an exposure model.

2.3.11 Comparison of common parameters: Summary

In this chapter some exposure parameters which are found in several models have been compared and discussed.
The average quality of input parameters (i.e. level of detail, vagueness of model inherent parameter definition) is found to be improvable in case of RISKOFDERM, medium in case of ECETOC TRA and MEASE and good in case of the EMKG-EXPO-TOOL and STOFFENMANAGER®, with the definition of RMMs (PPE and local controls) being parameters which are of low quality for each of the tools. To which extent the model inherent reflection of implemented parameters is able to provide accurate (or at least conservative) results, cannot be decided for most parameters. However, some general facts have been discussed which may help users to identify weaknesses related to their specific exposure situation and to interpret the uncertainty of their exposure estimate in a realistic way.
Concerning the resolution, the discussion in Chapter 2.3.10 indicates that the tools, which are considered to be at the border between Tier 1 and Tier 2 level ("Tier 1.5")

such as RISKOFDERM, STOFFENMANAGER® and partly MEASE tend to use more categories per parameter and a higher number of parameters than other models.
On the one hand this may be able to decrease the uncertainty of the model estimate because these models are able to define an exposure situation in a more specific way. However, depending on the parameter quality, knowledge about an exposure situation (e.g. air change rate, level of training concerning glove usage) and the general experience of the model user this aspect may also be able to increase the uncertainty or at least balance the positive effect of a higher model complexity. This effect is partly supported by the results of BURE, which indicate higher levels of uncertainty for models with many parameters (RISKOFDERM, STOFFENMANAGER©, MEASE). However, on the other hand subjective uncertainty of the model users is not always correlating with actual variation of the exposure estimates for a given situation. Moreover, there is also noticeable variability for models with few parameters or parameters with few categories (e.g. EMKG-EXPO-Tool, control approach).

2.4 Omission of parameters having potential relevance for exposure estimation

2.4.1 Parameters relevant at tier 1 level

Theoretically, the number of details which can be reported about an exposure situation and which might influence the resulting exposure value, can be very high. It is not reasonable to expect that any kind of exposure model, especially the evaluated tier 1 models, can or should be able to reflect all these possible parameters.
One criterion to decide which parameters should be implemented in a tier 1 exposure model can be the definition of “tier 1 level” as described in ECHA guidance R14 (ECHA (EUROPEAN CHEMICALS AGENCY), 2010a) and the information that is required for an exposure assessment at this level. A comparison of the parameters listed there and the parameters found in the evaluated models can be found in Table 2.10.

Table 2.10 Information required about an exposure situation to do a tier 1 assessment and models which do not use these parameter.

Parameter which should be known about a situation to do a tier 1 exposure assessment	Models which do not offer this parameter (or where the parameter does not influence the exposure estimate)
physical state of the substance and/or the product handled	ECETOC TRA v.2+3, dermal part
vapour pressure/dustiness	ECETOC TRA v.2+3, dermal part MEASE, dermal part
concentration of the substance in the preparation	RISKOFDERM EMKG-EXPO-TOOL
the level of containment	- (for some models this parameter is included in the use description)
presence and efficiency of local exhaust ventilation (LEV)	MEASE, dermal part
duration	ECETOC TRA v.2, dermal part; (STOFFENMANAGER® version 4.5: not in REACH part)
description of the process/task	EMKG-EXPO-TOOL (external cgs)

The summary provided in Table 2.10 shows that, although most parameters are implemented in the majority of evaluated models there are some cases, where single parameters are not present. The most important questions – which can only partly be answered in this work package – is now, if and how the omission of these parameters will influence the exposure estimate and its uncertainty and if there are further parameters which are considered to be of relevance (e.g. according to published information) but do not fall under the tier 1 definition given above and are not implemented in the majority of the models.

Concerning the omission of Tier 1 parameters some information has already been collected in the prior chapter (Sections 2.3.1-2.3.8).

The physical state is only neglected in case of the dermal part of ECETOC TRA v.2 and 3 and the dermal part of MEASE. No general statement can be made to which extent the exposure estimate and its uncertainty will be influenced by this.

Vapour pressure and dustiness are not influencing the exposure estimates of the same model parts (dermal part of TRA v.2 and 3 and MEASE), however, in case of TRA v.3 a certain influence via the combination with the duration modifier is present. It is considered to be likely that some uncertainty is introduced by this fact. However, direction and magnitude of the uncertainty cannot be evaluated in detail without further information as the connection between volatility/dustiness and dermal exposure may be influenced by a number of other details (e.g. adsorption effects).

The process temperature is implemented in the EMKG-EXPO-TOOL, in ECETOC TRA v.3 in form of the vapour pressure at process temperature and partly in MEASE and ECETOC TRA v.2. However, for all models which offer a parameter "vapour pressure" it is possible to use the vapour pressure at process temperature. In addition to the usual influence of volatility on inhalation and dermal exposure, an increased temperature can also lead to lower dermal exposure because direct skin contact may sometimes lead to burns. However, the omission of this effect only leads to overestimations and is therefore consistent with a conservative Tier 1 approach

Concentration modifiers are not implemented in the EMKG-EXPO-TOOL and RISKOFDERM which may lead to overestimations in case of diluted mixtures. Magnitudes of uncertainty can be very high. However, the RISKOFDERM user guidance gives advice on the external consideration of this aspect which decreases the probability that this case will occur.

The level of containment can be expressed in all models, although in some cases it is combined with the use description (e.g. PROC1: Closed system).

Local exhaust ventilation is only left out in the dermal part of the MEASE algorithm. If control measures are present in reality but cannot be described within an exposure model this usually leads to overestimations. However, no detailed evaluation of the expected magnitudes of exposure is possible without further information, e.g. exposure reduction may also depend on the major form of dermal exposure (droplets, surface contact, vapour etc.).

The duration of a task or process is not taken into account in case of STOFFENMANAGER version® 4.5 and ECETOC TRA v.2 (dermal part). Leaving out this parameter usually leads to overestimations for durations shorter than 8h, which is the common assumption for a maximum exposure duration per day. The exact level of overestimation however depends on the exposure route (dermal vs. inhalation) and in case of process based models also on the distribution of underlying tasks over the complete working day and/or the corresponding time window which shall be assessed. For both models duration has been implemented in later versions (TRA v.3 and STOFFENMANAGER® version 5.0), i.e. the level of uncertainty due to

the omission of this aspect has been decreased. The way this parameter is now implemented in both models of course may introduce other uncertainties, however, these are discussed in other sections of this report (see chapter 2.3.5).
A use description is implemented in all models except the EMKG-EXPO-TOOL which refers to the external control guidance sheets to define the assessed task. This separation between tool and use description may increase the uncertainty of the exposure estimate. However, this effect cannot be quantified.
Not always an explanation is given in the model documentation or manual why parameters are left out or do influence only one exposure route. In some cases the reason may be an increased user friendliness due to less complicated model structure and less information requirements (→ Tier 1 approach).
Other reasons that are reported in some cases are that a specific measure may not be universal applicable or not robust enough concerning the scientific basis (e.g. specific worker training in case of TRAv3, see Ref. (ECETOC, 2013)) or that no measured data was available which allowed for the derivation of an exposure reduction (e.g. RISKOFDERM (WARREN ET AL., 2006); see also Appendix 1, Section "RISKOFDERM version 2.1").
Overall it can be summarised that the parameters which are considered to be Tier 1 relevant according to ECHA guidance R14 are implemented in the majority of the evaluated models. In some cases where parameters were not taken into account this is considered to result mostly in positive directions of uncertainty, i.e. an overestimation of exposure, which is in line with the conservative Tier 1 concept (LEV, concentration, duration). However, for some parameters (physical state, use description, vapour pressure/dustiness) no prediction of expected directions or magnitudes of uncertainty concerning their omission can be made without further information.

2.4.2 Other parameters

In this subsection a short summary of other parameters will be given, which may be of relevance for an accurate exposure estimation but are not implemented in some or all of the evaluated models. As these parameters are at least partly not consistent with the Tier 1 approach (see Chapter 2.4.1) only a short overview will be given and no detailed discussion of the different parameters.
Some limited information about further parameters which are probably of relevance for exposure estimations can be found in published literature:
Marquart et al. (MARQUART ET AL., 2003) summarise some determinants which are considered to be relevant for dermal exposure. The mentioned determinants are listed in Table 2.11. According to Marquart et al. they are based on evidence in the analysed literature as well as scientific judgement and the possibility of gathering information about this parameter in the course of a risk assessment.
Burstyn and Teschke (BURSTYN AND TESCHKE, 1999) report a summary about relevant determinants of exposure (mostly for inhalation, see Table 2.12.). Influence of product type, protective clothing, outdoor/indoor application, ventilation, concentration, wood shapes, filter bag types, right/left handedness of the worker, humidity, gas pressure, training and other parameters are described. Many of the determinants are very specific and not applicable to generic exposure models, especially if these are intended to operate at Tier 1 level (see also footnote 22).

Table 2.11 Dermal exposure: Determinants of relevance (MARQUART ET AL., 2003). Determinants not implemented in any of the models are marked in orange. Determinants which are included in the list of Tier 1 parameters as discussed in chapter 2.4.1 are marked green.

Direct contact	
Substance and product characteristics	Physical state: liquid, solid
	Liquid characteristics: viscosity and other properties
	Particle characteristics: particle size distribution, moistness[21]
Task done by the worker	Distinguished tasks
	Amount of substance handled (or underlying determinants, e.g. volume of product and concentration of substance)
	Intensity of contact: frequency, i.e. the number of events (for both contacts with contaminant and clean surfaces)
Process, technique/ equipment	Distinguished process/equipment
Exposure control measure	Gloves: use, material
	Clothing: use, surface area covered, material
Worker characteristics	Accuracy of working: training
	Skin characteristics: moistness
	Personal care: (frequency of) hand washing
Surface contact	
Substance and product characteristics	Physical state: liquid, solid
	Liquid characteristics: viscosity and related properties
	Particle characteristics: particle size distribution, moistness[21]
Task done by the worker	Intensity of contact: duration of contact, exerted force
	Frequency: number of contacts or objects
	Treated area or objects: level of contamination
Exposure control measure	Gloves: use, material
	Clothing: use, surface area covered, material
	Organization of work: interval between event and contact
Worker characteristics	Accuracy of working: touching contaminated or treated surfaces
	Skin characteristics: moistness
	Personal care: (frequency of) hand washing
Area and situation	Type of surface: roughness
Deposition	
Substance and product characteristics	Physical state: liquid, solid
	Liquid characteristics
Task done by the worker	Distinguished tasks
	Amount of substance handled (or underlying determinants, e.g. volume of product and concentration of substance)
Process, technique/equipment	Distinguished type of process/equipment
	Process/equipment: pressure, orientation of application
Exposure control measure	Gloves: use, material

[21] May be implemented as dustiness of a solid substance or product.

Direct contact	
	Clothing: use, surface area covered, material
	Segregation
	Ventilation (including LEV)
Worker characteristics	Accuracy of working: training
	Personal manner of work: place relative to source
	Skin characteristics: roughness, electrical chargeability
	Personal care: (frequency of) hand washing
Area and situation	Weather conditions: temperature, wind speed

Table 2.12 Inhalation exposure: Determinants of relevance (BURSTYN AND TESCHKE, 1999). Determinants not implemented in any of the models are marked in orange.[22] Determinants which are included in the list of Tier 1 parameters as discussed in chapter 2.4.1 are marked green.

Substance and product characteristics
contaminant/ type of product and substance
concentrations
specific gravity (the ratio of the density of a substance compared to the density (mass of the same unit volume) of a reference substance.)
powder type/dustiness
aerodynamic diameter
moisture content of solids
Task, process and technical equipment
duration
gas pressure release, application pressure
process/technique
mass flow rates
automation
spills
vessel volume
dropping air heights
volume/amount
Exposure control measure
general ventilation
exhaust air ventilation (different configurations)
level of dust extraction
low/high ventilation outlet position

[22] Branch- or process specific parameters: rock wool production with and without oil, fiberisation process parameters, latex coating weights on carpet, injection points (embalming), presence of germicidal lamps,
autopsy or intact body (embalming), CO^2 concentration (exposure to germs + fungi), off gassing time of carpets, number of occupants (exposure to germs + fungi), sander type, sandpaper type, type of filter bag, wood shape, amount and type of flour, type of sterilising equipment, equipment isolation, stage of construction (construction site), asphalt industry category, type of machining fluid, number of plate changes (printing plants), number of presses in operation, machinery, contact with wet resins gasket conditions, solvent transport method, plant construction, feeding methods, flooring, type of wood cutting machines, type of body (embalming)

makeup air rates
room fan operation
airwashers
enclosure
gas recirculation
presence of engineering controls
Worker characteristics
activity level
seniority
right- left handedness
Worker characteristics
maintenance practices
worker training
reason for survey
work practices
distance from machines/sources of exposure
shift
distance from sources of exposure
hand washing
Area and situation
temperature
outdoor/indoor
humidity
number of windows
machine age
calendar year
season
day of week
location
month

There is a number of parameters (marked orange) which are not present in any of the models. As expected these parameters are mostly quite specific (e.g. skin moistness/roughness, frequency of hand washing, weather conditions) and will – although they may be relevant for the exposure estimation – usually not be known during a risk assessment process under REACH.

In addition to these publications, quite detailed information about exposure situations assigned to certain tasks/processes and expected equipment is summarised e.g. in the ECHA guidance on intermediates (ECHA, 2010) concerning containment strategies and RMMs. A detailed (experimental) evaluation or quantification of their influence is not documented, however, some qualitative judgements are provided.

The omission of the parameters listed above may induce over- as well as underestimations of exposure, depending on model and actual scenario.

Further substance characteristics

Apart from the standard parameters (dustiness/volatility) there are other determinants which are expected to influence the exposure results. An example are the viscosity and adsorption behaviour of a substance: These properties may influence the size of surfaces available for evaporation, i.e. the inhalation exposure, as well as the behaviour during skin contact (adsorption to skin, removal when other objects are touched).
Other parameters from this category are the particle characteristics, e.g. moistness of a dust, which can partly be expressed via the dustiness categorisation but may also influence adsorption on and subsequent removal from skin.

Operational conditions/use description

A number of additional details may be of relevance in this area.
As an example, the droplet spectrum in case of spray applications is expected to be of relevance for inhalation exposure to liquid aerosols (KOCH, 2012). It can depend on a number of other parameters, e.g. the spray pressure, viscosity, vapour pressure of the spray components etc. The droplet size distribution is not implemented in any of the evaluated models. In principle both over- and underestimations are possible which can go up to three orders of magnitude. However, a detailed evaluation of the influence of this parameter would go beyond the scope of this project.
Other parameters from this category are the vessel size, the day of the week or age of the employee (for further examples see Table 2.11 and Table 2.12). However, for none of them a simple estimation of the expected magnitudes of exposure is possible.

Personal protective equipment and local controls

Personal protective equipment (RPE, gloves) and localised controls (general ventilation, LEV, wetting techniques etc.) lead, if they are applied in a correct way, to a reduction of individual exposure, i.e. if a model does not offer a measure which is found in an exposure situation the exposure estimation for this situation will tend to overestimate the risk and be more conservative.
On the other hand in case of gloves it is also possible that their presence may increase or at least not change exposure, e.g. due to contamination of the glove inside (see also Chapter 2.3.8). However, to which extent this will play a role in reality cannot be assessed.
Concerning respiratory protection ECETOC TRA (both versions), MEASE and STOFFENMANAGER® include different options for their implementation. Gloves are implemented in the dermal part of MEASE and ECETOC TRA v.3 but not in RISKOFDERM or ECETOC TRA v.2.
These parameters fall partly under the Tier 1 definition as described in Guidance R14 (see reference (ECHA (EUROPEAN CHEMICALS AGENCY), 2010a) and chapter 2.4.1). However, how many possibilities (e.g. LEV, general ventilation, wetting of the source or even certain weather characteristics) are required for a Tier 1 model is not explained in detail. All evaluated models include at least a rough characterisation of the level of control for a specific situation while of course none of them offers all possible determinants.

Personal behaviour of worker

Parameters belonging to this area are not directly implemented in any of the evaluated exposure models. However, this aspect is to a certain extent included in the assumption of occupational hygiene and in the description of glove categories in case of ECETOC TRA v.2 and v.3. Details like personal hygiene/hand washing, handling of equipment and positioning of the worker are not part of the models but are sometimes included in the external control guidance sheets in case of the EMKG-EXPO-TOOL.

The simplification caused by the omission of these parameters is expected to cause some uncertainty as a worker with better training, and a certain level of personal hygiene is expected to show lower exposures than a worker without these characteristics. However, the level of detail which would be required to describe the mentioned differences in model parameters is considered to be much higher than necessary and desirable for a Tier 1 model. The resulting variability within the exposure estimates should be covered by the conservativeness of the estimate or the percentiles in case of RISKOFDERM and STOFFENMANAGER®. However, the final magnitude and direction cannot be judged for this source of uncertainty.

2.4.3 Summary/Discussion

In the paragraphs above some aspects have been discussed which may be of relevance for an exposure estimation but are omitted in at least some of the models.

Omitted parameters as potential source of uncertainty are generally difficult to evaluate, as it is often not known or still under discussion which parameters may influence exposure and how this influence may be implemented in the various exposure models. Moreover, this source of uncertainty is connected with the resolution and general level of detail of the various models.

All evaluated models are intended to keep the balance between the necessary level of detail and the Tier 1 approach which requires simplifications in order to increase the usability of a model. However, the boundary between tier 1 and higher tier models is not always clearly defined: Almost all of the models use at least one parameter which is not a tier 1 level parameter according to ECHA guidance R14 (e.g. ECETOC TRA uses RPE and gloves, RISKOFDERM uses the direction of application and the distance between worker and exposure source).

Moreover, also the ECHA guidance is not completely unambiguous. As an example, personal protective equipmen is not seen to be Tier 1 relevant in the general list of Tier 1 parameters it is recognised later in the same document that e.g. gloves are not implemented as a refinement option in ECETOC TRA v.2. In general, also the list of parameters required for Tier 1 models may include some uncertainty as it is not known if this list is sufficiently simple and/or sufficiently detailed and/or even too detailed for a Tier 1 exposure estimation.

Overall it is recognised that there is a number of parameters probably relevant for the final exposure value which is not implemented in any or only in 1 or 2 of the evaluated models. Most of these are quite sophisticated and clearly beyond the scope of a Tier 1 model. However, at least for some of them it may not be reasonable to include them into an exposure model as they cannot be changed for certain processes (e.g. moistness of skin: It cannot be completely prevented that workers transpire during work, i.e. moistness may be unavoidable.).

However, there are also some less complex determinants, e.g. the ones suggested in Guidance R14, which will probably influence exposure but are not implemented in some of the models.
The influence of these omissions may vary, i.e. they may cause over- and underestimations of different magnitudes. For some parameters their omission results in worst case estimates (e.g. 100% substance if concentration is not implemented, no exposure reduction for RMMs which are not implemented). This should lead to conservative results, which are in general consistent with the Tier 1 approach. But not for all potentially relevant parameters the influence of their omission is completely clear and independent of other factors (e.g. the process or task).
However, the question of conservatism will be evaluated in the external validation and cannot be answered in this report.
Apart from this, as already discussed in Chapter 2.3.10, a higher level of detail concerning the number of parameters may also lead to a higher number of wrong decisions during the exposure assessment and thus, lead to a higher uncertainty. The influence of this aspect cannot be evaluated at this point. However, results of BURE suggests, that at least subjective uncertainty of model users is increased for tools with a high number of input parameters.
It cannot be decided at this point if the Tier 1 approach including the suggested list of parameters is sufficient for an adequate exposure estimation or if more details (e.g. droplet spectrum for spray applications, personal behaviour) would improve the overall quality of an average risk assessment.

2.5 Common assumptions

2.5.1 Ideal gas law

Some models (ECETOC TRA v.2 and v.3, MEASE) use the ideal gas law and a temperature of ~298 K (i.e. molar volume of 24 l/mole) for the conversion of units in case of inhalation exposure to liquids. Usually no justification for this approach is documented. However, the ideal gas law is common knowledge and a lot of information about its applicability is available in published literature (depending on substance/mixture).
This source of uncertainty does not reflect an uncertainty of the model itself but of the ideal gas law. Its influence may vary and cannot be assessed at this point. However, deviations are expected to be small compared to other sources of uncertainty and affect only the conversion of units, but not the result in ppm.

2.5.2 Good occupational hygiene

Some Tier 1 models assume at least to a certain extent that a good occupational practice is present at the workplace. This applies to ECETOC TRA (v.2 and v.3) and the EMGK-EXPO-TOOL and partly also to MEASE (e.g. glove efficiency).
It has been identified in the course of the project, that already the definition of “good occupational hygiene” is not unambiguous, e.g. there has been a discussion within the advisory board if correct design of ventilation systems etc. also belongs to the area of “good hygiene”. There is no common, obligatory definition of this term and the available descriptions term differ concerning vagueness and level of detail.

As an example, the British Occupational Society (BOHS)[23] describes good occupational hygiene as something that has the aim to recognise, assess and control risks from exposures to hazards in the workplace such as chemicals, dusts, fumes, noise, vibration and extreme temperatures.
Information provided by COSHH[24] is more detailed and includes also the suggestion to consider insufficient technical design of ventilation systems as a possible reason for high exposure. Similar descriptions are found in the guidance provided by the Occupational Safety and Health Branch Labour Department[25], which also includes short visual suggestions concerning correct placement of ventilation systems.
Therefore, overall it cannot be excluded, that uncertainties may appear concerning the definition and implementation of good occupational hygiene practice, even if it is recognised at a workplace, that good practice is necessary to fulfil standards set by the communicated exposure scenarios.
If GOHP has been an assumption within the development of an exposure model, this approach is by definition not a conservative one as it does represent a good standard and not a worst case. On the other hand, the correct application of safety – and cleaning standards is at least partly also laid down in European law (application of best available techniques is mandatory[26] (EU, 2010)). Therefore it should theoretically be the common case and this assumption should not lead to underestimations in the majority of exposure situations.
Moreover, a concept including the possibility of misuse may sometimes be closer to the average, actual exposure for a certain exposure situation. But on the other hand it is not requested under REACH to assess unintended use or misuse of an evaluated substance, therefore it is not considered to be strictly necessary to include situations with bad practice into an exposure model.
However, as stated above the inclusion of such situations into a model basis will not lead to less conservatism, i.e. the changes of the exposure estimate which may be introduced are compatible with the idea of conservative Tier 1 estimates. Furthermore it is legitimate for different models to include different purposes, i.e. as long as it is clearly documented (which is the case for all models) both approaches are possible.
A similar argumentation can be made concerning the amount of information on good practice which is made available by the model developers:
As an example, the specific design required for LEV systems or general ventilation to REACH the assigned efficiency is not further described in some of the models. Partly only a “LEV: yes/no” decision can be made. The parameter quality has therefore been identified to be “medium” or even “low” (see Chapter 2.3.7 and Appendix 1), as the level of detail is not very high in these cases.
On the other hand it may be disputable if it would not be sufficient to refer to “good occupational hygiene” and the officially recommended techniques (via BAT documents, suppliers of ventilation systems etc.) to define localised control measures including their set-up and design. The parameter definition in the model may then still have a low level of detail but as long as expected techniques are described in other sources of information in an unambiguous, easy to find way uncertainty resulting

[23] http://www.bohs.org/
[24] http://www.hse.gov.uk/coshh/detail/goodpractice.htm
[25] http://www.labour.gov.hk/eng/public/oh/GOHP_eng.pdf
[26] Commission Directive 2010/75/EU on industrial emissions (integrated pollution prevention and control): Best available technique is required as laid down in BAT conclusions. See also http://eippcb.jrc.ec.europa.eu/reference/ and http://www.bvt.umweltbundesamt.de/.

from this could be avoided. Similar arguments can be used in cases were confidence limits or percentiles representing different points on the real-life distribution of exposure situations have to be chosen (e.g. MEASE, STOFFENMANAGER©).
Furthermore the technical design of the exposure models often does not allow for the inclusion of long descriptions or figures, therefore it may be even necessary to refer to external documents to a certain extent.
As a summary, both approaches (external guidance or all information within the model (documentation)) may work if they are applied in the correct way. More details within a model may increase the amount of available information, but also decrease user friendliness, therefore the impact on the uncertainty of the result of an exposure assessment under REACH cannot be evaluated within this project.
In the context of this report the categorisation of parameter quality only refers to information given in the model or in references directly linked to it (e.g. user guidance) as the work package refers only to the model itself and details directly connected to it. However, it is recognised that the "individual parameter quality" is closely linked to personal experience about workplaces, exposure assessment and the model as well as knowledge about other sources of information.

2.6 Uncertainty under REACH

As already mentioned in Chapter 0, an evaluation of uncertainty of exposure models under REACH may differ in some points from a general uncertainty analysis which evaluates the ability of a model to provide accurate estimates with a preferably low tendency to over- or underestimate exposure. As laid down in ECHA guidance R14 (ECHA (EUROPEAN CHEMICALS AGENCY), 2010a) Tier 1 tools are meant to be conservative and therefore expected to overestimate exposure. A tendency to overestimate exposure is therefore not considered to be a disadvantage but only an indication if the model can be regarded as a Tier 1 model. As long as a model gives only overestimations the safe use of the corresponding substance will be granted and thus, it is considered to be suitable for application under REACH.
Moreover the situation under REACH obliges the downstream user to follow the scenario used for exposure estimation, i.e. errors or vagueness during the documentation of the exposure situation are expected to have much less influence on the exposure estimate.
As an example, if a duration modifier has been used to modify dermal exposure, measures are to be taken at the workplace that dermal exposure indeed stops within the given exposure duration and possible contamination is removed.
However, on the other hand vagueness or a lack of detail concerning the input parameters and the exposure result may have a second layer of uncertainty along the chain of communication: As an example, the downstream user may communicate wrong PROC numbers to the registrant and as a consequence, exposure assessments for his process may not be appropriate. If he communicates more detailed descriptions there is still uncertainty when the exposure assessor choses the PROCs and other parameters for the exposure assessment and, depending on the level of detail of the scenario description communicated back to all downstream users, misinterpretations or wrong assignments of the scenarios to workplaces are theoretically possible. Overall, at some point of the whole communication process at least one person must have understood how to transform the exposure situation into model parameters and vice versa in a correct and sufficiently detailed way.

Otherwise the obligation of downstream users to follow the communicated scenarios may not be enough to remove all uncertainties which may arise.
The variability induced by misinterpretation of a scenario and its categories/ parameters is expected to REACH similar orders of magnitude like the variability induced during the input of parameters in the BURE exercise (see other chapters and BURE report).
Furthermore, exposure scenarios which have been prepared with models which do not use fixed modifiers are less easy to communicate as there is already an inherent but not always transparent assumption about commonly applied techniques in specific situations. Parameters such as air change rates or efficiencies which can be laid down in the eSDS may not be directly available.

An additional issue during the risk assessment in this context is the derivation of the used DNEL which is usually derived for full shift exposure and from studies which usually include one specific exposure duration. To which extent this influences the validity of the final risk assessment can however not be assessed within this project.

2.7 Conclusion and outlook

In this work package a qualitative assessment of the model uncertainty has been performed.
It has been shown that for each tool a number of possible sources of uncertainties exists, which in many cases can theoretically lead to large magnitudes of uncertainty of the exposure estimate. These sources of uncertainty can be vagueness or low level of detail concerning the parameter definition, model inherent parameters, assumptions, dependencies, omitted parameters or general uncertainties in the model basis (algorithm/knowledge base).
However, sources of uncertainty are located in different parts of the tool (e.g. parameter quality, uncertainty of knowledge base) and it has to be taken into account that it always depends on the model and the situation itself which sources of uncertainty for an exposure situation are dominant and how uncertain the final exposure estimate may be (e.g. the size and quality database for RISKOFDERM may differ between DEO units, a standard efficiency for ventilation systems may be accurate for some situations and highly uncertain for others).
A derivation of overall magnitudes of uncertainty for all models which combine the influences of several sources of uncertainty is not possible on the basis of the available information. The analyses of the isolated influences of various sources of uncertainty showed that a large number of them may lead to small or medium magnitudes of uncertainty. Thus, it is considered to be likely that overall deviations of this size are quite common during exposure assessments.
For some models (e.g. ECETOC TRA, MEASE) the tendency to overestimate exposure is – based on the available information – expected to be higher than for others (e.g. STOFFENMANAGER®, RISKOFDERM, see Appendix 1) and thus, the level of protection for the affected workers as expected on the basis of model related uncertainties is higher as well.
However, in reality error compensation may to a certain extent reduce the impact of some uncertainty sources. Therefore a final conclusion on direction and magnitude cannot be made without results of an external validation exercise.

In addition, there are many parameters and underlying datasets without sufficient information to allow for an estimation of the influence on the exposure estimate and thus on the uncertainty, i.e. as expected none of the evaluated models is perfectly transparent.

Overall, the assumption that all evaluated models are to some extent uncertain is supported by the various aspects discussed in this report. However, in the context of this project it is important to note that Tier 1 tools are even intended to be uncertain to some extent. Tier 1 tools should provide conservative results. Thus, as long as the overall direction of uncertainty is positive, i.e. underestimations of exposure and risk are negligible, uncertainty is not a concern but even wanted to ensure an appropriate conservativeness.

The exemplary exposure situations discussed in Appendix 1 show, that model uncertainty is for the same exposure situation variable between models and also within the same model variable between the exposure situations. However, for many sources of uncertainty, in particular high quality input parameters, it is suspected that uncertainties related to the assessed workplaces (i.e. scenarios uncertainty: statistical errors during vapour pressure sampling, incomplete or vague documentation of the exposure situation etc.) will be more relevant for the overall uncertainty of the exposure estimate than the model uncertainties (see also WPI.6; Between user reliability).

Information collected in the course of BURE teaches that the major source of variability is the assignment of the correct use category. Therefore, apart from the provided information about a workplace the definition of tasks or processes within a model is quite essential. Although no general advice can be drawn from BURE, how a perfect set of use categories should look like (task or process based? how many categories?) and how to improve the currently established PROC system it seems clear that this is a crucial point in order to reduce between user variability during exposure assessments.

Some further indications can be drawn from BURE, which input parameters may be major sources of uncertainty, e.g. dustiness, RMMs and the type of setting, and thus, should probably be improved concerning vagueness and level of detail.

However, when interpreting results of BURE it has to be kept in mind that the between user reliability represents always a balance between available information on the exposure situation, user characteristics and model characteristics, i.e. although some part of the resulting variability may be caused by unclear parameter definitions an improvement on this side will not lead to less overall uncertainty if corresponding contextual information (e.g. dustiness measurements) are not available or model users are not able to interpret information and model input or results in an appropriate way.

Furthermore, less ease of translation into model parameters was observed for dermal models than for inhalation models. This may suggest a higher average parameter quality for inhalation models but may also be a consequence of a lower level of experience of the model users with dermal exposure. However, this experience was not reflected in a lower variability for the inhalation models. Similar observations have been made concerning the number of parameters implemented in the models and their resolution: Users are more uncertain about models with a higher number of input parameters and higher numbers of categories per input parameter (e.g. STOFFENMANAGER©), but this is not supported by a higher variability.

Wrong input parameters can easily lead to variations around three orders of magnitude in the exposure estimates (see BURE report) and therefore can be at

least equally relevant to the overall uncertainty of an exposure estimate like uncertainties within the model algorithm. In addition persons responsible for occupational safety (mainly downstream users) should be able to interpret the model result and/or the communicated scenario in an appropriate way (which PROC represents my workplace?). A lower between user variability can be supported by decreasing the vagueness of model input parameters and implemented tool guidance but also has to be accompanied by further measures, e.g. information about the exposure situations, model user trainings.
As a consequence, the results of the model uncertainty described in this work package should not be interpreted isolated but only in combination with the other work packages of the eteam project and within the regulatory context.

References

ARNONE, M.K., D.; GABRIEL, S., (2013): Der GESTIS-Stoffenmanager als Werkzeug zur quantitativen Abschätzung von Gefahrstoffkonzentrationen am Arbeitsplatz. In: *Gefahrst. Reinhalt. Luft*. 73(4), 10p.

BELL, N.; VAUGHAN, N.P.; MORRIS, L.; GRIFFIN, P., (2012): An assessment of workplace programmes designed to control inhalation risks using respiratory protective equipment. In: *Ann Occup Hyg*. 56(3), 350-361.

BOOGAARD, P.J., (2008): Biomonitoring as a tool in the human health risk characterization of dermal exposure. In: *Human & Experimental Toxicology*. 27(4), 297-305.

BROUWER, D.H.; MARQUART, H.; VAN HEMMEN, J.J., (2001): Proposal for an approach with default values for the protection offered by PPE, under European new or existing substance regulations. In: *Ann Occup Hyg*. 45(7), 543-553.

BURDORF, A., (2005): Identification of determinants of exposure: consequences for measurement and control strategies. In: *Occup Environ Med*. 62(5), 344-350.

BURSTYN, I.; TESCHKE, K., (1999): Studying the determinants of exposure: a review of methods. In: *Am Ind Hyg Assoc J*. 60(1), 57-72.

CHANG, H.Y.; LIN, C.C.; SHIH, T.S.; CHAN, H.; CHOU, J.S.; HUANG, Y.S., (2004): Evaluation of the protective effectiveness of gloves from occupational exposure to 2-methoxyethanol using the biomarkers of 2-methoxyacetic acid levels in the urine and plasma. In: *Occup Environ Med*. 61(8), 697-702.

CHERRIE, J.W.; SEMPLE, S.; BROUWER, D., (2004): Gloves and dermal exposure to chemicals: proposals for evaluating workplace effectiveness. In: *Ann Occup Hyg*. 48(7), 607-615.

CLAYTON, M.; (2012): *APFs and the new ISO standards. The way forward.* Health & Safety Laboratory. (http://www.isrp.com/europe/docs/2012_eur_spring_meet_paper_clayton.pdf).

CREELY, K.S.; CHERRIE, J.W., (2001): A novel method of assessing the effectiveness of protective gloves--results from a pilot study. In: *Ann Occup Hyg*. 45(2), 137-143.

CRUMP, K.S., (2007): Statistical issues with respect to workplace protection factors for respirators. In: *J Occup Environ Hyg*. 4(3), 208-214.

EBRC; (2008): *Proposed metal-specific refinements ECETOC TRA*.

EC (EUROPEAN COMMISSION); (2003): *Technical guidance document (TGD) on risk assessment in support of Commission Directive 93/67/EEC on risk assessment for new notified substances*. (Part 1), 303p.

ECETOC; (2001): *Exposure Factors Sourcebook for European Populations (with Focus on UK Data)*. (Technical Report No. 79).

ECETOC; (2004): *Targeted Risk Assessment*. Brussels: European Centre for Ecotoxicology and Toxicology of Chemicals. (Technical Report No. 93), 223p.

ECETOC; (2009): *Addendum to ECETOC Targeted Risk Assessment No. 93*. Brussels: European Centre for Ecotoxicology and Toxicology of Chemicals. (Technical Report No. 107), 128p.

ECETOC; (2013): *ECETOC TRA version 3: Background and Rationale for the Improvements*. (Technical Report No. 114).

ECHA; (2008a): *Guidance information requirements and chemical safety assessment. Chapter R.19: Uncertainty analysis*. Helsinki.

ECHA; (2008b): *Guidance on information requirements and chemical safety assessment Chapter R.19: Uncertainty analysis*. Helsinki.

ECHA; (2010): *Guidance on intermediates*. Helsinki.

ECHA (EUROPEAN CHEMICALS AGENCY); (2010a): *Guidance on information requirements and chemical safety assessment. Chapter R.14: Occupational exposure estimation*. 62p.

ECHA (EUROPEAN CHEMICALS AGENCY); (2010b): *Guidance on information requirements and chemical safety assessment. Chapter R.12: Use descriptor system*. 47p.

EFSA; (2008): *Project to assess current approaches and knowledge with a view to develop a Guidance Document for pesticide exposure assessment for workers, operators, bystanders and residents*. (EFSA AGREEMENT NUMBER EFSA/PPR/2007/01 FINAL REPORT).

EFSA, (2010): Scientific Opinion on Preparation of a Guidance Document on Pesticide Exposure Assessment for Workers, Operators, Bystanders and Residents. In: *EFSA Journal*. 8(2).

EPA; (2011): *Exposure Factors Handbook*. U.S. Environmental Protection Agency, Washington, DC, , (EPA/600/R-09/052F).

EU, (2010): *Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on industrial emissions (integrated pollution prevention and control) (Recast)*, Directive 2010/75/EU, 103

FRANSMAN, W.; SCHINKEL, J.; MEIJSTER, T.; VAN HEMMEN, J.; TIELEMANS, E.; GOEDE, H., (2008): Development and evaluation of an exposure control efficacy library (ECEL). In: *Ann Occup Hyg*. 52(7), 567-575.

GARROD, A.N.; PHILLIPS, A.M.; PEMBERTON, J.A., (2001): Potential exposure of hands inside protective gloves-a summary of data from non-agricultural pesticide surveys. In: *Ann Occup Hyg*. 45(1), 55-60.

GMEHLING, J.; WEIDLICH, U.; LEHMANN, E.; FRÖHLICH, N., (1989a): Verfahren zur Berechnung von Luftkonzentrationen bei Freisetzung von Stoffen aus flüssigen Produktgemischen. In: *Staub - Reinhaltung der Luft*. 49(9), 227-230.

GMEHLING, J.; WEIDLICH, U.; LEHMANN, E.; FRÖHLICH, N., (1989b): Verfahren zur Berechnung von Luftkonzentrationen bei Freisetzung von Stoffen aus flüssigen Produktgemischen. In: *Staub - Reinhaltung der Luft*. 49(9), 295-299.

HASHIMOTO, H.; GOTO, T.; NAKACHI, N.; SUZUKI, H.; TAKEBAYASHI, T.; KAJIKI, S.; MORI, K., (2007): Evaluation of the control banding method - comparison with measurement-based comprehensive risk assessment. In: *J Occup Health*. 49(6), 482-492.

HERAG; (2007): *Assessment of occupational dermal exposure and dermal absorption for metals and inorganic metal compounds*. (Fact sheet 01), 49p.

HIDAYANTO, E.T., T.; KAWAI, J., (2010): Measurement of viscosity and sucrose concentration in aqueous solution using portable brix meter. In: *Berkala Fisika*. 13(2), A23-A28.

HOFSTETTER, E.; SPENCER, J.W.; HITESHEW, K.; COUTU, M.; NEALLEY, M., (2013): Evaluation of recommended REACH exposure modeling tools and near-field, far-field model in assessing occupational exposure to toluene from spray paint. In: *Ann Occup Hyg*. 57(2), 210-220.

HSE; (2011): *Controlling airborne contaminants at work - A guide to local exhaust ventilation (LEV)*. 109p.

JONES, R.M.; NICAS, M., (2006): Evaluation of COSHH Essentials for vapor degreasing and bag filling operations. In: *Ann Occup Hyg*. 50(2), 137-147.

JRC; (2007): *Human exposure to biocical products. Technical notes for guidance.*, 102p.

JRC; (2010): *HEEG opinion. Default protection factors for protective clothing and gloves*. ISPRA: EC JRC.

KINDLER, P.; (2010): *Anwendbarkeit von Expositionsmodellen für Chemikalien auf Schweizer Verhältnisse. Teilprojekt 1: Überprüfung der Modelle "EASE" und "EMKG-Expo-Tool"*. 56p.

KOCH, W.B., W.; BERGER-PREIß, E.; KOCH, H.; GERLING, S.; HAHN, S.; SCHRÖDER, K.; (2012): *Validation of an EDP assissted model for assessing inhalation exposure and dermal exposure during spraying process*. Dortmund/Berlin/Dresden.

KOPPISCH, D.; SCHINKEL, J.; GABRIEL, S.; FRANSMAN, W.; TIELEMANS, E., (2012): Use of the MEGA exposure database for the validation of the Stoffenmanager model. In: *Ann Occup Hyg*. 56(4), 426-439.

KUPCZEWSKA-DOBECKA, M.; CZERCZAK, S.; JAKUBOWSKI, M., (2011): Evaluation of the TRA ECETOC model for inhalation workplace exposure to different organic solvents for selected process categories. In: *Int J Occup Med Environ Health*. 24(2), 208-217.

LECHTENBERG-AUFFARTH, E.; RUHL, R., (2007): Safety of Gloves for chemical protection. In: *Ann Occup Hyg*. 51(8), 739-740.

LEE, E.G.; HARPER, M.; BOWEN, R.B.; SLAVEN, J., (2009): Evaluation of COSHH essentials: methylene chloride, isopropanol, and acetone exposures in a small printing plant. In: *Ann Occup Hyg*. 53(5), 463-474.

LEE, E.G.; SLAVEN, J.; BOWEN, R.B.; HARPER, M., (2011): Evaluation of the COSHH Essentials Model with a Mixture of Organic Chemicals at a Medium-Sized Paint Producer. In: *Annals of Occupational Hygiene*. 55(1), 16-29.

MAIDMENT, S.C., (1998): Occupational hygiene considerations in the development of a structured approach to select chemical control strategies. In: *Ann Occup Hyg*. 42(6), 391-400.

MARQUART, H.; HEUSSEN, H.; LE FEBER, M.; NOY, J.; TIELEMANS, E.; SCHINKEL, J.; WEST, J.; VAN DER SCHAAF, D., (2008): "Stoffenmanager", a web-based control banding tool using an exposure process model. In: *Ann Occup Hyg*. (52(6)), 429-441.

MARQUART, J., (2003): Determinants of Dermal Exposure Relevant for Exposure Modelling in Regulatory Risk Assessment. In: *Annals of Occupational Hygiene*. 47(8), 599-607.

MARQUART, J.; BROUWER, D.H.; GIJSBERS, J.H.; LINKS, I.H.; WARREN, N.; VAN HEMMEN, J.J., (2003): Determinants of dermal exposure relevant for exposure modelling in regulatory risk assessment. In: *Ann Occup Hyg*. 47(8), 599-607.

MONEY, C.D.; MARGARY, S.A., (2002): Improved Use of Workplace Exposure Data in the Regulatory Risk Assessment of Chemicals within Europe. In: *Annals of Occupational Hygiene*. 46(3), 279-285.

NELSON, T.J.; JAYJOCK, M.A.; COLTON, C.E., (2000): How protective are respirator assigned protection factors: an uncertainty analysis. In: *AIHAJ*. 61(3), 388-393.

NICAS, M.; NEUHAUS, J., (2004): Variability in respiratory protection and the assigned protection factor. In: *J Occup Environ Hyg*. 1(2), 99-109.

PACKHAM, C., (2006): Gloves as chemical protection--can they really work? In: *Ann Occup Hyg*. 50(6), 545-548.

PASZKIEWICZ, P., (2012): Alles gemeinsam in der EU - auch die Schutzfaktoren für Atemschutz. In: *Gefahrst. Reinhalt. Luft*. 72(4), 121.

POPENDORF, W.; SELIM, M.; LEWIS, M.Q., (1995): Exposure While Applying Industrial Antimicrobial Pesticides. In: *Am Ind Hyg Assoc J*. 56(10), 993-1001.

POPENDORF, W.S., M, (1995): Exposure while applying commercial disinfectants. In: *Am Ind Hyg Assoc J*. 56, 1111-1120.

RAJAN-SITHAMPARANADARAJAH, R.; ROFF, M.; DELGADO, P.; ERIKSSON, K.; FRANSMAN, W.; GIJSBERS, J.H.; HUGHSON, G.; MAKINEN, M.; VAN HEMMEN, J.J., (2004): Patterns of dermal exposure to hazardous substances in European union workplaces. In: *Ann Occup Hyg*. 48(3), 285-297.

SCHINKEL, J.; FRANSMAN, W.; HEUSSEN, H.; KROMHOUT, H.; MARQUART, H.; TIELEMANS, E., (2010): Cross-validation and refinement of the Stoffenmanager as a first tier exposure assessment tool for REACH. In: *Occup Environ Med*. 67(2), 125-132.

TIELEMANS, E.; NOY, D.; SCHINKEL, J.; HEUSSEN, H.; VAN DER SCHAAF, D.; WEST, J.; FRANSMAN, W., (2008a): Stoffenmanager exposure model development of a quantitative algorithm. In: *Ann Occup Hyg*. 52(6), 443-454.

TIELEMANS, E.; SCHNEIDER, T.; GOEDE, H.; TISCHER, M.; WARREN, N.; KROMHOUT, H.; VAN TONGEREN, M.; VAN HEMMEN, J.; CHERRIE, J.W., (2008b): Conceptual model for assessment of inhalation exposure: defining modifying factors. In: *Ann Occup Hyg*. 52(7), 577-586.

TIELEMANS, E.M., H.; DE COCK, J.; GROENEWOLD, M.; VAN HEMMEN, J., (2002): A proposal for evaluation of exposure data. In: *Ann Occup Hyg*. 46(3), 287-297.

TISCHER, M., (2011). Personal communication: Model calculations for the EMKG-Expo tool in the case of large-area use of liquids. (01.11.2011), 4p. (unpublished)

TISCHER, M.; POPPEK, U.; (2003): *Inhalative and dermal exposure at different control strategies - Part 1: Control strategy related evaluation of existing exposure information - Report*. 43p.

TISCHER, M.; POPPEK, U.; (2007): *Schutzniveau von Maßnahmenkonzepten: Evaluierung anhand von empirischen Daten und durch probabilistische Modellierung*. (Forschung Projekt F 1914), 81p.

TISCHER, M.; BREDENDIEK-KAMPER, S.; POPPEK, U., (2003): Evaluation of the HSE COSHH Essentials exposure predictive model on the basis of BAuA field studies and existing substances exposure data. In: *Ann Occup Hyg*. 47(7), 557-569.

TISCHER, M.; BREDENDIEK-KAMPER, S.; POPPEK, U.; PACKROFF, R., (2009): How safe is control banding? integrated evaluation by comparing OELs with measurement data and using Monte Carlo simulation. In: *Ann Occup Hyg*. 53(5), 449-462.

TNO; (2006): *The RISKOFDERM Dermal Exposure Model. Version 2.0 - Guidance document*. 23p.

TNO; (2007): *Effective Personal Protective Equipment (PPE)*. AJ Zeist, (V7333).

VERMEULEN, R.; STEWART, P.; KROMHOUT, H., (2002): Dermal exposure assessment in occupational epidemiologic research. In: *Scand J Work Environ Health*. 28(6), 371-385.

VINK, S.R.; MIKKERS, J.; BOUWMAN, T.; MARQUART, H.; KROESE, E.D., (2010): Use of read-across and tiered exposure assessment in risk assessment under REACH--a case study on a phase-in substance. In: *Regul Toxicol Pharmacol*. 58(1), 64-71.

WARREN, N.D.; MARQUART, H.; CHRISTOPHER, Y.; LAITINEN, J.; JJ, V.A.N.H., (2006): Task-based dermal exposure models for regulatory risk assessment. In: *Ann Occup Hyg*. 50(5), 491-503.

WHO; (2008): *Uncertainty and data quality in exposure assessment [Part 1: Guidance document on characterizing and communicating uncertainty in exposure assessment. Part 2: Hallmarks of data quality in chemical exposure assessment]*. IPCS (International Programm on Chemicals Safety). Geneva, (Harmonization project document no.6).

ZEIGLER, B.P.; PRAEHOFER, H.; KIM, T.G., (2000): *Modeling and Simulation. Integrating Discrete Event and Continuous Complex Dynamic Systems.* 2nd ed, Academic Press, 330 pp.

ZHAO, Y.C.; FREY, H.C., (2006): Uncertainty for data with non-detects: Air toxic emissions from combustion. In: *Human and Ecological Risk Assessment*. 12(6), 1171-1191.

Abbreviations

APF	assigned protection factor
ACH	Air changes per hour
BAuA	„Bundesanstalt für Arbeitsschutz und Arbeitsmedizin“ (Federal Institute for Occupational Safety and Health)
BURE	Between user reliability
CGS	control guidance sheet
DEO unit	dermal exposure operation unit
ECHA	European Chemicals Agency
ECETOC	ECETOC – European Centre for Ecotoxicology and Toxicology of Chemicals
EMKG	“Einfaches Maßnahmenkonzept Gefahrstoffe” (Easy to use workplace control scheme for hazardous substances)
GOH	good occupational hygiene
GOHP	good occupational hygiene practice
HERAG	Health Risk Assessment Guidance
IOM	Institute of Occupational Medicine
ITEM	Institute of Toxicology and Experimental medicine
LEV	local exhaust ventilation
LOD	Limit of detection
LOQ	Limit of quantification
MEASE	The metals’ EASE
n.a.	n.a.
n.a.p.	no assessment possible
PPE	personal protective equipment
PROC	Process category
RAR	Risk assessment report
RCR	Risk characterisation ratio
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RMM	risk management measure
RPE	respiratory protective equipment
SMEs	Small and medium sized enterprises
TGD	Technical Guidance Document
TNsG	Technical Notes for Guidance
TRA	Targeted Risk Assessment
WPF	workplace protection factor

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Appendix 1 Discussion of separate models

In the following Chapters a general discussion of the uncertainty of each evaluated model will be provided as well as an evaluation of example situations.

General considerations

A high amount of expert judgement within a tool does not necessarily lead to a less accurate exposure estimation. However, some aspects of uncertainty (e.g. the uncertainty of the knowledge base) cannot be judged in these cases.
If information is missing, sometimes no upper border for the magnitude of uncertainty of the exposure estimate can be determined. Therefore it has not been marked as "very high magnitude" in the corresponding column but as "cannot be judged".
Furthermore, some aspects of input parameters (knowledge base, transparency, variability/uncertainty) are marked as being "not relevant for model uncertainty", as uncertainties of the exposure situation (e.g. how a vapour pressure has been measured) are beyond the scope of this work package. However, model inherent reflections of input parameters (e.g. efficiencies of risk management measures) are influenced by the way of derivation (e.g. fitting to a database, expert judgement) which has to be documented in a transparent way to allow evaluation of the knowledge base and may also include variability. These cases are labelled as "input parameter and model inherent reflection" in contrast to the "pure" input parameters, which represent only the moment when the information is entered into the model. The latter can influenced by uncertainties related to the situation and its documentation and the experience of the model user, but also by the description of the input parameter in the corresponding model.
If a parameter influences the inhalation exposure estimate but not the dermal estimate it will be marked with a magnitude of uncertainty of 0 for dermal exposure.
Direction and magnitude of the exposure estimate's uncertainty are indicated using plus- and minus-signs with plus signs representing positive deviations/ overestimations due to the source of uncertainty and minus-signs possible underestimations.
The number of "+" and "-" indicates the magnitude of uncertainty, i.e. one, two or three orders of magnitude deviation to the actual exposure value is expected as a maximum.
Sometimes the uncertainty or at least the part of it that can be evaluated are mainly caused by the possibility of a wrong assignment of the parameter category (e.g. dustiness). This type of uncertainty represents an overlap between model uncertainty and scenario uncertainty, as it is influenced by the documentation of a situation as well as user experience and input parameter quality.

List of example scenarios/situations

As explained in the Introduction the uncertainty of a model estimate always depends on the situation that should be assessed. Therefore it was decided to include a selection of defined exposure situations to show possible differences. However, this selection of scenarios is far too limited to be seen as representative and should therefore only be regarded as a set of illustrative examples.
The situations have been selected from the eteam database used for the external validation exercise. If available, identical codings into model parameter have been used. Although for all situations only measured exposure values for one exposure route (inhalation or dermal) is available a discussion of uncertainty has been done for both routes to allow for a comparison of all models.
Situations which are clearly beyond the scope of a specific model have been excepted from this comparison to avoid misinterpretations.

Appendix 1, Table 1 Scenario 1: Spraying of locomotives with paint (toluene exposure used for external validation)[27]

ECETOC TRA v.2	
Molecular weight (g/mol)	92
solid?	no
dustiness	n.a.
volatility (Pa)	2910
PROC	7 (industrial spraying)
type of setting	industrial setting
indoors or outdoors	indoors
LEV?	no
duration	>4 h
type of resp. protection	none
preparation?	yes
concentration range	5-25%
ECETOC TRA v.3	
Molecular weight (g/mol)	92
solid?	no
dustiness	n.a.
volatility (Pa)	2910
PROC	7 (industrial spraying)
type of setting	industrial setting
indoors or outdoors	indoors with enhanced general ventilation
LEV?	no
duration	>4 h
type of resp. protection	none
preparation?	yes
concentration range	5-25%
Dermal PPE/gloves?	no
consider LEV for dermal exposure?	no

[27] Red letters refer to codings also used in the external validation.

MEASE	
Scenario beyond scope (see Chapter "MEASE version 1.02.01")	
EMKG-EXPO-TOOL	
volatility	medium
scale of use	1-1000 l
surfaces	yes
duration less then 15 minutes	no
level of control	general ventilation
STOFFENMANAGER®	
location	painting area
solid?	no
vapour pressure (Pa)	2910
% concentration in product	50
task characterisation (liquid)	handling of liquids at high pressure resulting in substantial generation of mist or spray/haze
duration of task	4-8 h/day
frequency of task	4-5 days/week
Is the working room cleaned daily?	no
Is the machine inspected monthly?	no
Takes the task place in the breathing zone of an employees?	yes
Is more than 1 employee doing the same task?	yes
Is the task followed by a period of evaporation/drying/curing?	yes
volume of work room	>1000 m3
type of general ventilation	good general ventilation
Other available control measure?	no controls at source
Is the worker located in a cabin?	no cabin
PPE applied?	no PPE
RISKOFDERM	
DEO unit	4 (Spray applications)
indoor/outdoor	indoor
volatility of carrier liquid	not highly volatile
ventilation/air flow away from worker or not?	yes
spray direction	level
distance	less than 1 m
physical state	liquid
use rate (l/min)	25.22
duration (minutes)	240
segregation?	no

Appendix 1, Table 2 Scenario 2: Small scale surface wiping (potassium peroxomonosulphate exposure used for external validation)[27]

ECETOC TRA v.2	
Scenario beyond scope (see chapters “Evaluation matrix”, “Example situations”)	
ECETOC TRA v.3	
Scenario beyond scope(see chapter “Evaluation matrix”, “Example situations”)	
MEASE	
Molecular weight (g/mol)	614.77
solid?	no
dustiness	
volatility (Pa)	10
PROC	10 (wiping)
type of setting	professional use
indoors or outdoors	indoors
LEV?	no
duration	> 4 h
type of resp. protection	none
preparation?	yes
concentration range	< 1%
Pattern of use	non dispersive use
Pattern of exposure control	direct handling
Contact level	intermittent contact
Implemented RMMs	General ventilation
RMM efficiency based on	low confidence
Respiratory protective equipment (RPE)	no
Use of gloves	no
EMKG-EXPO-TOOL	
volatility	low
scale of use	1-1000 ml
Application of more than 1 l per shift on surfaces of more than 1 m^2?	yes
duration less then 15 minutes?	no
level of control	general ventilation
STOFFENMANAGER®	
location	no information
solid?	no
vapour pressure (Pa)	10
% concentration in product	1%
task characterisation (liquid)	handling of liquids on small surfaces or incidental handling of liquids
duration of task	4-8 h/day
frequency of task	4-5 days/week
Is the working room cleaned daily?	no
Is the machine inspected monthly?	no
Takes the task place in the breathing zone of an employees?	yes
Is more than 1 employee doing the same task?	yes

Is the task followed by a period of evaporation/drying/curing?	yes
volume of work room	<100 m^3
type of general ventilation	good general ventilation
other available control measures?	no
Is the worker located in a cabin?	no
PPE applied?	no
RISKOFDERM	
DEO unit	2 (wiping)
application rate (l/min)	0.1
extensive body contact?	no
duration of scenario (minutes)	5

Appendix 1, Table 3 Scenario 3: Sieving of plastic powders and filling of barrels (overall dust exposure used for external validation)[27]

ECETOC TRA v.2	
Molecular weight	1000000
solid?	yes
dustiness	medium
volatility (Pa)	n.a.
PROC	8a (transfer of substance from/to vessels or large containers at non-dedicated facilities)
type of setting	industrial setting
indoors or outdoors	indoors
LEV?	no
duration	> 4 h
type of resp. protection	none
preparation?	n.a.
concentration range	n.a.
ECETOC TRA v.3	
Molecular weight (g/mol)	1000000
solid?	yes
dustiness	medium
volatility (Pa)	n.a.
PROC	8a (transfer of substance from/to vessels or large containers at non-dedicated facilities)
Ind/prof	ind
indoors or outdoors	indoors with good general ventilation
LEV?	no
duration	> 4 h
type of respiratory protection	none
preparation?	n.a.
concentration range	n.a.
PPE/gloves	no
consider LEV for dermal exposure?	no
MEASE	
Molecular weight (g/mol)	1000000
solid?	yes
dustiness	medium
volatility (Pa)	
PROC	8a (transfer of substance from/to vessels or large

	containers at non-dedicated facilities)
Type of setting	industrial use
indoors or outdoors	indoors
LEV?	no
duration	> 4 h
type of resp. protection	none
preparation?	n.a.
concentration range	n.a.
Pattern of use	wide dispersive use
Pattern of exposure control	direct handling
Contact level	extensive contact
Implemented RMMs	general ventilation
RMM efficiency based on	low confidence
Respiratory protective equipment (RPE)	no
Use of gloves	no
EMKG-EXPO-TOOL	
dustiness	medium
scale of use band	> 1000 t
duration less than 15 minutes	no
level of control	general ventilation
STOFFENMANAGER®	
location	powder production area
solid?	solid
dustiness?	coarse dust
Is the product diluted in water?	no
task characterisations / solids	handling of product or treatment of objects, where due to high pressure, speed or force large quantities of dust are generated and dispersed
cutting or shaping involved?	no
duration of task	4-8 h
frequency of task	4-5 d
Is the working room cleaned daily?	no
Is the machine inspected monthly?	no
Takes the task place in the breathing zone of an employees?	yes
Is more than 1 employee doing the same task?	yes
Is the task followed by a period of evaporation/drying/curing?	no
volume of work room	> 1000 m^3
type of general ventilation	general ventilation
other available control measures?	no
Is the worker located in a cabin?	no
PPE applied?	none
RISKOFDERM	
DEO unit	1 (filling, mixing, loading)
rare or more than rare contact?	more than rare contact
light or more than light contact?	more than light contact
type of substance	low or moderately dusty
Splashes/aerosol generated?	yes
Ventilation	normal or good ventilation
level of automation?	manual task
use rate (kg/min)	8.3
duration	240

ECETOC TRA

ECETOC TRA v.2

Two versions of ECETOC TRA (v.2 and v.3) are part of the eteam project. Issues related to ECETOC TRA version 2 or both versions will be discussed in the following section. Changes between version 2 and 3 will be discussed afterwards.

General aspects: general model approach and uncertainty of datasets

The basic approach of ECETOC TRA is the assignment of initial exposure estimates to a certain combination of process description (PROC), type of setting (professional vs. industrial) and volatility (vapour pressure or dustiness). These initial exposure estimates are then refined by a set of modifiers which are partly process specific (LEV efficiency) and partly independent of process and substance.
If this approach is in principle able to reflect exposure estimates in a correct way or if other approaches (e.g. logic trees) would be more accurate cannot be finally assessed.
Some parts of the model have been derived based on partly published measured exposure data. However, as these datasets do not refer to the complete model they will be discussed separately in the evaluation matrix.

Evaluation matrix

Appendix 1, Table 4 ECETOC TRA v.2 Evaluation matrix

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
Input parameters							
physical state (volatile/solid)	Input parameter / intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high: Wax like compounds may have unsharp boundaries; substances with low melting points may be solid at room temperature but however used as liquid at higher temperatures. However, overall these are special cases.	**inhalation:** Direction and magnitude of a possible deviation of the exposure estimate depend on the substance and its molecular weight, which is used to convert units from ppm to mg/m^3. Theoretically, there are no upper or lower limits for the magnitude of uncertainty. However, a detailed assessment is not possible at this point. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	n. a. p.
						dermal: no influence	0
dustiness (high/medium/ low)	Input parameter/ intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	medium: Qualitative description, high vagueness, medium level of detail	**Inhalation**: The magnitude of uncertainty of the exposure estimate can go up to two orders of magnitude based on the difference of initial exposure estimates assigned to two neighbouring dustiness bands.	**++/--**
						Dermal: No influence.	**0**

[28] Direction of deviation is indicated by "+" (overestimations expected) and "-" (underestimations expected) signs. "+/-" means that both directions are possible. The number of +/- signs indicates the magnitude of uncertainty (factor up to 10, up to 100, more than 100 between estimate and actual exposure value). 0 refers to no influence on uncertainty of the exposure estimate.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
vapour pressure (high/medium/ low/very low)	Input parameter/ intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high: quantitative number	**Inhalation:** Assignment of a wrong vapour pressure category would lead to deviations up to two orders of magnitude, based on the difference of initial exposure estimates assigned to two neighbouring dustiness bands. However, wrong assignments are considered to be unlikely in this case. Errors are expected to refer mostly to uncertainties in the measurement of vapour pressure and not to model related uncertainty.	++/--
						Dermal: No influence	0
Process temperature for PROCs 21-25 (Tproc<Tmelt; Tproc≈Tmelt; Tproc>Tmelt)	Input parameter/ process description + operational conditions	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	medium: Quantitative numbers but "$T_{melt} \approx T_{proc}$" is an ambiguous categorisation.	**Inhalation**: The assignment of a wrong fugacity band could lead to deviations of the exposure estimate of up to one order of magnitude.	+/-
						Dermal: no influence of volatility	0
PROC number (PROC 1-25)	Input parameter/ process description + operational conditions	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	medium: Medium level of detail in explanation, some vague descriptions	**Dermal and inhalation:** A wrong PROC assignment could lead to exposure deviations up to three orders of magnitude for both inhalation and dermal exposure.	+++/---
type of setting (industrial/ professional)	Input parameter/ process description + operational conditions	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	low: Qualitative description	**Inhalation**: The assignment of a wrong type of setting could lead to an exposure deviation up to one order or magnitude.	+/-
						dermal: no influence	0
Molecular weight (only for unit conversion	Input parameter/ intrinsic	not relevant for model uncertainty	not relevant for model uncertainty	not relevant for model uncertainty	high: quantitative parameter	**inhalation**: No assessment is possible of the impact of a wrong entered molecular weight as this	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
in case of liquids)	substance property					input is a free number. Uncertainties are expected to refer only to user handling and measurement uncertainties and not to the exposure model.	
						Dermal: no influence	0
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction)	Input parameter and model inherent reflection/use description and operational condition	n. a. p. both possible	medium: explanation available in TRA107, however, no experimental basis shown.	n.a.p.	medium/high: quantitative description, but only partly given if w/w or other percentage (given in worker stand-alone tool and guide but not in integrated tool and user guide).	**Inhalation/liquids:** A thorough investigation of the influence of liquid mixtures on vapour pressure would be beyond the scope of this project. However, the implemented factors will lead to estimations above the ideal, linear approach (i.e. $p_{vap} \sim c_{substance}$), thus, an overestimation of exposure is considered to be more likely than an underestimation. Overestimations of exposure up to three orders of magnitude are possible (especially for very low concentrations below 1%) and underestimations down to one order of magnitude, if p_{vap} (mixture) is assumed to be identical to p_{vap}(pure substance). As the input parameter quality is considered to be medium/high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	+++/-
						Inhalation/solids: no influence	0
						Dermal: no influence.	0
duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% exposure	Input parameter and model inherent reflection/Use description and	n. a. p. both possible	medium: explanation available in TRA93, however, no experimental	n.a.p.	high: quantitative description	**Inhalation**: Homogeneous emission of exposure would be an appropriate basis for a linear dependency of duration and inhalation exposure. However the	+++/-

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
reduction), maximum 8h	operational condition		basis shown.			implemented modifiers lead to higher exposure estimates than suggested by such an approach which makes overestimations more likely than underestimations. PROCs may include several sub-activities, i.e. exposure may not be distributed evenly over the considered duration (e.g. sampling for PROC2/3, see also Chapter "ECETOC TRA v.3", peak exposure). Overestimations up to three orders of magnitude are possible (especially for very short durations). Underestimations may go up to one order of magnitude (based difference between 90% reduction and a worst case of 0% reduction in reality) (HOFSTETTER ET AL., 2013)[29]. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	0
						Dermal: no influence	0

[29] see also Hofstetter et al.: measurement of spray paint exposure (inhalation): TWA 8h 8.3 ppm vs. TWA 15min 117.7 ppm. This corresponds roughly to one order of magnitude deviation.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
LEV for inhalation exposure, PROCs 1-20 (present or not)/ efficiency defined by physical state, process description, type of setting	Input parameter and model inherent reflection/ localised controls	n. a. p. both possible	low: no detailed explanation available	n.a.p.	medium: Yes/no decision necessary for input.,no detailed description of requested design in model itself or model related documentation, however, reference to HSE guidance from 2008 is made (updated version from 2011 (HSE, 2011)) where more detailed explanations are laid down.	**inhalation**: Efficiencies range from 75-97% and are depending on PROC and volatility/dustiness. A very worst case efficiency would be 0% which would lead to an underestimation of exposure about two orders of magnitude. Overestimation of exposure is also possible and can theoretically go up to three orders of magnitude. However, a final assessment is not possible at this point.	n.a.p.
LEV for dermal exposure, PROCs 1-20 (present or not)/ efficiency defined by process description	Input parameter and model inherent reflection/ localised controls	n. a. p. both possible	low: no detailed explanation available	n.a.p.	medium: discussion see above	**Dermal**: Efficiencies range from 50 to 97.5% and are depending on the PROC. Underestimations down to two orders of magnitude are theoretically possible and overestimations up to three orders of magnitude. However, a final assessment is not possible.	n.a.p.
Outdoors (30% efficiency)	Input parameter and model inherent reflection/ localised controls	n. a. p. both possible	low: no detailed explanation or measured background available	n.a.p.	medium/high: outdoors is more or less unambiguous, only rare examples may exist were it is not clear how to assign this parameter (half-open areas with 3 walls and a roof or similar)	**Inhalation**: Both over- and underestimations are possible because of different wind conditions, surroundings etc. over and underestimations theoretically up to three orders of magnitude. However, a final assessment is not possible. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	n.a.p.
						dermal: no influence	0

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
LEV for inhalation, PROCs 21-25 (present or not)/ efficiency defined by physical state, process description, type of setting	Input parameter and model inherent reflection/ localised controls	n. a. p. both possible	low: no detailed explanation or measured background available. Contradictions in documentation (ECETOC, 2009)	n.a.p.	medium: high vagueness. Parameter requires a yes/no decision; it is not defined of which type the LEV should be, how many air changes per hour it should induce etc. Reference to HSE guidance from 2008 is made (updated version from 2011 (HSE, 2011)) where more detailed explanations are laid down	**inhalation**: Efficiencies lie between 97% and 75% and are depending on PROC and volatility/dustiness., The worst case would be 0% efficiency. This results in a theoretical underestimation of exposure of two orders of magnitude (if 97% efficiency are selected but only 0% apply) and a maximum overestimation of three orders or magnitude (if 75% are selected but ~100% apply). However, a final assessment is not possible.	n.a.p.
LEV for dermal, PROCs 21-25 (present or not)/ efficiency defined by process description	Input parameter and model inherent reflection/ localised controls	n. a. p. both possible	low: limited explanation in TR 107 (ECETOC, 2009)	n.a.p.,	medium: for explanation see above	**dermal**: Efficiencies range from 99.5% to 50% and are depending on PROC. The worst case would be that LEV has efficiency 0. This would result in possible underestimations of three orders of magnitude. However, this scenario is considered to be unlikely. The lowest value of 50% leads to a possible overestimation of exposure up to three orders of magnitude (See above). However, is not possible.	n.a.p.
Respiratory protection equipment (90%, 95% efficiency according to APFs 10 and 20)	Input parameter (and model inherent reflection)/ personal protective equipment	n. a. p. both possible	high: assigned protection factors (APFs) are given in the ECETOC documentation (ECETOC, 2009). APFs are documented for each type of respiratory protection by the	n.a. no common agreement within EU	high: APFs are available together with other product related information when a respiratory protection is bought. Derivation of appropriate APFs for a certain equipment is not an issue of the model developers.	**inhalation**: APFs are based on low percentile (5^{th}) of workplace protection factor (WPF). Thus, overestimations are expected. Uncertainty depends on the situation and the country. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category – which may REACH one order of magnitude - is considered to be mainly related to scenario	+/-

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
			corresponding producers. They may differ between countries. However, this does not affect the ECETOC documentation.			uncertainty.	
						Dermal: no influence	0
Model inherent parameters							
Breathing rate (10 m^3 per 8h shift) (only used for overall exposure per kg and day)	Model inherent parameter/ process description + operational condition	n. a. p. both possible	low: no information about value origin given	n.a.p.	n.a.	**Inhalation**: Common limit values for inhalation exposure are given in ppm or mg/m^3, i.e. the breathing rate does not have an influence on the risk characterisation. However, internal doses can be under- as well as overestimated. The ECETOC European exposure factors handbook (ECETOC, 2001) lists breathing rates between 0.4 (rest) and 6.7 m^3/hour (heavy exercise), i.e. the (unlikely) maximum of deviation would be around a factor of 20 (two orders of magnitude). The exposure factors handbook from US EPA (EPA, 2011) suggests lower deviations, however two orders of magnitude may be considered to be the upper border of the deviation of the exposure estimate.	++/--
						Dermal: no influence	0
70 kg body weight worker	Model inherent parameter/ process description + operational	n. a. p. both possible	low: no information about value origin given	n.a.p.	n.a.	**Dermal and inhalation:** As a human beings normally only shows body weights within a certain range, only exposure deviations up to one order of magnitude are	+/-

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
	condition					expected. This influences only internal mg/kg doses, i.e. the dermal risk characterisation but not necessarily the inhalation risk characterisation. The ECETOC European exposure factors handbook (ECETOC, 2001) lists mean body weights above 70 kg for adult males but mean body weights between 60 and 70 kg for females, i.e. underestimations of the exposure per kg bw are possible. Inhalation exposure estimates are only affected if internal exposure is assessed.	
Initial exposure estimate (PROC1-20 for inhalation and dermal exposure)/ defined by fugacity, physical state, process description, type of setting for inhalation; defined by PROC for dermal)	Model inherent parameter/ process description + operational condition	n. a. p. both possible	medium: Some data sources are given but no single datasets. A certain amount of scientific knowledge of the model developers was involved (ECETOC, 2009)	n.a.p.	n.a.	**Dermal and inhalation:** Deviation of the exposure estimate cannot be defined. It depends very specifically on situations, occupational hygiene, etc. As ECETOC TRA is a tier 1 tool it is expected that initial exposure estimates are at the upper border of possible exposure estimates for a situation or a process. However, a final assessment is not possible at this point. Theoretically, up to three orders of magnitude deviation are possible.	n.a.p.
Initial exposure estimate (PROC21-25 for dermal and inhalation exposure): defined by	Model inherent parameter/ process description + operational condition	n. a. p. both possible	medium: In general most of the underlying datasets are published (in (ECETOC, 2009)	medium: Inhalation datasets are only published in EU risk assessment reports.	n.a.	**Inhalation and dermal:** Direction and magnitude of the uncertainty of the exposure estimate depend on situation and if this situation is represented in the underlying datasets, thus, it cannot be assessed. Maximum exposure	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
fugacity, physical state, process description, type of setting for inhalation; defined by PROC for dermal			and (HERAG, 2007) some underlying reports/publications) however not all steps used for the derivation of initial exposure estimates have been published. Some contradictions are present in (ECETOC, 2009) (different values assigned to the same PROC, see Conceptual evaluation).	Numbers of datasets for one process vary between 146 and 2544 (inhalation) and 0 and 125 (dermal) respectively. Sometimes only information about one metal is available. Scientific judgement has been involved.		variability within one process category is around one order of magnitude, however, theoretically the deviations can go up to three orders of magnitude. A final assessment is not possible at this point.	
Skin areas, Exposed body parts (defined by PROC; palm(s), fingers, hand(s), hands and forearm(s))	Model inherent parameter/ process description + operational condition	n. a. p. both possible	medium: skin areas are given but no explanation about their assignment.	n.a.p.	n.a.	**Dermal**: Direction and magnitude of uncertainty depend on the situation. The total skin surface of an adult is approximately 2 m^2 (ECETOC, 2001) the smallest considered skin area for worker exposure is 240 cm^2, i.e. the theoretical underestimation of exposed skin area can only go up to approximately two orders of magnitude if in reality the complete body would be exposed and up to one order of magnitude, if the complete hands and forearms area (1980 cm^2) instead of only 240 cm^2 is exposed. Overestimations are also possible and depend also on the situation. Theoretically they can go up to three orders of magnitude (e.g. 10 cm^2 exposed instead of 1980cm^2). According to Creely and Cherrie (Creely and Cherrie, 2001) hand	+++/--

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	transparency of documentation	Certainty of knowledge base	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[28]	
						exposure to pesticides may account for approximately 50% of total body exposure, sometimes up to 90%. However, the resulting deviation strongly depends on the process and other (protective) clothing.	
						Inhalation: no influence	0
Presentation of results	Model inherent parameter/ Model assumption	variability/ uncertainty	low: no indication of the point on the real life distribution of exposure values (percentile) which the result is intended to reflect in TR107.	n.a.p.	medium/low: Only one value, i.e. no choice of "wrong" value within a range possible. However, there is no indication of the point on the real life distribution of exposure values (percentile) which the result is intended to reflect in TR107. Vague description.	**Inhalation and dermal:** According to TR114 ECETOC TRA results are intended to represent the 75th percentile of the exposure distribution. However, this is not reported in earlier documentations, i.e. it is not known how model users interpreted the level of conservativeness of the model (90th percentile is often regarded to be the "reasonable worst case"). The induced uncertainty is not quantifiable.	n.a.p.
Model equation, assumptions							
Ideal gas law and approximately 298 K (i.e. molar volume of 24 l/mole) assumed for conversion of units in case of liquids	Model/ assumption	uncertainty	high: No justification documented. However, the ideal gas law is common knowledge.	n.a.p. Depends on the substance. Many publications exist about the ideal gas in general, however not for all substances experimental data may be available.	n.a.	**inhalation**: This uncertainty source does not reflect an uncertainty of the model itself but of the ideal gas law. Its influence may vary and cannot be assessed at this point. However, deviations are expected to be small compared to other sources of uncertainty and affect only the conversion of units, but not the result in ppm.	n.a.p.
						dermal: no influence	0

Source of uncertainty	**Type of uncertainty source**	**Variability/ uncertainty**	**transparency of documentation**	**Certainty of knowledge base**	**Quality of parameter definition (vagueness/level of detail)**	**Direction and magnitude of the caused uncertainty**[28]	
GOHP	Model/ assumption	uncertainty	Medium: The assumption is documented in TR 114 (ECETOC, 2013) but not in the earlier TR107 (ECETOC, 2009). The basis for the derived exposure values is however not documented (see “initial exposure estimates”), no statistics on GOHP are given.	n.a.p.	n.a.	**Inhalation and dermal:** No occupational hygiene would lead to an underestimation of exposure, which can theoretically the deviation can reach three orders of magnitude. No data on GOHP in Europe are available.	n.a.p.

Summary

It can be summarised that no source of uncertainty in ECETOC TRA v. 2 could be identified that is expected to lead predominantly to underestimations. On the other hand several sources of uncertainty could be identified which are expected to produce overestimations of exposure. This indicates that the model is indeed conservative as intended by the tier 1 approach. It will tend to err on the side of caution and thus, should at least theoretically ensure a sufficient protection of the affected workers.

Dermal exposure is influenced by less parameters than inhalation (no concentration, no duration influence dermal estimate in version 2, no gloves are implemented), which also reduces the potential sources of uncertainty but on the other hand also increases the model resolution (see Chapter 2.3.10). Overall the resolution of ECETOC TRA v.2 is considered to be medium for inhalation, while it is considered to be medium/low for dermal exposure.

Large parts of the model cannot be assessed as not all information that would be needed for such statement has been available for this analysis. Some main parts of the model (e.g. initial exposure estimates, efficiencies for RMMs) are at least partly based on scientific judgement. Therefore, the transparency is considered to be medium and the estimation of the magnitude of uncertainty is hampered. However, according to the available literature the model including its assumptions and default parameters has been designed as a conservative tier 1 model.

Besides the scientific judgement, measured exposure data were used for the derivation of the model defaults. Not all of these data are publicly available and not all derivation steps from data to exposure estimate are reproducible. Thus, a detailed assessment of the knowledge base or the magnitude of uncertainty of ECETOC TRA v.2 is not possible. However, the uncertainty of the model's overall knowledge base is considered to be medium.

As comparable numbers of parameters have been assigned to the upper and lower category of uncertainty related to the parameter quality, the average quality of the input parameters was assessed as medium.

ECETOC TRA v.3

In this chapter only changes relative to version 3 of ECETOC TRA and there likely impact on the uncertainty will be discussed.

Evaluation matrix

Appendix 1, Table 5 ECETOC TRA v.3 Evaluation matrix

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty[30]	
Input parameters							
Process temperature for PROCs 1-20 (not explicitly implemented, however vapour pressure at process temperature can be entered)	Input parameter/process description + operational conditions	not relevant for model uncertainty	see transparency of the initial exposure estimates	n.a.	high: vapour pressure is a quantitative parameter, low vagueness.	**inhalation:** The process temperature is now reflected in the assignment of the correct volatility band, i.e. the possible directions and magnitude of uncertainty are identical to the initial exposure estimates. If no vapour pressure at process temperature is known it will lead to uncertainties comparable to those discussed for the missing parameter “process temperature” in Chapter “ECETOC TRA v.2”. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	n.a.p.
						dermal: no influence	0
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40,	Input parameter and model inherent reflection/Use	n.a.p. both possible	medium:	n.a.p.	medium/high::	**dermal and inhalation (solids):** A lower concentration is	+++/-

[30] Direction of deviation is indicated by “+” (overestimations expected) and “-“ (underestimations expected) signs. “+/-“ means that both directions are possible. The number of +/- signs indicates the magnitude of uncertainty (factor up to 10, up to 100, more than 100 between estimate and actual exposure value). 0 refers to no influence on uncertainty of the exposure estimate.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty[30]	
0% exposure reduction) for dermal exposure and solids in general.	description and operational condition		explanation available in TRA107, however, no experimental basis shown.		not mentioned if v/v or m/m percentages are required.	expected to decrease dermal exposure linearly as it does not depend on the vapour pressure. and the concentration in air (at least for contamination via splashed, aerosol, contaminated surfaces which are assumed to be the main sources of exposure). For solids the exposure may also depend on things like the particle size, thus, in principle the linear approach might lead to both over and underestimations of exposure. However, the implemented factors are chosen conservatively (less exposure reduction than a linear approach would suggest), thus, underestimations cannot be excluded but are assumed to be less likely. Theoretically underestimations up to one order of magnitude (90% estimated exposure reduction vs. worst case 0%) and overestimations up to three orders of magnitude (if a non-linear dependency would be assumed) are possible. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty[30]	
duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% efficiency), maximum 8h; for dermal exposure	Input parameter and model inherent reflection/Use description and operational condition	n.a.p. both possible	medium: explanation available in TRA93, however, no experimental basis shown.	n.a.p.	high: quantitative description, low vagueness	**dermal**: Now also applicable to dermal exposure in case of low/medium dustiness or high volatility substances. The connection between dermal exposure and duration of exposure is more difficult to describe than for inhalation, as it depends on substance properties, saturation effects etc. Both under- and overestimations are possible, resulting in a theoretical maximum of one order of magnitude for underestimations and three orders of magnitude for overestimations (90% reduction if 0% would be appropriate; 0% reduction if more than 99% would be appropriate). As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	+++/-
short term duration for inhalation (peak exposure for duration <15min = 4 x 8h average)	Input parameter and model inherent reflection/Use description and operational condition	both possible	high: underlying publications are given including main results.	medium: published datasets but only one publication with a limited set of measurements. in general there is a complex relation between full shift and short term exposure	medium: quantitative description, however the word "peak exposure" seem not to be clear to everyone (see last eteam meeting).	**inhalation**: It is differentiated between task-based and process based PROC numbers, however a (compared with cited measured values) conservative upper end factor of 4 is chosen. On the other hand other published values indicate that a factor of more than 4 may be appropriate for spray painting (HOFSTETTER ET AL., 2013). Overall the comparison of examples given by ECETOC (ECETOC, 2013) and Hofstetter	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty[30]	
				depending on percentile and process/task.		et al. suggests possible over- and underestimations up to one order of magnitude. However, as no thorough literature search was possible within the scope of this project a final assessment cannot be made.	
						dermal: no influence	0
LEV for inhalation, PROCs 1-20 (present or not)/ defined by physical state, process description, type of setting	Input parameter and model inherent reflection/localised controls	both possible	low: no explanation or background for derivation of efficiencies.	n.a.p.	medium (see v. 2 for explanation)	**inhalation**: Some minor, PROC dependant changes have been applied, however, the general tendencies stay the same as in version 2 of the tool. Efficiencies for version 3 range from 75 to 95%, which theoretically may result in magnitudes of uncertainty up to three orders of magnitude overestimation and two orders of magnitude underestimations. However, a final assessment without an external validation is not possible.	n.a.p.
LEV for dermal, PROCs 1-20 (present or not) / defined by process description	Input parameter and model inherent reflection/localised controls	both possible	low: no explanation or background for derivation of efficiencies.	n.a.p.	medium (see v. 2 for explanation)	**dermal**: Efficiencies have been modified depending on PROC, in general the efficiency has been decreased. They are now identical to inhalation efficiencies which ranges from 75-95%, therefore the maximum magnitude of uncertainty is identical to the inhalation values. However, also in this case a final assessment is not possible.	n.a.p.
General ventilation (good general vent. 30%, enhanced 70%, good or enhanced + LEV)	Input parameter and model inherent reflection/localised controls	both possible	medium: no measurements or detailed algorithms are explained, but comparison with other models (e.g.	Medium: established other models are cited, however their	high: in contrast to the LEV description air change rates	**inhalation**: The implemented efficiencies result in theoretical underestimations up to one order of magnitude (worst case: assuming 70% when 0% would be appropriate). For	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty[30]	
			COSHH), air changes per hour are given (3-5 ach, 5-10 ach),	background is not evaluated, thus, a thorough understanding of the basis of these efficiencies and if they are realistic is not possible.	are given in this case.	overestimations no upper border can be determined, theoretically they can range up to three orders of magnitude. Available literature (ECETOC, 2013; Fransman et al., 2008) suggest efficiencies above 30% for good general ventilation. However, a final assessment of this parameter is not possible. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	
						dermal: no influence	0
Gloves (95, 90, 85, 80 % efficiency, corresponding to different levels of personal behaviour/level of supervision)	Input parameter and model inherent reflection/personal protective equipment	both possible	Low no references are given in the ECETOC documentation.	n.a.p.	low: qualitative description, no detailed explanation of expected behaviour related to levels of supervision.	**dermal**: The efficiency of gloves is a quite complicated topic: although a number of different defaults for various exposure models are in use only a limited number of publications is available. Overall overestimations of exposure can theoretically go up to three orders of magnitude while underestimations can go up to two orders of magnitude (95% instead of 0%). It is expected that under- and overestimations of more than one order of magnitude are unlikely, however, a final assessment of magnitude and direction of the uncertainty is not possible at this point.	n.a.p.
						inhalation: no influence	0
Model inherent parameters							

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty[30]	
Initial exposure estimates (all PROCs, dermal and inhalation)	Model inherent parameter/ process description + operational condition	both possible	see ECETOC v.2	see ECETOC v.2	n.a.	**dermal and inhalation:** Some minor changes have been implemented compared to version 2 of ECETOC TRA, however, the in general the expected/possible maximum deviations is not expected to have changed. Moreover still no detailed documentation about the derivation of initial exposure estimates is available, thus, an upper border for the magnitude of uncertainty cannot be determined at this point. Theoretically, both under- and overestimations are possible.	n.a.p.
Presentation of results	Model inherent parameter/ Model assumption	variability/ uncertainty	medium/high: Information is given in TR114 (results should represent the 75th percentile). However, information about underlying data (75th percentile of what?) is limited.	n.a.p.	medium/high: Only one value, i.e. no choice of “wrong” value within a range possible. Information about interpretation of the result is given in TR114 (75th percentile).	**Inhalation and dermal:** According to TR114 ECETOC TRA results are intended to represent the 75th percentile of the exposure distribution. The information about underlying data (75th percentile of what?) is limited. The induced uncertainty is not quantifiable.	n.a.p.
Model							
Connection/dependency between dustiness/volatility and the implementation of duration in combination with dermal exposure:	Model/assumption	both possible	Low: no detailed explanation or experimental background	n.a.p.	n.a.	**dermal**: The magnitude of uncertainty can be up to a factor of 10 if it is assumed that the modifying factor 0.1 is applied where exposure should not have been reduced (or that the factor has been applied by mistake). Both over- and underestimations	+/-

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency	Certainty of knowledge base	Quality of parameter definition	Direction and magnitude of the caused uncertainty[30]	
						are generally possible. As dermal exposure also depends on saturation processes this cannot be evaluated without a very detailed investigation of the specific situation and substance that would be beyond the scope of this project.	
						inhalation: no influence	0

Summary

ECETOC TRA v.3 offers more exposure reducing determinants, especially for dermal exposure, than v.2 (e.g. gloves, concentration for dermal exposure and general ventilation for inhalation). This consequently means that the conservativeness and level of protection of the model is slightly decreased. However, the level of detail and the general resolution have been increased and the general tendency of the model is still considered to be conservative, as none of the newly introduced parameters seems to suggest a major tendency for underestimations.

Overall the resolution of ECETOC TRA v.3 is considered to be medium for inhalation, while it is considered to be comparably high for dermal exposure.

The documentation of TRA v.3 (ECETOC, 2013) offers a well-structured summary of the model's scope and limitations that was not included in this form in earlier documentations, i.e. the transparency has been slightly increased. However, most issues concerning the knowledge base and expected deviations of the exposure estimate identified for v.2 also apply to v.3 of ECETOC TRA.

Example situations

Scenario 2: Small scale surface wiping:
Exposure to potassium peroxomonosulphate in aqueous solution should be assessed (in accordance with the external validation), i.e. a mixture of a solid substance with liquids.
This is beyond the scope of ECETOC TRA, therefore the scenario has not been included into the evaluation matrix.

Appendix 1, Table 6 Magnitudes of uncertainty: ECETOC TRA v.2 (red text refers to comments)

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
			Scenario within scope For this situation toluene vapour exposure should be assessed (in accordance with the external validation). This substance is within the scope of ECETOC TRA. However, exposure to liquid aerosols is not covered, i.e. the overall exposure to toluene may be higher than estimated.	**Scenario partly beyond scope:** The scenario describes sieving and filling (handling) of plastic granules (polyester or polyethylene) mixed with pigments. In the external validation exercise inhalable dust concentrations have been assessed for this situation without exposure values for single components. This dust concentration probably reflects mostly plastic dust but can be used as a worst case value referring to single components like pigments. ECETOC TRA is not designed to estimate combined exposure values, i.e. an overall inhalable dust estimate is beyond its scope. However, single components can be estimated, therefore the situation has not been removed from the evaluation matrix.	
Input parameters					

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
physical state (volatile/solid)	input parameter	**dermal and inhalation**	n. a. p.	n. a. p.	n. a. p.
			liquid. Quantitative parameter, therefore it is assumed that assignment of a wrong category will be mainly related to scenario uncertainty. High parameter quality.	solid. Quantitative parameter, therefore it is assumed that assignment of a wrong category will be mainly related to scenario uncertainty. High parameter quality.	
dustiness (high/medium/low)	input parameter	**Inhalation**	n.a.	+/-	**++/--**
			n.a.	medium dustiness assigned, PROC8a	
		Dermal: No influence.	n.a.	n.a.	**0**
			n.a.	n.a.	
vapour pressure (high/ medium/low/very low)	input parameter	**Inhalation**	n.a.p.	n.a.	++/--
			uncertainty mostly scenario uncertainty	n.a.	
		Dermal: No influence	0	n.a.	0
			no influence on exposure estimate	n.a.	
Process temperature for PROCs 21-25 (Tproc<Tmelt; Tproc≈Tmelt; Tproc>Tmelt)	input parameter	**Inhalation**	n.a.	n.a.	+/-
			PROC7	PROC8a	
		Dermal: no influence of volatiliy	n.a.	n.a.	0
			PROC7	PROC8a	
PROC number (PROC 1-25)	input parameter	**Dermal and inhalation**	+++/---	+++/---	+++/---

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
			comparison with PROC11 estimates: small order of magnitude underestimation. However, no detailed assessment possible.	comparison with PROC8b/9 estimates: small order of magnitude underestimation. However, no detailed assessment possible.	
type of setting (industrial/ professional)	input parameter	**Inhalation**	-	0	+/-
			comparison with PROC11 estimates (See above): small order of magnitude underestimations.	comparison with PROC8a, industrial. no difference for medium dustiness.	
		dermal: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
Molecular weight (only for unit conversion in case of liquids)	input parameter + model inherent reflection	**inhalation**	n.a.p.	n.a.p.	n.a.p.
			92 g/mol. Quantitative parameter, therefore it is assumed that input of a wrong number will be mainly related to scenario uncertainty.	1000000. Quantitative parameter, therefore it is assumed that assignment of a wrong number will be mainly related to scenario uncertainty.	
		Dermal: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction)	input parameter + model inherent reflection	**Inhalation**	+++/-	0	+++/-

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
			5-25 % (i.e. 40% reduction) assigned. "Worst case": no reduction of exposure estimate would be appropriate, i.e. underestimation of small magnitude. "Best case": Reduction > 40%, i.e. overestimations up to three orders of magnitude possible. No detailed information about mixture available, however, component in excess often follows Raoults law, i.e. the applied factor is expected to lead to overestimations. Quantitative parameter, therefore it is assumed that assignment of a wrong category will be mainly related to scenario uncertainty.	no influence on exposure estimate for solids.	
		Dermal: no influence.	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% exposure reduction), maximum 8h	input parameter + model inherent reflection	**Inhalation**	0	0	+++/-
			>4 h, i.e. full shift duration assigned, no exposure reduction due to this parameter. Quantitative parameter, therefore it is assumed that input of a wrong number will be mainly related to scenario uncertainty.	>4 h, i.e. full shift duration assigned, no exposure reduction due to this parameter. Quantitative parameter, therefore it is assumed that input of a wrong number will be mainly related to scenario uncertainty.	
		Dermal: no influence	n.a.	n.a.	0

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
LEV for inhalation exposure, PROCs 1-20 (present or not)/ efficiency defined by physical state, process description, type of setting	input parameter + model inherent reflection	**inhalation**	n.a.p.	n.a.p.	n.a.p.
			no LEV indicated, assignment of a wrong category would lead to overestimations in this case. However, no detailed assessment possible.	no LEV indicated, assignment of a wrong category would lead to overestimations in this case. However, no detailed assessment possible.	
LEV for dermal exposure, PROCs 1-20 (present or not)/ efficiency defined by process description	input parameter + model inherent reflection	**Dermal**	n.a.p.	n.a.p.	n.a.p.
			no LEV indicated, assignment of a wrong category would lead to overestimations in this case. However, no detailed assessment possible.	no LEV indicated, assignment of a wrong category would lead to overestimations in this case. However, no detailed assessment possible.	
Outdoors (30% exposure reduction)	input parameter + model inherent reflection	**Inhalation**	n.a.p.	n.a.p.	n.a.p.
			indoor, i.e. no reduction of exposure. High parameter quality, therefore it is assumed that input of a wrong number will be mainly related to scenario uncertainty.	indoor, i.e. no reduction of exposure. High parameter quality, therefore it is assumed that input of a wrong number will be mainly related to scenario uncertainty.	
		dermal: no influence	0	0	0

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
LEV for inhalation, PROCs 21-25 (present or not)/efficiency defined by physical state, process description, type of setting	input parameter + model inherent reflection	**inhalation**.	n.a.	n.a.	n.a.p.
			PROC7	PROC8a	
LEV for dermal, PROCs 21-25 (present or not)/ efficiency defined by process description	input parameter + model inherent reflection	**dermal**	n.a.	n.a.	n.a.p.
			PROC7	PROC8a	
Respiratory protection equipment (90%, 95% efficiency according to APFs 10 and 20)	input parameter (+ model inherent reflection)	**inhalation**	+	+	+/-
			no RPE present. High parameter quality, therefore uncertainty due to assignment of wrong category is expected to be mainly scenario uncertainty.	no RPE present. High parameter quality, therefore uncertainty due to assignment of wrong category is expected to be mainly scenario uncertainty.	
Model inherent parameters					
Breathing rate (10 m^3 per 8h shift) (only used for overall exposure per kg and day)	model inherent parameter	**Inhalation**	++/--	++/--	++/--
			only internal dose affected, not air concentration affected. No detailed evaluation possible.	only internal dose affected, not air concentration affected. No detailed evaluation possible.	

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
		Dermal: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
70 kg body weight worker	model inherent parameter	**Dermal and inhalation**	+/-	+/-	+/-
			No information about male/female workers or details about weight. No detailed assessment possible.	No information about male/female workers or details about weight. No detailed assessment possible.	
Initial exposure estimate (PROC1-20 for inhalation and dermal exposure) / defined by fugacity, physical state, process description, type of setting for inhalation; defined by PROC for dermal)	model inherent parameter	**Dermal and inhalation**	n.a.p.	n.a.p.	n.a.p.
Initial exposure estimate (PROC21-25 for dermal and inhalation exposure): defined by fugacity, physical state, process description, type of setting for inhalation; defined by PROC for dermal	model inherent parameter	**Inhalation and dermal**	n.a.	n.a.p.	n.a.p.
			PROC7	PROC8a	

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
Skin areas, Exposed body parts (defined by PROC; palm(s), fingers, hand(s), hands and forearm(s))	model inherent parameter	**Dermal**	+++/--	+++/--	+++/--
			1500 cm^2, hands and forearm(s) assumed. No detailed evaluation possible.	960 cm^2 assumed (two hands). No detailed evaluation possible.	
		Inhalation: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
Presentation of model results	model output	Inhalation and dermal	n.a.p.	n.a.p.	n.a.p.
Model equation, assumptions					
Ideal gas law and approximately 298 K (i.e. molar volume of 24 l/mole) assumed for conversion of units in case of liquids	model/assumption	**inhalation**	n.a.p.	n.a.	n.a.p.
			only for conversion of units	solid, no vapour pressure used	
		dermal: no influence	0	n.a.	0
			no influence on exposure estimate	solid, no vapour pressure used	
GOHP	model/assumption	**Inhalation and dermal**	n.a.p.	n.a.p.	n.a.p.
Exposure to liquid aerosol is beyond scope	Model /scope		n.a.p.	n.a.	

Source of uncertainty	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
			underestimations likely, magnitude cannot be assessed.	solid.	

Appendix 1, Table 7 Magnitudes of uncertainty: ECETOC TRA v.3 (italic type refers to comments)

Parameter	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
Input parameters					
Process temperature for PROCs 1-20 (not explicitly implemented, however vapour pressure at process temperature can be entered)	Input parameter	**inhalation**	n.a.p.	n.a.p.	n.a.p.
			process at room temperature	room temperature or lower (liquid nitrogen). However, dustiness not influenced by temperature	
		dermal: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction) for dermal exposure and solids in general.	Input parameter and model inherent reflection	**dermal and inhalation (solids)**	+++/-	0	+++/-
			dermal, 5-25 %. no detailed assessment possible.	dermal/inhalation. 100 % concentration (plastic dust assessed), i.e. no uncertainty introduced by this parameter.	

Parameter	**Type of uncertainty source**	**Exposure route**	**Magnitudes of uncertainty**		**Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix**
			Scenario 1: Spray painting of locomotives	**Scenario 3: Sieving of plastic powders and filling of barrels**	
duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% exposure reduction), maximum 8h; for dermal exposure	Input parameter and model inherent reflection	**dermal**	0	0	+++/-
			>4 h	>4 h	
short term duration for inhalation (peak exposure for duration <15min = 4 x 8h average)	Input parameter and model inherent reflection	**inhalation**	n.a.p.	n.a.p.	n.a.p.
			n.a.p.	n.a.p.	
		dermal: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
LEV for inhalation, PROCs 1-20 (present or not)/defined by physical state, process description, type of setting	Input parameter and model inherent reflection	**inhalation**	n.a.p.	n.a.p.	n.a.p.
			n.a.p.	n.a.p.	
LEV for dermal, PROCs 1-20 (present or not)/ defined by process description	Input parameter and model inherent reflection	**dermal**	n.a.p.	n.a.p.	n.a.p.
			n.a.p.	n.a.p.	
General ventilation (good general vent. 30%, enhanced 70%, good or enhanced + LEV)	Input parameter and model inherent reflection	**inhalation**	n.a.p.	n.a.p.	n.a.p.
			general ventilation indicated (enhanced)	general ventilation indicated (good)	

Parameter	Type of uncertainty source	Exposure route	Magnitudes of uncertainty		Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
			Scenario 1: Spray painting of locomotives	Scenario 3: Sieving of plastic powders and filling of barrels	
		dermal: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
Gloves (95, 90, 85, 80 % efficiency, corresponding to different levels of personal behaviour/level of supervision)	Input parameter and model inherent reflection	**dermal**	0	0	n.a.p.
			no glove indicated.	no glove indicated.	
		inhalation: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	
Model inherent parameters					
Initial exposure estimates (all PROCs, dermal and inhalation)	Model inherent parameter	**dermal and inhalation**	n.a.p.	n.a.p.	n.a.p.
Presentation of model results	model parameter/ output	Inhalation and dermal	n.a.p.	n.a.p.	n.a.p.
Model					
Connection/ dependency between dustiness/volatility and the implementation of duration in combination with dermal exposure:	Model/ assumption	**dermal**	0	0	+/-
			low volatility, i.e. no influence on exposure estimate	medium dustiness, i.e. no influence on exposure estimate	
		inhalation: no influence	0	0	0
			no influence on exposure estimate	no influence on exposure estimate	

MEASE version 1.02.01

General model approach and uncertainty of datasets

For the inhalation part a modified version of the ECETOC TRA v.2 algorithm has been used, i.e. initial exposure estimates have been assigned to combinations of dustiness/volatility, type of setting and PROC number which are modified afterwards by risk management measures of the application or different operational conditions. Efficiencies for localised controls are based on the work of Fransman et al. (FRANSMAN ET AL., 2008). Initial exposure estimates are identical to ECETOC TRA v.2 defaults for PROCs 1-20 and have been replaced by the results of exposure measurements at metal related workplaces for PROCs 21-27a. Initial exposure estimates for PROC27b are based on expert judgement.

The dermal part on the other hand is based on the logic tree implemented in EASE which has been adapted to include exposure outputs fitted to a set of measured data collected in the metal industry. Affected skin areas are again based on ECETOC TRA v.2 defaults for PROCs below PROC 21. Dermal exposure estimates may also be influenced by the reflection of additional modifiers describing operational conditions (e.g. duration, concentration) and the presence of gloves.

Therefore, the model algorithm implemented in MEASE differs for both exposure routes but is based on the same basic principle (initial exposure estimate + fixed modifiers).

This approach is commonly used, however, if it is in principle able to reflect exposure estimates in a correct way cannot be finally assessed. Details of the model algorithm, i.e. parameters and involved datasets, will be discussed in Chapter “Evaluation matrix”.

Evaluation matrix

Appendix 1, Table 8 Evaluation matrix MEASE version 1.02.01

Source of uncertainty	Type of uncertainty source	Variability/ uncertainty	Transparency of documentation	Certainty of knowledge base	Parameter quality (vagueness and level of detail)	Direction and magnitude of the caused uncertainty[31]	
Input parameters and model inherent parameters							
physical form (liquid/solid/ aqueous solution/gas)	Input parameter / intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high: Wax like compounds may have unsharp boundaries; some substances with low melting points may be solid at room temperature but still be used as liquid. However, overall these are special cases which do not represent common scenarios.	**inhalation**: Direction and magnitude of a possible deviation of the exposure estimate depend on the substance and its molecular weight, which is used to convert units from ppm to mg/m^3. Thus, there is no general way of estimating a maximum magnitude for this source of uncertainty. Theoretically, there are no upper or lower limits for the magnitude of uncertainty.	n.a.p.
						Dermal: Only a differentiation between gas and non-gas products is made. Deviations can reach three orders of magnitude. However, as the input parameter is of high quality the uncertainty is considered to be mainly user – and scenario based.	n.a.p.

[31] Direction of deviation is indicated by “+” (overestimations expected) and “-“ (underestimations expected) signs. “+/-“ means that both directions are possible. The number of +/- signs indicates the magnitude of uncertainty (factor up to 10, up to 100, more than 100 between estimate and actual exposure value). 0 refers to no influence on uncertainty of the exposure estimate.

molecular weight (free number, default of 24.45 g/mol)	Input parameter and model inherent reflection / intrinsic substance property	not relevant for model uncertainty	not relevant for model uncertainty	not relevant for model uncertainty	high: quantitative parameter	**inhalation**: No assessment is possible of the impact of a wrong entered molecular weight as this input is a free number. Uncertainties are expected to refer only to user handling and measurement uncertainties and not to the exposure model (high parameter quality). Moreover, this parameter is only used for conversion of units for liquid substances and thus, will not influence assessments within the main applicability domain of the model.	n.a.p.
						Dermal: no influence	0
dustiness (high/medium/low/massive object (i.e. very low))	Input parameter / intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high: Quantitative description in the MEASE glossary, low vagueness	**Inhalation**: The magnitude of uncertainty of the exposure estimate can go up to two orders of magnitude based on the difference of initial exposure estimates assigned to two neighbouring dustiness bands.	++/--
						dermal: not influenced	0
vapour pressure (high/ medium/ ow)	Input parameter / intrinsic substance property	see initial exposure estimate	see initial exposure estimate	see initial exposure estimate	high: quantitative number	**Inhalation:** Assignment of a wrong vapour pressure category would lead to deviations up to three orders of magnitude, based on two neighbouring categories. However, wrong assignments are considered to be unlikely in this case, as the required input is of quantitative nature. Errors are expected to refer mostly to uncertainties in the measurement of vapour pressure and not to model related uncertainty.	++/--
						Dermal: no influence	0
Process temperature for PROCs 21-25, 27a (Tproc<Tmelt; Tproc≈Tmelt; Tproc>Tmelt)	Input parameter and model inherent reflection / process description + operational conditions	n.a.p. both possible	For transparency of assigned exposure values see initial exposure estimates. Categorisation criteria for the three volatility bands are not given in one of the literature sources officially available, however have been made available during the project.	see initial exposure estimates	high: The process temperature is directly entered into the tool, i.e. the input parameter is quantitative and of low vagueness.	**Inhalation:** Differences between two neighbouring fugacity categories do not exceed one order of magnitude. However, wrong assignments are considered to be unlikely in this case due to the high parameter quality.	+/-
						Dermal: no influence	0

PROC number (PROC 1-27b)	Input parameter / process description + operational conditions	see initial exposure estimates	see initial exposure estimates	see initial exposure estimates	medium/high: Medium level of detail in explanation in the PROC description itself, some vague descriptions. However, metal specific examples are given in the MEASE glossary.	**inhalation:** A wrong PROC assignment could lead to exposure deviations up to three orders of magnitude for both inhalation and dermal exposure.	+++/---
						Dermal: A wrong PROC number may result in the assignment of a wrong skin area/exposed body part. This can result in over- or underestimations of up to one order of magnitude (1980 cm^2 vs. 240 cm^2).	+/-
scale of operation (industrial/professional)	Input parameter / process description + operational conditions	see initial exposure estimates	see initial exposure estimates	see initial exposure estimates	low: Qualitative description	**Inhalation**: The assignment of a wrong type of setting could lead to an exposure deviations up to one order or magnitude.	+/-
						Dermal: no influence	0
Pattern of use	Input parameter / Use description and operational conditions	see initial exposure estimate	See initial exposure estimate	See initial exposure estimate	Low: Rough definition of four categories. Some additional explaining words can be found in the MEASE glossary, however still no clear separation between the different pattern of use categories is possible.	**Dermal**: Theoretically, deviations can reach three orders of magnitude (based on difference between two categories). However, confusion of the highest and lowest categories (“wide dispersive use” vs. “closed system without bREACHes”) is considered to be unlikely due to the definition of these use patterns. Thus, overall not more than two orders of magnitude are expected. Both over- and underestimations are possible.	++/--
						Inhalation: No influence	0
Contact level (extensive, intermittent, incidental, none	Input parameter / Use description and operational conditions	see initial exposure estimate	See initial exposure estimate	See initial exposure estimate	High: The explanation in the MEASE glossary includes contact numbers, i.e. this parameter is defined in a quantitative way.	**Dermal**: The differences between two categories can reach three orders of magnitude, however, as this parameter is quantitatively defined the major source of uncertainty is expected to be on the side of the exposures situation (i.e. measurement errors etc.).	+++/---
						Inhalation: no influence	0

Pattern of control (direct/non-direct handling)	Input parameter / Use description and operational conditions	see initial exposure estimate	See initial exposure estimate	See initial exposure estimate	Medium: description of these parameter categories available in MEASE glossary, medium level of detail including some vague wording.	**Dermal**: The difference between the two categories can go up to three orders of magnitude. Both under- and overestimations are possible.	+++/---
						Inhalation: no influence	0

concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction)	Input parameter and model inherent reflection / Use description and operational condition	n.a.p. both possible	medium no detailed explanation or experimental basis available in MEASE context, some background in ECETOC documentation.	N.a.p.	medium: quantitative parameter but it is not mentioned if the substance content should be given in volume/volume, as mole fraction or as mass /mass.	**Inhalation:** A thorough investigation of the influence of mixtures on the exposure estimate for the single components would be beyond the scope of this project. The applicability domain of MEASE is inorganic substances, i.e. in most cases the assessment will be done based on dustiness for a solid product or for an aqueous solution. In case of solid mixtures actual exposure values may be influenced by varying particle sizes (different sizes for different components) and the interactions between the particles (e.g. adhesion). For aqueous solutions exposure estimates are assumed to be identical to very low dustiness results in most cases. Again interaction between the solvent (water) and the solved substance may influence the result and the dependency on the concentration. No final assessment is possible. However, the implemented factors will lead to estimations above the linear approach, thus, an overestimation of exposure is expected to be more likely than an underestimation. Overestimations of exposure up to three orders of magnitude are possible (especially for very low concentrations below 1%) and underestimations down to one order of magnitude, if exposure (mixture) is assumed to be identical to exposure (pure substance). See also section “ECETOC TRA” in Appendix 1.	+++/-

						Dermal: A lower concentration is expected to decrease dermal exposure linearly as it does not depend on the vapour pressure and the concentration of a substance in air (at least for contamination via splashes, aerosol and contaminated surfaces which are expected to be the main sources of exposure). For solids the exposure may also depend on parameters such as the particle size, thus, in principle the linear approach might lead to both over and underestimations of exposure. However, the implemented factors are chosen conservatively (less exposure reduction than a linear approach would suggest), thus, underestimations cannot be excluded but are expected to be of minor significance. Theoretically underestimations up to one order of magnitude (90% estimated exposure reduction vs. worst case 0%) and overestimations up to three orders of magnitude (if a non-linear dependency would be assumed) are possible. See also section “ECETOC TRA” in Appendix 1.	+++/-

duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% exposure reduction), maximum 8h	Input parameter and model inherent reflection / Use description and operational condition	n.a.p. both possible	medium: no detailed explanation or experimental basis available in MEASE context, some background in ECETOC documentation.	N.a.p.	high: quantitative description	**Inhalation**: Homogeneous emission of exposure would be an appropriate basis for a linear dependency between duration and inhalation exposure. The implemented factors lead to higher exposure values than suggested by such an approach which makes overestimations more likely than underestimations for situations, where emissions are distributed evenly over the assessed timeframe. Most PROCs may include several sub-activities, i.e. exposure may not be distributed evenly over the considered duration (e.g. sampling for PROCs 2/3, use in closed continuous or batch processes). Theoretically, overestimations up to three orders of magnitude are possible (especially for very short durations) (see also Hofstetter et al. (HOFSTETTER ET AL., 2013)). Underestimations may go up to one order of magnitude (based difference between 90% reduction and a worst case of 0% reduction in reality). See section “ECETOC TRA” in Appendix 1.	+++/-

		n.a.p. both possible	low/medium: no detailed explanation or experimental basis. Difficulties concerning dermal exposure sampling (e.g. saturation phenomena) are described in Ref. (HERAG, 2007) but no relation to the implemented modifiers is given. Some background is given in ECETOC documentation, however, this only refers to version 2, where no duration modifier is implemented for dermal exposure.	N.a.p.	high: quantitative description, low vagueness	**Dermal**: The connection between dermal exposure and duration of exposure is more difficult to describe than for inhalation, as it depends on substance properties, saturation effects etc. Both under- and overestimations are possible, resulting in a maximum of one order of magnitude for underestimations and three orders of magnitude for overestimations (90% reduction if 0% would be appropriate; 0% reduction if more than 99% would be appropriate). See section “ECETOC TRA” in Appendix 1.	+++/-
LEV (ECETOC values)	Input parameter and model inherent reflection/ localised controls	See section “ECETOC TRA” in Appendix 1.for details.					

Localised control measures for inhalation exposure: LEV (generic, exterior, interior), enclosure, containment, General ventilation, Suppression techniques: generic suppression, capture sprays (wetting system at point release), wet suppression of contaminant (after emission), Separation of workers	Input parameter and model inherent reflection/ localised controls	n.a.p. both possible	Medium: The origin of efficiency values and a basic overview of the included datasets is given in Fransman, 2008, however, details about the evaluated workplaces and underlying reports or publications are not documented.	The number of samples varies between the different control techniques (from 14 for enclosure up to133 for LEV). Compared to datasets for other model(parts) evaluated in this project this is not a high number (see Table 2.7), however, as far as the authors know no alternative publication about RMM efficiencies is currently available. A final assessment of the uncertainty of underlying datasets is not possible, as no detailed information is given by Fransman et al., however, medium or low uncertainty, i.e. medium or high certainty is expected as the values are not based on expert judgement.	medium: Basically only a yes/no decision is needed (and information about the confidence), short examples in the MEASE glossary, however, no description is given, how the included ventilation, suppression technique etc. has to be designed to be represented by the model.	**Inhalation**: Confidence intervals reported by Fransman et al..(FRANSMAN ET AL., 2008) suggest deviations of the exposure estimate of not more than one order of magnitude. However, the possible deviation for each exposure situation depends on the underlying datasets and if the assessed situation is represented adequately within these datasets. Therefore, no detailed assessment of expected magnitudes and direction of uncertainty is possible at this point. Efficiencies do not depend on the type of exposure or the process. In general the uncertainty depends on the specific local control measure whereas a large confidence interval means a high uncertainty (low number of data, high variation). Considering this the highest uncertainty is expected for “Enclosure” (4-74 % confidence interval) and “General ventilation” (17-61% confidence interval) while the lowest uncertainty is expected for “LEV” (75-84 % confidence interval) and the LEV-subcategory “integrated LEV” (84-90% confidence interval).	n.a.p..
						Dermal: No influence	0

Average with median confidence or upper or lower confidence limits may be chosen for the inhalation risk management measures	Input parameter/ localised controls	n.a.p. both possible	Medium: see “localised control measures inhalation”, Fransman et al are clearly cited in the MEASE glossary.	medium: Statistical parameters related to the chosen control measures. See “localised control measures inhalation”	Medium/high: The categorisation includes a certain vagueness as it is not clearly defined how the design of specific situations can be assigned to the different confidence levels. Moreover, one category is described in a misleading way ("Median estimate" instead of "average with median confidence"), which is however not expected to lead to a large number of wrong assignments. However, the statistical term “confidence limit” is generally accepted and well-defined and furthermore, in case of doubts the user is referred to the lower confidence limit.	**Inhalation**: The differentiation between average, the upper and the lower confidence limit can be used to reflect the variability within the underlying datasets, however, of course it is also possible to assign a wrong category for a situation. In the MEASE glossary the user is advised to insert the lower confidence limit for a first Tier assessment, therefore overestimations of exposure are expected to be more likely than underestimations. Overall, no deviations of more than one order of magnitude are expected if the wrong confidence category is assigned. The unclear definition of one of the categories (“Median estimate” instead of “average with median confidence”) may lead to misinterpretations, however this is expected to be of minor importance as common differences between average and median are expected to be clearly below one order of magnitude. The MEASE glossary advises the user to use the lower confidence limit for a first tier exposure assessment, therefore underestimations due to a wrong assignment of this parameter are considered to be unlikely.	+/-
						Dermal: no influence	0

Respiratory protection equipment (75%, 80%, 90%, 95%, 97.5% efficiency according to APFs 4, 5, 10, 20 and 40)	Input parameter and model inherent reflection / personal protective equipment	n.a.p. both possible	high: assigned protection factors (APFs) are given. APFs are documented for each type of respiratory protection by the corresponding producers. They may differ between countries. However, this does not affect the transparency of the model documentation.	n.a.: derivation of APFs has not been done by the MEASE developers.	high: APFs are available together with other product related information when a respiratory protection is bought.	**Inhalation**: APFs are uncertain themselves, however this is not directly model related. An accurate evaluation of the uncertainty depends not only on the situation but also on the country where an APF has been assigned, i.e. it cannot be assessed at this point. See also section “ECETOC TRA” in Appendix 1. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category – which may REACH two orders of magnitude - is considered to be mainly related to scenario uncertainty.	++/--
						Dermal: no influence	0

Gloves (90%)	Input parameter and model inherent reflection / personal protective equipment	n.a.p. both possible	Low: The MEASE glossary refers to the TGD (EC (EUROPEAN COMMISSION), 2003), however there are no detailed explanations or experimental background given for the derivation of this value.	n.a.p.	low: yes/no decision but no further explanation how gloves have to be designed and used to REACH the assigned efficiency.	**Dermal**: The efficiency of gloves is a quite complicated topic: although a number of different defaults for various exposure models are in use only a limited number of publications is available. Underestimations of exposure will not exceed one order of magnitude (90% instead of 0% efficiency). Overestimations of exposure can theoretically go up to three orders of magnitude. It is expected that overestimations of more than one order of magnitude are unlikely, however a final assessment of direction and magnitude of uncertainty is not possible at this point. An additional point in case of MEASE is the missing clarity about the inclusion of samples measured under gloves into the derivation of exposure estimates. According to the HERAG factsheet (HERAG, 2007) which describes the datasets used for the dermal part of MEASE exposure estimates were based on measurements of actual exposure, i.e. on the skin. This would have been affected by the use of personal protective equipment, such as the rigger gloves, that have been used at some of the workplaces included in the HERAG document. A detailed evaluation of all underlying studies and reports listed in (HERAG, 2007) is beyond the scope of this work package, therefore it is not possible to assess the number and types of affected exposure situations. Not enough information is available for an evaluation of the maximum magnitude of uncertainty due to this circumstance, however, underestimations (probably small magnitude) are expected to be more likely than overestimations for affected situations. See also section "ECETOC TRA" in Appendix 1.	n.a.p.
						Inhalation: no influence	0
Model inherent parameters							

Initial inhalation exposure estimate (Inhalation, PROC1-20)/ defined by fugacity, physical state, process description, type of setting. Values are mostly identical to ECETOC TRA	Model inherent parameter	n.a.p. both possible	medium (as these values are adopted from ECETOC TRA v.2 see also section “ECETOC TRA” in Appendix 1..) Some data sources are given but no single datasets. It is not explicitly mentioned in the documentation of ECETOC TRA (ECETOC, 2009) how the values were derived, however it has been clarified in TR107 that a certain amount of scientific knowledge of the model developers was involved.	n.a.p. due to missing information about measured data and involved experts	n.a.	**Inhalation:** Deviation of the exposure estimate cannot be defined. It depends very specifically on situations, occupational hygiene, etc. As MEASE is a tier 1 tool it is expected that initial exposure estimates are at the upper border of possible exposure estimates for a situation or a process. Theoretically, up to three orders of magnitude deviation cannot be excluded, however, a final judgement of the possible derivation without the results of an external validation would only be further expert judgement.	n.a.p.
Initial exposure estimate (Inhalation, PROC21-27a) / defined by fugacity, physical state, process description, type of setting	Model inherent parameter	N.a.p. both possible	medium: no model related publication for underlying datasets. A background report (EBRC, 2008) had been made available for this project, however, it does not include all relevant datasets. It is documented in the MEASE glossary that for PROC 21-27a the initial exposure estimate refers to the 90th percentile of measured data of the inhalable fraction	high: The overall number of datasets is high compared to the other models evaluated in this project (>7000, see Table 2.7) and although not all information could be evaluated it is known that the used datasets have been published in EU risk assessment reports before. The final derivation of the exposure estimate is based on statistical methods (90th percentile).	n.a.	**Inhalation**: As the 90th percentile of the inhalable fraction of measured exposure data has been used to derive these values that they tend to be conservative and overestimate exposure. The magnitude of uncertainty can theoretically REACH three orders of magnitude, however, without external data no final assessment is possible.	n.a.p..

Initial inhalation exposure estimate (Inhalation, PROC27b) / defined by fugacity, physical state, process description, type of setting	Model inherent parameter	N.a.p. both possible	high: It is clearly stated in the MEASE draft documentation that this value is based on expert judgement	low: expert judgement	n.a.	**Inhalation**: The magnitude of uncertainty can theoretically REACH three orders of magnitude, however, without external data no final assessment is possible".	n.a.p.

Initial exposure estimate (dermal, defined by pattern of use, pattern of control, contact level)	Model inherent paramter / Use description and operational conditions	N.a.p. both possible	Medium/high: dermal datasets are described in Ref. (HERAG, 2007) and in the underlying reports. Some detail information about the derivation of the exposure estimates was made available for this project but is not published.	Medium: The used datasets are already published in various EU risk assessment reports and are considered to be of reasonable quality. The number of datasets is high or normal compared to the other dermal tools in this project, however medium if compared also to the inhalation models (or model parts). Different sampling techniques have been used for the values listed in Ref. (HERAG, 2007) (wipe and bag wash), however, it is noted that no major differences between these two methods could be determined (Vetter and Battersby, 2012; personal communication). For some categories (e.g. closed system) no measurements were available, thus, scientific judgement of the model developers has been used.	n.a.	**Dermal**: Direction and magnitude of the uncertainty of the exposure estimate depend on the situation and if this situation is represented in the underlying datasets, thus, no final assessment is possible at this point. Maximum exposure variability within one process category is around one order of magnitude according to the HERAG fact sheet and the upper border of each derived process category is used within the MEASE algorithm. Thus, although theoretically large deviations may be possible, overestimations of exposure are considered to be more likely than underestimations of exposure.	n.a.p.
						Inhalation: no influence	0

Skin area, exposed body parts (defined by PROC; palm(s), fingers, hand(s), hands and forearm(s))	Model inherent parameter/Use description and operational conditions	n.a.p. both possible	medium: skin areas are given in the tool itself but no explanation of their derivation or assignment to the PROC codes.	n.a.p. due to lack of information.	n.a.	**Dermal**: Most skin areas are identical to the ECETOC TRA defaults (See also section "ECETOC TRA" in Appendix 1), however the exposed skin area for some products (aqueous solutions and liquids) is limited to 480 cm². Only hands and forearms are considered for all processes (in varying extent). Direction and magnitude of uncertainty depend on the situation. The total skin surface of an adult is approximately 2 m^2 (ECETOC, 2001). Therefore, if the smallest considered skin area for worker exposure is 240 cm^2,has been used for an assessment but in reality the whole body surface would be exposed the theoretical underestimation of exposed skin area would be two orders of magnitude and this would also be the deviation of the exposure estimate, if the exposure is assumed to be homogenously. However, this scenarios is highly unlikely because not all body areas are ususally homogenously exposed and especially in case of MEASE often dusts are assessed against which already normal clothing will offer some protection. If the complete hands and forearms area (1980 cm^2) instead of the minimum skin area of 240 cm^2 were be exposed this would lead to theoretical underestimations up to one order of magnitude. Overestimations are also possible and depend also on the situation. Theoretically they can go up to three orders of magnitude (e.g. 10 cm^2 exposed instead of 1980cm^2). According to Creely and Cherrie (CREELY AND CHERRIE, 2001) hand exposure to pesticides may account for approximately 50% of total body exposure, sometimes up to 90%. However, the resulting deviation strongly depends on the process and other (protective) clothing and a final assessment	+++/- (--)

						Inhalation: no influence	0
Presentation of results	Model inherent parameter / Model assumption	variability / uncertainty	high: Used percentile of underlying data is given in the glossary and datasets are mostly given in the HERAG and EU RARs about metals (see Chapter 2.2.1).	n.a.p.	high: Only one value, i.e. no choice of "wrong" value within a range possible. Used percentile of underlying data is given in the glossary and datasets are mostly given in the HERAG and EU RARs about metals.	**Inhalation (PROCs21-27) and dermal:** Model results are based on 90^{th} percentiles of dermal and inhalation data from the metals industry. Magnitude of uncertainty not assessable, however, conservative results are expected due to the relatively high percentile..	n.a.p.
			low: For this part of the model no information about the reflected percentile is available.	n.a.p.	medium/low: Only one value, i.e. no choice of "wrong" value within a range possible. However, no information about the interpretation of results available for this model part.	**Inhalation (PROCs1-21):** The results are based on ECETOC TRA v.2, however, the two models use different refinements and have different scopes. Thus, not statement can be made about the reflected percentile. No evaluation of the magnitude and direction of uncertainty is possible.	n.a.p.
Model equation, assumptions							
Ideal gas law and approximately 298 K (i.e. molar volume of 24 l/mole) assumed for conversion of units	Model	uncertainty	high: Reasons for this assumption are not documented in any of the MEASE specific publications, however, the ideal gas law is considered to be common knowledge and presented in a number of books and publications, thus, it is considered to be of high transparency.	n.a.p. Depends on the substance. Many publications exist about the ideal gas in general, however not for all substances experimental data may be available. No general assessment is possible.	n.a.	**inhalation**: This uncertainty source does not reflect an uncertainty of the model itself but of the ideal gas law. Its influence may vary and cannot be assessed at this point. However, deviations are expected to be small compared to other sources of uncertainty.	n.a.p.
						dermal: no influence	0

exposure estimates for aqueous solutions of inorganic substances are based on the same values as assigned to very low dustiness (massive objects) for all PROCs except 7 and 11 (spray processes)	Model / assumptions	n.a.p. both possible	low: No explanation or underlying database.	n.a.p.	n.a.	**Inhalation and dermal**: Different approaches are found in literature to describe the behaviour of aqueous solutions of inorganic substances (another quite common one is the treatment as liquids in a mixture, see e.g. STOFFENMANAGER®). Changing between these two approaches would results in differences up to two orders of magnitude within the MEASE algorithm. Without external data it cannot be assessed which of these approaches will result in more accurate exposure estimates and/or if a third, not considered approach would be more appropriate.	n.a.p.
exposure estimates for aqueous solutions of inorganic substances are based on the same values as assigned to substances of medium dustiness for PROCs 7 and 11 (spray processes)	Model / assumptions	n.a.p. both possible	low: No explanation or underlying database.	n.a.p.	n.a.	see above.	n.a.p.

Summary

It can be summarised that the general model approach of MEASE (initial exposure estimate and modifiers) is commonly used for exposure estimation purposes but cannot be assessed concerning its uncertainty aspects.
Some details concerning model background and development are not publicly available; however, for some underlying datasets and a number of details concerning the algorithm sufficient information is (or has been made) available which leads to medium overall transparency.
In general MEASE is partly based on measured data. Not all details about these datasets are publicly available, however, the main source of information (EU RARs) is expected to provide data of reasonable quality which leads in general to a medium overall uncertainty of the model's knowledge base.
MEASE's input parameters are overall of medium quality with almost equal numbers assigned to high and low uncertainty.
The relative resolution of MEASE is considered to be between high and medium for inhalation and high for dermal while the absolute number of parameters is also medium (see Chapter 2.3.10).
As detailed in the evaluation matrix, no source of uncertainty could be identified that is expected to lead predominantly to underestimations but on the other hand some exist (e.g. the concentration modifiers) which are expected to result predominantly in overestimations. In addition, the user is advised by the MEASE glossary to use the lower confidence limit for RMM efficiencies in case of inhalation exposure, i.e. to choose the most conservative option.
This suggests that the overall direction of uncertainty will tend to be positive as intended by the tier 1 approach and thus, at least theoretically the model should ensure a sufficient protection of the affected workers.

Example situations

Comment concerning scenario 1: Spray painting of locomotives:
For this situation toluene vapour exposure should be assessed (in accordance with the external validation).
MEASE only applicable to metals and inorganics, therefore this scenario is beyond its scope and has not been included into the evaluation matrix.

Appendix 1, Table 9 Magnitudes of uncertainty: MEASE (red text refers to comments)

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
			Scenario within scope: Exposure to potassium peroxomonosulphate in aqueous solution should be assessed (in accordance with the external validation). As this is an inorganic substance the scenario is within MEASEs scope.	**Scenario partly beyond scope:** The scenario describes sieving and filling (handling) of plastic granules (polyester or polyethylene) mixed with pigments. In the external validation exercise inhalable dust concentrations have been assessed for this situation without exposure values for single components. This dust concentration reflects mostly plastic dust but can be used as a worst case value referring to single components like pigments. MEASE is only applicable to metals or inorganic substances, i.e. the plastic powder itself is not within its scope. However, inorganic ingredients like pigments or other additives are within the scope of MEASE, i.e. MEASE can be used to assess those components, therefore this exposure situation has not been removed from the evaluation matrix.	

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
Input parameters					
physical form (liquid substance / solid substance / aqueous solution (solid in water)/ gas)	Input parameter	inhalation	n.a.p.	n.a.p.	n.a.p.
			aqueous solution. Uncertainty due to assignment of wrong category is expected to be mainly caused by scenario uncertainty. High parameter quality.	solid product and substance. Uncertainty due to assignment of wrong category is expected to be mainly caused by scenario uncertainty. High parameter quality.	
		dermal	0	0	n.a.p.
			aqueous solution. only differentiation gas/no gas in MEASE. High parameter quality.	solid substance. only differentiation gas/no gas in MEASE. High parameter quality.	
molecular weight (free number, default of 24.45 g/mol)	Input parameter and model inherent reflection / intrinsic substance property	inhalation	n.a.	n.a.	(n.a.p.)
		dermal	0	0	0
			exposure estimate not influenced by parameter	exposure estimate not influenced by parameter	
Dustiness (high/ medium/ low/ very low)			n.a.	+/-	++/--
			liquid product, aqueous solution	medium dustiness	
		dermal: no influence	0	0	0
vapour pressure (high / medium / low)	Input parameter	Inhalation	+/-	n.a.	++/--
			low volatility	solid product	
		Dermal: no influence	0	0	0
			exposure estimate not influenced by	exposure estimate not influenced by	

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
			parameter	parameter	
Process temperature for PROCs 1-20 (not explicitly implemented)	Input parameter and model inherent reflection / Missing parameter / Use description and operational conditions	inhalation	0	0	N.a.p.
			Scenario at room temperature	The substance will have temperatures between room temperature and the temperature of liquid nitrogen (77 K). However, no influence of temperature on dustiness.	
		Dermal: no influence of volatility	0	0	0
			exposure estimate not influenced by parameter	exposure estimate not influenced by parameter	
Process temperature for PROCs 21-25 (Tproc<Tmelt; Tproc≈Tmelt; Tproc>Tmelt)	Input parameter and model inherent reflection / process description + operational conditions	inhalation	n.a.	n.a.	+/-
			PROC10	PROC26	
		Dermal: no influence of volatility	0	0	0
			exposure estimate not influenced by parameter	exposure estimate not influenced by parameter	
PROC number (PROC 1-27a)	Input parameter / process description + operational conditions	inhalation	+++/---	+++/---	+++/---

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
			no obvious alternative, no detailed assessment possible.	comparison with PROC8a/8b/9 estimates: small order of magnitude underestimation. However, no detailed assessment possible.	
		dermal	+/-	+/-	+/-
			affected via assigned skin area.	affected via assigned skin area.	
scale of operation (industrial/professional)	Input parameter / process description + operational conditions	inhalation	-	0	+/-
			comparison with PROC10, professional. small order of magnitude underestimations.	comparison with PROC8a, industrial. no difference for medium dustiness.	
		Dermal: no influence	0	0	0
			exposure estimate not influenced by parameter	exposure estimate not influenced by parameter	
Pattern of use	Input parameter	Dermal	+/-	+	++/--
			“non dispersive use” assigned. Alternative categories can lead to higher or lower estimates, depending on the exact category.	“wide dispersive use” Conservative choice of input parameter, all alternative choices would lead to lower results, i.e. only an overestimation is possible with this category.	
		Inhalation: No influence	0	0	0
Contact level (extensive, intermittent, incidental, none	Input parameter		+/-	+	+++/---

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
			“intermittent” assigned. Over- and underestimations are possible. However, due to the quantitative definition of the parameter scenario uncertainty is expected to be more relevant.	“extensive” assigned. Only overestimations expected, however, due to the quantitative definition of the parameter scenario uncertainty is expected to be more relevant.	
		Inhalation: no influence	0	0	0
Pattern of control (direct/non-direct handling)	Input parameter	Dermal	+	+++	+++/---
			“direct handling” assigned. Wrong category would mean an overestimation of one order of magnitude.	“direct handling” assigned. Wrong category would mean an overestimation of three orders of magnitude.	
		Inhalation: no influence	0	0	
concentration (<1%, 1-5%, 5-25%, >25%; 90, 80, 40, 0% exposure reduction)	Input parameter and model inherent reflection	Inhalation	+++/-	+++/-	+++/-

Source of uncertainty	**Type of uncertainty source**		**Scenario 2: small scale surface wiping**	**Scenario 3: Sieving of plastic powders and filling of barrels**	**Direction and magnitude of the caused uncertainty according to common evaluation matrix**
			< 1 % assigned. No exact concentration known, thus, no detailed assessment possible. Quantitative parameter, therefore it is assumed that assignment of a wrong category will be mainly related to scenario uncertainty.	No concentration of single components known, thus, no detailed assessment possible. Quantitative parameter, therefore it is assumed that assignment of a wrong category will be mainly related to scenario uncertainty.	
		dermal	+++/-	0	+++/-
			<1%; no detailed assessment possible.	100 % concentration (plastic dust assessed), i.e. no uncertainty introduced by this parameter.	
duration (<15min, 15-60min, 1-4 h, >4h; 90, 80, 40, 0% exposure reduction), maximum 8h	Input parameter and model inherent reflection	inhalation	0	0	+++/-
			>4 h, i.e. full shift duration assigned, no exposure reduction due to this parameter. Quantitative parameter, therefore it is assumed that input of a wrong number will be mainly related to scenario uncertainty.	>4 h, i.e. full shift duration assigned, no exposure reduction due to this parameter. Quantitative parameter, therefore it is assumed that input of a wrong number will be mainly related to scenario uncertainty.	
		dermal	0	0	+++/-
			>4 h	*>4 h*	
LEV (ECETOC values)	Input parameter and model inherent reflection / localised controls	inhalation	n.a.p.	n.a.p.	n.a.p.

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
			no LEV indicated, assignment of a wrong category would lead to overestimations in this case. However, no detailed assessment possible.	no LEV indicated, assignment of a wrong category would lead to overestimations in this case. However, no detailed assessment possible.	
		dermal: no influence	0	0	
Localised control measures for inhalation exposure: LEV (generic, exterior, interior), enclosure, containment, General ventilation, Suppression techniques: generic suppression, capture sprays (wetting system at point release), wet suppression of contaminant (after emission), Separation of workers	Input parameter and model inherent reflection / localised controls	inhalation	n.a.p.	n.a.p.	n.a.p.
			general ventilation present	general ventilation present	
		dermal: no influence	0	0	0
Average with median confidence or upper or lower confidence limits may be chosen for the inhalation risk management measures	Input parameter	inhalation	+	+	+/-
			"low" assigned, assignment of wrong category would mean an overestimation of exposure	"low" assigned, assignment of wrong category would mean an overestimation of exposure	
		dermal: no influence	0	0	0

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
Respiratory protection equipment (75%, 80%, 90%, 95%, 97.5% efficiency according to APFs 4, 5, 10, 20 and 40)	Input parameter (and model inherent reflection)	inhalalation	+	+	++/--
			"no PPE" assigned. assignment of wrong category would mean an overestimation of exposure. High input parameter quality.	"no PPE" assigned. assignment of wrong category would mean an overestimation of exposure. High input parameter quality.	
		dermal: no influence	0	0	0
Gloves (90%)	Input parameter and model inherent reflection / personal protective equipment	inhalation: no influence	0	0	0
		dermal	n.a.p.	n.a.p.	n.a.p.
			"no gloves" assigned. Wrong assignment would mean an overestimation of exposure. No detailed assessment possible.	"no gloves" assigned. Wrong assignment would mean an overestimation of exposure. No detailed assessment possible.	
Model inherent parameters					
Initial exposure estimate (Inhalation and dermal, PROC1-20)/ defined by fugacity, physical state, process description, type of setting. Values are mostly identical to ECETOC TRA v.2	Model inherent parameter	Inhalation	n.a.p.	n.a.p.	n.a.p.
Initial dermal exposure estimates (defined by pattern of use/ contact level / pattern of control)	Model inherent parameter	Dermal	n.a.p.	n.a.p.	n.a.p.

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
			Potassium salt is assessed, but no strictly metal related process. A high level of uncertainty is expected. However, no detailed assessment of the magnitude of uncertainty is possible.	Only metal data included in dermal model, i.e. a high level of uncertainty is expected. However, no detailed assessment of the magnitude of uncertainty is possible.	
Initial exposure estimate (Inhalation, PROC21-27a) / defined by fugacity, physical state, process description, type of setting	Model inherent parameter	Inhalation	n.a.	n.a.p.	n.a.p.
			PROC10	PROC26	
Initial exposure estimate (Inhalation, PROC27b) / defined by fugacity, physical state, process description, type of setting	Model inherent parameter	Inhalation	n.a.	n.a.	N.a.p.
			PROC10	PROC26	
Initial exposure estimate (dermal, defined by pattern of use, pattern of control, contact level)	Model inherent paramter / Use description and operational conditions	dermal	n.a.p.	n.a.p.	n.a.p.
			dermal exposure estimates are based on metals and metal specific processes, therefore uncertainties are expected. However, no detailed assessment is possible.	dermal exposure estimates are based on metals and metal specific processes, therefore uncertainties are expected although “loading” scenarios are included in the underlying datasets. However, no detailed assessment is possible.	
Skin area, exposed body parts (defined by PROC; palm(s), fingers, hand(s), hands and forearm(s))	Model inherent parameter/Use description and operational	dermal	+++/-(--)	+++/-(--)	+++/-(--)

Source of uncertainty	Type of uncertainty source		Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	Direction and magnitude of the caused uncertainty according to common evaluation matrix
	conditions				
			960 cm^2 assumed (two hands). No detailed evaluation possible.	960 cm^2 assumed (two hands). No detailed evaluation possible.	
		Inhalation: no influence	0	0	
Presentation of model results	model/ assumption	Inhalation and dermal	n.a.p.	n.a.p.	n.a.p.
Model equation, assumptions					
Ideal gas law and approximately 298 K (i.e. molar volume of 24 l/mole) assumed for conversion of units	Model	inhalation	n.a.	n.a.	n.a.p.
			Potassium salt in aqueous solution assessed. i.e. ideal gas law is not used	solid substance assessed, i.e. ideal gas law is not used.	
		dermal: no influence	0	0	0
aqueous solutions are assumed to behave similar to substances of very low dustiness	Model / assumptions		n.a.p.	0	n.a.p.
			aqueous solution	solid substance	
		dermal: no influence	0	0	0

EMKG-EXPO-TOOL

General aspects

The EMKG-EXPO-TOOL and the corresponding EMKG approach are based on the COSHH system which originates in the UK. The model is based on a simple logic tree which assigns exposure ranges to specific combinations of input parameters. As this approach, its knowledge base and the related uncertainties apply to a large part of the model, they will be discussed together. If further details should become obvious which only apply to single parameters or aspects of the tool, this will be discussed in the evaluation matrix.

General model approach

The EMKG-EXPO-TOOL and the corresponding EMKG approach are based on the COSHH system which originates in the UK.
The model algorithm is based on the assumption that exposure is determined by two principle factors: **exposure potential** of the substance and **control strategy** (TISCHER AND POPPEK, 2003), whereas the scale of use is assumed to be the most important operational factor.
The derivation of the exposure estimate is based on a decision tree, i.e. most parts of it cannot be described by an actual equation. However, the estimation of the volatility at different temperatures for liquids is based on laws of physics (Clausius-Clapeyron and Trouton Rule), while the option for application on surfaces are based on a mechanistic transfer model (GMEHLING ET AL., 1989a, 1989b; TISCHER, 2011).
The transparency of the general model is considered to be medium/high, as there are some parts of the algorithm (application on large surfaces) which are not openly published, but have been made available to the authors in the course of this project.
The uncertainty of the knowledge base n.a.p., as it depends on the specific situation and substance if the used model (Clausius-Clapeyron / transfer model) are applicable in a reasonable way and there is no simple way to decide to which extent the principle of decision trees is better or worse than other models equipped to provide correct exposure estimates.
Thus, the overall uncertainty of the model algorithm as well as direction and magnitude of the deviation of the exposure estimate can also not be judged.

Uncertainty of datasets

The output ranges of COSHH Essentials and therefore also of the EMKG-EXPO-TOOL have been derived by debate among the occupational hygienists in 23 the working group without any known underlying database (MAIDMENT, 1998). Thus, it cannot be assessed to which extent experimental data may have influenced the uncertainty of the original exposure estimate. The transparency of the underlying datasets is therefore considered to be low.
If there is indeed no database and the exposure ranges have been derived by pure expert assessment the uncertainty of the knowledge base would be considered to be low as well. However, as it cannot be determined if there is no data or if it only has not been published the uncertainty of the knowledge base cannot be assessed.

There are several validation studies published which increase the general knowledge about expected uncertainties for a number of workplaces (see Chapter 2.2.1).

Evaluation matrix

Appendix 1, Table 10 Evaluation matrix EMKG-EXPO-TOOL

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	transparency of documentation	Certainty of knowledge base	quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[32]	
physical state (Solid/ liquid)	Input parameter / intrinsic substance properties	See exposure outcomes.	See chapter "General aspects". See exposure outcomes.	See chapter "General aspects". See exposure outcomes.	High: There are only some rare borderline cases (wax-like substances or substances with melting points around room temperature) where the assignment of this category is expected to be unclear.	A comparison of outcomes for solids and liquids is not possible as outputs are in mg/m3 for solids and in ppm for liquids, i.e. the value depends on the molecular weight. Deviations up to three orders of magnitude cannot be excluded, but overall the direction and magnitude of exposure n.a.p. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	N.a.p
Vapour pressure at process temperature or boiling point and process temperature (low, medium, high)	Input parameter / intrinsic substance properties	See exposure outcomes.	High: Information about this part of the model algorithm have been made available for this project, i.e. the transparency is considered to be high. See also chapter "General aspects".	high: For situations with operating temperatures deviating from the room temperature the Clausius Clapeyron and Trouton rules have been used, which are still simplifications but established laws of physic which are	High: Quantitative numbers for boiling points, operating temperatures, vapour pressures.	Deviations caused be the assignment of a wrong volatility band will not exceed one order of magnitude if neighbouring bands are compared. However, uncertainties related to the input of the vapour pressure are considered to be mainly on the side of the exposure situation and not model relevant.	+/-

32 Direction of deviation is indicated by "+" (overestimations expected) and "-" (underestimations expected) signs. "+/-" means that both directions are possible. The number of +/- signs indicates the magnitude of uncertainty (factor up to 10, up to 100, more than 100 between estimate and actual exposure value). 0 refers to no influence on uncertainty of the exposure estimate.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	transparency of documentation	Certainty of knowledge base	quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[32]	
			See also exposure outcomes.	considered to be appropriate for a Tier 1 model. See also in exposure outcomes. See also chapter "General aspects".			
dustiness (low, medium, high)	Input parameter / intrinsic substance properties	See exposure outcomes.	See chapter "General aspects". See exposure outcomes.	See chapter "General aspects". . See exposure outcomes.	medium: Qualitative description, high vagueness, medium level of detail	Deviations due to the wrong assignment of a dustiness category will not exceed one order of magnitude (neighbouring dustiness bands and exposure ranges).	+/-
application on surfaces (for liquids)	Input parameter / Use description and operational conditions	See exposure outcomes.	medium: See chapter "General aspects". See exposure outcomes. This part of the exposure algorithm is considered to be of medium transparency. The publications referring to the used equations have been made available for the project. However, the exact derivation of this category (< 1 l substance AND > 1 m^2 surface) are not documented.	high: See chapter "General aspects". . The uncertainty of the knowledge base for this part of the algorithm is considered to be low (mechanistic model + some assumptions). The overall uncertainty of this parameter and its reflection in the model is also reflected in the exposure ranges assigned to it, however, in this case the numbers can be derived directly from the model equations with some assumptions.	high: Quantitative description. The substance amount during whole working interval (shift) is needed – in contrast to the "scale of use", which refers to substance per event. However this is mentioned in the help text (red "?"-button).	Deviations due to the wrong assignment of this parameter will not exceed one order of magnitude (neighbouring exposure ranges). Uncertainties caused by the used model equation (transfer model) n.a.p. at this point. According to the used Gmehling model for application on surfaces and its assumptions for the lowest tested ventilation number (2 /h), in case of highly volatile liquids the upper level (50 ppm) of the corresponding concentration band without the "larges surface"-option is still exceeded if the amount used is less than 1 litre. Thus, low ventilation numbers are a possible source of uncertainty for surface applications, however, in industrial sites it is usually expected that this level of ventilation will be reached.	N.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	transparency of documentation	Certainty of knowledge base	quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[32]	
						As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	
Scale of use (g, kg, t, solid and liquid)	Input parameter / Use description and operational conditions	See exposure outcomes.	See chapter “General aspects”. See exposure outcomes.	See chapter “General aspects”. See exposure outcomes.	medium/high: Quantitative description. The substance usage per event is needed for this input parameter. This is explained in the help function, however in a not completely unambiguous way (“categories are related to the corresponding batch or operation”).	Deviations due to the wrong assignment of this parameter will not exceed one order of magnitude (neighbouring exposure ranges).	+/-
Short term application (<15 minutes; liquid and solid)	Input parameter / Use description and operational conditions	See exposure outcomes.	See chapter “General aspects”. See exposure outcomes.	See chapter “General aspects”. See exposure outcomes.	high: Quantitative description.	Deviations due to the wrong assignment of this parameter will not exceed one order of magnitude (neighbouring exposure ranges). As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	+/-
Control strategy (general ventilation, LEV, closed system; liquid and solid)	Input parameter / localised controls	See exposure outcomes.	See chapter “General aspects”. See exposure outcomes.	See chapter “General aspects”. See exposure outcomes.	Model parameter: low: qualitative, short	Deviations due to the wrong assignment of this parameter will not exceed one order of magnitude (neighbouring exposure ranges).	+/-

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	transparency of documentation	Certainty of knowledge base	quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[32]	
			Assignment has to be done according to COSHH contol guidance sheets which are not implemented directly into the model but mentioned in the help function (red “?”).		description of required situation.		
Control guidance sheets	Input parameter / localised controls / Use description and operational condications	see above.	see above.	see above.	high/medium: The control guidance sheets offer a high level of detail, however, they are not implemented or linked directly into the model and have to be searched in an extra step, which lowers their usability and thus, their overall quality as an additional “input parameter”.	See above The control guidance sheets are a special case as they are, strictly speaking, not a part of the model but are however not only intended to be an additional help, but required to use the tool in an appropriate way. Therefore they are, in contrast to underlying literature for the other models within this project, discussed separately. If the user refers to control guidance sheets the assignment of an wrong sheet is considered to be unlikely due to their high level of detail. If cgs are indeed usually used is not known (no further information from BURE available).	+/-
Resulting exposure ranges	Model inherent parameter / exposure result	Uncertainty	See chapter “General aspects”. Low: It is stated that the ranges were adopted from COSHH essentials. However,	low/medium: Expert judgement. It is not known if there exists any data that may have been used for the original model development. Even if such data exists it is	N.a.	Direction and magnitude of uncertainty cannot be assessed, as it is not known in detail how the exposure ranges were derived.	n.a.p.

Source of uncertainty	**Type of uncertainty source**	**Variability / uncertainty**	**transparency of documentation**	**Certainty of knowledge base**	**quality of parameter definition (vagueness/level of detail)**	**Direction and magnitude of the caused uncertainty[32]**	
			the derivation is stated to be based on a debate between occupational hygienists which is not documented any further. Only later validation studies are documented.	expected to be comparably old (1990s or older). However, some validation studies of COSHH Essentials and the EMKG-EXPO-TOOL are published.			
Presentation of results	Model inherent parameter / exposure result/ Model assumption	uncertainty	low: It is explained that the upper border of the range should be chosen ("the important figure is the upper level of the exposure range. This is the value that has to be compared with the DNEL later on. However, it is not documented which percentile the model is intended to represent.	n.a.p.	low: No explanation or documentation, which percentiles are represented, i.e. high vagueness. Exposure range is given.	If the result is interpreted as intended, i.e. the upper border of the exposure range is chosen, overestimations are considered to be more likely than underestimations. However, no quantification possible.	n.a.p.

Source of uncertainty	Type of uncertainty source	Variability / uncertainty	transparency of documentation	Certainty of knowledge base	quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[32]	
GOHP	Model / assumption	uncertainty	High: Techniques and other details of the expected level of GOHP are laid down in cgs and other documents related to the EMKG.	n.a.p.	n.a.	**Inhalation and dermal:** No occupational hygiene would lead to an underestimation of exposure, which can theoretically the deviation can reach three orders of magnitude. However, the probability of this is low, as long as the user uses the model in a correct way, i.e. refers to the control guidance sheets and the set-up described in these. No data on GOHP in Europe are available.	n.a.p.

Summary

The EMKG-EXPO-TOOL is a model with a comparably low resolution (low resolution score and small overall number of parameters), i.e. comparably high deviations of the exposure estimate can be expected due to the broad exposure ranges.
The transparency of the EMKG-EXPO-TOOL is considered to be low. Algorithm details have been made available for the project but the origin and derivation process of the final exposure estimates is not documented.
Both over- and underestimations of exposure are possible and due to information gaps concerning the derived exposure estimates no assessment about a preferred direction of deviation can be made. Thus, it cannot be evaluated at this point if uncertainties of the tool itself are expected to be sufficiently protective or not. In general two neighbouring exposure bands differ by one order of magnitude, i.e. a wrong assignment of one parameter usually results in a small magnitude of uncertainty (positive or negative). However, this may be overlain by the uncertainty already included in the exposure estimates themselves which cannot be assessed due to a lack of information concerning the underlying knowledge base. Moreover, most of the input parameters are of good quality and the user is advised by the introductory text in the tool to use the upper value of the output exposure range, which suggests that the wrong assignment of parameter categories or wrong interpretation of the result may not be the major source of model uncertainty.

Example situations

Appendix 1, Table 11 Magnitudes of uncertainty for example situations: EMKG-EXPO-TOOL. (red text refers to comments)

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty / maximum according to common evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping (used in RISKOFDERM)	Scenario 3: Sieving of plastic powders and filling of barrels	
		Scenario is within the scope: Toluene vapour should be assessed (in accordance with the external validation exercise). As vapour exposure can be estimated as long as the advice in the control guidance sheets is followed this scenario is within the model's scope. However, aerosol exposure resulting from open spray applications ist not covered by the EMKG-EXPO-TOOL, i.e. the overall toluene exposure may be underestimated. The model is intended to estimate SME exposures, i.e. usually no industrial settings. This may result in overestimations as professional companies are often assumed to show less strict safety conditions.	**Scenario is within the scope:** Exposure to potassium peroxomonosulphate in aqueous solution should be assessed (in accordance with the external validation). Solutions of solids in liquids are not explicitly addressed in the EMKG-EXPO-TOOL. However, they are also not excluded.	**Scenario is within the scope:** Overall inhalable dust should be estimated (in accordance with the external validation exercise). The model is intended to estimate SME exposures, i.e. usually no industrial settings. This may result in overestimations as professional companies are often assumed to show less strict safety conditions.	
Model parameters					
physical state (Solid/ liquid)	Input parameter	n.a.p.	n.a.p.	n.a.p.	n.a.p.

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty / maximum according to common evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping (used in RISKOFDERM)	Scenario 3: Sieving of plastic powders and filling of barrels	
		liquid product. Uncertainty due to assignment of wrong category is expected to be mainly caused by scenario uncertainty. High parameter quality.	liquid product / aqueous solution. Uncertainty due to assignment of wrong category is expected to be mainly caused by scenario uncertainty. High parameter quality.	solid product. Uncertainty due to assignment of wrong category is expected to be mainly caused by scenario uncertainty. High parameter quality.	
Vapour pressure at process temperature or boiling point and process temperature (low, medium, high)	Input parameter	+/-	-	n.a.	+/-
		Medium assigned. Quantitative parameter, scenario uncertainty is expected to be more relevant.	Low assigned. Quantitative parameter, scenario uncertainty is expected to be more relevant.	n.a.	
dustiness (low, medium, high)	Input parameter	n.a.	n.a.	+/-	+/-
		n.a.	n.a.	comparison of two neighbouring dustiness categories.	
application on surfaces (for liquids)	Input parameter and model inherent reflection	n.a.p.	n.a.p.	n.a.	n.a.p.
		“yes” assigned. wrong assignment of this category would lead to overestimations of small magnitude. However, the parameter is quantitative and thus, scenario uncertainty is expected to be more relevant. Basis of model algorithm cannot be assessed.	“yes” assigned. wrong assignment of this category would lead to overestimations of small magnitude. However, the parameter is quantitative and thus, scenario uncertainty is expected to be more relevant. Basis of model algorithm cannot be assessed.	n.a.	

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty / maximum according to common evaluation matrix
		Scenario 1: Spray painting of locomotives	**Scenario 2: small scale surface wiping (used in RISKOFDERM)**	**Scenario 3: Sieving of plastic powders and filling of barrels**	
Scale of use (g, kg, t, solid and liquid)	Input parameter	+/-	-	+	+/-
		1-1000 kg assigned. Positive and negative deviations up to one order of magnitude possible. However the parameter is quantitative, i.e. scenario uncertainty is expected to be more relevant.	1-1000 g assigned. Underestimations up to one order of magnitude are possible, however the parameter is quantitative, i.e. the scenario uncertainty is expected to be more relevant.	> 1 t assigned. Overestimations up to one order of magnitude are possible, however the parameter is quantitative, i.e. the scenario uncertainty is expected to be more relevant.	
Short term application (<15 minutes; liquid and solid)	Input parameter	+	+	+	+/-
		"no" assigned. Quantitative parameter, therefore scenario uncertainty is expected to be more relevant.	"no" assigned. Quantitative parameter, therefore scenario uncertainty is expected to be more relevant.	"no" assigned. Quantitative parameter, therefore scenario uncertainty is expected to be more relevant.	
Control strategy (general ventilaion, LEV, closed system; liquid and solid)	Input parameter	+	+	+	+/-
		"general ventilation" assigned. Assignment of wrong category would mean an overestimation.	"general ventilation" assigned. Assignment of wrong category would mean an overestimation.	"general ventilation" assigned. Assignment of wrong category would mean an overestimation.	
Control guidance sheet	Input parameter / localised controls / use description and operational conditions	+	+	+	+/-
		see above	see above	see above	
Resulting exposure ranges	Model inherent parameter	n.a.p.	n.a.p.	n.a.p.	n.a.p.
Presentation of model results	model/	n.a.p.	n.a.p.	n.a.p.	n.a.p.

Source of uncertainty	**Type of uncertainty source**	**Magnitudes of uncertainty**			**Direction and magnitude of the caused uncertainty / maximum according to common evaluation matrix**
		Scenario 1: Spray painting of locomotives	**Scenario 2: small scale surface wiping (used in RISKOFDERM)**	**Scenario 3: Sieving of plastic powders and filling of barrels**	
	assumption				
Model / equation / assumptions					
GOHP	model/ assumption	n.a.p.	n.a.p.	n.a.p.	n.a.p.
Further comments	Model	open spray applications are not covered by the model, no liquid aerosols covered. Underestimations likely.		model is intended to estimate SME exposures, i.e. usually no industrial settings. This may result in overestimations as professional companies are often assumed to show less strict safety conditions.	n.a.p.

STOFFENMANAGER® version 4.5

General aspects

The STOFFENMANAGER® basic algorithm and equations for the estimation of the geometric mean are given below.
Due to the nature of the model algorithm (see Appendix 1, Equation 2, fitting procedure of logarithmised exposure score) maximum deviations depend specifically and in a not obvious way on the exposure situation, i.e. there are no general efficiencies or modifiers for model parameters but the effects on the exposure estimate depend on the combination of model parameters used for the assessment. The order of magnitude of the uncertainty may vary with the substance and various other aspects.

Model equation:
Appendix 1, Equation 1: STOFFENMANAGER® algorithm: Conceptual basis
$C_t = (E \cdot H \cdot \mu_{gv\text{-}nf} \cdot \mu_{LC} + E \cdot H \cdot \mu_{gv\text{-}ff} \cdot \mu_{LC} + E \cdot a)\, \mu_{PPE}$

This equation is calibrated with experimental exposure values resulting in the following exposure estimation model:

Appendix 1, Equation 2: STOFFENMANAGER® algorithm: Geometric mean
$Y_{GM} = \exp(\beta_0 + \beta_1 \ln C_t) = \exp(\beta_0) \cdot C_t^{\beta 1} = \exp(\beta_0) \cdot (E \cdot \mu_{PPE})^{\beta 1} \cdot (H \cdot \mu_{gv\text{-}nf} \cdot \mu_{LC} + H \cdot \mu_{gv\text{-}ff} \cdot \mu_{LC} + a)^{\beta 1}$

C_t: Concentration score
E: Emission score
H: handling score
$\mu_{gv\text{-}nf}$: general ventilation score, near field
μ_{LC}: local control score
μ_{PPE}: score for personal protective equipment
a: passive emission score
β_0: Intercept
β_1: fixed effect of the STOFFENMANAGER® scores
Y_{GM}: Geometric mean of exposure estimate

There are four different model equations relating to handling of powders and granules, handling resulting in comminuting, handling of highly volatile liquids and handling of low volatile liquids (SCHINKEL ET AL., 2010).
A final assessment of the maximum deviation has not been made for most parameters, as it would require a detailed evaluation of possible scores and beta-values as well as the corresponding worst case. However, some test calculations using the maximum and minimum score for the corresponding parameter have been carried out to derive a rough impression of the possible deviations.
Some common tendencies can be extracted from the model algorithm: The exposure estimate consists of three contributions, the near-field, the far-field and the passive emission ($E \cdot a$). If the passive emission score is very small or the handling/localised

control scores of the direct emission contributions are comparably large, the passive emission and also the correlated uncertainties do not have a significant influence.
The emission score *E* (based on volatility or dustiness) is represented in all three terms, i.e. *E* to the power of β_1 as well as the expected uncertainty of this term will linearly influence the exposure estimate.
In general, uncertainties related to the STOFFENMANAGER® exposure algorithm can occur due to the variability and uncertainty of the underlying datasets, the general approach (linear mixed effect models) and due to the amount of expert assessment involved in the assignment of the scores to a specific situation before the fitting procedure. As the influence of the dataset cannot be treated separately for the different parameters and scenarios (no list with datasets and corresponding exposure scores available in published literature) they will be discussed together in the following paragraphs.

Uncertainty of datasets used for model development

General uncertainty/limitations of included datasets

The transparency of the documentation is considered to be medium-high. Not all details of the single measured datasets are available, however the main parts of information and statistical information are available in Refs. (TIELEMANS ET AL., 2008a) and (SCHINKEL ET AL., 2010).
The uncertainty of the knowledge base is considered to be low, as overall, according to Tielemans et al. (TIELEMANS ET AL., 2008a) and Schinkel et al. (SCHINKEL ET AL., 2010) high quality standards have been applied to select exposure data for the quantification of STOFFENMANAGER®.
The authors of the relevant publications (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a) consider the uncertainty during sampling to be small compared to the true variability within the datasets. It is also noted that within one category substantial variability is possible within a certain STOFFENMANAGER® score (TIELEMANS ET AL., 2008a). However, variability within the set of measured data can be reflected by choosing different percentiles.
Some parameter classes are not or only to a limited extent covered by data, thus, for these categories the uncertainty of the knowledge base is higher than for other situations. This applies for example to the following areas (TIELEMANS ET AL., 2008a):

- For solids: outside work, solids with very low intrinsic emission scores (e.g. firm granules or flakes), enclosure, LEV in combination with enclosure and wetting, no respirable dust concentration.
- For liquids: handling score 0.1 (small amounts of substances/release highly unlikely), enclosure and LEV in combination with enclosure.
- No glove boxes were within the database, no wet suppression techniques, no processing of melted or burning materials, no hot work techniques.

Respirable dust measurements are only available for a limited number of scenarios (comminuting activities on stone, see Report “Conceptual evaluation”). All other samples represent inhalable dust exposure.
No gases or fibres are present in the database (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a) and therefore for these situations no algorithms could be derived. However, it is clearly stated that such situations are outside of the applicability domain of the model..

No ventilation rate and no personal behaviour could be assessed due to missing information.

The datasets include only exposure measured in SMEs and all measurements were done in one country. Assessments of situations outside these areas are expected to show higher uncertainties than those that are covered by measured data (-> usage outside of the scope).

It is stated by Schinkel et al. that the included datasets contain both shift- and task based measurements which would normally be considered as a source of uncertainty. However, Schinkel and co-workers showed by test wise fitting of the models only with task-based data no significant increase in performance for three of the four models (no results shown), and decided to use both types of datasets for the final model calibration.

Overall it can be summarised that the underlying datasets include some sources of uncertainty concerning the exposure estimate. However, no general statement can be made about the resulting magnitude of uncertainty of the exposure estimates due to these sources.

Variability

The variability of underlying dataset is reflected in the percentiles given for the resulting exposure. I. e. although this is still a source of uncertainty for the exposure estimates it is possible for the user to reflect the impact of the variability and to choose a percentile that he thinks will reflect his situation best. This additional option increases the flexibility of the model. However, the chance to underestimate exposure rises if lower percentiles are chosen by the user.

Tielemans et al. recommend to choose the 75^{th} percentile for a reasonable worst case estimate (in contrast to the TGD (EC (EUROPEAN COMMISSION), 2003)). Only in cases where only average inputs of broadly described scenarios are available the 90^{th} percentile should be used. For typical situations the 50^{th} percentile is suggested. Differences between the 50^{th} percentile and the 90^{th} percentile were found to be a factor of 8.8 (solids) and 14.8 (liquids) while differences between the 50^{th} and the 75^{th} percentile can go up to ~3.1 (solids) and 4.1 (liquids). Thus, according to Tielemans et al., in most cases the deviation of the exposure estimate will not exceed one order of magnitude (low magnitude of uncertainty) but can also REACH two orders of magnitude (medium magnitude of uncertainty). As the STOFFENMANAGER® model has been adapted since its quantification procedure (TIELEMANS ET AL., 2008a) has been published and additional measured data have been implemented (SCHINKEL ET AL., 2010), the numbers are not expected to reflect the actual situation in detail. However, the general order of magnitude of uncertainty is expected to be still in a similar range.

Treatment of values below the limit of detection

The limit of detection (LOD) was defined by Tielemans et al. as the average weight difference of the blank filters plus three times the standard deviation. For exposure values below this detection limit a value of 0.5 x LOD was used. Schinkel et al., 2010 does not include a description of approaches used to deal with results below the LOD.

There is some information published about the influence of different methods of dealing with values below the limit of detection. According to REACH Guidance R19

(ECHA, 2008b) it would decrease the exposure estimate if all not detected are set to zero. If they are set equal to the limit of detection it will in on the other hand increase the exposure result.
Zhao and Frey (ZHAO AND FREY, 2006) published a comparison of different ways of dealing with limits of detection in the context of the derivation of air toxic emission factors. The applied methods were to ignore the LOD, to replace it with 0, with 0.5 times detection limit, with the detection limit itself or the maximum likelihood estimation calculated with different functions (log-normal, Gamma or Weibull function). These approaches led to different results for the confidence intervals and the mean results. However, the deviations did not exceed one order of magnitude (factor < 2 difference between lowest and highest result). Thus, although the actual uncertainty level also depends on the number of values below the limit of detection it is expected that deviations caused by this source of uncertainty will not exceed one order of magnitude.

Validation studies

Some validation studies are available which partly also represent a step within the development process of STOFFENMANAGER® (Schinkel et al.). Underestimations were reported, but were at least partly within the expected number of underestimates suggested by the chosen percentile (see Chapter 2.2.2).

General model approach, development and assignment of scores to underlying datasets

Most parts of the model algorithm are documented in a similar way (same publication and level of detail concerning background information), thus, they will also be discussed together:

Model equation and score assignment

The uncertainty of the general model type n.a.p. in a detailed way. By definition all models can only reflect reality to a limited extend. However, to which extent this influences magnitude and direction of uncertainty of the exposure estimate is not possible to decide.
For most variables the logarithmic scale is used. This approach is commonly accepted for exposure estimation models although it does not reflect a specific law of nature. It is expected that this assumption includes some uncertainty. However it is not possible to judge the magnitude and preferred direction of the resulting deviation.
The uncertainty concerning the assignment of the correct score during model development is difficult to judge as a detailed evaluation of the development process is not possible. Problems that will be present during usage of the tool are also expected to have influenced the model development, e.g. gaps in documentation of datasets or roughly given information (e.g. concentration range).
The transparency of this aspect of model development is only low, as the scores assigned to specific exposure situations used for the calibration of STOFFENMANAGER® have not been published as well as details about the documentation of the underlying datasets.
The uncertainty of the knowledge base is considered to be high, as the assignment of scores basically followed the scientific knowledge of the model developers.

Overall, the resulting deviation of the exposure estimate is expected to be in a similar order of magnitude than a wrong assignment of a parameter category (e.g. medium instead of high dustiness) by the potential user. Therefore it is assumed that uncertainties concerning these assignments would basically lead to a deviation of the corresponding parameter score of one category up or down.

Statistical information

Some statistical information about the STOFFENMANAGER® models can be found in Refs. (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a). They include exposure ranges for certain measured scenarios which have been used for calibration purposes (e.g. Table 1 in Ref. (SCHINKEL ET AL., 2010): “Carbon black industry”), the corresponding geometric mean and standard deviations and thus, allow for a general overview of expected variation within one scenario.

In addition, information about the explained variance, i.e. the part of the variation which can be explained by the determinants used in the model, is laid down for all four equations. The numbers show that the STOFFENMANAGER® models are in general better equipped to discriminate between scenarios in different premises. Discrimination between workers in one scenario is considered to be too sophisticated to be reflected in the STOFFENMANAGER® algorithm (SCHINKEL ET AL., 2010). The total explained variance varied between 26 and 48%, while the unexplained variance was comparable with a geometric standard deviation of 5.7-8.2.

Evaluation matrix

Variability/uncertainty: Mostly “no assessment possible”; variability and uncertainty are possible but it cannot be decided which will be the predominant source of uncertainty. Exceptions are marked with a footnote.

Uncertainty of knowledge base: See Chapter “General aspects”. Exceptions are explained in footnotes.

Appendix 1, Table 12 Evaluation matrix STOFFENMANAGER® Version 4.5

Source of uncertainty	Type of uncertainty source	Transparency of documentation	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[33]	
Model parameters					
vapour pressure of component (Pa), model internal reflection (intrinsic emission score ε_i for liquids)[34]	Input parameter and model inherent reflection/ intrinsic substance property	high: The equation for the derivation of the emission score is published by Tielemans et al. as well as the underlying datasets (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a). Not all single substances and corresponding vapour pressure used for the fitting procedure are listed in the documents openly	high: quantitative description	Direct influence on all contributing aspects of the exposure estimate (far field, near field, passive emission). Both over- and underestimation s are possible for this approach whose accuracy basically depends on the correct assignment of the 30000 Pa border. Without further information a final assessment of the general tendency (more over- or more underestimations) is not possible at this point. Underestimations of the emission score and also the exposure estimate may theoretically REACH one order of magnitude if the upper border is assumed to be around 1 bar instead of 30000 Pa. Overestimations can theoretically go up to three	n.a.p.

[33] Direction of deviation is indicated by “+” (overestimations expected) and “-“ (underestimations expected) signs. “+/-“ means that both directions are possible. The number of +/- signs indicates the magnitude of uncertainty (factor up to 10, up to 100, more than 100 between estimate and actual exposure value). 0 refers to no influence on uncertainty of the exposure estimate.

[34] Uncertainty of knowledge base:
low/medium: The emission score is mostly linear dependent on the vapour pressure (except for sustances with vapour pressures above 30000 Pa and below 10 Pa).
However, the assumption that substances with vapour pressure above 30000 Pa are completely evaporated is not explained further.
The overall uncertainty of the knowledge base is considered to be low with some tendencies to the medium category.
See also Chapter 0.

Source of uncertainty	Type of uncertainty source	Transparency of documentation	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[33]	
		available and it is not explained how the upper and lower border for the linear approach (10 vs. 30000 Pa) have been derived. However, the main details of the algorithm are provided and thus, the transparency is still considered to be high. See also Chapter "General aspects"..		orders of magnitude, if very low vapour pressure substances are assessed and the assignment of the 10 Pa border is assumed to be too high. The linear dependency between vapour pressure and score in the range between 10 and 30000 represents the ideal case, whose accuracy cannot be assessed at this point. See also Chapter "General aspects". and 2	
concentration of a component within a product[35]	Input parameter and model inherent reflection / Use description and operational conditions	high: The equation for the implementation of the concentration is published by Tielemans et al. as well as the underlying datasets (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a).. It is already recognised in Tielemans et al., 2008, that this approach bears a certain uncertainty.	Medium: In general this is a quantitative parameter, however it is not defined if the concentration should be provided as mole % or weight %, although the underlying publications (SCHINKEL ET AL., 2010; TIELEMANS ET AL., 2008a). suggest the latter.	This parameter has direct influence on all contributing aspects of the exposure estimate (far field, near field, passive emission), as it is assumed to be linearly dependant on the exposure score. Both over- and underestimations are possible. For the maximum magnitude of uncertainty three orders of magnitude cannot be excluded. However, a final and general assessment of this issue is not possible. See also Chapter 2. Applies only to liquid mixtures. [36]	n.a.p.

[35] Uncertainty of knowledge base: low: The concentration is implemented via the mass fraction of a substance, although it is already recognized by Tielemans et al. (2008) that the mole fraction would be more appropriate. The linear dependency between concentration and partial vapour pressure is a an ideal approach which is often used but not appropriate for all substances. However, as a lot of common information about ideal or not ideal behaviour of vapour pressure in relation to the concentration in a mixture is available the overall uncertainty of the knowledge base is considered to be low.

[36] STOFFENMANAGER® 5.0 uses the concentration also to estimate substance exposure values in case of solids.

Source of uncertainty	Type of uncertainty source	Transparency of documentation	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[33]	
dustiness of product	Input parameter and model inherent reflection/ intrinsic substance property	See Chapter "General aspects".	medium: Qualitative description, high vagueness, medium level of detail	Both over- and underestimations are possible due to assignment of a wrong dustiness category. Based on two neighbouring dustiness bands the magnitude of uncertainty is not expected to exceed one order of magnitude.	+/-
handling categories (7 for liquids, 7 for solids, 6 for wood, 4 for stone)	Input parameter and model inherent reflection / Use description and operational conditions	See Chapter "General aspects".	Low/medium: qualitative description of limited level of detail, some examples given in (MARQUART ET AL., 2008)	Differences between two (not necessarily neighbouring) handling categories are not expected to lead to deviations larger than two orders of magnitude, however, as the deviation depends on the specific combination of exposure scores a final assessment is not possible at this point. Both over- and underestimations are possible.[37]	n.a.p.
room size (4 categories including outdoor use)	Input parameter and model inherent reflection/ Use description and operational conditions	See Chapter "General aspects".	High: Quantitative description, the room volume borders are given. Some uncertainty exists for the "outdoor" category (e.g. concerning the question if three walls are considered to be outdoor), however, overall the parameter definition of this category is still considered to be of high quality.	Room size, outdoor applications and the presence of general ventilation are linked within the STOFFENMANAGER® algorithm, i.e. the combination of both input parameter is assigned to one score for general ventilation. Test calculations revealed that no deviations above one order of magnitude are expected if a wrong category is assigned, however a final assessment is not possible at this point and the uncertainty is expected to be mainly related to the scenario uncertainty.	n.a.p.

[37] In STOFFENMANAGER® 5.0 the task categories can be linked with the PROC system (medium parameter quality). Suggestions for combinations between certain PROC codes and the STOFFENMANAGER® tasks are made. However, theoretically the user can chose every combination he thinks is appropriate. The model algorithm is still based on the original task categorisation.

Source of uncertainty	Type of uncertainty source	Transparency of documentation	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[33]	
General ventilation (4 categories)	Input parameter parameter and model inherent reflection / localised controls	See Chapters "General aspects".	Low: Yes/No-decision, but no air change rate or detailed description of desired workplace design is given.	See above. As in case of the room size the assignment of a wrong category is not expected to lead to deviations exceeding one order of magnitude. However a final assessment is not possible at this point.	n.a.p.
situation of worker (cabin, no cabin, other room)	Input parameter parameter and model inherent reflection / Use description and operational conditions	See Chapters "General aspects".	high: Qualitative description of medium level of detail, however, the main facts are included (i.e. open or closed, fresh air supply or not).	Test calculations revealed that no deviations above one order of magnitude are expected if a wrong category is assigned. However, a final assessment is not possible at this point. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	n.a.p.
RMMs (LEV, product that reduces emission, containment, containment and LEV, no RMM)	Input parameter parameter and model inherent reflection / localised controls	See Chapters "General aspects".	low/medium: no detailed description about the way a ventilation system of other reducing method has to be arranged to guarantee the assigned efficiency. Only short examples in Ref. (Marquart et al., 2008)	Test calculations revealed that no deviations above one order of magnitude are expected if a wrong category is assigned. However, a final assessment is not possible at this point.	n.a.p.
Respiratory protection (6 categories)	Input parameter parameter and model inherent reflection / personal protective equipment	See Chapters "General aspects".	high: Unambiguous description of type of respiratory protection	No deviations above one order of magnitude are expected if a wrong category is assigned (efficiencies range from 38-90%). Uncertainties may be present in the suggested scores for PPE. However, their efficiencies have been adopted from the Dutch occupational hygiene society and thus, their uncertainty cannot be assessed at this point.	+/-

Source of uncertainty	Type of uncertainty source	Transparency of documentation	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[33]	
				As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	
Is the working room being cleaned daily?	Input parameter parameter and model inherent reflection / Use description and operational conditions	See Chapters “General aspects”.	Medium: Qualitative description, the way of cleaning is not further described. Cleaning e.g. with brooms may even increase the exposure.	A score representing the influence of diffusive sources is assigned to specific combinations of the “cleaning” and the “maintenance” parameter. Wrong assignment of one or both parameters is not expected to lead to deviations of more than one order or magnitude.	n.a.p.
Take inspections or maintenance of machines place once monthly?	Input parameter parameter and model inherent reflection / Use description and operational conditions	See Chapters “General aspects”.	High: Quantitative description.		n.a.p.
Is the task carried out in the breathing zone of an employee? (if “no” is chosen, the next two options (more than one employee is carrying out the task, period of evaporation) are n.a. anymore. If ‘yes’ is chosen, the option ‘the employee does not work in a cabin’ is chosen automatically	Input parameter parameter and model inherent reflection / Use description and operational conditions	See Chapters “General aspects”.	High: Quantitative description, distance that defines the border of the breathing zone is given.	Task is defined as near- or far field. Test calculations revealed that the assignment of a wrong category is not expected to lead to deviations larger than one order of magnitude. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	n.a.p.
Is more than one employee carrying out the task?	Input parameter parameter and model inherent reflection / Use description and operational conditions	See Chapters “General aspects”.	High: Quantitative description	The presence of far field emissions is indicated. Test calculations revealed that the assignment of a wrong category is not expected to lead to deviations larger than one order of magnitude. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	n.a.p.

Source of uncertainty	Type of uncertainty source	Transparency of documentation	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[33]	
Is the task followed by a period of evaporation, drying or curing?	Input parameter / Use description and operational conditions	See Chapters “General aspects”.	High: Clear description of considered processes (hardening etc.)	The presence of far field emissions is indicated which affects only substances with a vapour pressure above 10 Pa (MARQUART ET AL., 2008). Test calculations revealed that the assignment of a wrong category is not expected to lead to deviations larger than one order of magnitude. As the input parameter quality is considered to be high, uncertainty due to assignment of a wrong category is considered to be mainly related to scenario uncertainty.	n.a.p.
Is the product diluted with water? (free text field)	Input parameter parameter and model inherent reflection / Use description and operational conditions	See Chapters “General aspects”.	Medium: It is not mentioned if the fraction should be given in mole-, volume- or mass percentages.	The concentration of the assessed substance is not linearly connected with the exposure value but with the exposure score which is logarithmised before fitting it to the underlying dataset. Thus, the exposure deviations which would be caused by wrong input of the substance fraction could theoretically only slightly exceed one order of magnitude if 1 % instead of 100% would be entered. This very worst case is considered to be unlikely, moreover such a wrong input would not be related to the model itself but most probably to the exposure situation (testing methods etc.). For the uncertainty caused by using the wrong fraction type (mole fraction vs. mass fraction) no assignment is possible without mixture specific information (fraction, molecular weight), but it can theoretically go up to three orders of magnitude.	n.a.p.

Source of uncertainty	**Type of uncertainty source**	**Transparency of documentation**	**Quality of parameter definition (vagueness/level of detail)**	**Direction and magnitude of the caused uncertainty**[33]	
Presentation of results	Model inherent parameter / Model assumption	high: See Chapters "General aspects".	high: Different percentiles can be chosen. A higher number of options always means a higher possibility that a wrong option is chosen. However, background information which may help to interpret the suggested percentiles in relation to the assessed situation is available.	Theoretically, the choice of a wrong percentile or a wrong interpretation of it can lead to deviations up to three orders of magnitude. However, no final assessment is possible. The 75^{th} percentile as a reasonable worst case is recommended by Tielemans et al. (TIELEMANS ET AL., 2008a).	n.a.p.
Model equation / assumptions					
It is assumed that the exposure score is linearly dependent on the mass fraction of substance in a mixture (and not the mole fraction)	Model/ assumption[38]	See Chapters "General aspects".	n.a.	The impact of this assumption n.a.p. without detailed knowledge about type of mixtures. Mole fraction and mass fraction may indeed give very different numbers (see above) however, it cannot be said in which way this will influence the fitting procedure. Moreover already the assumption of a linear connection in case of the mole fraction is only valid for ideal mixtures. Overall, deviations up to three orders of magnitude cannot be excluded but a final assessment is not possible at this point.	n.a.p.

[38] Uncertainty of exposure estimate mainly caused by uncertainty of this assumption, no variability.

Source of uncertainty	Type of uncertainty source	Transparency of documentation	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[33]	
Exposure estimates for solutions of solids in liquids are based on the solids' vapour pressure (such as for liquid/liquid mixtures)	Model/ assumption[38]	See Chapters "General aspects".	n.a.	No assessment possible. To which deviations this approach may lead cannot be assessed with the available information and is probably situation- and substance dependent. Different approaches are found in literature to describe the behaviour of solutions of solid substances (another quite common one is the assignment of estimates according to very low dustiness, see e.g. MEASE). Without external data it cannot be assessed which of these approaches will result in more accurate exposure estimates and/or if a third, not considered approach would be more appropriate.	n.a .p.

Changes in tool version 5.0[39]

Some changes/ additional features have been implemented in the most recent version of STOFFENMANAGER®, which will be shortly described in this section.

Mixtures

STOFFENMANAGER® 5.0 estimates the exposure of a solid substance in a mixture now based on the fraction of the substance in the mixture whereas version 4.5 only provided overall dust concentrations. This reduces the possible level of overestimation (see also Chapter 2.4) in these cases.

Use description

STOFFENMANAGER® 5.0 offers the possibility to use the PROC system (input parameter of medium/high quality) to describe the corresponding task. Suggestions are made for possible links between PROC codes and STOFFENMANAGER® task categories, however, the choice of the appropriate PROC has still to be made by the user.
The algorithm remains based on the task categorisation, i.e. an influence on the direction and magnitude of uncertainty of the exposure estimate is only expected in cases where the starting point of an exposure assessment is the PROC code and not the original task categories.

Duration

STOFFENMANAGER® 5.0 uses an 8 h duration for the initial exposure estimate. However, in a second step other task durations can be entered which are then used to calculate a daily average concentration. Task durations are then implemented into the model algorithm in a linear way.

Summary

Sources of uncertainty were already discussed by Schinkel et al. (SCHINKEL ET AL., 2010). According to this publication they include uncertainty in input information, uncertainty in measurement data (analytical errors etc.) which is believed to be of minor importance compared to the true variability and model uncertainty, which is believed to be a fundamental reason for discrepancies. The factors mentioned in this context are missing determinants (e.g. personal behaviour, ventilation rate) and the assignment of exposure scores during model development.
Although there are certainly parameters which are not included STOFFENMANAGER® offers a comparably high level of detail concerning possible sources of exposure (depening on cleaning activities and/or distance to worker) and the description of the exposure situation. The model offers the highest number of parameters and a high relative resolution score, thus, it is considered to be of comparably high resolution.
The quality of implemented parameters is predominantly good.

[39] Source of information: H. Marquart, personal communication, 12.08.2013

Underlying datasets as well as the model algorithm and the results of the fitting procedure are published in peer reviewed journals and although there are certain aspects that cannot be found (yet) in publicly available documents (e.g. inclusion of respirable stone and wood dust measurements) the transparency of model background and algorithm is considered to be comparably high.

According to Schinkel et al. and Tielemans et al. the datasets used for the calibration procedure were chosen based on strict criteria so the knowledge base is also considered to be of a reasonable quality. The definitions of the input parameters include some points where improvement might be possible.

The detailed evaluation of sources of uncertainty showed that most sources will only lead to deviations around one order of magnitude (mostly based on wrong assignments of input categories). There are some issues whose influence n.a.p. at the moment, but on the other hand a large source of uncertainty, the variability within the underlying datasets, can be addressed by choosing the appropriate percentile. As a reasonable worst case usually the 75th percentile is recommended by Tielemans et al while the 90th percentile is suggested for broadly described scenarios, higher variability within input parameters or less conservative inputs. By default the model offers the 90th percentile as a result (TIELEMANS ET AL., 2008a) to ensure an appropriate level of protection.

As detailed in Chapter “General aspects”., an overall magnitude of deviation cannot be determined for STOFFENMANAGER® as well as a generally preferred direction of the uncertainty of the exposure estimate. The conservativeness and thus, the level of protection of STOFFENMANAGER® can to some extent be regulated by choosing appropriate percentiles. Moreover, as STOFFENMANAGER® intends to reflect actual exposure values instead of worst case estimates it is expected that less conservative results and a lower tendency to overestimate exposure will be derived.

There are usually other details influencing the overall possible uncertainty (e.g. quality of database for the specific situation or model scope for certain parameters, implementation of volatility and concentration, general model uncertainty), therefore a final assessment of a preferred direction of uncertainty is not possible.

Example situations

For most parameters the model inherent reflection could not be evaluated in detail due to the complex nature of the model algorithm (see Chapter "General aspects"). Thus, listed uncertainties refer mostly to the influence of the parameter quality (type of uncertainty source: input parameter; assignment of wrong category assessed). Uncertainties concerning the reflection of parameters in the model are discussed in Chapter "General aspects". A detailed discussion is not consistent with the qualitative approach of uncertainty evaluation.

Appendix 1, Table 13 Magnitudes of uncertainty for example situations: STOFFENMANAGER® (red text refers to comments)

Source of uncertainty	**Type of uncertainty source**	**Magnitudes of uncertainty**			**Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix**
		Scenario 1: Spray painting of locomotives	**Scenario 2: small scale surface wiping**	**Scenario 3: Sieving of plastic powders and filling of barrels**	
		Scenario is within the scope: Toluene vapour should be assessed (in accordance with the external validation exercise). STOFFENMANAGER® provides results in mg/m3 which include exposure to aerosols, i.e. the result is expected to be higher than the pure vapour exposure. However, the scenario in general is within the scope of the model.	**Scenario is within the scope:** Exposure to potassium peroxomonosulphate in aqueous solution should be assessed (in accordance with the external validation).	**Scenario is within the scope:** Overall inhalable dust should be estimated (in accordance with the external validation exercise). This can be done using STOFFENMANAGER® 4.5. Version 5.0 of the model also allows the estimation of single components in a solid mixture.	
Model parameters					
vapour pressure of component (Pa), model internal reflection (intrinsic emission score ei for liquids)	Input parameter and model inherent reflection	n.a.p.	n.a.p.	n.a.	n.a.p.

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
		Scenario 1: Spray painting of locomotives	**Scenario 2: small scale surface wiping**	**Scenario 3: Sieving of plastic powders and filling of barrels**	
		2910 Pa vapour pressure[40]	10 Pa vapour pressure, i.e. border between linear and fixed emission score.	n.a.	
concentration of a component within a product	Input parameter and model inherent reflection	n.a.p.	n.a.p.	n.a.	n.a.p.
		n.a.p.	n.a.p.	n.a.	
dustiness of product	Input parameter	n.a.	n.a.	+/-	+/-
		n.a.	n.a.	medium assigned. differences between neighbouring categories	
handling categories (7 for liquids, 7 for solids, 6 for wood, 4 for stone)	Input parameter	+	+/-	+	n.a.p.
		highest exposure score, no underestimations due to wrong category possible	assignment of wrong handling category assumed	highest exposure score, no underestimations due to wrong category possible	
room size (4 categories including outdoor use)	Input parameter	(-)	(-)	(-)	n.a.p.

[40] italised text refers to comments.

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	
		> 1000 m^3, for general ventilation 100-1000 m^3, offers the same score for near field. Far field induces small orders of magnitude (underestimations) due to assignment of wrong category. However, due to the quantitative parameter definition model uncertainty is considered to be less relevant than scenario uncertainty.	< 100 m^3, only underestimations for general ventilation (near field) due to assignment of wrong category possible. Far field influence negligible. However, due to the quantitative parameter definition model uncertainty is considered to be less relevant than scenario uncertainty.	> 1000 m^3, for general ventilation 100-1000 m^3,offers the same score. Far field induces small orders of magnitude (underestimations) due to assignment of wrong category. However, due to the quantitative parameter definition model uncertainty is considered to be less relevant than scenario uncertainty.	
General ventilation (4 categories)	Input parameter	+/-	+/-	+/-	n.a.p.
		assignment of wrong category assumed	assignment of wrong category assumed	assignment of wrong category assumed	
situation of worker (cabin, no cabin, other room)	Input parameter	0	0	0	n.a.p.
		no further control measure indicated, task in breathing zone -> only one option possible.	no further control measure indicated, task in breathing zone -> only one option possible.	no further control measure indicated, task in breathing zone -> only one option possible.	
RMMs (LEV, product that reduces emission, containment, containment and LEV, no RMM)	Input parameter	+	+	+	n.a.p.
		No further control measure indicated. Wrong assignment of this category would mean an overestimation.	No further control measure indicated. Wrong assignment of this category would mean an overestimation.	No further control measure indicated. Wrong assignment of this category would mean an overestimation.	
Respiratory protection (6 categories)	Input parameter	(+)	(+)	(+)	+/-

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	
		No RPE indicated, i.e. only overestimations possible. However, due to the high parameter quality model uncertainty is considered to be less relevant than scenario uncertainty.	No RPE indicated, i.e. only overestimations possible. However, due to the high parameter quality model uncertainty is considered to be less relevant than scenario uncertainty.	No RPE indicated, i.e. only overestimations possible. However, due to the high parameter quality model uncertainty is considered to be less relevant than scenario uncertainty.	
Is the working room being cleaned daily?	Input parameter	0	+	0	n.a.p.
		"no" assigned. negligible influence of wrong category.	"no" assigned. Small overestimations due to assignment of wrong category possible.	"no" assigned. negligible influence of wrong category.	
Take inspections or maintenance of machines place once monthly?	Input parameter	(0)	(+)	0	n.a.p.
		"no" assigned. negligible influence of wrong category, quantitative parameter.	"no" assigned, i.e. only overestimations possible. quantitative parameter.	"no" assigned. negligible influence of wrong category, quantitative parameter.	
Is the task carried out in the breathing zone of an employee?	Input parameter	(+)	(+)	(+)	n.a.p.
		"yes" assigned. Overestimations of one order of magnitude possible due to wrong assignment of category. However, high parameter quality (quantitative description of breathing zone), i.e. uncertainty is expected to be more scenario – than model related.	"yes" assigned. Overestimations of one order of magnitude possible due to wrong assignment of category. However, high parameter quality (quantitative description of breathing zone), i.e. uncertainty is expected to be more scenario – than model related.	"yes" assigned. Overestimations of one order of magnitude possible due to wrong assignment of category. However, high parameter quality (quantitative description of breathing zone), i.e. uncertainty is expected to be more scenario – than model related.	
Is more than one employee is	Input parameter	(0)	(0)	(0)	n.a.p.

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	
carrying out the task?					
		"yes" assigned. negligible influence of wrong category. parameter of high quality.	"yes" assigned. negligible influence of wrong category. parameter of high quality.	"yes" assigned. negligible influence of wrong category. parameter of high quality.	
Is the task followed by a period of evaporation, drying or curing?	Input parameter	(0)	(0)	(0)	n.a.p.
		yes assigned. negligible influence of wrong category. parameter of high quality.	yes assigned. negligible influence of wrong category. parameter of high quality.	yes assigned. negligible influence of wrong category. parameter of high quality.	
Is the product diluted with water? (free text field)	Input parameter and model inherent reflection	(n.a.p.)	(n.a.p.)	(n.a.p.)	n.a.p.
		no assigned, i.e. no influence. Input of wrong number would mean an overestimation of exposure (n.a.p.), however, due to the quantitative parameter definition scenario uncertainty is expected to be more relevant.	no assigned, i.e. no influence. Input of wrong number would mean an overestimation of exposure (n.a.p.), however, due to the quantitative parameter definition scenario uncertainty is expected to be more relevant.	no assigned, i.e. no influence. Input of wrong number would mean an overestimation of exposure (n.a.p.), however, due to the quantitative parameter definition scenario uncertainty is expected to be more relevant.	
Presentation of model results	model/ assumption	n.a.p.	n.a.p.	n.a.p.	n.a.p.
Model equation / assumptions					

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	
It is assumed that the exposure score is linearly dependent on the mass fraction of substance in a mixture (and not the mole fraction)	Model/ assumption	n.a.p.	n.a.p.	n.a.p.	n.a.p.
		influence of unknown impact	no spray application	no spray application	
Additional comments		Volatile organic compounds are included in the STOFFENMANAGER® datasets and paint application and in particular high exposure activities (handling score 10) are also well represented (Tielemans et al., 2008).	Biocides in general are a part of the STOFFENMANAGER® database and the corresponding handling score is represented in the STOFFENMANAGER® datasets (~7% of samples according to Tielemans et al., 2008).	There are some samples from the rubber/plastic industry included in the STOFFENMANAGER® datasets and a comparably large fraction of the underlying datasets (~30%) corresponds to this handling score.	
		To which extent this specific situation and this mixture are represented in STOFFENMANAGER® cannot be assessed.	To which extent this specific situation and this mixture are represented in STOFFENMANAGER® cannot be assessed.	To which extent this specific situation and this mixture are represented in STOFFENMANAGER® cannot be assessed.	
		STOFFENMANAGER® represents small and medium sized companies, i.e. usually no industrial setting. As small companies are often assumed to have less strict safety conditions this may lead to an overestimation of exposure in this case. However, no detailed assessment of this aspect is		STOFFENMANAGER® represents small and medium sized companies, i.e. usually no industrial setting. As small companies are often assumed to have less strict safety conditions this may lead to an overestimation of exposure in this case. However, no detailed assessment of this aspect is	

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	
		possible.		possible.	

RISKOFDERM version 2.1

General aspects

Uncertainty of datasets used for model development

General uncertainty/limitations of included datasets

The transparency of the documentation is considered to be between medium and high. Not all details of the measured single datasets are openly available. However, the main facts and statistical information have been published by Warren et al. (2006), Kromhout et al. (2000) and Rajan-Sithamparanadarajah et al. (2004). This includes industry sectors and workplaces as well as the used sampling techniques.

The uncertainty of the knowledge base is considered to be medium-low: Dermal exposure sampling methods often include a higher uncertainty than inhalation sampling due to method dependent exposure results and a lack of standartised techniques. However, according to Sithamparanadarajah et al. (RAJAN-SITHAMPARANADARAJAH ET AL., 2004), patch sampling as well as storage stability tests of the sampling media followed the corresponding OECD guidance document.
Certain areas are not covered by measured samples and thus, these categories are considered to be outside the scope of RISKORDERM:

- Body exposure for DEO unit 1 and hand exposure for DEO unit 6.
- For DEO units 2, 3 and 5 only data for liquids were available.
- As no substances with very high vapour pressure are included in the overall database, evaporation from the skin surface is not addressed in the model for the exposure estimation (ECHA guidance R14). A comparison with bio monitoring data published by Boogaard et al. (BOOGAARD, 2008) suggests that the RISKOFDERM estimates may indeed overestimate relevant exposures for volatiles, but the comparison of internal values with external values introduces several additional uncertainties that preclude a firm conclusion.
- For DEO unit 5 all available data are for machining tasks, so the tool should not be applied to low energy processes (WARREN ET AL., 2006).

Using RISKOFDERM for exposure estimations related to the uses described above will increase the uncertainty and the possible deviation of the exposure estimate to an unknown extent.
The DEO unit with the smallest dataset is “Immersion”. The majority of measurements for body exposure in this DEO unit was collected from two studies of electroplating containing widely differing exposures. One explanation for this level of scattering is that in one study only the specific immersing tasks were measured while in the other study longer periods, possibly including also other activities that might lead to decreased or even increased exposure, were sampled. Additional reasons might have been differences in the methodologies for sampling of dermal exposure and chemical analysis (WARREN ET AL., 2006).
It cannot be excluded that due to different sampling methods or other, unknown sources of uncertainty deviations of the exposure estimates will occur, however, these influences cannot be assessed at this point.

For body exposures a higher uncertainty is expected as the values have been extrapolated from a series of patches and not completely measured. However this is not reflected in the within worker variance components for body and hands, which show larger components for the body only for DEO 2 (“wiping”).
For DEO 2 (“Wiping”) saturated gloves have been suggested as a possible source of uncertainty during measurements (RAJAN-SITHAMPARANADARAJAH ET AL., 2004).
Some parameters could not be studied due to a lack of data (see Appendix 1, Table 14). It cannot be judged to which magnitudes or directions of uncertainty this may lead, however, it is expected that the general uncertainty will be higher for situations where substances are used that to not resemble substances within the RISKOFDERM database concerning these parameters.
Overall it can be summarised that the quality and number of the data sets varies between the DEO units (WARREN ET AL., 2006). The data collection was complicated by the general difficulties of dermal exposure sampling (no standardised sampling method etc., see Chapter 2), however already a comparatively large area of tasks and workplaces could be covered.

Appendix 1, Table 14 Determinants whose influence could not be studied due to a lack of data according to Warren et al. (WARREN ET AL., 2006).

DEO unit 1	mixing, filling, loading	nothing published
DEO unit 2	wiping	viscosity (only water based products present)
DEO unit 3	dispersion using a hand-held tool	overhead (only 12 data points)
DEO unit 4	spraying	nothing published
DEO unit 5	immersion	level of automation (proximity was used instead)
DEO unit 6	mechanical treatment of objects	particle size, manual tasks

Variability

The variability of underlying datasets of RISKOFDERM is reflected in the percentiles given for the resulting exposure. This means, that although this is still a source of uncertainty for the exposure estimates it is possible for the user to reflect the impact of the variability and to choose a percentile that he thinks will represent his situation best. This additional option increases the flexibility of the model. However, the chance to underestimate exposure rises if lower percentiles are chosen.
The model developers themselves suggest to choose the 75th percentile for a reasonable worst case, the 50th percentile for a typical situation and the 90t if average input parameters are used which vary within a broad range (TIELEMANS ET AL., 2008a). According to Tielemans et al. differences between the 50th and the 90th percentile can reach two orders of magnitude.

Treatment of values below the limit of detection

For the development of RISKOFDERM exposure values below the limit of detection have been addressed via the method of multiple imputation. The imputed values have been drawn from a log-normal distribution conditional upon being less than their LOD (WARREN ET AL., 2006). As published by Zhao and Frey (ZHAO AND FREY, 2006), the choice of method of dealing with values below the limit of detection does not

induce differences of more than a factor of 2 between the highest and the lowest result, i.e. the expected magnitude of uncertainty is expected to be low.
Overall it cannot be excluded that the datasets underlying RISKOFDERM will induce some uncertainty in the exposure estimate. However direction and magnitude of deviations caused by dataset related uncertainties cannot be judged.

Validation studies

No comparison of RISKOFDERM results with measured exposure values is available, however, the available information suggests no tendency to underestimate exposure (see Chapter 2.2.2).

General model approach

Model equation and Statistical information

As the model algorithm including all parameters has been published in one publication (TIELEMANS ET AL., 2008a). and moreover almost the complete model follows one single approach (linear mixed effect models), it will be discussed together in the following paragraphs and not separately for each parameter.
The uncertainty of the general model type cannot be judged in a detailed way. By definition all models can only reflect reality to a limited extend, however, to which extent this influences magnitude and direction of uncertainty of the exposure estimate is not possible to decide.
For most variables in RISKOFDERM the logarithmic scale is used. This approach is commonly accepted for exposure estimation models although it does not reflect any law of nature. It is expected that this assumption includes some uncertainty, however it is not possible to judge the magnitude and preferred direction of the resulting deviation at the moment.
In general, some problems that will be present during usage of the tool are also expected to have influenced the model development, e.g. gaps in documentation of measured data and the corresponding exposure situation or imprecise documentation of the given information (e.g. concentration range).
The transparency of this aspect of model development is only low, as details about documentation of the underlying datasets have not been published. However, as the general model algorithm as well as included (fitting) parameters are listed in detail in Ref. (TIELEMANS ET AL., 2008a)., the overall transparency of the model algorithm is considered to be high.
The RISKOFDERM tool is based on a set of linear mixed effects models which are fitted to the measured data (TIELEMANS ET AL., 2008a). The equations, the fitting process and the tool development are described by Warren et al. where the generic form of the linear mixed effect models are given as follows:

$$Y_{i,j} = \alpha_0 + \alpha_1 X_1 + \alpha_2 I_{2,ij} + ... + \beta_i + \Sigma_{ij}$$

- $Y_{i,j}$: jth log-transformed measurement on the ith worker
- α_0: mean log-transformed potential dermal exposure for the corresponding DEO unit. $\alpha_{i,0}$ includes a default setting for each implemented determinant.
- α_n: n^{th} fixed effect (n = 1,2, ...; defines the determinants of an exposure setting, e.g. quality of ventilation)

- $I_{1,ij}$: becomes 1, if the first fixed effect was present for the jth measurement on the ith worker and 0 otherwise.
- X_1: logarithm of the application rate
- β_i: random effect for the ith worker; describes the scattering of exposure values caused by the fact that different individuals were measured.
- Σ_{ij} : random error associated with the jth measurement on the ith individual; describes the scattering of exposure values caused by the fact that different measurements on one single individual were performed.

Σ_{ij} and β_i are independent and normal distributed with means of zero and standard deviations of σ_{BW} and σ_{WW}, respectively (between-worker and within-worker variability).
The use- or application rate of a chemical during the process is also included as a fixed effect in the model algorithms, i.e. it will influence the exposure estimate in a linear way. It is recognised that there is ongoing discussion about this parameter, if it is in general necessary to describe exposure scenarios and in which way it should be implemented. It is not possible to make final assessments about the expected accuracy of this approach with the current knowledge. It is expected that overestimations are more likely than underestimations, as saturation processes on the skin surface will not be taken into account at higher durations and/or application rates. However, also depending on the way this problem was handled during the measurements used for model fitting also underestimations may be possible.
In general the performance of the different model equations can be judged by the percentage of variance that can be explained by fixed effects (i.e. the part of the exposure values that can be captured by the implemented parameters and the fitting procedure), the 95% percentile confidence interval of the anti-log of the intercept term (which equals the confidence intervals for median exposures without the presence of any fixed effects) and the overall geometric standard deviation. In particular a good model should have a high percentage of explained variance, a small confidence interval and a small geometric standard deviation (TNO, 2006). Taking into account these three factors, DEO units 1, 2 and 6 are performing good, DEO units 3 and 4 moderate and DEO unit 5, “Immersion”, shows a poor performance ((TIELEMANS ET AL., 2008a; TNO, 2006); see also Appendix 1, Table 15).

Appendix 1, Table 15 Quality of performance for different DEO units – summary (TNO, 2006)

Process	Percentage explained variance	Geometric standard deviation		95 % confidence interval for intercept	Remarks
		Body	Hands		
Filling, mixing and loading	61%	-	5.4	0.06 – 1.73	Overall good performance
Wiping	50%	5.8	3.5	453 – 1464	Overall good performance
Dispersion hand-held tools	75%	5.9	11.2	20.4 – 181	High GSD for hands; other parameters reasonable to good
Spraying	31%	6.0	6.0	14.7 – 39.3	Moderate percentage explained variance; other parameters good
Immersion	29%	9.4	34.2	0.8 -76.7	Poor performance in all of the parameters
Mechanical treatment	53%	4.9	-	6.4 – 34.4	Overall good performance

Moreover, the median exposure estimate for each DEO unit can be estimated by the following equation:

$$E_m = e^Y = e^{(\alpha_0 + \alpha_1 X_1 + \alpha_2 I_{2,ij} + \dots)} = e^{\alpha 0} \cdot e^{\alpha 1 X1} \cdot e^{\alpha 2 I2} \cdot \dots$$

All parameters of the equation are connected by multiplication, therefore a rough impression of the statistical part of the model uncertainty can be obtained by consideration of standard errors of the various alpha-values as published by Warren et al.:

$$\frac{\Delta E_m}{E_m}(\alpha_0) = \frac{\Delta(\exp(\alpha_0))}{(\exp(\alpha_0))} = \frac{\exp(\alpha_0 + \Delta\alpha_0) - \exp(\alpha_0 - \Delta\alpha_0)}{(\exp(\alpha_0))}$$

This error propagation approach of course does not cover systematic errors, e.g. concerning measurement techniques or the uncertainty of the input parameter definition. A general evaluation of the expected deviation of the mean as expressed by the standard deviation revealed that this is expected to be smaller than one order of magnitude for all considered parameters and all DEO units.

However, as according to Warren et al. it is difficult to use the standard errors to make general statements about the accuracy

of the models as each instance of a model's use will use a specific combination of exposure determinants and so CIs must be calculated on a case-by-case basis.

These calculations are considered to be not trivial as the parameter estimates for each determinant are not independent but instead have their own correlation structure and are therefore beyond the scope of this work package. Calculating CIs for estimates of exposure percentiles other than the 50^{th} (median) also necessitates consideration of the uncertainty in the variance parameter.

Overall, only a basic overview of the expected order of magnitude of uncertainty of the RISKOFDERM exposure estimates will be given in this chapter.

Concerning the confidence intervals it has already been mentioned that the CI of the intercept gives information about the general uncertainty of the model. For most DEO units this is also the largest confidence interval of all model inherent parameters. The only exception is DEO unit 1 (filling, mixing, loading), for which the the confidence interval of the “liquids” parameter is larger than for the intercept, which leads to a higher uncertainty for liquids than for solids.
Overall it can be summarised that the uncertainty of the general model approach can only partly be judged, as it is not known, which impact the usage of some basic approaches like the linear mixed effect models will have on the possible exposures estimates. A general estimation of the possible deviations or direction of this deviation is not possible.

Validation studies

No comparison of RISKOFDERM results with measured exposure values is available. However, the available information suggests no tendency to underestimate exposure.

Evaluation matrix

Variability/uncertainty of uncertainty source: Always “no assessment possible; both possible”. Exceptions are indicated as footnotes. Transparency of a certain source of uncertainty is always “high”. Exceptions or additional information are indicated as footnotes. Uncertainty of knowledge base: Always “See Chapter “General aspects”. No assessment possible”. Exceptions and additional information are indicated as footnotes.

Appendix 1, Table 16 Evaluation matrix RISKOFDERM version 2.1

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
DEO 1 (mixing, filling, loading)				
Intercept (includes: more than light contact, frequent contact, good ventilation, low/moderately dusty, solid, no aerosol generation, manual task)	Model inherent parameter	N.a.	The intercept defines a complete scenario as it includes some default values for all possible model parameters. The standard error of the intercepts in RISKORDERM have been shown to not induce deviations of more than one order of magnitude, however, this statistical parameter may not cover all possible sources of uncertainty, i.e. a final assessment of magnitude and direction is not possible.	n.a.p.
Kind of skin contact (more than light or light)	Input parameter and model inherent reflection/Use description and operational conditions	Low: A short description is given, however there are no clear boundaries between the categories and the definitions are of a low level of detail.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”) . Deviations caused by the assignment of a wrong category do not exceed one order of magnitude.	n.a.p.
Contact frequency (rare or more than rare)	Input parameter and model inherent reflection/Use description and operational conditions	high: In the help-text beside the pull-down menue numbers are indicated to show, when the contact is considered to be more than rare.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category do not exceed one order of magnitude. However, wrong assignment is considered to be unlikely due to the quantitative character of the parameter – uncertainties on the side of the documentation of the exposure situation (and not on the model-side) are considered to have more influence.	n.a.p.

[41] Direction of deviation is indicated by “+” (overestimations expected) and “-“ (underestimations expected) signs. “+/-“ means that both directions are possible. The number of +/- signs indicates the magnitude of uncertainty (factor up to 10, up to 100, more than 100 between estimate and actual exposure value). 0 refers to no influence on uncertainty of the exposure estimate.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
Ventilation (normal or good ventilation / poor or no ventilation)	Input parameter and model inherent reflection/localised controls	Low: Qualitative description with a low level of detail. It is not clearly defined what is considered to be a good ventilation.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category do not exceed one order of magnitude.	n.a.p.
Dustiness (highly dusty, low or moderately dusty)	Input parameter and model inherent reflection/Intrinsic substance property	Low/medium: qualitative description with a low to medium level of detail. No particle size, examples or further quantifications (e.g. definition of “briefly visible”) are given.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category do not exceed one order of magnitude.	n.a.p.
Physical state (solid/liquid)	Input parameter and model inherent reflection/Intrinsic substance property	High: There are only some rare borderline cases (wax-like substances or substances with melting points around room temperature) where the assignment of this category is expected to be unclear.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category may REACH two orders of magnitude, however, this type of uncertainty is considered to be based mainly on the description and documentation of the exposure situation.	n.a.p.
Aerosol generation	Input parameter and model inherent reflection/Use description and operational conditions	Medium: Qualitative description. Examples of handling types which may lead to aerosol production are given, however it is not further defined where the border to “significant aerosol generation” is.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category do not exceed one order of magnitude.	n.a.p.
Application/use rate (free number)[42]	Input parameter and model inherent reflection/Use description and operational conditions	high: Quantitative parameter.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong input number are considered to be mainly caused by uncertainties on the exposure situation side (i.e. sampling methods, documentation of situation). Thus, although deviations may theoretically go up to three orders of magnitude this is not relevant for the model uncertainty.	n.a.p.

[42] Transparency: High. Limitations of the model (i.e. used rates contained in the underlying datasets) are indicated in the tool itself.
see Chapter 0

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
Level of automation (automated or semi-automated / manual)	Input parameter and model inherent reflection/Use description and operational conditions	Medium: Qualitative description with medium level of detail. The type of automation is not explained in detail (e.g. filling of large amounts chemical with a machine in open systems vs. automated filling in closed systems)	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category do not exceed one order of magnitude.	n.a.p.
only hand exposure is estimated for this DEO unit[43]	Model	N.a.	Direction and magnitude of uncertainty depend on the situation. The total skin surface of an adult is approximately 2 m^2 (ECETOC, 2001) while the skin surface used by RISKOFDERM for hands is not documented but is expected to be between 500 and 2000 cm^2 , (based on published skin areas for hands and forearm; see e.g. Refs. (ECETOC, 2001) and (EPA, 2011)) i.e. the theoretical underestimation of exposed skin area can go up to approximately two orders of magnitude if in reality the complete body would be exposed. An overestimation of the exposed area is of course also possible and would possibly lead to an overestimation of exposure. However, as it is not known to which extent the skin surface played a role during the fitting procedure (extrapolation from patches or wipes?) and as a comparison of skin areas may only lead to information about the exposure estimate deviations if the per skin exposure distribution over the complete body is known. According to Creely and Cherrie (CREELY AND CHERRIE, 2001) hand exposure to pesticides may account for approximately 50% of total body exposure, sometimes up to 90%. However, the resulting deviation strongly depends on the process and other (protective) clothing and thus, cannot be finally assessed.	n.a.p.
DEO2 (wiping)				
Intercept (hands, no extensive body contact)	Model inherent parameter	n.a.	The intercept defines a complete scenario as it includes some default values for all possible model parameters. The standard error of the intercepts in RISKORDERM have been shown to not	n.a.p.

[43] Source of uncertainty only represents uncertainty itself, no variability.
Transparency: High. It is clearly stated for which scenarios only hand exposure can be estimated and why (no body data available)
Uncertainty of knowledge base: N.a.. The model does not estimated body exposure because there is no corresponding data and thus, no knowledge base

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
			induce deviations of more than one order of magnitude, however, this statistical parameter may not cover all possible sources of uncertainty, i.e. a final assessment of magnitude and direction is not possible.	
Body exposure	Model inherent parameter and model inherent reflection/Use description and operational conditions	n.a..	Uncertainty induced by datasets cannot be judged (see Chapter “General aspects”). Warren et al. refer only to potential exposure, i.e. no protective clothing is taken into account. As the body is usually covered to a large extent at least by normal clothing and efficiencies for this type of skin cover are less established than gloves this means an additional source of uncertainty. It can lead to overestimations (skin contact is reduced due to clothing) and underestimations (skin contact is enhanced, e.g. because fabric is soaked with liquid substance) of exposure. Magnitudes of uncertainty of more than three orders of magnitude cannot be excluded, however a final assessment is not possible.	n.a.p.
Extensive Body contact	Input parameter and model inherent reflection/Use description and operational conditions	low: Qualitative description. It is not explained in detail, what “extensive” contact means in this context.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category go up to two orders of magnitude.	n.a.p.
Application/use rate (free number)[44]	Input parameter and model inherent reflection/Use description and operational conditions	high: Quantitative parameter.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong input number are considered to be mainly caused by uncertainties on the exposure situation side (i.e. sampling methods, documentation of situation). Thus, although deviations may theoretically go up to three orders of magnitude this is not relevant for the model uncertainty.	Not relevant for model uncertainty
DEO 2: Wiping				
Intercept (hands, viscosity like honey, overhead orientation, more than 30 cm handle)	Model inherent parameter	n.a.	The intercept defines a complete scenario as it includes some default values for all possible model parameters. The standard error of the intercepts in RISKORDERM have been shown to not induce deviations of more than one order of magnitude, however, this statistical parameter may not cover all possible sources of uncertainty, i.e. a final assessment of magnitude and direction is not possible.	n.a.p.

[44] Transparency: high: Limitations of the model (i.e. used rates contained in the underlying datasets) are indicated in the tool itself.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
Body exposure	Model inherent parameter/Use description and operational conditions	n.a..	Uncertainty induced by datasets cannot be judged (see Chapter "General aspects"). Warren et al. refer only to potential exposure, i.e. no protective clothing is taken into account. As the body is usually covered to a large extent at least by normal clothing and efficiencies for this type of skin cover are less established than gloves this means an additional source of uncertainty. It can lead to overestimations (skin contact is reduced due to clothing) and underestimations (skin contact is enhanced, e.g. because fabric is soaked with liquid substance) of exposure. Magnitudes of uncertainty of more than three orders of magnitude cannot be excluded. However, a final assessment is not possible.	n.a.p.
viscosity (like water, like honey, like oil)	Input parameter and model inherent reflection/Intrinsic substance property	low: Qualitative description, no clear boundaries between categories.	Uncertainty induced by datasets cannot be assessed (see Chapter "General aspects"). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
Orientation (overhead/level or downwards)	Input parameter and model inherent reflection/Use description and operational conditions	medium-high: Qualitative description, however, quite clear definitions are used. Only in some cases (direction of application almost level) wrong assignment of categories is possible.	Uncertainty induced by datasets cannot be assessed (see Chapter "General aspects"). Deviations caused by the assignment of a wrong category go up to two orders of magnitude.	n.a.p.
Distance to source (tools with handles more or less than 30 cm)	Input parameter and model inherent reflection/Use description and operational conditions	Medium: Quantitative description (30 cm), however, an additional comment advices users to use the "less than 30 cm" category if the handle is generally located close to the contaminated parts without definition how close this should be.	Only hand exposure is influenced by this parameter. Uncertainty induced by datasets cannot be assessed (see Chapter "General aspects"). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
Application/use rate (free number)[45]	Input parameter and model inherent reflection/Use description and operational conditions	high: Quantitative parameter.	Uncertainty induced by datasets cannot be assessed (see Chapter "General aspects"). Deviations caused by the assignment of a wrong input number are considered to be mainly caused by uncertainties on the exposure situation side (i.e. sampling methods, documentation of situation). Thus, although deviations may theoretically go up to three orders of magnitude this is not relevant for the model	(n.a.p.)

[45] Transparency: High: Limitations of the model (i.e. used rates contained in the underlying datasets) are indicated in the tool itself.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
			uncertainty.	
DEO4 (Spray dispersion)				
Intercept (work indoors, not highly volatile substance, no segregation, level orientation, no airflow or LEV)	Model inherent parameter	n.a.	The intercept defines a complete scenario as it includes some default values for all possible model parameters. The standard error of the intercepts in RISKORDERM have been shown to not induce deviations of more than one order of magnitude, however, this statistical parameter may not cover all possible sources of uncertainty, i.e. a final assessment of magnitude and direction is not possible.	n.a.p.
Work environment (Outdoors/indoors)	Input parameter and model inherent reflection/Use description and operational conditions	medium – high: “outdoors” is more or less unambiguous, only rare examples may exist were it is not clear how to assign this parameter (half-open areas with 3 walls and a roof or similar)	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
Volatility (highly volatile, not highly volatile)	Input parameter and model inherent reflection/Intrinsic substance property	Medium: Semi-quantitative description. The boundary between categories is the volatility of water, however, vapour pressure and boiling point for comparison are not given in the tool.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
Segregation (physical barrier, no physical barrier)	Input parameter and model inherent reflection/localised controls	Low: No detailed description of possible “segregation”, only one example is given (“in another room”).	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
Body exposure	Model inherent parameter/Use description and operational conditions	n.a..	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Warren et al. refer only to potential exposure, i.e. no protective clothing is taken into account. As the body is usually covered to a large extent at least by normal clothing and efficiencies for this type of skin cover are less established than gloves this means an additional source of uncertainty. It can lead to overestimations (skin contact is reduced due to clothing) and underestimations (skin contact is	n.a.p.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
			enhanced, e.g. because fabric is soaked with liquid substance) of exposure. Magnitudes of uncertainty of more than three orders of magnitude cannot be excluded, however a final assessment is not possible.	
Orientation (overhead, level, downwards)	Input parameter and model inherent reflection/Use description and operational conditions	low: Qualitative description. In contrast to DEO 3, where two categories are given, here are three categories mentioned. Boundaries between categories are not clearly defined, especially the “level”-category (which would strictly speaking only refer to exaclty identically application height and height of the individuals head.).	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category (estimated by using the difference between two neighbouring categories) will not exceed one order of magnitude.	n.a.p.
Airflow (clearly away from the worker or not clearly away from the worker)	Input parameter and model inherent reflection/localised controls	low: It is not defined how strong this airflow should be and would “clearly away from the worker” means in detail (natural ventilation, mechanical ventilation, LEV, only internal fluctuations or removal of contaminated air from room air).	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
Application/use rate (free number)[46]	Input parameter and model inherent reflection/Use description and operational conditions	high: Quantitative parameter.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong input number are considered to be mainly caused by uncertainties on the exposure situation side (i.e. sampling methods, documentation of situation). Thus, although deviations may theoretically go up to three orders of magnitude this is not relevant for the model uncertainty.	Not releva nt for model uncert ainty
DEO5 (immersion)				
Intercept (represents the following scenario: hands, no LEV, distance between 30 and 100 cm)	Model inherent parameter	n.a.	The intercept defines a complete scenario as it includes some default values for all possible model parameters. The standard error of the intercepts in RISKORDERM have been shown to not induce deviations of more than one order of magnitude, however,	n.a.p.

46 Transparency: high: Limitations of the model (i.e. used rates contained in the underlying datasets) are indicated in the tool itself.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
			this statistical parameter may not cover all possible sources of uncertainty, i.e. a final assessment of magnitude and direction is not possible.	
adequate LEV used or not	Input parameter and model inherent reflection/localised controls	low: Qualitative description. It is not further defined, what is expected of an “Adequate” LEV.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
body exposure	Model inherent parameter/Use description and operational conditions	n.a..	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Warren et al. refer only to potential exposure, i.e. no protective clothing is taken into account. As the body is usually covered to a large extent at least by normal clothing and efficiencies for this type of skin cover are less established than gloves this means an additional source of uncertainty. It can lead to overestimations (skin contact is reduced due to clothing) and underestimations (skin contact is enhanced, e.g. because fabric is soaked with liquid substance) of exposure. Magnitudes of uncertainty of more than three orders of magnitude cannot be excluded, however a final assessment is not possible.	n.a.p
Distance to source (more than 100 cm, less than 100 cm, less than 30 cm)	Input parameter and model inherent reflection/Use description and operational conditions	High: Quantitative description (distance between worker and source). Small uncertainties may arise during to identification of the main source of exposure.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
DEO6 (mechanical treatment)				
Intercept (represents the following scenario: less than 100 cm distance, infrequent contact, liquid formulation)	Model inherent parameter	n.a.	The intercept defines a complete scenario as it includes some default values for all possible model parameters. The standard error of the intercepts in RISKORDERM have been shown to not induce deviations of more than one order of magnitude, however, this statistical parameter may not cover all possible sources of uncertainty, i.e. a final assessment of magnitude and direction is not possible.	n.a.p.
Distance to source (more than 100 cm, less than 100)	Input parameter and model inherent reflection/Use description and operational conditions	low: definition in the tool is not quantitative (more or less than an arm’s length), i.e. no clear boundaries are defined.	Uncertainty induced by datasets cannot be assessed (see Chapter “General aspects”). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
Contact frequency (infrequent or frequent)	Input parameter and model inherent reflection/Use description and operational conditions	low: qualitative description, no further definition of "frequent" or "rare".	Uncertainty induced by datasets cannot be assessed (see Chapter "General aspects"). Deviations caused by the assignment of a wrong category will not exceed one order of magnitude.	n.a.p.
Physical state (solid/liquid)	Input parameter and model inherent reflection/Intrinsic substance property	high: clear separation between solid objects and metalworking fluids used for the process. Borderline cases like wax-like substances are expected to play a negligible role in this DEO unit (mechanical treatment of solid objects).	Uncertainty induced by datasets cannot be assessed (see Chapter "General aspects"). Deviations caused by the assignment of a wrong category may REACH two orders of magnitude. However, this type of uncertainty is expected to be unlikely.	n.a.p.
Only body exposure can be estimated for DEO 6, only hand exposure can be estimated for DEO 1.[47]	Model equation/scope	n.a.	Neglected body parts which may be exposed to a substance will always lead to underestimations. However, direction and magnitude of uncertainty depend on the situation. The total skin surface of an adult is approximately 2 m^2 = 20000 cm^2 (ECETOC, 2001), while the skin area for the hands is approximately 2000 cm^2, i.e. the theoretical underestimation of exposed skin area can only go up to one order of magnitude. Overall exposure is also influenced by the loading per skin area, which is not estimated by RISKOFDERM and can be very different for various body parts. According to Creely and Cherrie (CREELY AND CHERRIE, 2001) hand exposure to pesticides may account for approximately 50% of total body exposure, sometimes up to 90%. However, the resulting deviation strongly depends on the process and other (protective) clothing, i.e. a final assessment is not possible.	n.a.p.

[47] Source of uncertainty only represents uncertainty itself
Knowledge base: N.a.: body - or hand exposure has been left out if no data was available, i.e. this is not an assumption for which a certain knowledge base has to be evaluated.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
Duration (free text, linear dependency assumed); (WARREN ET AL., 2006). Implemented for all DEO units.[48]	Input parameter and model inherent reflection/Use description and operational conditions	High: Quantitative input parameter.	Uncertainty induced by datasets cannot be judged (see Chapter "General aspects"). Deviations caused by the assignment of a wrong category do not exceed one order of magnitude. However, wrong assignment is considered to be unlikely due to the quantitative character of the parameter – uncertainties on the side of the documentation of the exposure situation (and not on the model-side) are considered to have more influence.	n.a.p
only body exposure is estimated for this DEO unit[49]	Model	N.a.	Direction and magnitude of uncertainty depend on the situation. The total skin surface of an adult is approximately 2 m^2 (ECETOC, 2001) while the skin surface used by RISKOFDERM for hands is not documented by is expected to be between 500 and 2000 cm^2 , (based on published skin areas for hands and forearm; see e.g. Refs. (ECETOC, 2001) and (EPA, 2011)) i.e. the theoretical underestimation of exposed skin area can go up to approximately one order of magnitude if in reality the complete body and hands would be exposed. An overestimation of the exposed area is of course also possible and would possibly lead to an overestimation of exposure. However, as it is not known to which extent the skin surface played a role during the model fitting procedure (extrapolation from patches or wipes?) and as a comparison of skin areas may only lead to information about the exposure estimate deviations if the per skin exposure distribution over the complete body is known. According to Creely and Cherrie (CREELY AND CHERRIE, 2001) hand exposure to pesticides may account for approximately 50% of total body exposure, sometimes up to 90%, which suggests a major potential for underestimations of exposure. However, the	n.a.p.

[48] Transparency: High. It is recognised by Warren et al. that there are different opinions about this approach, however, for pragmatic reasons it has been used anyway.
Durations included in the underlying datasets are also indicated in the tool as the valid range of the model algorithms.
Knowledge base: Uncertainty of datasets: Cannot be assessed, see Chapter 0.
Uncertainty of general approach (linearity): situation- and substance dependant, see also Chapter 0.
The overall uncertainty of the knowlegde base for this assumption is considered to be medium.
[49] Source of uncertainty only represents uncertainty itself.
Transparency: High: It is clearly stated for which scenarios only hand exposure can be estimated and why (no body data available)
Knowledge base: N.a.. The model does not estimated body exposure because there is no corresponding data and thus, no knowledge base

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
			resulting deviation strongly depends on the process and other (protective) clothing and thus, cannot be finally judged.	
General sources of uncertainty for all DEO units				
Linear dependency between exposure and weight fraction of a substance in the formulation (WARREN ET AL., 2006)[50]	Input parameter and model inherent reflection/process description and operational condition	N.a. (not implemented in tool	This assumption is not implemented within the tool but according to the manual (TNO, 2006) it can be applied manually after the exposure estimation with the tool. This assumption can be a source of uncertainty as the dependence between skin contact (and contact duration) and weight fraction does not have to be completely linear. It also may depend on volatility, dustiness, particle size or other parameters. Both over- and underestimations of exposure may be caused by this assumption and theoretically deviations can go up to three orders of magnitude, however, a final assessment is not possible.	n.a.p
DEO unit	Input parameter and model inherent reflection/Use description and operational condition	medium: some examples are given, thus, the level of detail is considered to be of medium quality	Theoretically the deviations can go up to three orders of magnitude if a wrong DEO unit is entered. However, this heavily depends on the specific exposure situation and cannot be generally assessed, as available input parameters differ between DEO units and therefore a variation only of the DEO unit is not possible.	n.a.p.
The density of liquid substances is assumed to be 1 mg/ml (WARREN ET AL., 2006) [51]	Parameter/intrinsic substance properties	N.a.	Both under- and overestimations are possible and can theoretically go up to three orders of magnitude, however, a final assessment is not possible.	n.a.p.

[50] Source of uncertainty only represents uncertainty itself.
Transparency: High: It is stated by Warren et al. that this approach is only valid for non-volatiles, however it has been used anyway for pragmatic reasons.
Knowledge base: Uncertainty of datasets: Cannot be judged, see Chapter 0.
Uncertainty of general approach (linearity): situation- and substance dependant, see also Chapter 0.
The overall uncertainty of the knowlegde base for this assumption is considered to be medium.

[51] Source of uncertainty only represents uncertainty itself.
Transparency: Medium: See also Chapter 0. Generally the model approach is documented with a high level of transparency. However, the basis of this assumption has not been explained explicitly, although it has been mentioned by Warren et al. (2006) which default value has been chosen. The overall transparency of this assumption is considered to be medium.
Knowledge base: See Chapter 0. Cannot be assessed. The density of water is a default that is often used, however, how appropriate this assumption is, depends on the substances it is intended to represent. As not for all included substances a density is known, the uncertainty of the knowledge base cannot be finally judged.

Source of uncertainty	Type of uncertainty source	Quality of parameter definition (vagueness/level of detail)	Direction and magnitude of the caused uncertainty[41]	
Presentation of results	Model inherent parameter/Model assumption	high: Different percentiles can be chosen. A higher number of options always means a higher possibility that a wrong option is chosen. However, background information which may help to interpret the suggested percentiles in relation to the assessed situation is available.	Theoretically, the choice of a wrong percentile or a wrong interpretation of it can lead to deviations up to three orders of magnitude. However, no final assessment is possible.	n.a.p.

Summary

RISKOFDERM is a model with a comparably good resolution and number of parameters. The transparency concerning underlying datasets, algorithm and model development is high

The quality of the input parameter varies from DEO to DEO unit. The fact that in at least one case the same fixed effect is described by different wordings is an inconsistency within the tool (> 100 cm in DEO 4 and 5 vs. “more than an arm’s length” in DEO 6) and decreases the overall quality of input parameters which is no longer homogeneous for more or less identical parameters. Another inhomogeneous description of parameters is found for LEV in DEO units 4 and 5. Overall there are slightly more parameters of low quality than of high quality, what suggests a potential for improvement at this point.

The uncertainty of the underlying knowledge base varies between the DEO units. There are some details that cannot be assessed. However, description of the sample collection process as well as the used model algorithm (whose accuracy cannot be assessed but which is a commonly used approach to simulate exposures) suggest a medium-low uncertainty.

The majority of sources of uncertainty are not expected to induce deviations (positive or negative) of more than one order of magnitude. However, the overall uncertainty including expected magnitudes and direction of deviation cannot be assessed as there are some potential sources of uncertainty which do not allow for a detailed prediction (e.g. accuracy of the general model approach).

Moreover, as the model intends to reflect actual exposure values instead of worst case estimates it is expected that less conservative results and a lower tendency to overestimate exposure than for traditional Tier 1 models will be derived. The level of protection is also influenced by the percentile which can be chosen in addition to the median (50^{th} percentile, always given). However, no guidance on a specific percentile suggested for more or less conservative outputs which would ensure a certain level of protection is provided.

Example situations

For most parameters the model inherent reflection could not be evaluated in detail. Thus, listed uncertainties refer mostly to the influence of the parameter quality (type of uncertainty source: “input parameter”; assignment of wrong category assessed). Uncertainties concerning the reflection of parameters in the model are discussed in Chapter “General aspects”. A detailed discussion is not consistent with the qualitative approach of uncertainty evaluation.

All scenarios are within the scope of the model.

Appendix 1, Table 17 Magnitudes of uncertainty: RISKOFDERM. Scenario 1: Spray painting of locomotives (red text refers to comments)

Source of uncertainty	Type of uncertainty source	Magnitude of uncertainty	Magnitude of uncertainty: Maximum according to general evaluation matrix
DEO4: Spray dispersion			
Intercept (work indoors, not highly volatile substance, no segregation, level orientation, no airflow or LEV)	Model inherent parameter	n.a.p.	n.a.p.
Work environment (Outdoors/indoors)	Input parameter	(+)	
		"indoor" assigned. Due to high parameter quality scenario uncertainty is expected to be more relevant. Assignment of wrong input category may lead to overestimations of one order of magnitude.	n.a.p.
Volatility (highly volatile, not highly volatile)	Input parameter	-	
		"not highly volatile" assigned. Wrong category assignment may lead to underestimations of one order of magnitude.	n.a.p.
Segregation (physical barrier, no physical barrier)	Input parameter	+	
		"no" assigned. assignment of wrong category may lead to overestimations of one order of magnitude.	
Body exposure	Model inherent parameter	n.a.p.	n.a.p.
Orientation (overhead, level, downwards)	Input parameter	+/-	
		"level" assigned. Assignment of wrong category would lead to uncertainties of small magnitude.	n.a.p.
Airflow (clearly away from the worker or not clearly away from the worker)	Input parameter	-	
		"yes" assigned. Assignment of wrong category would mean an underestimation of one order of magnitude.	
Application/use rate (free number)	Input parameter and model inherent reflection	n.a.p.	
		Quantitative parameter. Uncertainties due to wrong input are expected to be mainly scenario based. No detailed assessment possible.	

Appendix 1, Table 18 Magnitudes of uncertainty: RISKOFDERM. Scenario 2: Small scale surface wiping (red text refers to comments)

Source of uncertainty	Type of uncertainty source	Magnitude of uncertainty	Magnitude of uncertainty: Maximum according to general evaluation matrix
DEO unit 2: Wiping			
Intercept (hands, no extensive body contact)	Model inherent parameter	n.a.p.	n.a.p.
Body exposure	Model inherent parameter	n.a.p.	n.a.p.
Extensive Body contact	Input parameter	-	n.a.p.
		"no" assigned. Assignment of wrong category would mean underestimations of one order of magnitude.	
Application/use rate (free number)	Input parameter and model inherent reflection.	n.a.p.	Not relevant for model uncertainty
		Quantitative parameter. Uncertainties due to wrong input are expected to be mainly scenario based. No detailed assessment possible.	

Appendix 1, Table 19 Magnitudes of uncertainty: RISKOFDERM. Scenario 3: Sieving of plastic powders and filling of barrels (red text refers to comments)

Source of uncertainty	Type of uncertainty source	Magnitude of uncertainty	Magnitude of uncertainty: Maximum according to general evaluation matrix
DEO 1: mixing, filling, loading			
Intercept (includes: more than light contact, frequent contact, good ventilation, low/moderately dusty, solid, no aerosol generation, manual task)	Model inherent parameter	n.a.p.	n.a.p.
Kind of skin contact (more than light or. light)	Input parameter	+	
		"more than light" assigned. Assignment of a wrong category would mean overestimations of one order of magnitude.	n.a.p.
Contact frequency (rare or more than rare)	Input parameter	(+)	

Source of uncertainty	Type of uncertainty source	Magnitude of uncertainty	Magnitude of uncertainty: Maximum according to general evaluation matrix
		“more than rare contact” assigned. Assignment of a wrong category would mean overestimations of one order of magnitude. Due to quantitative nature of the parameter scenario uncertainties are expected to be more relevant.	n.a.p.
Ventilation (normal or good ventilation / poor or no ventilation)	Input parameter	-	
		“normal or good ventilation” assigned. Assignment of wrong category would mean an underestimation of one order of magnitude.	n.a.p.
Dustiness (highly dusty, low or moderately dusty)	Input parameter	-	
		“low or moderately” assigned. Assignment of wrong category would mean an underestimation of one order of magnitude.	n.a.p.
Physical state (solid/liquid)	Input parameter	(--)	
		Assignment of wrong category may cause uncertainties of two orders of magnitude. High parameter quality, therefore scenario uncertainty is expected to be more relevant. Low model uncertainty.	n.a.p.
Aerosol generation	Input parameter	+	n.a.p.
		“yes” assigned. Assignment of wrong category may lead to uncertainties of one order of magnitude.	
Application/use rate (free number)	Input parameter	n.a.p.	n.a.p.
Level of automation (automated or semi-automated / manual)	Input parameter	-	
		“manual task” assigned. Assignment of wrong category may lead to uncertainties of one order of magnitude. Automated tasks for powders are not included in RISKOFDERM datasets.	
only hand exposure is estimated for this DEO unit	Model		n.a.p.

Appendix 1, Table 20 Magnitudes of uncertainty: RISKOFDERM. Common sources of uncertainty. (red text refers to comments)

Source of uncertainty	**Type of uncertainty source**	**Magnitudes of uncertainty**			**Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix**
		Scenario 1: Spray painting of locomotives	**Scenario 2: small scale surface wiping**	**Scenario 3: Sieving of plastic powders and filling of barrels**	
Linear dependency between exposure and weight fraction of a substance in the formulation (Warren et al., 2006).	Input parameter and model inherent reflection / process description and operational condition	n.a.p.	n.a.p.	n.a.p.	n.a.p
DEO unit	Input parameter and model inherent reflection / Use description and operational condition	n.a.p.	n.a.p.	n.a.p.	n.a.p.
		Assessment of potential assignment of wrong DEO unit cannot be assessed.			
The density of liquid substances is assumed to be 1 mg/ml (Warren et al., 2006).	Parameter / intrinsic substance properties	n.a.p.	n.a.p.	n.a.p.	n.a.p.
		Density of product not available. Model for Spraying shows moderate performance (see Table 2). Spray paint scenarios are also part of the RISKOFDERM datasets, however, no detailed assessment is possible.	Density of product not available. Model for Wiping shows overall good performance (see Table 2). Small scale wiping scenarios are also part of the RISKOFDERM datasets, however, no detailed assessment is possible.	Density of product not available. Model for Filling/mixing/loading shows overall good performance (see Table 2). Loading/filling of solids is also part of the RISKOFDERM datasets. However, the use rate is slightly smaller than those indicated in Warren et al. (2006) and a detailed assessment is not possible.	
Gloves, protecting	Model / missing	0	0	0	n.a.p.

Source of uncertainty	Type of uncertainty source	Magnitudes of uncertainty			Direction and magnitude of the caused uncertainty: maximum according to general evaluation matrix
		Scenario 1: Spray painting of locomotives	Scenario 2: small scale surface wiping	Scenario 3: Sieving of plastic powders and filling of barrels	
clothing	determinants				
		no gloves indicated	no gloves indicated	no gloves indicated	
Presentation of results	Model / assumption	n.a.p.	n.a.p.		

Appendix 2 Resolution of exposure models

Appendix 2, Table 1 ECETOC TRA v.2: Resolution

Input parameter resolution		**Model inherent parameter resolution**			
Input parameter	**number of categories**	**Corresponding model inherent parameter**	**influenced substance types**	**number of categories: inhalation**	**number of categories: dermal**
Molecular weight[52]	free number	**Exposure modifier**	liquid	linear dependency	no influence
			solid	no influence	no influence
vapour pressure	free number	**initial exposure estimates**	liquid	4	no influence
			solid	no influence	no influence
Dustiness	3	**initial exposure estimates**	liquid	no influence	no influence
			solid	3	no influence
Type of setting	2	**initial exposure estimates**	liquid	2	no influence
			solid	2	no influence
Process description (PROC)	26	**initial exposure estimates**	liquid	8	8
			solid	8	8
		Overall number of initial exposure estimates	liquid	15	8
			solid	12	8
Ventilation (LEV)	yes/no	**Exposure modifiers**	liquid and solid	1+"no LEV"	1+"no LEV"
		Overall number of different efficiencies	liquid and solid	4+"no LEV"	4+"no LEV"
Outdoor	1+"no outdoor application"	**Exposure modifiers**	liquid and solid	1+"no outdoor application"	no influence
RPE	2+"no RPE"	**Exposure modifiers**	liquid and solid	2+"no RPE"	no influence
		Skin surface	liquid and solid	no influence	5
concentration	4	**Exposure modifiers**	liquid	4	no influence
		Exposure modifiers	solid	no influence	no influence
duration	4	**Exposure modifiers**	liquid and solid	4	no influence

[52] only for conversion of units

Appendix 2, Table 2 ECETOC TRA v.3: Resolution (parameters which are new compared to v.2 are marked in red)

Input parameter resolution		**Model inherent parameter resolution**			
Input parameter	**number of categories**	**Corresponding model inherent parameter**	**influenced substance types**	**number of categories: inhalation**	**number of categories: dermal**
Molecular weight[52]	free number	**Exposure modifiers**	liquid	linear dependency	no influence
			solid	no influence	no influence
vapour pressure	4	**initial exposure estimates**	liquid	4	no influence
			solid	no influence	no influence
Dustiness	3	**initial exposure estimates**	liquid	no influence	no influence
			solid	3	no influence
Type of setting	2	**initial exposure estimates**	liquid	2	2
			solid	2	2
Process description (PROC)	26	**initial exposure estimates**	liquid	8	9
			solid	8	9
		Overall number of initial exposure estimates	liquid	15	9
			solid	12	9
LEV	yes/no	**Exposure modifiers**	liquid and solid	1+"no LEV"	1+"no LEV"
General vent.	2+"basic general ventilation"	**Exposure modifiers**	liquid and solid	2+"basic general ventilation"	no influence
		Overall number of different efficiencies for ventilation		6	2
Outdoor	1+"no outdoor application"	**Exposure modifiers**	liquid and solid	1+"no outdoor application"	no influence
RPE	2+"no RPE"	**Exposure modifiers**	liquid and solid	2+"no RPE"	no influence
		Skin surface	liquid and solid	no influence	5
Gloves	3+"no gloves"	**Exposure modifiers**	liquid and solid	no influence	3+"no gloves"
concentration	4	**Exposure modifiers**	liquid and solid	4	4
duration	4	**Exposure modifiers**	liquid and solid	4	4

Appendix 2, Table 3 MEASE: Resolution

Input parameter resolution		**Model inherent parameter resolution**			
Input parameter	**number of categories**	**Corresponding model inherent parameter**	**influenced substance types**	**number of categories: inhalation**	**number of categories: dermal (exposure per skin area)**
Molecular weight[52]	free number	**Exposure modifiers**	liquid, gas	linear dependency	no influence
			solid, aqueous solution	no influence	no influence
fugacity: vapour pressure (free number)	3	**Initial exposure estimate**	only liquids	3	no influence
fugacity: dustiness	4	**Initial exposure estimate**	only solids	4	no influence
fugacity: solid/process temperature is high	3	**Initial exposure estimate**			
process description: PROCs	29	**Initial exposure estimate**	solids, aqueous solution	18	no direct influence (via skin area)
			liquids, gas	14	no direct influence (via skin area)
concentration	4	**Exposure modifiers**	liquid, aqueous solution, gas and solid	4	4
Duration	4	**Exposure modifiers**	liquid, aqueous solution, gas and solid	4	4
process description: pattern of use	4	**Initial exposure estimate**	liquid, aqueous solution, and solid	no influence	3
			gas	no influence	no influence
process description: contact level	4	**Initial exposure estimate**	liquid, aqueous solution, and solid	no influence	4
			gas	no influence	no influence
process description: level of control	2	**Initial exposure estimate**	liquid, aqueous solution, and solid	no influence	2
			gas	no influence	no influence
		Overall number of initial exposure	liquid, aqueous solution and	no influence	4

Input parameter resolution		Model inherent parameter resolution			
Input parameter	**number of categories**	**Corresponding model inherent parameter**	**influenced substance types**	**number of categories: inhalation**	**number of categories: dermal (exposure per skin area)**
		estimates	solid		
			gas	no influence	no influence
confidence (refers to inhalation RMMs)	3	**Exposure modifiers**	liquid, aqueous solution and solid	3	no influence
Enclosure[53]	1+"no RMM"	**Exposure modifiers**	liquid, aqueous solution and solid	1+"no influence"	no influence
LEV[53]	3 (generic, exterior, interior) +"no RMM"	**Exposure modifiers**	liquid, aqueous solution and solid	3+"no influence"	no influence
general ventilation[53]	1+"no RMM"	**Exposure modifiers**	liquid, aqueous solution and solid	1+"no influence"	no influence
wet suppression (after emission)[53]	1+"no RMM"	**Exposure modifiers**	liquid, aqueous solution and solid	1+"no influence"	no influence
capture spray (at point of release)[53]	1+"no RMM"	**Exposure modifiers**	liquid, aqueous solution and solid	1+"no influence"	no influence
generic suppression[53]	1+"no RMM"	**Exposure modifiers**	liquid, aqueous solution and solid	1+"no RMM"	no influence
separation of workers[53]	1+"no RMM"	**Exposure modifiers**	liquid, aqueous solution and solid	1+"no influence"	no influence
RPE	5 + „no RPE"	**Exposure modifiers**	liquid, aqueous solution and solid	5+"no influence"	no influence
Gloves	1 + „no gloves"	**Exposure modifiers**	liquid, aqueous solution and solid	no influence	1+"no influence"

[53] All localised controls/RMMs are collected in one pull-down menue, i.e. there is only one "no RMM" option and not one for each measure.

Appendix 2, Table 4 EMKG-EXPO-TOOL: Resolution

Input parameter resolution		**Model inherent parameter resolution**		
Input parameter	**number of categories**	**Corresponding model inherent parameter**	**influenced substance types**	**number of categories**
Volatility (can be defined by the boiling point in relation to the process temperature or the vapour pressure at process temperature)	3	**Exposure potential**	liquid+solid	4
Dustiness	3			
scale of use	3			
short term exposure	**1+"no short term"**	**Exposure modifiers**	solid and liquid	2[54]
application of surfaces	**1+"no application of surfaces"**	**Exposure modifiers**	liquid	2[54]
		Exposure modifiers	solid	no influence
Control strategy (overall number of categories, no option without any control available)	**3 (broken down from 65 external control guidance sheets)**	**Exposure modifiers**	solid and liquid	3
containment	**1**	**Exposure modifiers**		
LEV	**1**	**Exposure modifiers**		
general ventilation	**1**	**Exposure modifiers**		

Appendix 2, Table 5 STOFFENMANAGER®: Resolution

Input parameter resolution		**Model inherent parameter resolution**	
Input parameter	**Number of categories**	**influenced substance types**	**Number of categories**
vapour pressure of substance	free number	solid	no influence
		liquid	low/high and linear dependency between these two borders
dustiness of product	6	solid	6
		liquid	no influence
concentration of substance in products/dilution with water	free number	solid	no influence (overall dust concentration estimated)
		liquid	linear
molecular weight	free number	solid and liquid	no influence
handling categories (substance dependant)[55]	8 (no cutting, solid)	solid	8

[54] Factor 10 or no change of exposure result

Input parameter resolution		**Model inherent parameter resolution**	
Input parameter	**Number of categories**	**influenced substance types**	**Number of categories**
	6 (cutting, wood)	solid, wood	4
	4 (cutting, stone)	solid, stone	3
	18 (overall number of categories for solid products)	solid, overall	14
	8 (liquids, no sub categorisation)	liquid	7
room size	3	solid and liquid	1 - 3 or no influence (depending on ventilation)
outdoors	1 + "no outdoor application"	solid and liquid	no influence
general ventilation	3 + "no general ventilation"	solid and liquid	"no influence" or 3 (depending on room size)
Other RMMs	4 + "no further measures"	solid and liquid	2 + "no influence"
containment	1 + "no measures"	solid and liquid	1 +"no influence"
LEV	1 + "no measures"	solid and liquid	1 +"no influence"
containment and LEV	1 + „no measures"	solid and liquid	1 +"no influence"
Use of product that limits emission	1 + "no measures"	solid and liquid	1 +"no influence"
worker situation	2+"not in a cabin"	solid and liquid	2 and "no influence"
PPE	6+"no PPE"	solid and liquid	4 and "no influence"
Is the task carried out in the breathing zone of an employee?	1 + "no"	solid and liquid	no influence
Is more than one employee is carrying out the task?	1+ "no"	solid and liquid	no influence
Is the task followed by a period of evaporation, drying or curing?	1 + "no"	solid and liquid	no influence
Is the working room being cleaned daily?	1 + "no"	solid and liquid	4
Regular inspections?	1 + "no"		

[55] Resolution of model inherent categorisation derived by test calculations with STOFFENMANAGER®.

Appendix 2, Table 6 RISKOFDERM: Resolution

Input parameter resolution			Model inherent parameter resolution
	Input parameter	**Number of categories**	**Number of categories**
Process description: DEO units		6	6
mixing/filling/ loading	**dustiness**	2	2
(solids and liquids)	**aerosol generation**	1 + "no"	2
	automation	1 + "no"	2
	ventilation	2	2
	type of contact (light/not light)	2	2
	contact frequency	2	2
	use rate	free number	linear dependency
	duration	free number	linear dependency
wiping	**body contact**	1 + "no"	2
	use rate	free number	linear dependency
	duration	free number	linear dependency
dispersion with hand held tool	**viscosity**	3	3
	use rate	free number	linear dependency
	distance to surface	2	2
	orientation	2	2
	duration	free number	linear dependency
spraying	**vapour pressure**	2	2
	outdoor/indoor	2	2
	LEV	1 + "no"	2
	Segregation	1 + "no"	2
	use rate	free number	linear dependency
	distance to surface	2	2
	orientation	3	3
	duration	free number	linear dependency
immersion	**LEV**	1 + "no"	2
	Segregation	1 + "no"	2
	distance to surface	2	2
	duration	free number	linear dependency
mechanical treatment	**contact frequency**	2	2
	distance to surface	2	2
	duration	free number	linear dependency

Appendix 3 Personal protective equipment

Respiratory protection: Available literature

- Some information concerning the safety of APFs has been published by Nelson et al. (NELSON ET AL., 2000), who modelled actual exposure under respiratory protection with APF10 using a Monte Carlo simulation and compared it with OELs. The calculations indicated a low risk of being exposed above an OEL, therefore the authors concluded that mean exposures would be controlled and well below an OEL.
- Nicas and Neuhaus (NICAS AND NEUHAUS, 2004) have carried out a random normal effect model on WPFs using the example half-masks. Two criteria are proposed: 95% of the WPFs should be above the APF for one wearer and this should apply to 95% of the respirator wearers.
- Crump et al. (CRUMP, 2007) compare in their publication the OSHA approach of defining RPE efficiencies with the approach published by Nicas and Neuhaus. Workplace protection factors depend not only on design of respirator but also on the size distribution of the contaminant, the substance, the individual worker and maybe other, unknown circumstances. The following method of deriving the WPF is suggested in this publication (following the approach of Nicas and Neuhaus (NICAS AND NEUHAUS, 2004)): 95% of the respirator wearers have 95% of their WPFs above the APF. In contrast to this the criterion used by OSHA requires that 95% of all WPFs are above the APF. This approach is recommended in cases where the 5% measurements which show lower APFs are expected to lead to some workers which are not sufficiently protected (i.e. receive exposure above the assigned limit value.).
- Bell et al. (BELL ET AL., 2012) reported study results which revealed that in many cases good occupational hygiene was not followed (i.e. training system, appropriate supervision, storing of RPE in clean area if not used etc.).
- Paszkiewicz (PASZKIEWICZ, 2012) noted that an APF of 1000 is used for pressed air respiratory protection in Germany while in GB an APF of 40 is commonly used.

Dermal models / gloves: Available literature

- Often breakthrough times are available for specific substances material combinations, e.g. in the RMM library developed by CEFIC[56]. Several links to information about general permeation for different materials and substances are listed. However no general efficiency is given, and personal behaviour is not taken into account
- In a publication by Lechtenberg-Auffarth (LECHTENBERG-AUFFARTH AND RUHL, 2007) several internet-links with advice for gloves and material which are sufficient for certain activities and substances are given.
- Cherrie et al. (CHERRIE ET AL., 2004) state that the break-through time of a glove differs with the composition of mixture, the substance, the material of a glove, the temperature and the process/task (handling of things with sharp edges etc.).
- The work of Packham (PACKHAM, 2006) disapproves glove usage due to the high number of misuses/failures. Exceptions where glove usage might be appropriate

[56] www.cefic.org

are emergency situations and temporary measures while other measures are introduced.

- Creely and Cherrie (CREELY AND CHERRIE, 2001) tested nitrile and PVC gloves with cotton gloves being used for the collection of samples over and under protective gloves. Resulting efficiencies of **99.7 %, 99.5 %** (Nitrile) and **99%** (PVC) are found. Moreover, the PVC gloves are reported to be shorter. In some cases lower efficiencies were found (96.9%). However, these were explained with equipment failure
- Chang et al. (CHANG ET AL., 2004) published a study about biomonitoring of exposure to 2-methoxyethanol. The evaluated gloves were cotton gloves and rubber gloves. Cotton was reported to show varying results but to have no actual protective effect while rubber gloves showed a protective efficiency of **74.76 %** (urine sample) and **68.9 %** (plasma sample). These test results were obtained during and "in field study" where no further information about the level of advice and training the workers experienced concerning the usage of gloves was available.
- The Technical guidance document on risk assessment for biocides (TGD (2003); part I (EC (EUROPEAN COMMISSION), 2003)): recommends **90%** without citation of any experimental data
- The technical notes for guidance concerning the human risk assessment for biocides (TNsG (2007) (JRC, 2007)) states that "compared to respiratory protection, determination of APFs for protective clothing and gloves is much more complex. This is in part due to the multi-compartment origin of dermal contamination and the effect of workers' behaviour. The assessment of protective properties for PPE (including gloves) relies on laboratory test data on penetration, permeation rates and break-through times." No further references are given but **90%** efficiency are recommended for gloves, **75%** for dry cotton coveralls and **95%** for impermeable coveralls. Common clothing (long-sleeved shirt and trousers, no gloves) is suggested to have **50%** clothing penetration. For cotton coveralls and normal clothing a protecting fuction can only be expected for dry substances. Furthermore it is recommended to "await the results of the development of guidance for Risk Management Measures"
- The human exposure expert group (HEEG) opinion (JRC, 2010) suggests the following default protection factors for protective clothing and gloves:
  - **90%** for liquids (refers to the TNsG (JRC, 2007));
  - **95%** for solids (refers to (EFSA, 2010))
  - **95%** (for liquids and solids if new gloves for each work shift are used; Garrod et al. (GARROD ET AL., 2001) and TNsG (JRC, 2007) are cited)). The work of Garrod et al. determines the difference between "existing gloves" and "new gloves" to be around a factor of 2 (based on experimental data). However, this factor is applied to the glove efficiency from the TNsG which is not based on experimental data.
  - Efficiencies for coveralls, ranging from **75** up to **99%** (depending on coverall material and substance) are also suggested.
- The EFSA Scientific Opinion on Preparation of a Guidance Document on Pesticide Exposure Assessment for Workers, Operators, Bystanders and Residents (EFSA, 2010) cites TNO (TNO, 2007) which includes a summary of a performed experimental studies and research is provided. The reported levels of reduction by gloves range from **38%** to **99%**. In general TNO summarises the

huge differences concerning the efficiencies used for glove, other clothing and RPE efficiency estimates in registration processes of pesticides

- The addendum to (TNO, 2007) which has been published by EFSA (EFSA, 2008) includes a review of literature published from 2005 to 2008. 20 publications were found to be of some relevance but only one offers concrete efficiency values (Driver et al., 2007) with penetration rates between 0.7 and 14 % (median), i.e. efficiencies between **99.3** and **86 %.** It is noted that the outer loading mass affects the degree of penetration.
- Brouwer et al. (BROUWER ET AL., 2001) state that high efficiencies can be reached (>/= **98%**) but also lower values have been reported (lowest reported efficiency is **60%** in general for fabric and **85%** for gloves). Often internal exposure is less reduced by gloves than external exposure, e.g. due to increased skin permeation because of more moisture or higher temperatures. The importance of traning programmes for RPE and gloves for companies is indicated. A default of APF 6 (i.e. **~83%** efficiency) for gloves (and 2,5 and 6 (i.e. **60** and **~63%** efficiency) for one or two layers of general clothing) is suggested as Tier 2 approach. On Tier 1 level no gloves or other PPE should be implemented.