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Guidance on Information Requirements and Chemical Safety Assessment

Chapter R.14: Occupational exposure assessment

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Guidance on Information Requirements and Chemical Safety Assessment
Chapter R.14: Occupational exposure assessment

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Preface

This document describes the information requirements under the REACH Regulation with regard to substance properties, exposure, use and risk management measures, and the chemical safety assessment. It is part of a series of guidance documents that are aimed to help all stakeholders with their preparation for fulfilling their obligations under the REACH Regulation. These documents cover detailed guidance for a range of essential REACH processes as well as for some specific scientific and/or technical methods that industry or authorities need to make use of under the REACH Regulation.

The original versions of the guidance documents were drafted and discussed within the REACH Implementation Projects (RIPs) led by the European Commission services, involving stakeholders from Member States, industry and non-governmental organisations. After acceptance by the Member States competent authorities the guidance documents had been handed over to ECHA for publication and further maintenance. Any updates of the guidance are drafted by ECHA and are then subject to a consultation procedure, involving stakeholders from Member States, industry and non-governmental organisations. For details of the consultation procedure, please see:

http://echa.europa.eu/documents/10162/13559/mb_63_2013_consultation_procedure_for_guidance_revision_2_en.pdf

The guidance documents can be obtained via the website of the European Chemicals Agency at:

http://echa.europa.eu/web/guest/guidance-documents/guidance-on-reach

This document relates to the REACH Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006[1] and its amendments until 27 December 2015.

1 Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006).

Document History

Version 1	First edition	May 2008
Version 2	• The material on worker exposure models in Part D of IR&CSA guidance (Chapter 5.3 and Appendix D-1 pp. 63-64) introduced to Chapter 14.4.	May 2010
Version 2	• In the text on exposure models "steps to run the tool" were removed, as they were not considered helpful in written guidance.	May 2010
Version 2	• Section 14.4.7 on the ECETOC TRA worker tool for exposure estimation at Tier 1 underwent a major revision and updating, with the inclusion of the new version of ECETOC TRA worker model	May 2010
Version 2	• The text on other models (Stoffenmanager, Riskofderm, ART) were updated	May 2010
Version 2	• The text on EMKG-Expo-Tool was edited	May 2010
Version 2	• The text on measurement data was updated (R 14.4.4 and R14.4.5)	May 2010
Version 2	• A new Section R14.4.6 on short term exposure data was introduced	May 2010
Version 2.1	Corrigendum: • (i) replacing references to DSD/DPD by references to CLP • (ii) further minor editorial changes/corrections	November 2012
Version 3.0	• New sections on assessment workflow and assessment principles have been introduced (Sections R.14.3 and R.14.4) • Section R.14.5 on Exposure determinants has been redrafted to include extended information on exposure scenarios and means of exposure control • New Section R.14.5.4 on SWEDs has been introduced • The section on measured data (R.14.6.3) has been redrafted to focus on principles to consider rather	August 2016

	than in number of data points required • The information on modelling tools (Section R.14.6.6) has been updated and streamlined • The BEAT model has been added to the list of tools (Section A.14-1.4.3 in Appendix R.14-1) • New section on exposure assessment for applications for authorisation has been added (Section R.14.7.)	

Notes on the updates

The updates in this version of the guidance either provide additional tools and parameters to support occupational exposure assessment and exposure scenario building under REACH, or provide further explanation to improve understanding. Other revisions are of an editorial nature.

A registrant having already finalised the occupational exposure estimation based on versions 2 or 2.1 of Chapter R.14 may therefore wish to take the following advice into account:

- Carefully read the document history to be informed on what has been updated;
- Check whether the changes in the guidance put into question:
  - the scope of the exposure assessment and scenarios already worked out, and
  - the outcome of the risk characterisation related to these exposure scenarios.

In this respect, it should be highlighted that an assessment carried out with previous versions of the exposure estimation tools can still be considered valid.

Registrants may decide on reading this guidance that they need to update their CSR, if consideration of the issues causes them to revise their assessment. Some possible issues are identified below:

- **Use of exposure estimation tools**: sources of uncertainty when using estimation tools and the domain of applicability of the tools have been further detailed in guidance. (See Appendix R.14-1)
- **Risk management measures:** Section R.14.5.2 includes information on closed systems and ventilation. The closed systems sub-section includes advice on the assignment on PROCs used for rigorous containment (PROCs 1-3), whilst the ventilation sub-section explains the expected effectiveness associated with certain types of ventilation.
- **Acute exposures:** the updated guidance further clarifies the applicability of estimation tools for the assessment of acute exposures.
- **Glove material:** Section R.14.5.3 on PPE clarifies that an effective glove for the registered substance should be described in the IUCLID dossier

If the conclusion of the check is that the scope of the exposure assessment and scenarios are satisfactory and the outcome of the risk characterisation is also satisfactory, then it is unlikely that an already existing Chemical Safety Report would need to be updated or amended. If none of the substantive issues outlined here affects an already existing Chemical Safety Report, amendments are not required due to this guidance update.

Convention for citing the REACH regulation

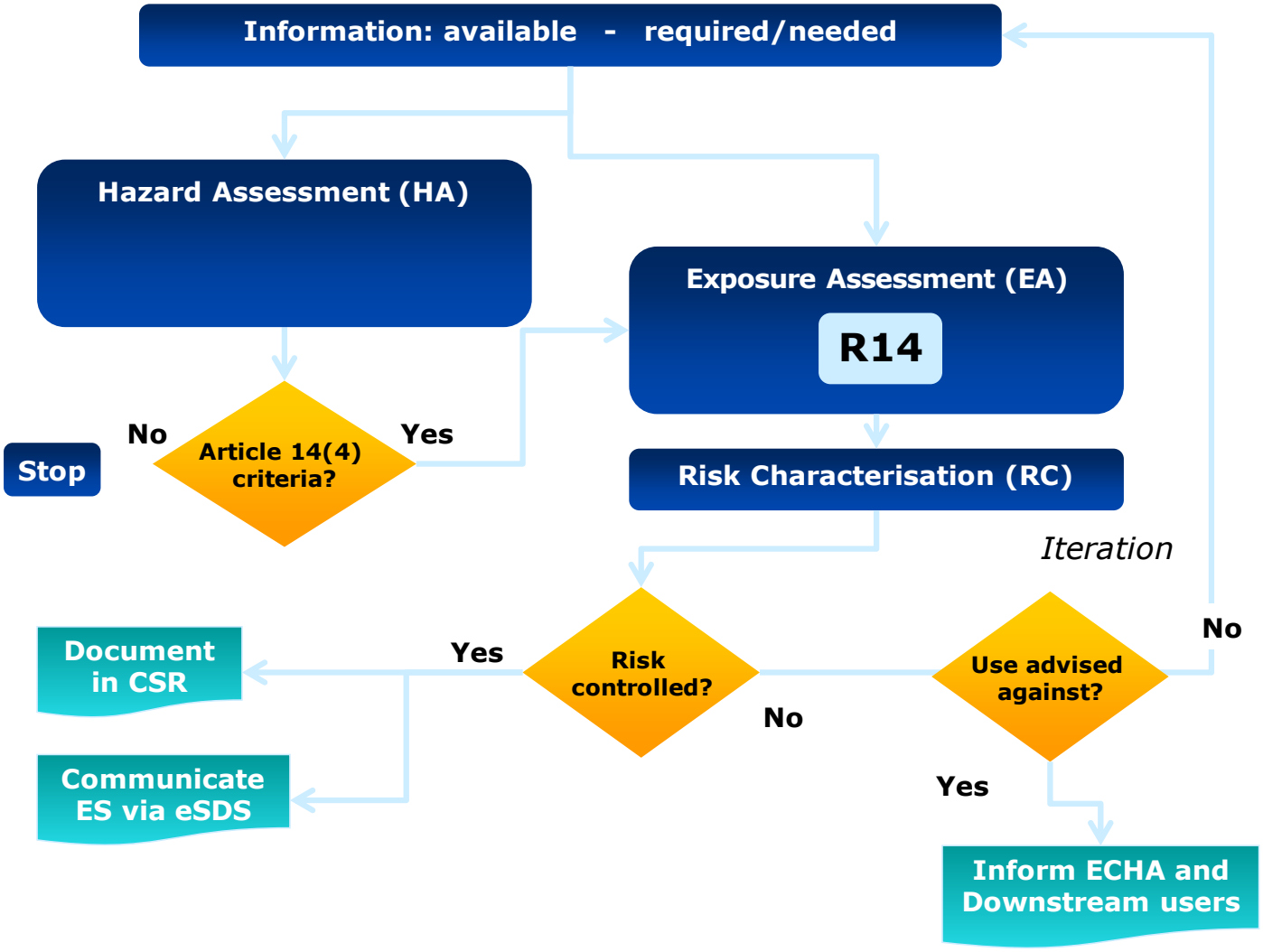
Where the REACH regulation is cited literally, this is indicated by text in italics between quotes.

Table of Terms and Abbreviations

See Chapter R.20

Pathfinder

The figure below indicates the location of chapter R.14 within the Guidance Document



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R.14.1 Aim of this guidance

This guidance gives advice to registrants on how to carry out an occupational exposure assessment under REACH. REACH requires, according to Article 14(4), exposure assessment and subsequent risk characterisation to be carried out for substances subject to registration, which are manufactured or imported in quantities equal to or greater than 10 tonnes/year, and where the substance fulfils the criteria for any of the hazard classes or categories listed in Article 14(4)[2] or is assessed to be a PBT or vPvB. It describes how to build the exposure scenario and estimate the exposure. The guidance also addresses aspects relating to the scope of the assessment, and the assessment workflow.

The guidance includes the following sections:

- Types and routes of exposure (Section R.14.2)
- Assessment workflow (Section R.14.3)
- Assessment principles (Section R.14.4)
- Exposure determinants (Section R.14.5)
- Exposure estimation (Section R.14.6)
- Exposure Assessment and Applications for Authorisation (Section R.14.7)
- Exposure estimation models

The main focus of the guidance is occupational exposure assessment in the context of REACH Registration (i.e. when required by Article 14(4)). However, occupational exposure estimation is also required in the context of applications for authorisation and the information contained in this guidance is, in general, also applicable to the exposure assessment in this context with specific considerations identified in Section R.14.7.

R.14.2 Types and routes of exposure

Substances in the workplace may come into contact with the body and possibly enter the body by inhalation, by contact with the skin (dermal route), or sometimes by swallowing (ingestion/oral route).

Exposure estimation will need to consider the following three separate exposure routes:

- inhalation exposure: usually represented by the average airborne concentration of the substance over a reference period in the breathing zone of a worker;
- dermal exposure : the amount of substance in contact with the skin surface, and/or
- oral exposure: but only to consider in the context of proposing appropriate risk management measures and strategies to avoid exposure in specific cases.

A fraction of the amount in contact (external exposure) will be absorbed into the body, either via the digestive system, the respiratory tract, or through the skin and can cause

[2] These are:
- hazard classes 2.1 to 2.4, 2.6 and 2.7, 2.8 types A and B, 2.9, 2.10, 2.12, 2.13 categories 1 and 2, 2.14 categories 1 and 2, 2.15 types A to F
- hazard classes 3.1 to 3.6, 3.7 adverse effects on sexual function and fertility or on development, 3.8 effects other than narcotic effects, 3.9 and 3.10
- hazard class 4.1
- hazard class 5.1

systemic effects (internal dose). This fraction is usually route and substance specific but may also depend on other factors. If no specific information is available, 100% is assumed.

Exposure to a particular substance is normally determined through estimating the "external" exposure, which needs to be compared to a toxicological threshold (DNEL) for quantitative risk characterisation. This may refer to local effects at the point of entry or to systemic effects. The DNELs for systemic effects are also expressed as external concentration or dose, in order to facilitate direct comparison. Depending on the available information such DNELs already take into account the fraction of substance absorbed into the body. When extrapolating systemic study results from one exposure route to another, the route specific absorption behaviour needs to be taken into account (See *Chapter R.8 of the Guidance on IR&CSA* [1]).

The routes of exposure and the nature of effect will dictate the risk management strategy that needs to be deployed. (See Section R.14.4.4).

In addition to the exposure routes, the duration and frequency of exposure after which the effect occurs (acute or chronic effect) needs to be taken into account. Acute effects (e.g. narcosis, irritation) occur rapidly as a result of short-term exposures while chronic effects generally occur as a result of long-term exposure (months, years) etc.

For comparison with hazards after repeated or continuous exposure (chronic effects), a reference period of a full shift (normally 8 hours) is generally used. Exposures that are typically longer or shorter than the 8-hour reference period can be adjusted in magnitude to provide an 8-hour time-weighted average estimate so they can be compared with chronic DNELs. If the substance has the potential to cause acute health effects (leading to classification), the peak exposure over shorter reference periods must be identified and evaluated and compared with an acute DNEL. This is often a 15-minute time weighted average exposure to be compared with the corresponding (15 min) acute DNEL. Shorter exposure periods may be more appropriate depending on the effect. Section R.14.6 on exposure estimation provides advice on how to assess the long-term exposure and gives specific advice for the assessment of acute exposures in Section R.14.6.5.

For certain effects, like for example irritation or corrosion to skin and eyes, usually no exposure estimate and risk quantification is needed to demonstrate control of risk. For uses of acids and bases in mixtures for example, control of local risks may be achieved by limiting the concentration to the classification threshold for mixtures, or by the presence of a buffer system in the mixture. The registrant is expected to provide arguments that the conditions of use described in the exposure scenario make it unlikely that adverse effects occur (qualitative risk characterisation). The same applies for other effects where no threshold can be derived.

R.14.2.1 Inhalation exposure

Inhalation exposure is generally expressed as mg/m^3 for particulates and in ppm (parts per million) or mg/m^3 for volatile substances. It may sometimes be useful to express exposures as ppm for vapours, especially when data are to be used in analogous situations – a conversion can then be made to account for molecular weight. Other metrics could also be relevant, such as cm^2/m^3 (relevant for nanomaterials) and/or particle number/cm^3 (especially relevant for fibres and also relevant for nanomaterials).

When assessing the exposure arising from aerosols (liquid and solid, including fumes, dust, and fibres), some considerations may need to be taken into account such as the aerodynamic particle size. Particle size may vary with time and place (for instance, when arising from processes such as evaporation, condensation or settling of particles). Particle size is important because, firstly it determines the uptake, as some particles will

not be inhaled due to their size. Secondly, once the particles are inhaled, the particle properties will determine the most likely location of deposition in the respiratory tract; which will in many cases determine the possible adverse health effects. For example, for an aerosol that is soluble in human fluids and can therefore be absorbed and have systemic effects, the whole amount of the substance inhaled, is relevant regardless of the particle size. However, for particles having an effect by accumulation in a specific area of the respiratory tract (may be regarded as local effects), only the particles within a certain size-range may be of interest in the exposure assessment. Examples of aerosols causing local effects in specific lung regions include crystalline silica on the alveolar region (respirable fraction, see below), causing silicosis, or sulphuric acid mist deposited in the thoracic region.

The particle size distribution of the aerosol does not need to be known in every situation. The general approach in occupational sites has been to use mass fractions (e.g., health related fractions as defined by EN 481) except in the case of fibres. For example, in Europe, from the publication of the EN 481 the OELs for powder materials have been defined for one or several mass fractions (inhalable, thoracic or respirable). Thus, if measurements of airborne dusts take place, it should be indicated for which aerosol fraction(s) (inhalable, thoracic or respirable as defined by the European standard EN 481 [2]) the measurements have been performed.

The assessment of exposure to aerosols that show mixed phases is more challenging and there is limited experience on how to tackle it. For example, in the case of volatile substances, the exposure assessment may need to take into account components that are both vapour and aerosol – either form may dominate the assessment, depending on the uses and the characteristics of the substance. European standard EN 13936 [3] provides advice on health-related sampling of mixed-phase aerosols, including advice on which phase(s) matter(s) depending on the substance properties and the conditions of use. CONCAWE report 8/15 [4] describes sampling and analysis methods for measurement of the personal exposure concentration of gas oil vapours and aerosols

The general requirements for methods to determine the concentration of airborne chemicals in the workplace are well described in European standards (e.g. EN 482 [5]) and are normally supported by published methods at a national or international level validated against the standards[3].

R.14.2.2 Dermal exposure

Substances may have local effects on the skin or may have the ability to penetrate skin (both intact and broken) and become absorbed into the body. The following two terms can be used to describe dermal exposure:

- **potential dermal exposure (PDE)** is an estimate of the amount of the substance or mixture being deposited on both the unprotected and protected body parts. It is the total amount of contaminant landing on the outside of work-wear and on the exposed surfaces of the various protected and unprotected skin, including hands, torso, face, neck and even feet;
- **actual dermal exposure (ADE)** is an estimate of the amount of contamination deposited on the skin.

[3] The GESTIS database contains validated lists of methods from various EU member states described as suitable for the analysis of chemical agents at workplaces (http://www.dguv.de/ifa/GESTIS/GESTIS-Analysenverfahren-für-chemische-Stoffe/index.jsp).

In regulatory assessment of chemicals, the current approach is to make an estimate to assess actual dermal exposure – i.e. what gets onto the skin. Potential dermal exposure is the most frequently available indicator of amount of deposition arising from real data and can be used to establish the necessary risk management measures (RMM) required to predict actual dermal exposure and demonstrate a safe use.

Dermal exposure is highly variable and often unpredictable; for example, it is often made up of splashes and smears and not an idealised evenly spread layer on the skin, or it may occur from spraying an aerosol that generates a high concentration which is then deposited widely on the exposed skin and clothing.

Dermal exposure may occur through direct skin contact with surfaces that have been previously contaminated. The three major routes of dermal contamination are:

- by deposition (from air),
- by direct contact with the contaminant (e.g. immersion, splashes), and
- by contact with contaminated surfaces (including clothing).

The level of dermal exposure is generally expressed in mg/kg bw/day (for systemic effects) and as a rate of contamination e.g. in mg/minute or µl/minute of a substance depositing as potential dermal exposure or sometimes as dermal load in terms of the mass of contaminant per unit surface area of the skin exposed (µg/cm^2 or mg/cm^2). Estimates of deposition may be arrived at through multiplying the rate of deposition (mg/min) by the duration of the task. Mg/cm^2 may be a common metric for substances that are applied to the skin in a known dose but, in an industrial context, such uniform application or deposition is rather unlikely.

In general, the quantitative assessment should be considered in the context of the uncertainties that exist. Proposals for personal protective measures for dermal exposure and especially for substances considered of high risk through the combination of hazard profile and potential for skin absorption will need to take this into account. It is better if the risk management strategy is decided first and the required measures are then reflected in the quantitative assessment.

R.14.2.3 Oral exposure

Oral exposure in the workplace is usually unintentional ingestion and is addressed through application of good occupational hygiene practice. In some cases where substances present particularly high risk by the oral route it may be necessary to consider specific RMM to prevent such exposure, or to implement measures that can warn when unacceptable oral exposure could occur. Quantitative estimation of unintentional ingestion is not required under REACH.

Unintentional ingestion exposure is important to consider when substances are, for example, accumulated in the body over time causing toxic effects. Unintentional ingestion usually occurs when substances are transferred from contaminated surfaces (including hands and gloves) to the peri-oral region of the face or through direct exposure resulting from aerosol release. Aerosols are, however, considered under exposure via inhalation.

It is not routinely possible to estimate exposure by the oral route quantitatively.

Where identified as a key route, oral exposure can be addressed through a qualitative approach aiming to identify the correct RMMs for each specified exposure scenario. Where substances have a cumulative toxic effect, and where a method is available, it may be possible to use biomonitoring as a means to assess the effectiveness of RMM through demonstration of absence of significant uptake and providing assurance over the effectiveness of the workplace control strategy. Whatever approach is taken, the

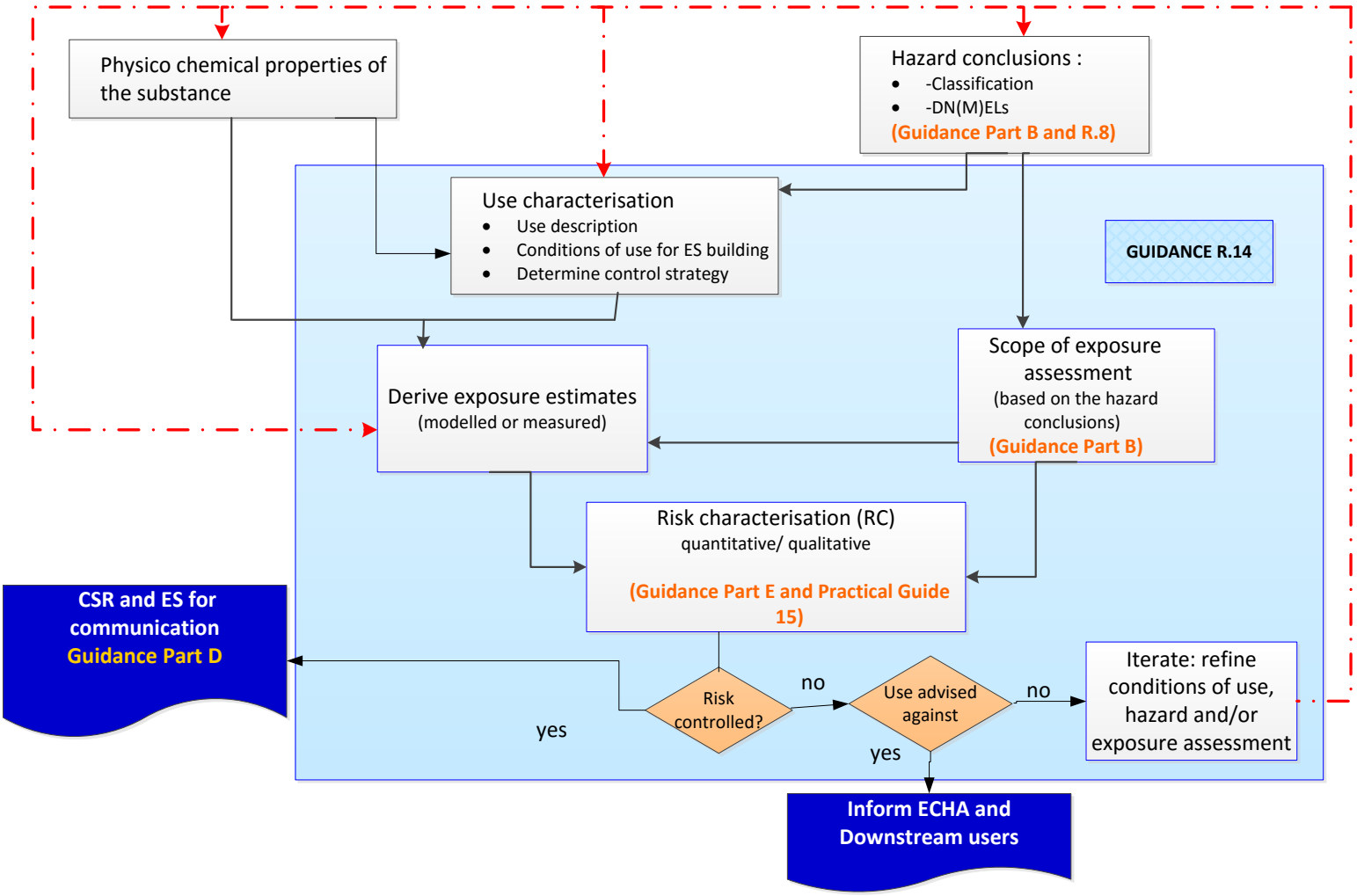
measures will always need to include effective occupational hygiene controls in the workplace.

R.14.3 Assessment workflow

The chemical safety assessment with regard to workers usually includes the steps explained below. The collection of information on the intrinsic properties of the substance and the hazard assessment is not addressed in this guidance but is mentioned because it generates information that is needed for the exposure assessment and risk characterisation.

The following flowchart (Figure R.14- 1) illustrates the steps described below; the light blue box contains all the steps related to the occupational exposure assessment (thus within the scope of this guidance), while the other boxes are related to other steps in the safety assessment that have an impact on the risk characterisation and are outside the scope of this guidance. The dotted red arrows show the different possibilities for the iteration of the assessment

Figure R.14- 1: workflow for occupational exposure assessment



- Collect information related to the intrinsic properties of the substance including:
  - physicochemical properties (e.g. physical form, vapour pressure, water

solubility, dustiness);
    - consider how the use conditions (e.g. process temperature, mechanical energy, concentration of substance in the mixture) may impact on vapour pressure, the (physical) form and the composition of the substance, including reaction products that may occur. This may affect the conclusions on the likely routes of exposure that need to be assessed.
    - toxicological outcomes (e.g. irritation, sensitisation, acute and chronic systemic effects, genotoxicity, carcinogenicity, reproductive toxicity);
- Determine the type and the severity of hazards, through classification and labelling and by deriving no-effect levels (DNELs) or derived minimal effect levels (DMELs) [4] (See *Part B and Chapter R.8 of the Guidance on IR&CSA* [6] and [1]).
- Determine the leading hazard for each exposure route to be addressed in the exposure assessment. It may be necessary to address both local and systemic effects at the same time.
- Determine the scope of exposure assessment (informed by hazard conclusions) (See Section B.8 of *Part B of the Guidance on IR&CSA* [6]):
    - Determine whether (serious) local effects on skin, eyes, respiratory tract may occur (e.g. due to irritation, corrosion or sensitisation).
    - Determine whether short-term high exposure events can cause serious systemic effects;
    - Determine routes and types of effects for which exposure quantification is required (i.e. where a DNEL/DMEL can be derived based on effects seen in the corresponding study(s).
- Determine the control strategy based on substance properties, hazard conclusions and use patterns: for example consider whether rigorous containment (or other means to prevent contact) is the required option; determine whether acute exposure may need to be addressed; determine the engineering controls required to reduce exposure below the DNEL/DMEL; determine where local effects can be prevented by limiting the concentration of the substance in a mixture;
- Define an exposure scenario for each use along the life cycle of the substance: Build a set of contributing scenarios (see Section R.14.5.1) for all tasks or processes under this use, relevant to worker exposure); start from the typical conditions currently found in the sectors of use; employ use maps and exposure assessment inputs available from DU sector organisations (e.g. sector specific exposure descriptions, SWEDs; or sector Generic Exposure Scenarios) or obtain information from customers that represent specific uses of the substance; See ECHA's illustrative example for CSR [7]
- Derive quantitative exposure estimates for all contributing scenarios where needed to support the risk characterisation (i.e. where DNELs/DMELs have been determined in the hazard assessment, and/or where the functioning of rigorous containment should be demonstrated). The exposure estimates can be based on modelling tools, or on measured data sets. It needs to be ensured, that the conditions described in the exposure scenario are consistent with the applicability domain of the modelling tool or with the conditions under which the measured data set has been obtained.
- Derive risk characterisation ratios (RCRs) per route and relevant type of effect. Derive combined risk characterisation ratio (RCR) for dermal and inhalation exposure

[4] DNELs represent the level of exposure above which humans should not be exposed. DNELs are derived for substances based on: population (workers, consumers and the general population), route (inhalation, dermal and ingestion exposure) and duration (acute and long-term exposure)

For non-threshold effects (e.g. non-threshold mutagens and non-threshold carcinogens) a no-effect level, and thus a DNEL, cannot be established. However, it may be possible, if data allow, to set a DMEL (derived minimal effect level), a reference risk level considered to be of very low concern

if systemic effects are relevant.

- Where qualitative risk characterisation is required, provide the key arguments why the conditions of use described in the exposure scenario are appropriate to limit/prevent exposure. Quantitative estimates of exposure are also helpful to support judgement on RMMs and OCs.
- Conclude whether further refinement of assessment is needed, and finalise the risk characterisation (quantitative and/or qualitative).
- Document the assessment in the CSR. Communicate conditions/measures for safe use down the supply chain. Ensure that customers receive information that is consistent with the CSR and can be interpreted in the workplace. This should also cover uses far down the supply chain where the concentration of a substance in a mixture is below the classification thresholds, but still the properties of the substance are such that workers would need particular advice to avoid health effects.

R.14.4 Assessment principles

R.14.4.1 Determine the scope of exposure assessment

The starting point for the registrant's exposure assessment is the outcome of the hazard assessment, which is based on the endpoint information required under REACH. The adverse effects identified for the substance determine the scope of the exposure assessment. In the hazard assessment the registrant should already have taken into account the likely routes of exposure, including consideration of the intrinsic properties of the substance (e.g. volatility, physical state, forms of the substance) and the anticipated conditions of use. The tendency for a substance to be absorbed through the skin may already have been considered in the hazard assessment.

For workers, the output of the hazard assessment consists of nine conclusions referring to the various combination of exposure route, location of effect and time needed to trigger the effect (see *Chapter B.8 of the IR&CSA Guidance* [6])

- types of effect (local on skin, in respiratory tract or eyes, or systemic effect)
- the duration and frequency of exposure after which the effect occurs (acute or chronic effect)
- the routes of exposure (inhalation, dermal, oral, eyes)

The outcome conclusion for each route and type of effect may be one of the following:

- No hazard has been identified. Consequence: no exposure assessment is needed
- Insufficient data are available to conclude on the hazard. Consequence: a testing proposal has been made and the exposure assessment needs to identify suitable interim measures to control the risk.
- Exposure is demonstrated to be negligible, and testing is therefore considered not needed (exposure based adaptation). A comprehensive justification should be provided: conditions of use (including exposure controls) to be described ensuring that the exposure is negligible, and quantification of the expected exposure level under these conditions.
- DNEL/DMEL can be derived quantifying the level of exposure where no effects are expected or where the likelihood of adverse effects is sufficiently low. Consequence: suitable exposure controls to be determined and corresponding exposure estimates to be derived, demonstrating that the expected exposure is below the DNEL/DMEL. If a DMEL is used as a reference, an additional argumentation is needed for why the exposure level represented by the DMEL leads to tolerable health risk.
- No DNEL/DMEL can be derived, but other toxicological threshold (e.g. a Toxicological Threshold of No Concern) is available for comparison with exposure estimate. Consequence: depending on the type of threshold it can be used as a surrogate DNEL (justification required) or a reference for assessing the level of expected exposure in a more qualitative way.
- No DNEL/DMEL can be derived, but the level of hazard is concluded from classification of the substance. Consequence: Suitable exposure controls to be determined and qualitative argumentation needed for why the measures are appropriate to ensure a low/tolerable likelihood of adverse effects. The physicochemical properties of the substance and its form during use are to be taken into account. Depending on the case, the expected exposure may benefit from being quantified to support the argumentation.
- For cases where the substance is corrosive or irritating to skin or eyes and where no information from an inhalation study on respiratory tract irritation is available, it should be appropriate to assume an irritation hazard also for the inhalation route. For substances identified as potential skin sensitizers, it is also advisable to take steps to prevent/minimise inhalation exposure. For low molecular weight

substances identified as respiratory sensitizers, it is appropriate to consider measures to prevent skin contact even if a specific hazard for the skin has not been identified.

By definition the systemic DNEL/DMELs derived under REACH are meant to be expressed as external concentration (mg/m^3 for inhalation) or deposition on skin (mg/cm^2 or mg/kg bw/day). Depending on the underlying toxicity data, such values may be based on the assumption that:

- 100% of the inhaled/deposited substance is transferred into the body or
- limited defined absorption into the body takes place.

If 100% absorption is assumed the derived DNEL is lower than the case where a DNEL is derived where partial absorption has been taken into account. Thus, when characterising the risk, the factors determining the DNEL need to be taken into account.

A comparable issue may occur when inhalation exposure of a dust/aerosol is to be assessed against a local DNEL for the deep lungs. Unless information on the particle size distribution or the aerosol fraction occurring in the workplace is available, it should be assumed that all particles are respirable (i.e. penetrate into the alveolar region in the lungs). Also, the particle size distribution of the airborne fraction released during use may be different from the distribution measured from stored samples of the manufactured material or from the test material in the toxicity study.

R.14.4.2 Particular case: Exposure considerations when determining testing needs

The exposure assessment may, on occasions, be used as a means to help determine the most appropriate route for administration during testing. The physicochemical properties of the substance and uses may lead to the conclusion that significant inhalation exposure is or is not expected (e.g. as a result of vapour pressure). In these cases, it should be clear from the conditions described in the exposure scenario when, for example, processing at elevated temperatures or when aerosol formation is predicted, that the correct conclusions are drawn. Extending the exposure scenarios into unnecessary uses may lead to the wrong conclusion on route of administration – especially by inhalation when it does not really exist to a great extent.

On occasions you may wish to rely on an exposure assessment to support a case for either a column 2 adaptation or for substance-tailored exposure-driven adaptation (Annex XI, Section 3).

Generally the need is to demonstrate that there is sufficient evidence of absence of exposure, as defined through the application of strictly controlled conditions (Article 18(4) (a) to (f)). Advice on how measurements may support an argument for strictly controlled conditions and absence of exposure is presented in *Practical Guide 16: How to assess whether a substance is used as an intermediate under strictly controlled conditions and how to report the information for the intermediate registration in IUCLID.* Various terms are used in the legal text as an indicator of the standard to be achieved, but in every case the evidence will need to be specific, adequate and suitable for that purpose. It is unlikely that exposure modelling alone will provide the level of proof required to demonstrate these highly controlled and rigorously contained conditions.

R.14.4.3 Integration of quantitative and qualitative hazard conclusions

Having DNELs or DMELs for all the required and available data on a substance makes it fairly easy to identify the leading health effect for that substance for the relevant exposure patterns. By contrast, for a substance having DNELs or DMELs for some

endpoints and data of a qualitative nature for other endpoints, it may be more challenging to identify the leading health effect for each route for the relevant exposure patterns.

The general approach when it is not possible to derive a DNEL or DMEL for an endpoint is to reduce/avoid contact with the substance. However, implementation of risk management measures (RMMs) and operational conditions (OCs) needs to be proportional to the degree of concern for the health hazard presented by the substance. For example, it is not appropriate to apply the same control strategy to irritating substances as to substances that are strong respiratory sensitizers or mutagenic.

A typical assessment situation in this respect occurs if a substance may cause local effects in the respiratory system due to its properties (but no DNEL is available) and causes systemic effects at the same time (for which an inhalation DNEL has been derived by route to route extrapolation). Often it may not be obvious upfront, which of the two effects would drive the risk management, and thus a concentration level at which local effects may occur needs to be estimated.

This means that the conditions of use (OCs and RMMs) as set out in the exposure scenario (that determine the exposure level) need to reflect the severity of the hazard. The severity of the hazard (and consequently the suggested extent of exposure controls) may be indicated:

- by one of the three hazard-levels (high, moderate or low) suggested in *Part E of the IR&CSA Guidance* [8] and based on the EU hazard classification system (hazard statements). These hazard levels reflect three factors:
  i) whether a threshold theoretically exists but available data do not allow to set a DNEL (e.g. for irritation);
  ii) the seriousness of the health effect and
  iii) the potency of the substance regarding a certain effect (e.g. strong sensitizer versus moderate sensitizer);
- and additionally by a DMEL (if available)

Based on DNELs, DMELs and the Classification and Labelling based hazard bands it should be possible to identify the critical hazard for each route of exposure and type of effect.

For more details see *Part E of the IR&CSA Guidance* [8], Table E.3-1.

R.14.4.4 Principles for determining the control strategy

The purpose of the exposure assessment in the CSR for registration is to describe the conditions for safe use under normal operating conditions. It assumes good practice in compliance with national occupational health and safety legislation. Based on this, the exposure estimates should be representative of the safe use conditions described.

Exposure resulting from misuse or abuse would not normally be considered during the assessment. Similarly, exposure which results from accidental release and serious failure of plant integrity leading to major loss of containment, does not need to be addressed in the exposure assessment.

The exposure assessment includes identifying the relevant exposure scenarios which can be based on knowledge of own use, information from key customers, or use maps developed by sector organisations (see Section 14.5.3). Depending on the routes of exposure, the nature of effect and the availability of data to determine a safe level of exposure, the appropriate control strategy can be determined. The principles for determining the control strategy are as follows, in order of priority (according to Directive 98/24/EC):

- Avoid any contact with the substance by containment and other strict controls; for example, applicable for substances classified as mutagens, non-threshold carcinogens, respiratory sensitizers, potent skin sensitizers and strong corrosives;
- Apply engineering controls (e.g. containment of the source, local exhaust ventilation (LEV), mechanical ventilation ; conditions avoiding splashes, spills and hand contact) to limit exposure to i) a safe level (if exposure can be compared with DNEL/DMEL) or ii) a level where the likelihood of effects occurring is sufficiently low (for qualitative assessment);
- Limit concentration of substances in mixtures when possible such that:
  - the classification thresholds for corrosion, irritation, sensitisation in mixtures is not exceeded;
  - the external concentration/loading of the substance is limited to a safe level for systemic exposure (to be verified by estimation of exposure).
- Apply management controls (e.g. reduction of the duration of the task)
- Apply appropriate personal protective equipment (PPE). It is important to note that PPE is always the last resort;

The operational conditions including the control strategy for the highest hazard on a given route will also be protective for lower hazards on the same route. Depending on the properties of the substance, a threshold effect (quantitative assessment) or a non-threshold effect (DNEL cannot be derived) can be the leading hazard.

If control of risk can be demonstrated for all routes and types of effect, the existing conditions of use are obviously sufficient. Where the DNEL/DMEL is exceeded, or the measures in place do not limit the likelihood of effects occurring at a low level, the corresponding exposure scenarios need to be refined until safe use is guaranteed.

R.14.5 Exposure determinants

Worker exposure is determined by many factors, including:

- inherent properties of the substances, in a mixture or in an article;
- the process type and the associated containment and degree of engineering control;
- operational conditions, e.g. temperature, in-use concentration, scale of use, duration and frequency;
- RMMs applied and the associated effectiveness.

To enable robust worker exposure estimation the following type of information is required:

- where is the substance used?
  - enclosed processes or plants;
  - indoor controlled environment;
  - indoor open sources;
  - outdoor; etc.
- how is the substance used?
  - high energy processing (e.g. spraying, grinding, hot processes) or low energy processing (e.g. assembly of article components, dipping of articles into vat);
  - remote or intimate contact during normal operation; etc.
- what are the operational conditions?

- characteristics of the substance (physical state/dustiness/vapour pressure)and its concentration in a mixture or an article (process materials, and finished products) under the operational conditions;
- duration and frequency of task;
- duration and frequency of exposure
- temperature of plant, process and surfaces; etc.

- what are the appropriate RMM?
  - engineering controls;
  - separation of operator from the emission points (cabin, control room);
  - impact of management systems (e.g. housekeeping, operators effectively trained in use of RMMs);
  - personal protective equipment (PPE) (provided to address residual risk), must be suitable and adequate [5] and associated with appropriate levels of instruction and training etc.

R.14.5.1 Exposure scenarios and contributing scenarios

For each of the identified uses in the life-cycle of a substance, the operational conditions and risk management measures ensuring control of risk must be determined. This set of information is called an exposure scenario (ES). An exposure scenario usually covers a number of contributing tasks/activities within the use (such as transfer, mixing, spraying, dipping, brushing, cleaning of equipment/machinery etc.). A set of conditions of use addressing one task/activity is called a contributing scenario (CS).

The contributing activities (described by a name and a process category) usually do not lead to the same exposure and do not necessarily take place under the same conditions of use (e.g. duration, ventilation, dermal protection). Therefore, usually a contributing scenario is generated for each of the activities/tasks, and corresponding exposure estimates are derived. Where all the activities contributing to a use take place under the same conditions, they are still to be described and assessed one by one, when the activity category or process category (PROC) as such drives the exposure estimate.

When the assessment is based on measured data, it is often the case that these measured data have been collected across several different tasks over a shift. In this case, the contributing activities that are relevant for the exposure scenario must still be described one by one, even if it is not possible to identify data points from the measured data set that are applicable to individual contributing activities. If the conditions are the same across all tasks, the contributing activities may be linked to one set of use conditions, which correspond to the conditions that are represented by the measured exposure data (covering both routes of exposure).

For a given use (and its contributing activities), different levels of exposure controls may be needed, depending on the hazard characteristics of the substance. The registrant is expected to choose the appropriate level of control that matches the properties of the substance (see also Section R.14.5.4 on SWEDs). It may also be appropriate to include contributing scenarios for different concentration levels of the substance, when this gives rise to different RMMs.

[5] **Suitable** means the right type of equipment taking into account operational conditions and personal factors. **Adequate** means capable of providing the right level of protection.

For most uses, manual cleaning and maintenance of equipment is needed from time to time. This will include, for example, interventions into closed systems and cleaning of machinery and vessels between batches. It may also include changing of filters, maintenance of reservoirs of processing fluids and similar tasks. The exposure assessment should include a contributing scenario describing conditions for this periodic (but not necessarily daily) cleaning and maintenance if such activities are not already covered in one or more of the other contributing scenarios. Repair due to accidental malfunction or renovation/reconstruction of production plants is however out of scope of the REACH safety assessment. The exposure assessment is required for both the substance to be removed and any substances used as cleaning agent. However these activities will normally be addressed by different registrants.

The updated *Chapter R.12 of the IR&CSA Guidance* [9] includes a new PROC (PROC 28) to be assigned to this type of activities.

R.14.5.2 Technical means and administrative controls

RMMs are a combination of design, engineering solutions and the administrative measures that deliver the required acceptable level of exposure.

Within the CSR, RMMs are required to be described; this is usually in generic terms such as LEV or personal protective equipment. These descriptions are interpreted in the workplace within the context of Chemical Agents Directive (98/24/EC). The Directive establishes a hierarchy in the application of control measures, this means that engineering controls such as closed systems, containment and use of ventilation arrangements (local exhaust at the point of emission and/ or general building ventilation (passive or mechanical)) are always the preferred primary means to control exposure.

A substantial amount of occupational health and safety guidance is widely available that provides information on conditions for safe use in the workplace[6]. Registrants are encouraged to link the RMMs in the CSR and in the ES for communication to such advice when possible. Information from downstream user sector organisation can support this (see also Section R.14.5.4).

R.14.5.2.1 Closed systems (rigorous containment)

Closed systems (including rigorous containment by technical means) generally relate to high integrity plant/machinery where the opportunity for exposure is negligible, both in terms of frequency and magnitude. Fugitive emissions do not occur under normal conditions of use and only occur due to loss of integrity and associated failures in the monitoring and management systems.

This section provides some particular guidance on the selection of a suitable PROC when describing uses and its contributing activities in closed processes (for more information on description of uses and for complete list of PROCs please see *Chapter R.12 of the IR&CSA Guidance* [9]). At the same time reference is made to the applicability domain of the PROC 1 to 3 when used as an input parameter to exposure estimated based on ECETOC TRA worker or other tools (See section A.14-1.1).

PROCs 1 to 3 refer to systems/plants that are intended to be closed (rigorously contained), such as synthesis of substances in closed reaction and purification vessels, drying towers or extraction of substances in distillation plants, where all transfers take place via fixed pipes. Releases may result from planned interventions (e.g. cleaning and maintenance, sampling), and if so, these would need to be assessed and managed separately. However, if such processes are not undertaken under contained/closed

[6] See for example: https://oshwiki.eu/wiki/Hierarchy_of_controls_applied_to_dangerous_substances

conditions PROCs 1 to 3 are not applicable, (e.g. for tray drying, dry milling and sieving, manual charging/discharging to and from containers, filter presses, stirred reactions in open or partially closed vessels), and a more suitable PROC, such as PROC 4 or PROC 8a/8b could be used.

Other process types occurring on end-use of substances (e.g. spraying, dipping, brushing, printing, lubricating) may be engineered using containment, automation, and ventilation so that a very low level of exposure can be achieved. When correctly operated, the exposure can be similar to that associated with processes/plants referred to as PROC 1 to PROC 3. However, it is not appropriate to just assign a PROC 1 to 3 in such cases: The name of the contributing activity/scenario should clearly refer to the actual type of process/task (e.g. industrial automated dip coating in closed system), the assigned PROC should correspond to the type of process (e.g. PROC 13), and the closed conditions need to be specifically described in the contributing scenario. An exposure estimate based on PROC 1 to 3 may be applicable, but would need an explicit justification. For the criteria that need to be checked and documented, see Section A.14-1.1.1 on applicability domain of ECETOC TRA. For further description of the different levels of containment, please refer to Section 2.1.1 of the ECHA *Guidance on Intermediates*[7] [10].

Enclosure, containment and process ventilation are most often inherent design features of the plant. When managed effectively, these combined features have the potential to prevent releases. Higher Tier models allow assessment of these types of circumstances.

Please note: The information on whether a substance is used under rigorous containment (only) may play a role for selection when identifying priority substances for one or more of the REACH processes following registration. Therefore, IUCLID 6 includes the possibility to explicitly flag to the authorities that a use takes place under rigorous containment. For claiming such conditions of use, the registrant would need to describe the containment and the related administrative controls in two dedicated fields of the IUCLID dossier.

R.14.5.2.2 Ventilation

Additional control of emissions through the use of ventilation arrangements is often ascribed a level of effectiveness (such as 80%, 90%, 95%) and mostly applies within the context of processes where there is anticipated release, with a subsequent need to control emissions at source. The levels of effectiveness will in themselves be associated with aspects of design, commissioning, maintenance, monitoring etc., to prove they deliver the necessary level of control. It is anticipated at well managed processes LEV would, in any case, be subject to periodic examination and testing to demonstrate the level of performance.

Effectiveness of LEV is determined by many factors such as type of emission, design of the enclosure, positioning of the worker and the correct flow of air throughout the system. This is to ensure that capture performance and transport of the substance is optimal. Best performance is associated with maximising enclosure, integration of ventilation arrangements into the process, good design, commissioning and management. Levels of effectiveness of LEV can however, be difficult to establish with certainty.

However, the characteristics generally associated with certain levels of effectiveness can be identified:

[7] Please note that the above mentioned section describes containment systems in general, not only closed systems

95% effectiveness or higher is, ordinarily, difficult to achieve. It is most likely to be achieved when the ventilation and engineering controls are specially designed and/or integrated into the equipment, expertly commissioned and tested regularly to prove it continues to operate at the intended high level of performance.

LEV around 90% effectiveness is associated with good design, although possibly employing retro-fitted equipment, good adjustment, and with routine examination and testing to ensure it delivers the required performance and continues to do so.

Levels of effectiveness at 80% to 90% are associated with retro-fitted equipment that has not necessarily been fully integrated into the plant. It may allow operators to alter the positioning of hoods or in other ways change the optimal effectiveness of the equipment.

Lower levels of effectiveness of LEV (below 80%) are often associated with poor design, inadequate selection of the composite parts and opportunities for worker interference with the system.

As an example, a spray-booth compliant to EN 12215 or EN 13355 is required to have a minimum downdraft air velocity of 0.3 m/s which should ensure a minimum 200 air exchanges per hour. This should deliver a 95 % reduction with a well-designed LEV. A spray-stand with efficient exhaust ventilation (0.5 m/s at exhaust screen) ensures 90% reduction. This is an equivalent efficiency to local exhaust ventilation even when it is not literally a local exhaust. It may be reasonable to manually reduce effectiveness values of LEV and engineering controls in the exposure assessment to provide more options during implementation. In this way where high effectiveness is not normal practice, and where the risk characterisation allows, the registrant can propose options that allow use of less sophisticated equipment than would be required, for instance, to otherwise achieve 90% reduction.

The effectiveness of the ventilation has a major influence on the predicted exposure. Default effectiveness values for LEV are incorporated into certain Tier 1 modelling tools. Registrants should as far as possible ensure that the effectiveness values they rely on in their assessment align with the type of ventilation arrangements foreseen at typical workplaces.

Some limited work has been carried out investigating effectiveness of LEV. A paper published in 2008, investigated published efficacy of RMMs and identified substantial variation, the reasons for which are however not always fully clear [11]. General ventilation arrangements may be a valid exposure modifying factor in some instances where there are uncontained releases to the general workplace environment. However, in cases where the operator is close to the source of emission, general ventilation may have very unpredictable impact and should be considered carefully as a means to further reduce exposure estimates when local exhaust ventilation is already selected as a risk management option.

R.14.5.2.3 Management controls

Management and administrative arrangements can also deliver reduced exposure.

It is generally assumed, that good occupational hygiene practice is implemented on site[8]. Nevertheless different levels and opportunities of management controls can be incorporated into the exposure scenario leading also to differences in the risk management effectiveness and hence the expected exposure levels. For example, in

[8] Principles for good occupational hygiene practice can be found in different OHS publications, see for example the UK COSHH *Approved Code of Practice and guidance* (pages 30 to 33) that provides eight generic principles to be followed as good occupational hygiene practice [49].

ECETOC TRA or MEASE a distinction is made between "industrial" and "professional" setting, which impacts on the i) basic exposure estimate for the single process category and ii) on the expected effectiveness of local exhaust ventilation. Together, the assumption on the "setting" may impact on the exposure estimate by an order of magnitude. In practice, the "industrial" setting means: advanced system to instruct, train and supervise workers; and proper installation, operation, maintenance and cleaning of equipment; and regular cleaning of rooms. (See also *Chapter R.12 of the Guidance on IR&CSA* [9])

Also, limiting the duration of an activity during the typical 8-hour working day to a shorter period may result in a lower exposure due to that activity. Some Tier 1 exposure estimation tools include an exposure modifier based on duration of the single task. Please note: If limiting the time is a pre-requisite for demonstrating control of risk for a particular contributing scenario, this may have an impact on the work organisation of the downstream user. It may mean that workers should not be exposed to the substance during the remainder of the shift to guarantee safe use. Under OHS legislation, an employer must assess the risk over the entire shift. The registrant may want to include suitable information that supports this need in the exposure scenario for communication. For instance, the risk characterisation ratios may be useful information and could be provided in section 3 of the exposure scenario. In general exposure estimates should not be reduced by applying unlikely time constraints that are not realistic for the expected conditions of use.

A further option for exposure reduction may be ensuring workers are remote from the process. Some models can provide refined exposure predictions based on this modifier and real data often reflects the proximity of the worker to the source of exposure throughout the working day.

R.14.5.3 Personal protective equipment

Personal protective equipment (PPE) is used when residual exposure cannot be avoided after application of other means. Thus, exposure scenarios that rely on PPE as a primary risk management option should be avoided whenever possible.

Selection and use of personal protective equipment will always need to be seen within the context of national OHS legislation where the full range of risks need to be considered. For example, the registrant may need to consider the additional physiological burden introduced by the use of PPE, such as heat stress, or impact on the hands due to long wearing of PPE, if appropriate breaks are not taken.

It is the responsibility of the employer to ensure such risks are avoided. This may be particularly relevant to exposures for extended periods, for example when wearing of impervious gloves national legislation requires that breaks are taken to avoid the effect of wet working (e.g. time for continuous wearing of the gloves may need to be limited e.g. 2 hours, 4 hours depending on the case).

For the risk characterisation, the RCR should be calculated including the reduction factor achieved by the use of the PPE. The reduction factors applied should be transparently reported in the CSR. Justification should be provided when PPE is specified within exposure scenarios as the primary method to achieve acceptable exposures. One such example is during professional car respraying operations, where RPE and protective clothing are a primary RMM. The use of respiratory protective equipment (RPE) should usually be a temporary measure, during short time intervals, until other technical measures are provided to ensure safe use. RPE should be proposed for use well within its designed performance. This may mean an exposure assessment that indicates a performance of 90% but additional good practice advice may suggest equipment providing 95% or better performance is preferred to meet the requirement of other

legislation, especially in cases where the exposures are close to the limit values.

PPE to protect against dermal exposure will often be needed due to the very variable and unpredictable nature of dermal exposure. The outcome of the quantitative assessment alone should not be the only information used to propose suitable and adequate gloves and clothing. Glove effectiveness is determined by the management systems in place to ensure the prescribed level of performance. The required level of management is described by the ESCom phrases (http://www.cefic.org/Industry-support/Implementing-reach/escom/) which are generally included in the exposure scenarios.

Gloves alone will not provide protection when other parts of the body are exposed.

It is an absolute requirement that the barrier properties of the glove material are known to be adequate to ensure the substance does not migrate through the material of the glove during the proposed use. It is important that gloves are sufficiently described in the IUCLID dossier and the CSR so that there is assurance that suppliers of substances and formulations, can effectively communicate (in section 8 of the Safety Data Sheet) the correct information to downstream users. Important information on gloves relates to those materials that are effective and over what duration they are effective. It is also useful to provide information on common glove materials that are known not to be effective as a barrier.

Note: Glove manufacturers' literature may provide indicative information but the best information derives from specific testing against the registered substance. Such information will also help producers of mixtures to select appropriate gloves for their products. Information such as "suitable chemical resistant gloves tested according to EN 374" alone does not give sufficiently concrete information to ensure the correct information is available to control the risk adequately down the supply chain.

R.14.5.4 Specific Worker Exposure Descriptions (SWEDs)

When registrants assess the exposure of downstream users further down the supply chain, they often do not have direct access to information on the condition of use and its variety within/across sectors. This is in particular true for uses of mixtures and articles into which the substance has been incorporated somewhere in the supply chain. Thus for registrants under REACH it is a challenge to i) base their assessment on realistic conditions of use and to generate sufficiently reliable exposure estimates (and hence risk characterisation) and ii) to provide practically helpful and use-specific safety advice to customers.

To address this challenge, some downstream user sector organisations map out the typical uses and describe the conditions of use in a way that registrants can feed into their CSAs; these are called "use maps". Use maps are developed using a template and describe the typical uses within sectors. They include the description of use and its contributing activities as well as the references to the corresponding inputs to the exposure assessment of workers, environment or consumers[9].

The conditions relating to worker exposure are provided in *specific worker exposure descriptions* (SWEDs), in the form of input values to the assessment tools used at registrant's level. The SWEDs are linked to the corresponding uses/activities from the relevant use maps.

SWEDs provide conditions of use to be used by registrants as input to the assessment of worker exposure in the CSA. The RMMs are linked to current occupational health and

[9] See also Part D of the Guidance on IR & CSA, Use Maps can be accessed at http://echa.europa.eu/csr-es-roadmap/use-maps

safety guidance when appropriate.

Registrants are encouraged to base their assessments on use maps and SWEDs where possible, to ensure that the assessments undertaken are realistic and relevant and the exposure scenarios communicated to downstream users provide useful information to promote the safe use of the substance. Use maps and SWEDs are a development of generic exposure scenario (GES) that were introduced in 2009.

R.14.6 Exposure estimation

R.14.6.1 Introduction

Clearly there are options for registrants to address the exposure assessment requirement by different means, such as modelled estimates of exposure levels, measured representative exposure data for the assessed substance, or monitoring data from substance with analogous use, exposure pattern or analogous properties. When adequately measured representative exposure data are available special consideration should be given to them, as they may best reflect the real life exposure situation.

In many cases it may be appropriate to use a Tier 1 modelling approach to support the REACH registrant's generic assessment for the different uses identified. In other cases however there may be a greater need for reliance on higher Tier modelling or appropriate data from measurements. In some cases, a combination of measured data and modelling approaches may lead to the most appropriate assessment.

A pragmatic work flow is to start with Tier-1 modelling and, on the basis of the results, to identify a limited number of (contributing) scenarios for which either higher Tier modelling or a measurement campaign is needed.

Most importantly, the exposure estimate has to be adequate for establishing safe use and be aligned with the anticipated real life situation described within the final exposure scenario. The exposure estimates are required to cover all the described uses and take account of the variability within and between tasks, and for users and sites. Where a worker carries out different tasks with the substance over a shift, the exposure resulting from the individual contributing scenarios will add up to a total exposure. In a generic assessment, control of risk should in general be demonstrated for a duration of 8h per task, to make the registrant's safety assessment independent of the work organisation downstream. Where a registrant however chooses to limit the duration of a task to reduce the estimated exposure concentration, he should make the DUs aware of the potential consequence: exposure to the substance during the rest of the shift may need to be avoided (see also section R.14.5.2.3).

In the context of application for authorisation, an estimate for the full shift cumulative exposure from the different tasks with the substance should be provided.

The exposure estimates should aim to be conservative and reliably cover the conditions described in the exposure scenario; the level of detail required may be limited, but it still needs to be clear which exposures are within scope of that assessment. More refined estimates will include additional information to allow revision of the exposure assessment.

Uncertainty of the exposure estimate needs to be considered to ensure that the conditions of use are sufficiently covered by the exposure estimate. Depending on the level of uncertainty around the various factors contributing to the exposure estimate and resulting RCR, it is recommended to refine (re-iterate) the exposure by alternative means, to reduce the uncertainty. This may include for example modelled exposure from higher Tier models, sensitivity considerations regarding input data in models, and by inclusion of or resorting to (additional) measurement data in a weight of evidence approach to increase reliability of the outcome and to guarantee safe use. Please note: A

risk characterisation ratio close to 1 may clearly indicate the need for such considerations, especially if the substance has particularly hazardous properties (or is very potent) and/or if the exposure estimates are not obviously conservative. In order to support the interpretation of the risk characterisation, the registrant should include in his CSR a reflection on the uncertainties around his assessment, and how they are dealt with (see also section 5.4 of *Part D of the Guidance on IR&CSA* [12]).

R.14.6.2 .Assessment of data and information quality

The confidence in a modelled or measured exposure estimate in the context of exposure assessment and risk characterisation under REACH depends on various considerations. For exposure estimates based on **measured** data, the confidence increases when:

- the exposure data has been collected and analysed according to recognised protocols;
- the data has been collected as personal exposure, or is directly related to it (e.g. representative static samples);
- appropriate information on the conditions of use is available;
- the number of data points is adequate (see Section R.14.6.4)

For exposure estimates based on **modelled** data, the confidence increases when:

- The model is well documented and tested against independent measured datasets;
- one or more peer-reviewed scientific publication is/are available

For both, measured and modelled data, the relationship between i) the actual conditions of use of the substance and ii) the substance/conditions to which the data source refers is also important, as shown in Table R.14- 1.

Where the source of the modelled or measured exposure estimates deviates from the general quality requirements, the data can still be used but a particular justification is needed in the CSR. Potentially a confirmation by other supportive exposure estimates could increase the confidence.

Table R.14- 1 Implications of the chosen information source

Data Source	Suitability of data source
MEASURED DATA	
Measured dataset for the substance used/generated for exposure scenario describing the conditions of use at a specific site or a range of very similar sites	Provides sufficient confidence, which is in particular needed when demonstrating safe use for highly hazardous substances not handled in a closed system. For establishing the similarity between sites the variability/distribution of the exposure estimates need to be analysed.

Data Source	Suitability of data source
Measured dataset for substance and/or uses and/or use conditions analogous to the substance/use to be assessed	Particular and detailed justification needed in the CSR regarding the similarity of substance properties and conditions of use. For establishing the similarity the variability/distribution of the exposure estimates need to be analysed.
Measured dataset with partial information only on context (use and conditions of use) and/or origin of data and/or method of sampling and analysis	Usually not suitable for an assessment under REACH. May, however, provide supportive evidence based on a detailed explanation why the data are interpretable despite the missing information.
MODELLED DATA	
Modelled dataset; input parameters match 1:1 with use and use conditions in the exposure scenario; model used in its applicability domain	Assessment can be based on a simple reference to the tool (including its version).
Modelled dataset; actual use/conditions of use need to be "translated" into input parameters; model used within its applicability domain;	Describe the use, independent of how the model/tool input parameters are expressed. Provide an argumentation how the suitable model/tool inputs have been chosen to properly reflect reality (i.e. the actual conditions of use). Potentially confirm by measured data, in particular when risk characterisation is close to 1 and/or substance is highly hazardous.
Assessment case outside the applicability domain of the model (substance properties, input parameters available)	Should be used as supportive evidence only. Provide a robust argumentation why nevertheless the exposure estimate is relevant in context of the assessment case.

R.14.6.3 Use of measured data

REACH does not require that registrants use measured data for the purpose of exposure assessment or that, if they are used, they are generated for that purpose. Thus, the measured data have often been generated for other purposes. If relevant data do exist, they should be interpreted as part of the exposure assessment reported within the CSR. Where no specific data exist, appropriate analogous data from similar conditions of use could be used.

As already mentioned in Section R.14.4.4, the purpose of the exposure assessment in the CSR for registration is the description of conditions under which safe use is possible

(exposure scenario). It is not the purpose to describe conditions covering companies with no or insufficient exposure controls. Based on this, the exposure estimates should be consistent and representative for the safe use conditions described and thus existing data from measurements aiming to identify unsafe conditions of use or (too) high exposure may not be suitable for a registration under REACH

Sources of measured data that may be useful in the context of REACH are:

- measured data taken under the actual exposure settings for the (contributing) exposure scenario to be developed. For example, data generated to comply with other legislation or to evaluate the effectiveness of the RMMs in place;
- exposure information from databases if information requirements enabling a robust assessment are fulfilled;
- biomonitoring data (see section R.14.6.4.4).

Workplace exposure data have a key role in the assessment of individual workplaces to help fulfil the provisions of the Chemical Agents Directive (98/24/EC) and in evaluating the effectiveness of the RMM in place and thus it can be assumed that exposure estimates for many workplaces exist already.

Exposure data is typically obtained from personal samples. Static samples may also be valid if they reflect the personal exposure and provide a conservative estimate for it.

For registrants, however, the data may not always be easily interpreted in the context of the final exposure scenario required by REACH. Under REACH, registrants may not have access to the measured exposure data from downstream users and are even less likely to have access to the full documentation related to the exposure estimates (e.g. data from individual measurements, OC/RMM of these data etc.).

There may be cases where information sources include reliable documentation of workplace measurements (databases), such as that collected by manufacturers, downstream users or sector organisations, to help fulfil the provisions of the Chemical Agents Directive (98/24/EC), the Carcinogens and Mutagens Directive (2004/37/EC) or for research purposes. Such data, if of a suitable quality and supported by sufficient information, may provide good evidence. A professional judgement needs to be made on the relevance and representativeness and to decide if the data correspond to the conditions of use described in the final exposure scenario and can therefore be used as an exposure estimate and /or to supplement modelled estimates.

R.14.6.3.1 Representativeness of the data and variability of exposure

Available exposure data, even in well-defined situations, have substantial variability. Additionally, the exposure data are associated with certain OCs and RMMs. Both the exposure distribution and the representativeness of the data to the exposure settings to be assessed need to be taken into account.

A key requirement for the final outcome of an assessment is to be representative of the (contributing) scenario to be assessed. For instance, the RMMs prevailing during sampling (i.e. the generation of the measured data), should be similar (provide at least the same efficiency) as the ones reflected in the (C)ES. The representativeness of the data is further discussed in Section R.14.6.4.1.

Variability of measured data is reflected by the spread of the distribution of the individual exposure data points. This variability may be introduced through a number of factors. These factors include differences in application of operational conditions, level of (substance) throughput, other local conditions, variability in performance of RMMs, (lack of) maintenance of plant over time, and behavioural differences between workers.

Exposure distributions can be reasonably described by the geometric mean (GM) and the geometric standard deviation (GSD). Whereas the GM is an estimate of the central tendency of the distribution, the GSD can be used as an indicator for the spread of the distribution (i.e. for the level of variability). Percentiles (e.g. 75th, 90th) show the percentage of the measured exposure levels that are at or below a certain value (e.g. the 90th percentile value indicates that 90% of the measured exposure levels are at or below that value). In general the 90th percentile value, representing the reasonable worst case exposure level of a distribution within a generally suitable dataset (i.e. a dataset corresponding to the conditions described in a contributing scenario), should be used as the exposure value for the risk characterisation. Under particular conditions other percentiles may be applicable as well. A justification should be provided in the CSR. For instance, the use of the 75th percentile may be justified when the data set reflects worst case situation only (e.g. data sets taken in companies suspected of being non-compliant).

High (e.g. maximum) values of a data set are part of the exposure distribution and, unless there is a reason to reject them, should remain in the distribution to help in defining that distribution. An assessor may judge that very high values are so far out of scope and caused by factors that are not possibly associated with the exposure scenario (not reasonably foreseeable or may represent sampling artefacts) that they may be removed, but only on that basis and with a sound justification.

Measurements below the detection limit are in principle also part of the exposure distribution. However, how to include them could be challenging. Accepted practice includes using the limit of detection (or fraction of it) to calculate the concentration to be included in the distribution or the use of more sophisticated tools (see for instance Excel tool Implementing the BOHS/NVvA Sampling Strategy[10] http://www.bsoh.be/?q=en/node/67)[11]. The procedure that has been used to take account of non-detects in the statistical analysis of a data set should be clearly described in the CSR.

R.14.6.3.2 Analogous data

When appropriate representative measured data for the registered substance are not available, an alternative is the use of measured data for analogous substances, that are used in the same way as the assessed substance, or from the assessed substance, that is used in analogous situations. Analogous substances should have close enough physico-chemical properties to the registered substance and be used in a similar enough way. In some cases, it may be possible to use measurement data for the substance taken from analogous situations. For example, with justification, gluing instead of painting may be a similar enough task in some cases given that other conditions of use are comparable as well. Justification needs to be provided to support an exposure assessment based on analogous data.

When using data from analogous substances, the registrant must justify that estimations provide an appropriately conservative outcome. For instance, an estimation based on data from a more volatile substance is on the safe side, while an estimation based on data from a less volatile substance is not on the safe side, and it may lead to an underestimation of risk. For example, using toluene data to support estimates for xylene may be possible if OCs and RMMs are similar. Toluene has a lower boiling point and

[10]The BOHS/NVvA Sampling Strategy implemented in the excel tool is available at: http://www.arbeidshygiene.nl/-uploads/files/insite/2011-12-bohs-nvva-sampling-strategy-guidance.pdf

higher vapour pressure than xylene with the expectation that exposure would be higher under the same conditions of use. However, the estimation of toluene exposure based on xylene exposure may not be equally appropriate, as toluene is more volatile. Volatility is an important parameter for inhalation exposure and comparability should be justified. However, care needs to be taken to ensure that the conditions of use are similar as some substances of higher volatility may be used in a more controlled way, possibly due to concerns over flammability, odour or toxicity.

R.14.6.4 Selection and interpretation of measured data

R.14.6.4.1 General aspects

The purpose for which data were collected needs to be taken into account when considering the representativeness of the data (and thus, it affects whether and how the data can be used in a REACH exposure assessment). Data sources need to be assessed carefully for relevance for the assessment to be done. For instance, data may have been collected for compliance purposes or to demonstrate good practice. They may also have been collected at a time when the OELs were higher and improvements in the working conditions could have been implemented since. The data may also be representative of worker exposure where the individual is involved in a number of tasks in a day and include periods where there is no activity. In the case of the assessment of a single site (e.g. registrant's own site), the use of measurements is simpler. In this case, the data are representative of the OC and RMM available in the company and the assessor will most likely have access to all the documentation related to the sampling.

When assessing a broader situation (for instance across a sector), care should be taken that the data are representative. Issues to be assessed include:

- The data set should be representative of the OC and RMM described in the exposure scenario. This is a basic condition for acceptance of the data. The similarity in tasks, the technology (e.g. level of automation), scale of the processes (gluing small parts is quite different from gluing flooring in buildings) and the potential variation this introduces needs to be considered.
- In order to be applicable to a sector, the data set should represent the typical conditions within the sector suitable to assure safe use. The tasks (or combination of tasks) that the data set represents should be made clear. The downstream user should be able to judge whether the data set is applicable for their own work arrangements (e.g. differences in frequency of tasks).

In a regulatory context, for substances of low concern, provision of reasonably foreseeable worst case exposure data may allow a simple assessment of risk to establish safe use.

Generally, there needs to be enough information to satisfactorily support the suitability and representativeness. Indicators of good quality data in this context are:

- reference to quality schemes and standard sampling and measurement methodologies;
- sufficient description to support the intended scope;
- clear description of monitored tasks;
- clear information on RMMs in operation during sampling;
- details of duration and frequency of tasks as well as an assessment if the sampling duration is representative of full-shift exposure or only for the task duration;

- data collected using static samplers should only be used in the exposure estimation if there is sufficient information provided to demonstrate how they reflect personal exposures or that they provide a conservative estimate of personal exposures (i.e. that in this situation personal exposure levels would be lower than results from static samples). Air samples should be taken at breathing zone height and in the immediate vicinity of workers. If there is a large quantity of pooled and statistically evaluated data available, these data may be used provided that the methods used to do this and reasons for using data from static sampling are made clear.

- whether data are current rather than historical (i.e. sampling period to be reported);
- collection from a wide range of the sites and processes covered by the use description;
- Individual values (data points) and/or statistical descriptors available.

The CSR should contain sufficient information for the reader to understand the decision making. For instance, in many cases, the single data points will not need to be reported and the statistical parameters characterising the distribution would be sufficient. However, if some data points had been removed from the data set (e.g. maximum values), the reader may need more information to be able to judge whether that was adequate.

R.14.6.4.2 Inhalation data and sample size

Inhalation exposure data to be used in occupational exposure assessments under REACH should relate to concentration of the substance in the breathing zone of the operator and before any respiratory protection is factored into the assessment. The concentration measured, time-weighted if appropriate, is compared with the appropriate DNEL.

Inhalation exposure data tend to be log-normally distributed. For regulatory decision-making, enough data are required to establish the key values from the distribution.

The confidence in the estimated exposure value, for regulatory purposes, generally increases with sample size, as long as the data truly represent the full variability across industry. This can only be assessed through good quality supporting information associated with the data set.

The number of data points required will differ depending on whether the ES is intended to cover a single company (e.g. assessment of its own site) or a broader situation (e.g. in a top-down assessment).

Guidelines on sampling strategy are available from many sources including the European Committee for Standardization (CEN). European national organizations have also publications on sampling strategy[12].

These publications provide advice that is in some cases directly applicable in a REACH context. For instance, how to calculate a TWA will follow the same mechanism (but within REACH it usually would refer to a task and not a full-shift) and the same considerations are applicable to the adequate duration of the sampling within REACH and

[12] See for instance the list of references/ Links for further reading in the EU-OSHA wiki page dedicated to sampling of airborne chemicals https://oshwiki.eu/wiki/Monitoring,_sampling_and_analysis_of_airborne_dangerous_substances#Sampling_strategy

OHS. Other aspects such as number of data points required for an adequate assessment would need adaptation.

For example, for the assessment of a single company, the European Standard EN 689 [13] (currently under revision) provides recommendations on how to choose the adequate number of workers for exposure measurements, which will vary depending on the strategy chosen (e.g. random sampling, use of homogeneous exposure groups etc.). As a possible approach, the standard recommends that at least six data points should be presented to adequately describe the exposure of a single work activity within one company. In this case, narrow distributions are expected (and required by the standard) as the sampling is based on homogeneous exposure groups, i.e. on a group of workers performing identical or similar task and that are expected to have similar exposure levels to the same substance.

On the other hand, assessing exposure for broad exposure situations needs more data to ensure sufficient coverage of the broad situation and to enable evaluation of potentially relevant subsets (for instance higher exposure situations). In this type of assessment, narrow distributions may indicate not all independent variables have been accounted for, such as the full range of activities and between worker or between site variability.

Another important factor is the quotient between the exposure level and the DNEL involved, called the RCR (risk characterisation ratio).

As explained in *Chapter R.19 of the IR&CSA guidance* [14] each step of the risk assessment process, including the exposure estimation has an associated uncertainty. In order to have a robust CS, the registrant needs to consider whether these sources of uncertainty are adequately addressed and provide enough confidence in the calculated RCR. Thus, when the RCR is close to 1, taking into account the uncertainty associated with the measured data is of high importance. This usually involves a critical consideration of the representativeness of the data and an increased number of measurement data points to verify that the DNEL will not be exceeded.

Regarding the assessment of one single site, various sampling protocols provide advice on this matter giving clear recommendations based on the RCR and the variability of the data (as GSD). These include for instance the standard EN 689[13].

For broader assessments, the number of data points needed to ensure that the data are robust enough to provide sufficient confidence that exposure is below the DNEL should be decided on the following principles:

- data from one company is unlikely to be representative of a whole industrial sector consisting of multiple sites;
- A higher number of data points is required:
    - the closer the RCR is to 1;
    - with higher variability of the data (represented by the geometric standard deviation of the exposure distribution);
    - if the representativeness of the data is suspected to be significantly uncertain for the situation to be assessed.

In order to obtain representative inhalation exposure measurements the duration and time of the monitoring should be carefully chosen.

[13] Other relevant document on sampling strategy is the BOHS/NVVA guidance http://www.arbeidshygiene.nl/-uploads/files/insite/2011-12-bohs-nvva-sampling-strategy-guidance.pdf

R.14.6.4.3 Dermal data

Dermal exposure data are rarely available and often difficult to interpret, because of missing contextual information and/or information on the measurement method. Some sectors are working to generate specific data sets based on agreed sampling protocols to address their needs. In most cases, the default approach in assessing dermal exposure should be to seek to use exposure models and particularly those that have been validated by publications and are based on, or benchmarked against, real data. Dermal exposure assessment has large uncertainty associated with it and results should be considered in that context.

Measured dermal data may be available for some analogous situations. Most often, these data reflect uses such as uses for biocides and plant protection products. With professional judgement, these data can be used to address similar situations for REACH registered substances. It is clear, in the case of dermal exposure data, that they may not adequately describe REACH compliant conditions as often they will have been collected without standard industrial controls in place. It could represent the wrong exposure distribution and lead to either under-prediction or over-prediction of exposure. Some tasks are well described by existing generic data, such as spraying and transferring of powders and liquids.

Measured dermal exposure data are most often presented as a rate of exposure in mg/min or µl/min of in-use formulation (i.e. allowing the user to take account of concentration of substance in the mixture).

In some cases measured dermal exposure data may include information on surface area sampled (cm^2) and mass of contaminant depositing (mg), allowing an estimate to be made of mass per unit area (mg/cm^2). This is mostly relevant where the exposure is expected to be evenly spread over the skin surface, such as with a specifically applied formulation. Information may also be available on duration and frequency of exposure.

A good source of pre-existing data is the RISKOFDERM project. The project resulted in development of an expert model for estimating potential dermal exposure (see Section 0). A further resource for dermal exposure data (which includes all the Riskofderm raw data) is the BEAT model (see Section A.14-1.4.3), originally developed for assessment of biocidal products. The data within that model are presented generically but the scenarios are mainly directly relevant to biocidal uses, however these data may still be used to help address some REACH-relevant exposure scenarios; for example, dermal exposure arising from professional spray painting. The raw BEAT data (over 1400 exposure estimates, including all RISKOFDERM data) can be fully accessed via the model but requires expert interpretation (see ECHA Guidance[14]).

R.14.6.4.4 Biological monitoring data

Biological monitoring may be employed as an exposure monitoring tool to help evaluate the effectiveness of risk management measures – exceedances of benchmark values prompting investigation into the causes of loss of control in the workplace. When available, biological monitoring data may be usable within exposure assessment but interpretation is often difficult in the context of comparison with DNELs. It generates results that may be compared with biological monitoring guidance values (BMGVs) or workplace biological monitoring exposure standards. It can add value to the exposure

[14] Guidance on the BPR: Volume III Human Health, Part B Assessment (Chapter 3 Exposure assessment) [http://echa.europa.eu/web/guest/guidance-documents/guidance-on-biocides-legislation]

Biocides Human Health Exposure Methodology Document [http://echa.europa.eu/about-us/who-we-are/biocidal-products-committee/working-groups/human-exposure]

assessment process by providing information that enables a better understanding of the nature and extent of the total exposure through all exposure routes. Most biological monitoring metrics cannot easily be compared to daily systemic dose for comparison with a DNEL as they relate to a concentration in the collected fluids (generally urine), but it may, for instance, demonstrate uptake is very low for specified tasks. It may allow tasks to be ranked in terms of their potential to cause exposure.

For some substances biological monitoring methods already exist. New methods may require a lengthy development phase and though achievable in principle, in practice, few new methods will be developed.

Biological monitoring results reflect total exposure to the substance through any relevant route and from any source, i.e. from consumer exposure, man via environment in addition to occupational exposure through inhalation, dermal absorption and ingestion. In the case of confounding variables it may be difficult to link biological monitoring data to specific exposure scenarios, even though in many cases occupational exposure is the most significant. In cases where there is an identified exposure from other sources (e.g. water, food) biomonitoring can act as a useful means to identify potential for occupational exposure to cause exceedance of any pre-existing limits.

Biological monitoring data need to be seen within context. Information should be provided on which metabolite is measured, the sampling strategy, the biological half-life of the metabolite and how to interpret the results against pre-defined standards. Where reference is made to pre-defined standards, the basis for the standard should be clearly described. Aspects to address may include whether the standard has any implications for health or is intended to act as a good practice benchmark, whether the marker is found in unexposed populations, and any confounding exposures have been identified. Biological monitoring data should be presented with the same core information as data on inhalation or dermal exposure to enable proper interpretation of the outcome in relation to working conditions.

In order to make best use of biological monitoring data, it is necessary to compare measured data against an appropriate standard. The toxicokinetic properties (e.g. absorption percentages) that form the basis for any relationship between the biomarker and external dose metrics should be clearly described. The comparison of biomonitoring data with DNELs is further described in *Chapter R.8 of the IR&CSA Guidance* [1].

R.14.6.5 Assessment of acute exposures

Exposure to some substances may lead to acute health effects. The assessment of acute exposures becomes necessary when either an acute DNEL or a DNEL for acute local effects have been derived.

For highly toxic substances that can produce serious effects after a very short exposure time (i.e. a few seconds), strictly controlled conditions would normally apply. System breaks (e.g. system leaks or loss of containment) will be treated as an accidental release and thus, short-term qualitative exposure assessment is not expected.

R.14.6.5.1 Assessment of acute inhalation exposure

Assessment of short-term (acute) inhalation exposure is required when an inhalation DNEL has been derived for acute effects. It is also relevant when the substance produces local effects and the concern is that knowledge of short intense exposure is at least as important as longer term exposures.

Short-term inhalation exposure is normally estimated over a 15-minute reference period (but shorter periods may be applicable depending on the effect). The short-term exposure profile may determine the risk management measures. For example, consider a limited-period high exposure solvent application task in a printing works that is carried out for only 15 minutes in a day. The predicted exposure for the 15 minutes of the task

may be many times higher than the predicted 8-hour time-weighted average for the whole shift, and specific risk management measures will need to be determined for that task.

Care should be taken when estimating the exposure. Most of the exposure modelling tools (see outputs for the tools in Section R.14.6.6) do not address the assessment of short-term exposures. In those cases, the exposure cannot be estimated by using the tool and choosing the option "less than 15 minutes" (or similar) for exposure duration; this is because the duration is not meant to address acute exposure but an activity that is performed less than 15 min per day (i.e. the concentration given by the tool is averaged for 8 hours instead of 15 min and is meant to be compared with a chronic DNEL).

The short-term exposure **can be modelled** by using the Advanced REACH Tool (ART) or Stoffenmanager (see Sections A.14-1.4.4 and A.14-1.4.1) or by extrapolation from the long-term exposure under certain conditions.

If the activity assessed is considered to lead to stable exposure levels (without any task leading to exposure peaks) extrapolation from the measured or modelled long-term exposure can be used consisting of a multiplier of the 8 hours exposure estimate for the task (ECETOC TRA uses a factor of 4).

If peaks of exposure are expected due to the nature of the activity (for example, opening vessels etc.), the extrapolation from the average shift exposure cannot be used. In such cases the exposure needs to be estimated by other means, for example, by using a tool like ART or Stoffenmanager that allows this type of assessment or by using measurements.

When using measurements, sampling strategy for acute exposures can be found in general occupational hygiene guidelines and it generally covers two options:

- If the higher exposure activities can be identified, measurements will be taken around these activities (in general 15 minute samples, or direct reading device measurements)
- If the higher exposure activities cannot be identified a more complicated strategy is needed (for example, a screening step to know the exposure pattern or taking 15 minute samples randomly during the whole task).

Measurement methods are usually similar for acute tasks but care needs to be taken to ensure the methods are accurate enough and provide an adequate limit of detection (see section R.14.2.1 for more information for requirements for analytical methods for comparison with a limit value).

R.14.6.5.2 Acute dermal exposure assessment

Inhalation and dermal exposure have very different characteristics. The derivation of short-term quantitative exposure estimates for the dermal route may be complex.

Exposure estimation for local effects on the skin uses other units (mg/cm^2 or $\mu g/cm^2$), which are difficult to assess and is driven to a large extent by the concentration of the assessed substance in the contamination reaching the skin. The exposure associated with the maximum percentage of substance in the product should be used as the basis for managing acute local skin effects. The assumption is that exposure needs to be prevented and a qualitative assessment is most often required to establish the appropriate risk management options leading to a situation where the likelihood of effects is avoided. Ideally, risk management strategies should aim to engineer out opportunities for high acute dermal exposures.

R.14.6.6 Use of exposure estimation tools

The currently available tools for occupational exposure estimation have been developed to be relatively simple to use. The tools are intended to provide appropriately conservative estimates when used correctly.

Exposure estimation tools have limitations to their domain of applicability, such as the scope of the intended use or to physico-chemical properties of the substances that may be assessed. Users are required to ensure that the assessment is within published boundaries. Where modelling tools are used for situations outside their applicability domains, the exposure estimates should only be used in the assessment as supporting evidence (it is anticipated that tool outputs reflect the appropriate application of good occupational hygiene practice within the prediction).

All tools allow the user to specify some input parameters often including operational conditions and risk management measures, although RMMs may need to be addressed externally to some tools. The inputs should reflect realistic and relevant exposure scenarios. To support this, use maps have been developed by sector organisations that describe typical conditions of use within their sectors and can be readily incorporated by registrants in their chemical safety assessment. Development of non-existent or unrealistic exposure scenarios within a Chemical Safety Report should be avoided and are unhelpful in the context of assessing the scenarios that matter.

The TREXMO tool may be a useful source of information on how the different tools define the exposure determinants. The tool establishes a common ground for all models by making the assumption that a set of input parameters in one model can be translated into another model. Further information about the TREXMO tool is available at https://www.seco.admin.ch/trexmo.

The common tools that are currently available are outlined in Appendix R.14-1, together with the domain of applicability (as claimed by tool owners), inputs and outputs. Newer versions of tools and other tools not included here can be used if appropriate. Referring to the tool owner user guidance is a necessity if they are to be used successfully. A basic overview of the different scope and domains of applicability of the tools based on [15] is given the Table R.14- 2 and Table R.14- 3 below.

Table R.14- 2: Applicability matrix (inhalation models)

Applicability	ECETOC TRA	MEASE	EMKG-EXPO-TOOL	STOFFENMANAGER	ART
PROC codes (as input)	Yes	Yes	No	No	No
Covered physical state	Solid /liquid=volatile	Solid /liquid	Solid /liquid	Solid /liquid	Solid /liquid
Beyond scope	• Fibres • aerosol mist • emissions from • hot processes (e.g. fumes) • gases • caution needs to be exercised when applying to CMRs and very high hazard substances • solids in liquids	• organic substances • some restrictions concerning special combinations of PROC/physical properties	• Dusts by abrasive techniques, • fumes (soldering, welding, acid fumes) • gases • open spray • pesticides • wood dusts • CMR substances	• Fibres • gases or hot working • techniques (welding, soldering, • acid fumes)	• Dust resulting from emissions during hot metallurgical processes • fibres • fumes • gases • solutions of solids in liquids
Basis of use description	process based	process based	task based (control guidance sheets)	task based	task based

Table R.14- 3 Applicability matrix (dermal models)

Applicability	ECETOC TRA	MEASE	RISKOFDERM	BEAT
PROC codes (as input)	Yes	Yes	No	No
Covered physical state	solid liquid = volatile	solid liquid	solid liquid	solid liquid
Beyond scope	• Fibres • liquid aerosols (if this is dermal – liquid deposition from aerosol is covered e.g. at spraying PROCs 7 and 11.) • or emissions from • hot processes (e.g. • fumes) • caution also needs to be exercised when applying to CMRs	• organic substances	• sometimes restrictions due to original data set ("only on manual tasks for powders") • fumes not covered	• Ultimately, the scope is determined by an understanding of the tool's capabilities. Unfamiliar situations can be addressed through professional judgement on degree of "likeness" and merging of data sets or inclusion of available real data.
Basis of use description	process based	process based	task based	task based

Experience from using the tools, along with increased research aimed at validating the outputs, is an ongoing process.

The E-TEAM project evaluated parts of the generic exposure estimation tools for inhalation that are currently widely used for chemical safety assessments under REACH in order to record the applicability domains of the models and to achieve more confidence about the accuracy and reliability of model predictions. The E-Team analyses appear to indicate that overall the tools investigated in the study are suitable for application at Tier 1 of REACH. However, results from the E-TEAM project have been interpreted as showing some Tier 1 models may not always produce sufficiently conservative exposure estimates. Furthermore, under the conditions of the study, high levels of variability between users were found. The reports of the project (see [15]) may assist registrants to choose the most appropriate model for a given exposure situation. The E-TEAM analyses have helped identification of elements in these tools that may benefit from review leading to possible revision and ultimately convergence between models.

The tools continue to be developed and it is the responsibility of the registrant to ensure the use of an appropriate tool and most recent version of tools are used to predict exposure. It is not the purpose of this guidance to endorse or assess the overall validity of outputs from any of the tools.

Variability and uncertainty in exposure estimation tools

All tools incorporate uncertainties and variability, and models can both over-predict and under-predict.

In regulatory exposure assessment, it is important not to erode any conservatism within the tool through application of artificial external mechanisms that modify the outputs. For example, many tools, including ECETOC TRA, employ a banded approach to take account of influence of duration and concentration on the model output. It is generally not admissible to further refine these outputs through, for example, applying linear reductions for elements such as concentration in mixtures or duration of exposure unless robust scientific justification is provided.

For similar inputs into various tools, there can be significant differences between the outputs. These differences may reflect the datasets that the model is based on, the algorithms used to predict exposures or the intended purpose. Also, users may interpret the tool-specific inputs differently and there can be differences introduced by experienced and inexperienced users. For these reasons, it is important that registrants provide a justification for the parameters they have used to generate exposure estimates, especially if diverging from tool defaults. Modelling tools should be used only when there is an understanding of the use conditions to being assessed.

Tool specific training can help reduce the between-user variability and improve the adequate use of the tools. Moreover, the variability can be further reduced by reviewing the exposure estimates with others (e.g. colleagues).

The registrant can help to reduce the uncertainty within risk characterisation by comparing the estimates from a range of sources, including other tools and measured data. Given the uncertainty inherent in many tools, generation of RCRs close to 1 may indicate that further investigation is necessary, such as further iteration within the tool or assessment by other means.

Use of single tool estimates is unlikely to be persuasive enough for the purposes of assessing circumstances related to strictly controlled conditions or for proving the low level exposures that may be demanded by authorisation processes under REACH or when justifying exposure based adaptation.

A factor that can have a significant impact on the estimated exposure is the selection of the task descriptor (see *Chapter R.12 of the IR&CSA Guidance* [9]). In Tier 1 assessments, very often Process Categories (PROCs) are used which are intended to cover the routine tasks carried out under that broad categorisation. These would include elements such as plant adjustments and routine daily cleaning tasks which are part of normal operation but would not be assessed separately.

Some forms of exposure assessment are not well addressed and the uncertainty is greater. This is currently the case for inhalation exposure to aerosol droplets, although recent approaches to modelling will allow generation of some estimates (SprayExpo)[15]. SprayExpo is able to estimate inhalation exposure and dermal exposure to non-evaporating substances and has been validated with measurement results from real workplaces in the fields of antifouling and stored product protection.

The BEAT model (see Section A.14-1.4.3) addresses some tasks where aerosol droplets are released (painting, spraying) and scenarios can sometimes be sufficiently analogous to industrial processes for the data to be useful at a screening level, even though possibly over-predictive for what is the usually more controlled industrial workplace environment.

Dermal Exposure Models

The models can be applied to a range of situations and their outputs used to help screen obviously lower level exposure scenarios. It will rarely be possible for measured data sets to challenge the validity of the generic data based exposure models. The current database models, though still limited in scope, are built around data specifically collected for the purpose of model development and the raw data may be considered analogous.

The preferred approach to quantitative assessment of dermal exposure is to use generic database models and to supplement the outputs with real data, but only if they are available. Exposure models such as Riskofderm use a set of database models.

Modelling techniques may help to further characterise the potential for systemic uptake following dermal deposition. This is important where there is no indication of absorption being taken account of in the derivation of the DNEL. The IH SkinPerm mathematical tool requires users to input physico-chemical properties of substances and predicts the fate of the substance, after impingement on the skin, through losses to evaporation, residence in the stratum corneum and absorption into the body [16]. Exposure reducing effects due to evaporation cannot be considered if workers have continuous direct contact with the substance. Furthermore, to take the evaporation of a substance into account, non-occlusive dermal exposure has to be the predominant exposure situation.

R.14.7 Exposure Assessment and Applications for Authorisation

R.14.7.1 Special requirements of Applications for Authorisation (AfA)

The previous sections of this guidance addressed registrants in general, however this section highlights some of the differences in the exposure assessment required in the authorisation process, which potential applicants may take into account when preparing an application for authorisation.

[15] http://www.baua.de/en/Topics-from-A-to-Z/Hazardous-Substances/SprayExpo.html

Under the 'adequate control' route an authorisation shall be granted if it is demonstrated that the risk to human health or the environment from the use of the substance arising from the intrinsic properties specified in Annex XIV is adequately controlled in accordance with section 6.4 of Annex I {Art. 60(2)}, taking into account Article 60(3). While this route may appear rather familiar, the second route for authorisation, the 'socio-economic' route, is a fundamentally different approach.
Under the socio-economic route an authorisation may be granted if it can be demonstrated that the risk to human health or the environment from the use of the substance is outweighed by the socio-economic benefits, provided there are no suitable alternative substances or technologies. Nevertheless, the appropriateness and effectiveness of the (RMM) will be assessed {Art. 60(4)} as well. Where the Risk Assessment Committee (RAC) will not concur with the claim of the applicant of adequate control in the CSR the application will leave the adequate control route and enter into the socio-economic route.

To demonstrate that the socio-economic benefits of the continued use of the substance outweigh the risks to human health (or the environment), an impact assessment must be performed in addition to a risk assessment, e.g. the risks must be evaluated and monetised to quantify the impact on human health or the environment. According to this requirement, in contrast to registration, the derivation of a DMEL is not a useful step, as it would preclude the impact assessment. Instead a dose response relationship may be used to assess the risk and the impact of the continued use of the substance. RAC aims to publish well in advance the dose response relationships to be used in the assessment of applications.

[For further information on the Authorisation process and the terminology used, the reader is referred to the ECHA Webpages [http://echa.europa.eu/applying-for-authorisation] and the Guidance on the preparation of an application for authorisation (http://echa.europa.eu/documents/10162/13637/authorisation_application_en.pdf).]

In the assessment of exposure for registration purposes, the focus is in general on the adequate control of exposure and on the derivation of appropriate Risk Management Measures (RMMs) and Operational Conditions (OCs) which are communicated throughout the supply chain to ensure safe use. In comparison, in the assessment of exposure for an authorisation application, it must be specified which RMMs and OCs have been implemented at all sites of use (e.g. site of manufacture and all downstream user (DU) sites) because the impact assessment is based on the actual implemented RMMs and OCs described in the application.

Pursuant to Annex I, 0.8 of REACH, the level of detail required in describing an exposure scenario will vary substantially from case to case, depending on the use of the substance and its hazardous properties. According to Annex I, 5.2.5 of REACH, where adequately measured, representative exposure data are available, special consideration must be given to them when conducting the exposure assessment.

Authorisation concerns substances of very high concern, and therefore adequately measured, representative occupational exposure data should be available, and need to be submitted in the application. This requirement is consistent with the requirements under the Chemical Agent Directive (98/24/EC) and Carcinogen and Mutagens Directive (2004/37/EC). For such substances, the exposure scenario needs to be detailed and conclusive.

Furthermore, as is noted in the note on a Common Approach of RAC and SEAC, incomplete or missing information and weak evidence could lead RAC and SEAC to advise on more stringent conditions or short review periods in the final opinion. [Ref.: Common Approach of RAC and SEAC in opinion development on applications for authorisations

(http://echa.europa.eu/documents/10162/13555/common_approach_rac_seac_en.pdf)]

In contrast to the registration process in which only some registration dossiers are assessed, all applications for authorisation are assessed by the Committee for Risk Assessment (RAC) and Committee for Socio-Economic Analysis (SEAC). The final opinion of the two Committees on the application is taken into account by the Commission who make the final decision on the application.

In view of the above and the fact that applying for authorisation is primarily the result of a complex business decision, it must be stressed that the resources to be employed in preparing an application, including the risk assessment, go beyond those traditionally available in the environmental, health and safety department of a company.

R.14.7.2 Assessment of Chemical Safety Reports by RAC

In contrast to the registration process, every CSR in an authorisation application is assessed by RAC to form an opinion on authorising the use(s) identified in the application. It is essential that RAC can understand the processes and tasks described in the CSR and the underlying assumptions, justifications and conclusions in the exposure assessment. Therefore this section, describes how authorisation applications are evaluated and what kinds of uncertainties might be considered.

1. Elements taken into consideration in the context of AfA

The following four tables have been taken from the template for draft opinions for agreement for RAC and may be subject to change. However, they highlight the structure of the information requested.

Table R.14- 4: Contributing Scenarios presented in the Use

Contributing scenario	ERC / PROC	Name of the scenario
ECS1		
WCS 1		
WCS 2		

Table R.14- 5: Operational Conditions and Risk Management Measures

Contributing scenario	Duration and frequency of exposure	Concentration of the substance*	LEV used + effectiveness	RPE used + effectiveness	Skin protection+ effectiveness	Other RMMs
WCS 1 + PROC						
WCS 2+ PROC						

**If changing through the process*

Table R.14- 6: Exposure – dermal and inhalation

Contributing scenario	Route of exposure	Method of assessment	Exposure value	Exposure value corrected for PPE	Exposure value corrected for PPE and frequency *
WCS 1	Inhalation				
	Dermal				
WCS 2	Inhalation				
	Dermal				

**And duration of the task – if not already considered*

Table R.14- 7: Combined exposure

Contributing scenario	Route	Exposure value corrected for PPE and frequency
WCS 1	Inhalation	
	Dermal	
WCS 2	Inhalation	
	Dermal	
Total exposure for 8 hours	Inhalation	
	Dermal	

- For the exposure assessment of workers, it is important to clearly describe the overall processes of the use applied for, as well as the sequence of tasks (and individual tasks – described in worker contributing scenarios (WCS)) performed by individual workers (Table R.14- 4). For this purpose, diagrams and photos or short videos would be very helpful, provided that they are representative of the tasks and workplaces at stake.

- In the individual working contributing scenarios, the operational conditions and risk management measurements (Table R.14- 5), aiming to either adequately control the risk or to minimise as low as is practically and technically possible, should be presented. It is important to follow the hierarchy of controls; for apparent deviations from this principle clear justification should be given. Article 5 of the Carcinogen and Mutagens Directive (2004/37/EC) provides advice on prevention and reduction exposure measures that could be used.

- In addition to the description of the exposure of individual workers through separate WCSs (Table R.14- 6), the combined exposure, resulting from various tasks performed by a worker during the 8 hour shift must also be presented (Table R.14-7). The remaining exposure should be clearly stated before and after the use of certain RMMs, especially in the case of using RPE.

- Some tasks are only performed a few times per year, (e.g. infrequent delivery of the substance, batch production or maintenance carried out once or twice a year). For carcinogenic substances, the dose response relationship may be used to correct for the frequency of these tasks and express the remaining risk (i.e. taking into consideration the implemented RMMs) and the associated dose using the whole year as a time basis. This may not be adequate for other substances such as reprotoxic substances, where a DNEL is normally used. In addition, it is important that the short-term and full-shift exposure levels that are experienced during infrequent tasks are properly understood and clearly stated to ensure suitable risk management measures are in place.

- It is recommended to employ all the tools available to describe the exposure; this includes use of measured data for exposure via inhalation or by the dermal route as well as biomonitoring and the various exposure models (Tier 1 or higher). A combination of different tools for individual working contributing scenarios may prove useful. The choice of the methods to estimate the exposure should be clearly justified, especially when using models, with respect to their domain of applicability.

- Remaining uncertainties, not necessarily being of a statistical nature in the exposure assessment (e.g. those related to the methodology used to estimate the exposure, the variability of tasks and their duration), should clearly be stated and critically discussed.

2. Indicators for weak evidence

The assessment of exposure for authorisation purposes is required to be detailed and therefore any deficiencies in the data submitted may cause concern and result in more stringent recommendations. The deficiencies may include:

- The assessment was not complete with respect to all relevant endpoints or routes of exposure, e.g. for man via the environment local or regional scale was not considered, or for workers, exposure through dermal route was omitted.
- The description of the use, processes and tasks were too brief and did not address variability in terms of OCs and RMMs.
- Possible changes (e.g. increase in the tonnage of the substance used) were not reflected in the exposure and impact assessment.
- The aggregation of tasks into an 8 hour shift value remained unclear: tasks were not clearly identified.
- The representativeness of measured data was not clearly demonstrated by the applicant, (e.g. too small a sample size, or contextual information on the measurements; for which set of tasks were OCs and RMMs covered and even more

importantly were not covered by certain measurements; limit of detection not specified).

- In cases covering multiple (hundreds/thousands) DU sites throughout Europe, measurement data from very few locations in one or two countries (without corroboration with modelling data), may be assessed as having "only limited geographical coverage" and judged to have only "limited informative value".
- Not providing raw data covering the measurements or information on the methodology of biomonitoring campaigns (in the application, or upon request).
- Information as to why a specific model was used in exposure assessment: e.g. either inadequate or completely missing explanation; input parameters not included or the choice of them was not explained, especially in relation to selection of PROCs; claimed effectiveness of certain RMMs not justified; A sensitivity analysis for important input parameters not provided.
- No justification for not using higher level RMM, e.g. containment in cases where the technology is available.
- Overreliance on Personal Protective Equipment.
- No corroboration of measurement data with modelling results, especially where the data set is limited to, for example, one measurement session.
- Mistakes made in calculations of exposure.

Whilst there is a possibility for RAC to ask for clarifications in relation to points of concern, the authorisation process does not allow sufficient time for the exchange of additional information or for obtaining such information. Therefore, potential applicants should carefully and comprehensively present their uses, and address potential issues in their applications.

For the assessment of applications, RAC has developed a checklist. In addition, RAC has developed an opinion tree to conclude on authorization opinions for non-threshold substances. Applicants may find these documents useful when preparing their applications (see [17] and [18]).

Appendix R.14-1. Exposure estimation models

A.14-1.1. ECETOC TRA tool for occupational exposure

The ECETOC TRA tool can be used to determine exposure through inhalation and by the dermal route. The ECETOC TRA tool can be downloaded from http://www.ecetoc.org/tra. The tool requires the user to input some basic information on the substance (molecular weight, vapour pressure, substance form). The user can then select contributing scenarios, as PROCs, which pre-define the point of departure exposure value. A range of exposure modifiers are sequentially applied to establish the set of operational conditions and risk management measures that appear in the final scenario.

A.14-1.1.1 Domain of applicability

Table R.14- 8 below summarises those circumstances where the use of the TRA is not advised based on the information in ECETOC TRA version 3: Background and Rationale for the Improvements. Technical Report No. 114 [19]. The table only deviates from the above-mentioned ECETOC report in two entries:

- *"CMRs and 'very high hazard' substances",* where the limitations have been further clarified
- *PROCs indicating closed systems (PROC 1-3).* This entry has been added to the table to provide advice on the applicability domain of a PROC 1-3 exposure estimate in the using ECETOC TRA.

Table R.14- 8: Domain of reliable application of the TRAv3.1

Domain Boundary	Comments
Gases	The TRA does not predict exposure to gases. The reason for this is that the EASE model did not extend to gases. However the TRA does allow exposures to very volatile liquids (vapour pressure >10kPa and with no upper bound set on vapour pressure) to be estimated. As these very volatile liquids might be assumed to be the equivalents of gases for many circumstances of use (PROCs), then provided users are able to assure themselves of such equivalencies, then it is reasonable to assume that the high volatility exposure prediction can also be used to predict exposures to gases in certain scenarios.
Aerosol mists	Although exposures to aerosol mists might be expected to be associated with certain uses which are open and associated with the release of significant amounts of energy (e.g. spraying, machining, etc.), the TRA does not address such exposures. However, in circumstances where users have available representative measured exposure data on mists, then these may be able to be used to 'calibrate' and read across to relevant PROCs e.g. by assessing whether medium dustiness values might offer a conservative approximation of actual data (but where consideration also needs to be given to the vapour component of such exposures).

Domain Boundary	Comments
Process fumes	Although exposures to process fumes might be expected to be associated with certain uses which are undertaken at elevated temperatures (e.g. handling hot materials when their melting point lies at or above ambient temperatures), the TRA does not address such exposures. Appendix E of [19] addresses this aspect in further detail.
Fibrous materials	The TRA does not predict exposure to fibrous solids.
Exposures above ambient temperature	The TRA predicts exposure at 20°C. Where a liquid substance is handled at temperatures significantly in excess of this, then users should apply the vapour pressure calculated at the operating temperature. The exception to this 'rule' is PROC6 (calendaring) where the TRA predictions already account for the elevated temperatures applied in this activity (see also 'process fumes' above when solid substances are handled).
Solids in liquids	The TRA cannot predict inhalation exposures to solids suspended or dissolved in liquids. If such exposures are considered relevant, then in circumstances where users have available representative measured exposure data, then these may be able to be used to 'calibrate' and read across to relevant PROCs, or alternatively users are referred to other tools capable of estimating such exposures. The model will predict dermal exposures.
CMRs and 'very high hazard' substances e.g. respiratory sensitizers	Although the TRA is a Tier 1 model and hence is intended to be conservative in the nature of its predictions, it requires judicious interpretation if applied to CMRs and other high hazard substances. For 'simple' substances such as readily volatile liquids (e.g. toluene, benzene, n-hexane), the TRA will be capable of offering valid predictions, provided the practical use/exposure situation has been correctly translated to a suitable TRA process category and suitable exposure modifiers (i.e. risk management measures). CMRs and other highly hazardous substances are often handled under specific conditions to prevent and control exposure. Such conditions often cannot be readily translated into the available TRA inputs. Therefore assessors should have access to sets of measured exposure data for at least some of the PROC/RMM combinations for the substance (or close analogues) to establish that they are broadly consistent with the TRA estimates.

Domain Boundary	Comments
UVCBs	The TRA estimates have been developed for mono-constituent substances. Where UVCB substances are being assessed using the TRA (in particular those substances having a range of volatilities) then users should apply the nominal VP for the substance (or the VP of most volatile component present at >1% when this is known). If a UVCB material is handled at elevated temperatures, then further correction will need to be applied consistent with the guidance contained elsewhere in this section.
Mixtures	The concentration modifier enables the TRA to predict exposures to a single substance within a (simple) mixture. However, the TRA is not intended to be applied to calculate combined exposures to different substances in a mixture beyond the 'concentration banding' that already exists
Fractions of airborne solids	The TRA exposure predictions for solids do not differentiate between total inhalable exposure (respirable and non-respirable) and respirable exposures fractions. Users should therefore assume that any output for solids describes the inhalable fraction.

Domain Boundary	Comments
PROCs indicating closed systems (PROC 1-3)	The TRA exposure prediction covers processes as typically applied in manufacturing and formulation of chemicals, pharmaceutical and mineral oil products (e.g. reaction, mixing, distillation purification, drying, charging/discharging) ***under closed conditions.*** If such processes are not undertaken under contained/closed conditions PROC 1-3 is not applicable: e.g. tray drying, dry milling and sieving, manual dis/charging to and from containers, filtration on Nutsche filters and filter presses; stirred reactions in open or partially closed vessels; The TRA predictions for PROC 1 to 3 may be also applicable to end-uses, which are typically carried out under closed conditions (e.g. dry cleaning, metal cleaning, where the level of containment of machines is indicated by a sector classification system (e.g. ECSA). The following criteria define the applicability domain of a PROC 1-3 exposure estimate in the TRA: • The process takes place in a high integrity contained, fully closed system (PROC 1) or in a closed system (PROC 2 and 3). It is not possible to break into the system during operation (PROC 1-3). • The transfers of materials into or from the system are undertaken by means of closed lines (PROC 1 and 2) or in an enclosed manner, where there is however some opportunity for exposure (e.g. during coupling/decoupling of lines (PROC 3). • Sampling is only done by i) means of dedicated, closed loop (fully closed) sampling systems, which prevent any contact of workers with the substance (PROC 1) or ii) by means of dedicated, enclosed sampling systems, which limit contact of workers with the substance (PROC 2 and 3) • Before breaking into (part of) the system for maintenance or cleaning, the system (or parts of it) is isolated, drained and flushed or purged to eliminate chemicals from the system (PROC 1-3). The drained/flushed/purged material is also contained (PROC 1)
Out of scope PROCs	The TRA does not cover certain PROCs, specifically PROC 25 (handling of solid inorganic substances at ambient temperature); PROC 27a (production of metal powders using hot processes) and PROC 27b (production of metal powders using wet processes). If these PROCs are considered relevant, then users are referred to other tools capable of estimating exposure in these circumstances (e.g. MEASE).

Additional observation on applicability of the tool

Some additional factors relating to exposure assessment require some consideration by registrants when using the ECETOC TRA tool. These are:

- The model allows the user to iterate a range of options leading to the final exposure scenario. The tool forbids some combinations of exposure modifiers.

Users should not deviate from defaults without strong justification and evidence – for example, enhancing glove effectiveness, amending duration of exposure, use of LEV outdoors, or through introducing a linear relationship between exposure output and concentration. The model applies its own means to adjust for these variables and forbids some combinations. Attempts to reduce exposures by application of unsupported and unjustified methods will make the assessment invalid, unless the tool developers expressly state the action is a possibility.

- The tool predicts dermal exposure only to the hands (and in a few cases forearms, depending on the PROC used). For some tasks, other body parts may be additional targets for deposition. This will not be predicted by the model and will need to be addressed separately if challenge to other body parts is a realistic concern.
- Users of the tool may elect to opt for dermal exposure modification through use of LEV. This may be a valid option in some cases, for example for highly volatile substances and during industrial spray use where aerosol release is anticipated. It is not often a justifiable choice for low volatility substances (low fugacity) where surface contamination levels are largely not affected by the rate of evaporation and are anticipated to be the primary source of potential exposure.
- Glove effectiveness is assigned within the model and associated with specific phrases related to the level of organisational and management control. For quantitative assessment it is anticipated that further exposure modification, through extension of model defaults, will require justification; for instance using a 98% effectiveness[16] modification factor outside of the model where this is associated with a phrase for enhanced intensive management supervision controls.

A.14-1.1.2 Inputs

The following determinants are needed as input data:

Substance identification and Physical-chemical properties:
As a minimum the following information should be included:

- Molecular weight
- Vapour pressure (Pa or hPa)

Assessment inputs

- Process Category (PROC)
- Type of setting (industrial/professional)
- Substance form (Solid or liquid)
- Vapour pressure at operation temperature (liquids/gases) or dustiness (solids)
- Duration of the activity
- Type of ventilation (Outdoors, general ventilation, LEV etc.)
- Respiratory protection (and if yes, minimum efficiency)
- Whether the substance is used in a mixture (then percentage of substance in the mixture is chosen)
- Dermal PPE/ Gloves (and if yes, assigned protection factor (APF))
- Whether LEV for dermal exposure has been considered

[16] This level of performance and associated ESCom phrase is appropriate where the substance is corrosive or a sensitizer and the intention is to prevent exposure through implementation of an intensive glove management programme. However, within quantitative estimation of exposure the 98% value has to be justified.

- Reference value(s) (normally DNEL). Exposure estimates will be derived, even without entering a reference value.

In addition to these inputs that are needed to calculate exposures, some additional (optional) information may be added such us substance name, CAS number and short scenario name.

A.14-1.1.3 Outputs

Table R.14- 9: ECETOC TRA Output

ECETOC OUTPUT	
Exposure estimates	
Output	**Unit**
Long-term inhalation exposure estimate	(ppm and mg/m^3 for volatiles) / (mg/m^3 for solids)
Short-term Inhalation exposure estimate	(ppm and mg/m^3 for volatiles) / (mg/m^3 for solids)
Long-term dermal exposure estimate	(mg/kg/day)
Local dermal exposure estimate	(µg/cm^2)
Risk characterisation ratio*	
RCR - Long-term Inhalation	
RCR -Long-term Dermal	
RCR - Long-term Total Exposure	
RCR - Short-term Inhalation	
RCR - Local Dermal	

(*) Please note that the tool will not provide all these RCRs in all cases, as in many situations not all possible DNELs will have been derived.

A.14-1.1.4 Status of validation

The inhalation estimates of the TRA have been evaluated in a number of independent studies and have generally been found to be conservative ([20], [21], [22], [23], [15] and [24]) , although these exercises have not examined all the use situations (PROCs) and substance types dealt with by the TRA. The validations have also highlighted that, in practice, the exposure reduction afforded by LEV can be significantly less than that assumed by the TRA, for example, when such LEV is incorrectly located or poorly maintained, or higher in particular in cases of well-designed systems. It has been agreed that for REACH registrants it is reasonable to expect a standard of good occupational hygiene practice in European workplaces driven by existing legal requirements. Such good practice includes periodic testing and maintenance of RMMs. The TRA's ability to estimate dermal exposures has not yet been evaluated, although a CEFIC LRI supported study is examining this aspect and is expected to conclude by summer 2016. ECETOC continues to review the TRA estimates in the light of new scientific understandings as

well as related developments, e.g. the updated PROC descriptions contained within the revised *Chapter R.12 of the IR&CSA Guidance* [9].

A.14-1.2. MEASE for metals and inorganic substances

MEASE has been developed to address first Tier exposure estimation of metals and inorganic substances. It combines the approaches from the ECETOC TRA tool, the EASE expert system and the health risk assessment guidance for metals (HERAG project) and generates first Tier inhalation and dermal occupational exposure estimates. For inhalation exposure, the tool follows the PROC approach of the TRA tool and selects initial exposure estimates from three fugacity classes (low, medium, high). The fugacity classes are defined based on the physical form, the melting point of the metal/inorganic substance, the temperature of the process, the vapour pressure and the selected PROC.

For dermal exposure, MEASE is based on a system of exposure bands. However, the generated exposure estimates are based on measured data from several metals, collated and plotted against the EASE exposure classes in the "dermal fact sheet" of the HERAG project. The MEASE tool can be downloaded from http://www.ebrc.de/mease.html and the REACH metals gateway http://www.reach-metals.eu/

A.14-1.2.1 Domain of applicability

Table R.14- 10: Domain of intended application of MEASE 1.02.01 and MEASE 2

Type of exposure	Applicability information
General applicability domain	The MEASE tool is a first Tier exposure assessment tool developed for the assessment of occupational inhalation and dermal exposure to metals and their inorganic compounds under REACH. It should not be used outside this applicability domain. The tool considers that existing parallel legislation to REACH (requiring, for example, a basic level of good occupational hygiene practice for compliance with the generic dust limit) is followed.
Gases	Exposure resulting from manufacture, processing and transfer of inorganic gases can be assessed for highly contained processes.
Aerosol mists	Exposure to aerosol mists is covered for the fraction of the (metal/inorganic) substance in airborne droplets. Compare with "Solids in liquids".
Solids in liquids	Exposure to solid (metal/inorganic) substances in liquids (e.g. aqueous solutions and suspensions) is covered by the tool.
Fibrous materials	Covered for inorganic materials.
Resulting from emissions from processes conducted above ambient temperature	Exposure resulting from emissions from processes conducted above ambient temperature is covered for the fraction of the (metal/inorganic) substance in airborne dust or droplets. It is assumed that workers are not exposed to hot aerosols for safety reasons. Compare with process fumes.

Process fumes	Exposure to process fumes is covered for the fraction of the (metal/inorganic) substance in airborne dust. It is assumed that workers are not exposed to hot fumes for safety reasons.
Mixtures	Covered, given that the substance in mixture falls into at least one of the covered types of exposure above.
UVCBs	Covered, given that the substance falls into at least one of the covered types of exposure above.
CMRs and 'very high hazard' substances e.g. respiratory sensitizers	Covered, given that the substance falls into at least one of the covered types of exposure above. However, it is strongly advised to confirm very low/no exposure situations, which are required in this case, by exposure monitoring data.
Fractions of airborne solids	Exposure estimates in MEASE are provided for the inhalable fraction of airborne dust (particles that can potentially be inhaled) according to EN 481.
Out of scope tasks/process (PROCs)	From the currently existing PROCs, none are generally out of scope. However, specific combinations of PROCs and physical forms are out of scope, e.g. combination of PROC 21 and physical form "Solid, high dustiness". A warning is given in these cases in the tool. PROC28 is in MEASE 2.

A.14-1.2.2 Inputs

The following determinants are needed as input data:

- **Substances characteristics:**
  - Molecular weight (g/mol)
  - Melting point (°C)
  - Vapour pressure (Pa)
  - Physical form
  - Content in preparation (including alloys) (%)
- **Operational conditions (OC)**:
  - Process category (the tool itself provides some guidance on choosing the right PROC)
  - Process temperature (°C)
  - Scale of operation (industrial/professional)
  - Duration of the exposure
- **OCs used for dermal exposure assessment**
  - Pattern of use (Wide dispersive, non-dispersive, inclusion into matrix or closed system
  - Pattern of exposure control (direct/non direct handling)
  - Contact level (extensive, intermittent, etc.)
- **Risk Management measures (RMM)**
  - Implemented RMMs
  - RMM efficiency (based on type of enclosure / ventilation)

- Respiratory protective equipment (APF)
- Use of gloves

A.14-1.2.3 Output

Table R.14- 11: MEASE output

MEASE OUTPUT	
Output	**Unit**
Long-term inhalation exposure estimate	mg/m³
Long-term dermal exposure estimate	µg/cm²/day
Exposed skin area	cm²
Total dermal loading	mg/day

A.14-1.2.4 Status of validation

MEASE has been developed based on experiences from several EU risk assessments of metals and their inorganic compounds (Ni, Cu, Zn, Pb, Sb). In these risk assessments, monitoring data for occupational exposure were peer-reviewed and used for the respective occupational exposure assessments. The associated databases were collated by incorporating available contextual information and used for the calibration of MEASE. The output of the MEASE model is constantly validated by comparison with more recent monitoring data and the results are taken into account when updating the tool. However, a systematic comparison of tool prediction and measured data sets has not been published so far.

A.14-1.3. EMKG-Expo-Tool

The exposure prediction model of the German EMKG-Expo-Tool[17] "Easy-to-use workplace control scheme for hazardous substances" is a generic tool that can be used to derive a Tier 1 inhalation exposure value for the workplace (EMKG, BAuA 2008). The tool was developed to help small and medium sized companies to comply with the Chemical Agents Directive. The EMKG-Expo-Tool is based on a chemical banding approach similar to COSHH Essentials, originally developed by the UK Health and Safety Executive (HSE 1999). While COSHH Essentials is seen as a qualitative approach to guide the assessment and management of workplace risks, the EMKG-Expo-Tool can also be used as a generic tool for assessing and comparing the level of exposure with limit values (OEL, DNEL). Hence, the EMKG-Expo-Tool should be seen as an approach for filtering the non-risky workplace situations from those requiring detailed attention. The tool only functions for inhalation exposure. The English version of the EMKG-Expo-tool is available

[17] The acronym EMKG stands for "Einfaches Maßnahmenkonzept Gefahrstoffe".

on the BAuA website: (www.baua.de), http://www.reach-helpdesk.de/en/Exposure/Exposure.html.

A.14-1.3.1 Domain of applicability

The EMKG-Expo-Tool is currently not appropriate for special situations, including activities where dusts are formed through abrasive techniques, open spray applications, gases, and pesticides. Operations that give rise to the generation of fumes (soldering, welding) and wood dusts are exempted as well. The tool is also not suited for CMR substances. These situations involve more complex exposures requiring additional considerations that are not yet fully addressed by the current tool.

A.14-1.3.2 Inputs

The following determinants are needed as input data:

- type of substance: solid/liquid
- dustiness (for solids), based on particle size and observation when substance is used, or
- volatility for liquids (estimated from the vapour pressure at process temperature or if this is not available from a combination of boiling point and process temperature)
- operational conditions (temperature, amount of substance/product used per task, size of the application surface)
- implemented RMMs (control strategy)
- exposure period (<15 min or > 15 min)

These general control solutions are underpinned by a series of Control Guidance Sheets (CGS) which provide practical examples of each control approach for common industrial unit operations such as weighing and filling. The CGS are essential to demonstrate a safe use and there are a number of key points that the user has to follow to control exposure, e.g. access to the work area, design and equipment, maintenance of equipment, examination and testing of equipment, cleaning and housekeeping, personal protective equipment, training, supervision. The Control Guidance Sheets can be accessed directly through the following link: http://www.reach-clp-biozid-helpdesk.de/en/Exposure/Exposure.html.

A.14-1.3.3 Outputs

Table R.14- 12: EMKG-Expo-Tool OUTPUT version 2.2

EMKG-Expo-Tool OUTPUT	
For solids	
Output	**Units**
Exposure band (for long-term inhalation exposure)	In mg/m^3 (for RCR take the higher value of the band)
For liquids	
Output	**Units**
Exposure band (for long-term inhalation exposure)	In ppm (for RCR take the higher value of the band)

A.14-1.3.4 Status of validation

For liquids, Lamb *et al* [15] carried out an extensive comparison of measured data (n= 905) with model predictions to examine the level of conservatism. "High", "medium" and "low" levels of conservatism were defined as where ≤ 10 %, 10 ≤ 25 % and > 25 % of the measurements exceeded the tool estimate, respectively. The EMKG-Expo-Tool showed a medium level of conservatism for PROC 4, PROC 13, PROC 14, PROC 19, and was highly conservative for PROC 5, PROC 8a, PROC 8b, PROC 9, and PROC 10 (see table 3.32 in [15]).

A number of further studies aimed at the evaluation of the exposure prediction model of COSHH Essentials. While Kindler [25], Lee et al [26] Hashimoto et al [27] and Tischer *et al* [28] generally confirm the conservatism of model estimates for volatile liquids as found by Lamb *et al*, the papers of Lee *et al* ([29]-batch-making and bucket washing), and Jones *et al* ([30]- vapour degreasing) described tasks where the tool tended to underestimate exposure.

For solids, according to Lamb *et al* [15] (n=246) the EMKG-Expo-Tool was of medium/high conservatism for powder handling tasks related to PROC 8b/9 respectively. By contrast, the tool showed a low level of conservatism for PROC 5, PROC 8a, and PROC 14 (s. table 3.32 in [15]).

Evaluation of COSHH Essentials[18] for bag filling operations carried out by Jones *et al* [30] identified 48 % of bag filling operations as "under-controlled".

For situation where the tool showed low levels of conservatism, it is recommended to estimate the exposure by alternative means as well, in order to reduce the uncertainty in the outcome. This may include, for example, comparison of modelled exposure values from different models and comparison between measured exposure data and modelled exposure estimates.

A.14-1.4. Higher Tier exposure assessment

If an initial assessment of exposure is not adequate, i.e. safe use is not reliably demonstrated, a refined assessment is necessary. This assessment is generally more specific than the initial assessment and may introduce new factors to be considered. The refined assessment can use any suitable method that is valid and provides sufficient accuracy. Higher Tier assessments usually require input from experienced assessors.

Four models are briefly discussed in this guidance:

- Stoffenmanager (Section A.14-1.4.1),
- RISKOFDERM (Section A.14-1.4.2)
- BEAT (Section A.14-1.4.3)
- Advanced REACH Tool (ART) (Section A.14-1.4.4)

Exposure assessment models that have been developed for the exposure assessment of biocides[19] and pesticides can be applied for some worker exposure assessments. These

[18] With regard to the EMKG-Expo-Tool it is important to note that the tool is almost identical to the exposure prediction model of the COSHH Essentials. Hence studies that aim at the validation of the COSHH Essentials can be used for the EMKG-Expo-Tool as well.

[19] Guidance on the BPR: Volume III Human Health, Part B Assessment (Chapter 3 Exposure assessment) [http://echa.europa.eu/web/guest/guidance-documents/guidance-on-biocides-legislation]

tools are particularly relevant for estimating dermal exposure and can estimate aerosol exposure. The tools exist either as individual models within the Biocides Human Health Exposure Methodology Document or have been further developed to be part of the Bayesian Exposure Assessment Toolkit (BEAT model). Biocides models specifically allow prediction of dermal exposure and to aerosols for analogous situations based on underpinning real generic data which can be fully accessed via the BEAT model.

In the USA, the Environmental Protection Agency (EPA) has supported development of a number of tools which may contain useful approaches for higher Tier exposure assessment. For these approaches see the EPA website: http://www.epa.gov/expobox/exposure-assessment-tools-routes

If an initial exposure assessment does not produce an acceptable outcome it may be possible to produce exposure predictions that are specific to the exposure scenario. Levels clearly above DNELs, will demand the further development of exposure scenarios implementing a different set of operational conditions and risk management measures.

A.14-1.4.1 Stoffenmanager

Stoffenmanager version 6.4 (Dutch for "substance manager") is a web-tool that is free to use following registration. Besides the free version, it also has a commercial Premium version. Stoffenmanager includes a quantitative model for estimating inhalation exposure to vapours, aerosols of low volatility liquids and inhalable dusts. The model is available in Dutch, English, German, Finnish, Polish and Swedish. The web-based tool has a specific REACH section and a section for exposure calculations in which full shift time-weighted averages can be calculated. An exposure database containing around 1000 measurements with all relevant Stoffenmanager parameters is used to further underpin and validate the model. The Stoffenmanager 6.3 exposure model tool is currently somewhere between first Tier and higher Tier models. The rationale of the underlying exposure algorithm is based on the work of Cherrie and Schneider (1999) but is adapted in several ways (see https://stoffenmanager.nl/Public/Explanation.aspx for more information). Stoffenmanager estimates task-based exposure levels in mg/m^3. A time-weighted average can be calculated for one, or several combined tasks with duration of less than 8 hours.

A.14-1.4.1.1. Applicability domain

The domain of application of Stoffenmanager [31] is summarized in Table R.14- 13.

Table R.14- 13: Domain of reliable application of Stoffenmanager® (the algorithms can only be found at www.stoffenmanager.nl in its most recent version)

Domain Boundary	Comments
Gases	Out of applicability domain
Aerosol Mists	Falls within applicability domain

Biocides Human Health Exposure Methodology Document [http://echa.europa.eu/about-us/who-we-are/biocidal-products-committee/working-groups/human-exposure]

Domain Boundary	Comments
Process fumes	Out of applicability domain
Fibrous materials	Out of applicability domain
Exposures above ambient temperature	Stoffenmanager predicts exposure at 20°C. Where a liquid substance is handled at temperatures significantly in excess of this, then users should apply the vapour pressure calculated at the operating temperature
Solids in liquids	Falls within applicability domain
CMRs and 'very high hazard' substances e.g. respiratory sensitizers	Falls within applicability domain
UVCBs	Falls within applicability domain
Mixtures	Falls within applicability domain
Fractions of airborne solids	Falls within applicability domain for abrasive activities using wood (inhalable dust) and stone (inhalable and respirable dust). Out of applicability domain for other abrasive activities like using plastic, glass or metal.

Domain Boundary	Comments
Out of scope tasks/process (PROCs)	- PROC 6 Calendering operations - PROC 12 Use of blowing agents in manufacture of foam - PROC 16 Using material as fuel sources, limited exposure to unburned product to be expected - PROC 20 Heat and pressure transfer fluids in dispersive, professional use but closed systems - PROC 21 Low energy manipulation of substances bound in materials and/or articles. Abrasive activities using wood (inhalable dust) and stone (inhalable and respirable dust) do fall within the scope. - PROC 22 Potentially closed processing operations with minerals/metals at elevated temperature. Industrial setting - PROC 23 Open processing and transfer operations with minerals/metals at elevated temperature - PROC 24 High (mechanical) energy work-up of substances bound in materials and/or articles. Abrasive activities using wood (inhalable dust) and stone (inhalable and respirable dust) do fall within the scope. - PROC 25 Other hot work operations with metals - PROC 27a Production of metal powders (hot processes) - PROC 27b Production of metal powders (wet processes

A.14-1.4.1.2. Input data

The following parameters are needed as input data for the quantification of exposure with the Stoffenmanager:

- Physical state of the substance (solid or liquid)
- Whether there are activities involving articles (= solid objects) that may cause emission of dust.
- Vapour pressure of liquids (in Pascal, used directly) or dustiness (solid articles, firm granules or flakes, granules or flakes, coarse dust, fine dust, extremely dusty products)
- Type of dust emitted from solid objects (presently only stone or wood)
- Percentage of the substance(s) in the product
- Level of dilution of liquid products with water (undiluted = 100%)
- Handling category
- Duration and frequency

- Local controls (including local exhaust ventilation (LEV) and containment)
- Distance of the worker from the source (within one meter or not)
- Presence of secondary emission sources:
    - Other workers using the same substance simultaneously
        - A period of evaporation, drying or curing after the activity (with prolonged emission of vapours)
- Room volume
- General ventilation
- Emission control measures (such as control rooms)
- Respiratory protective equipment (RPE) used
- Information on whether the work area is regularly cleaned
- Information on whether machinery and equipment are regularly inspected and kept in good order.

To calculate time weighted averages, separate assessments for each activity should first be made and then combined using the duration of each activity entered to calculate time weighted averages.

In addition to the required inputs for exposure estimation, a number of other inputs are needed. These are data on the product name, the date of the Safety Data Sheet, the name of the supplier as well as the department or work area for which the assessment is being made. Although these data will not influence the quantitative calculations, inputs are required for the software to function.

A.14-1.4.1.3. Stoffenmanager output

Table R.14- 14: Stoffenmanager output

STOFFENMANAGER OUTPUT	
Output	**Units / comments**
Long-term inhalation exposure estimate	mg/m^3 (90th percentile)
Short-term inhalation exposure estimate	mg/m^3 (90th percentile)
Data on the exposure distribution	The tool gives the 50-75-90 and 95th percentile values of the exposure distribution. The 90th percentile is given as default value

A.14-1.4.1.4. Status of validation

Stoffenmanager® is a continuous development platform and the algorithms in its most recent version can only be found at www.stoffenmanager.nl. The International Scientific Advisory Board is a guarantee that the tool complies with regulations and is in line with latest scientific developments. Several publications concerning the development and further refinement of the model are available. Originally the tool was based on a published scientific conceptual model of exposure [32] followed by a quantification of the model algorithms (i.e. the calibration with measured data) by [33]. Schinkel et al. [34] published a cross-validation and further refinement of the model and concluded that the 90th percentile estimates of the model are verified to be sufficiently conservative and therefore can be used as Tier 1 exposure assessment tool for REACH. This was again demonstrated by Koppisch et al. [35] who focussed on estimating workers' exposure to inhalable dust. In the ETEAM study all five REACH Tier 1 tools were evaluated and the authors concluded that Stoffenmanager® 4.5 appeared to provide the most balanced performance with regard to the level of conservatism and predictive power for volatile liquids and powders ([15] and [36]). In another study, Landberg et al. [37] evaluated the conservatism of Stoffenmanager® 5.1 by testing whether the 90th percentiles are above the measured exposure values. They showed that only two of the eleven scenarios tested had slightly higher measured median exposure values than modelled concentrations and concluded that the model performed well. Finally a sensitivity analysis on ECETOC TRA v3, Stoffenmanager® 4.5 and ART 1.5 was performed by Riedmann et al. [24] to determine dominant factors for the three models and to assess the robustness of each model. The authors stated that, "when the entry data are uncertain or difficult to use, practitioners should consider using Stoffenmanager as their default occupational exposure model since: (1) it provides mean exposure estimates and various CIs in a reasonable range, and (2) it is the most robust model. Besides, Stoffenmanager appears also to be the most balanced model with regard to physical phenomena such as source emission and dilution." Overall, the conclusion, on the basis of all available scientific literature, is that the Stoffenmanager® model is robust, has sufficiently predictive power and is conservative enough for a REACH Tier 1 tool.

A.14-1.4.2 RISKOFDERM

The RISKOFDERM dermal exposure model is the result of a European 5th framework programme project that focused on dermal exposures in industrial and professional settings [38]. The model assesses mainly potential dermal exposure, i.e. exposure on the skin and on the outer layers of clothing covering the skin in the target areas. It therefore does not take into account any protective effect of clothing or gloves, unless specified. Performance of protective clothing and gloves has to be introduced externally to the model to produce an estimate of actual dermal exposure (ADE) which can be used to compare with an external DNEL. The model is based on real datasets with known distributions that represent much of the current knowledge on dermal exposure in the professional and industrial setting.

An Excel spreadsheet version of, and a guidance document for, the model can be downloaded from http://www.eurofins.com/product-testing-services/services/research-development/projects-on-skin-exposure-and-protection/riskofderm-skin-exposure-and-risk-assessment.aspx

The basic estimate made by RISKOFDERM is the potential rate of exposure per minute (for hands and/or remainder of the body). Total exposure over a longer period is calculated by entering the duration of the activity leading to exposure.

Although the potential for deposition may, at times, appear high, especially when compared to other models, there is consistency between a wide range of studies in this area.

The exposure reducing effect of protective clothing and gloves needs to be included externally to the model. Advice, which may be useful by analogy, on the effectiveness of gloves and clothing can be found in work carried out in the context of biocides and incorporating findings from a number of studies on the effectiveness of protective clothing (Please see http://echa.europa.eu/documents/10162/19680902/heeg_opinion_9_default_protection_factors_for_clothing_and_gloves_en.pdf).

A.14-1.4.2.1. Domain of Applicability

Due to a lack of data on dermal exposure to volatile substances, the model is not optimally suitable for very volatile substances (e.g. > 500 Pa vapour pressure). Use with input values outside those found in the measured data sets should be avoided, though results may still be indicative. These boundaries are provided in the guidance document with the spreadsheet version (that can be downloaded from http://www.eurofins.com/product-testing-services/services/research-development/projects-on-skin-exposure-and-protection/riskofderm-skin-exposure-and-risk-assessment.aspx). Further refinement of predictions of actual dermal exposure may be provided through application of other external tools such as IH SkinPerm.

A.14-1.4.2.2. Input data

The first step in using the RISKOFDERM dermal exposure model is to input the type of exposure process (choice between one of six processes or DEO units). The next step depends on the exposure process input and the following items may be needed:

- type of skin contact
- frequency of skin contact
- type of product handled
- viscosity of the product
- volatility of the product
- dustiness of the product

- use rate of the product
- formation of aerosols
- manual or automated tasks
- direction of application
- tools used
- quality of ventilation
- direction of airflow
- segregation of worker from source
- distance of worker from sources

A.14-1.4.2.3. Output

The spreadsheet version of the RISKOFDERM dermal model provides exposure estimates for the median exposure level corresponding to the inputs provided and for any chosen percentile. Also, the values are presented for a number of fixed percentiles of the output distribution. Depending on the exposure process only hand exposure, only body exposure or both are estimated.

The web-based version provides a distribution of exposure estimates for the input distributions provided. The RISKOFDERM dermal exposure model makes calculations based on equations derived from mixed-model statistical analyses from a relatively large set of measured data.

A.14-1.4.2.4. Status of validation

The validity of the model has not been established with independent data. A benchmark study after a first draft version showed that in general the model appeared to be quite reasonable. The validity and adequacy of the model is relatively well-known for situations resembling those measured in the data set that was the basis for the model [38]

A.14-1.4.3 BEAT model

The Bayesian Exposure Assessment Tool (BEAT) was originally developed in 2002 by the United Kingdom's HSE for experienced assessors undertaking regulatory risk assessments carried out in connection with the European Biocidal Products Directive (EC, 1998a). The BPD has been replaced by the Biocidal Products Regulation (EU 528/2012) and new Guidance[20] has been published for the BPR replacing the TNGs. BEAT provides the option to search for appropriate generic data (suitable indicative exposure estimates) based on (task) analogy with measured exposure data. In addition, the software offers a hierarchical Bayesian model for probabilistic predictions by using various analogous data sets in a single exposure distribution. In addition, if sufficient data for an analysis are available, BEAT offers further statistical tools (e.g. Markov Chain Monte Carlo analysis). A feature of BEAT is that users are not restricted to using exposure values extracted from the measurement database; instead, the user may insert other data. Moreover, BEAT provides a visualization of the spatial distribution of dermal exposure of the body using three-dimensional mapping (IGHRC, 2010). General information about the

[20] Guidance on the BPR: Volume III Human Health, Part B Assessment (Chapter 3 Exposure assessment) [http://echa.europa.eu/web/guest/guidance-documents/guidance-on-biocides-legislation]

Biocides Human Health Exposure Methodology Document [http://echa.europa.eu/about-us/who-we-are/biocidal-products-committee/working-groups/human-exposure]

development and the underlying concept is provided in the help files integrated in the tool, but details about the underlying algorithm are not publicly available. The BEAT model is available at http://xnet.hsl.gov.uk/download/.

A.14-1.4.3.1. Input data

The following input data are required to run BEAT:

- physical state (liquid/solid)
- Particle size (e.g. sand like, pellets)
- Particle wetness (e.g.: dry, damp)
- viscosity of the product
- volatility of the product
- work environment (confined, restricted, open)
- automation of the process (e.g. fully manual, partly automated)
- type of ventilation
- whether liquid bases dust control is used
- Type of process (high energy/low energy)
- Spray pressure (e.g. showering, high pressure)
- Segregation of worker from source (e.g. partial segregation, containment)
- Surface area of contact (e.g. whole body, whole hands, fingertips)
- Level of contamination (e.g. invisible, thin layer)
- frequency of skin contact (e.g. rare, intermittent)
- Application use rate (l*min-1 or kg min-1)
- Distance to source
- Length of tool handle
- Orientation (e.g. overhead, level)
- Duration of exposure (in minutes)

A.14-1.4.3.2. Output

Dermal exposure is provided as actual dermal exposure (mass rate) of the hands and potential exposure of the body (in $mg \cdot min^{-1}$) for both a specific defined area of the skin and a specific application rate presented in the database.

A.14-1.4.3.3. Status of validation

The BEAT dermal exposure tool has not been validated

A.14-1.4.4 Advanced REACH Tool (ART)

The Advanced REACH Tool, ART (version 1.5) makes use of mechanistically modelled estimates of exposure and any relevant measurements of exposure. The tool provides estimates of the whole distribution of exposure variability and uncertainty, allowing the user to produce a variety of reasonably foreseeable realistic and worst-case exposure estimates, dependent upon the requirements of the particular risk assessment. ART does not take into account the effect of respiratory protective equipment (RPE). Performance of RPE has to be introduced externally to the model to produce an estimate of actual inhalation exposure which can be used to compare with an external DNEL. The approach facilitates the inclusion of any new data that become available in the future or during the

risk assessment process. The tool is suitable for expert assessors.

Since the tool allows the use of analogous exposure data from comparable scenarios, exposure assessments will not automatically require scenario-specific exposure data [39]. The tool incorporates both a mechanistic model and an empirical part with information from an exposure database.

ART is a web-tool that is free to use following registration. Registration is via the website http://www.advancedreachtool.com.

A.14-1.4.4.1. Domain of applicability

The domain of applicability of ART is summarized in Table R.14- 15 below.

Table R.14- 15: domain of applicability of ART

Type of exposure	Explanation
Exposure types within ART applicability domain	
Dust	Solid particles that are formed by aerosolization of already existing powders or by abrasion of solid objects.
Mist	Any airborne liquid particles. A water mist in the form of fog or a fine spray is a common example.
Vapour	This is the airborne state of a chemical, which, if a sufficiently large amount of liquid were released into a closed room at normal temperature, would not completely evaporate but rather would reach equilibrium with its liquid. Exposure during the application of various organic solvents is a common example.
Fume	Solid particles that are formed by condensation from high temperature vapour, such as from molten metal or smoke
Exposure types outside of ART applicability domain	
Gas	This is the airborne state of a chemical whose liquid is so volatile that its vapours cannot reach equilibrium with its liquid
Fibres	Elongated particles whose length-to-diameter ratio is at least 3:1 (e.g., asbestos, MMMF).

A.14-1.4.4.2. Input data

The inputs are arranged in sets of 'principal modifying factors' (MF) such as intrinsic emission rates, efficacy of local controls and methods of handling or processing of chemicals. Based on a relatively abstract definition of the MFs, specific inputs (determinants) have been derived. The user of the tool is guided through these inputs.

For calculation of exposure with the mechanistic model the following inputs are needed:

- Duration of activities (each will get a separate assessment) within the shift

- Type of material used (powdered, granular or pelletised material; solid objects; liquids; powders dissolved in a liquid or incorporated in a liquid matrix; paste, slurry or clearly (soaked) wet powder)
- For powdered, granular or pelletised material:
    - Dustiness (measured) or dustiness category
    - Moisture content of the material
- For solid objects:
    - Material of which the solid object is composed
    - Moisture content of the material
- For liquids:
    - Temperature of liquid in process (or relative compared to room temperature)
    - Vapour pressure of the liquid
    - Boiling point of the liquid
    - Viscosity of the liquid
    - Activity coefficient of the substance in the liquid
- For all materials: molar or weight fraction of the substance in the material
- Primary emission source in the breathing zone of the worker (yes/no)
    - If yes, secondary sources outside the breathing zone also need to be assessed.

For both primary and secondary emission sources, the following information has to be provided separately:

- Activity class of the activity
    - In some cases, also activity subclasses are defined
    - For some activity classes, further questions are asked, such as:
        - Spray direction (for spraying)
        - Drop height (for dropping of material, e.g. in transfer)
    - For several activity classes a parameter representing the 'scale' of the activity needs to be provided (in classes), e.g. 'use rate' or 'surface area'

For primary sources (both within and outside the breathing zone), the following information on RMM needs to be provided

- Any control measures close to the source with the following choices and sub-options
    - Suppression techniques (only for powdered, granular or pelletised material)
    - Containment without extraction
    - Local exhaust ventilation - three options, each with two to three sub-options
- Measures to limit surface contamination and fugitive emissions
    - Enclosure of process
    - Evidently effective housekeeping

    - General housekeeping
- Conditions and measures of dispersion
    - Working indoors, outdoors or in a spray room
        - For indoors: room size and ventilation rate
        - For outdoors: placement of source relative to buildings and of workers relative to source

For primary sources outside of the breathing zone, only the following RMMs need to be evaluated:

- Emission source segregated from the worker (several options)
- Worker separated from the emission source by a personal enclosure (several options)

For secondary sources (outside the breathing zone), the question regarding emission sources segregated from the worker also applies.

In addition, some administrative data on e.g. the name of the substance and the name of the assessment are also required to perform calculations.

A.14-1.4.4.3. Output data

ART version 1.5 (July 2014) provides the following outputs.

Table R.14- 16: ART output

ART OUTPUT	
Output	**Units**
Long-term inhalation exposure estimates (2 types)	**mg/m³** **Full-Shift exposure (recommended for REACH evaluations)**: ART calculates an overall distribution for full-shift exposures. Normally the 90th percentile (that provides the exposure level, which has a 10% probability of being exceeded by the exposure from a randomly selected worker on a randomly selected day) should be used for REACH purposes.
	mg/m³ **Long-Term Average exposure:** ART calculates the distribution of workers' long-term average (mean) exposure (e.g. over a period of months). In this case, the 90th percentile provides the long-term mean exposure level, which has a 10% probability of being exceeded by the long-term exposure from a randomly selected worker.
Short-term inhalation exposure estimates	**mg/m³**
Data on the exposure distribution	The tool generates values for 50th, 75th, 90th, 95th and 99th percentile exposures and applies a confidence interval around the reported value.

A.14-1.4.4.4. Status of validation

The mechanistic model of the Advanced Reach Tool (ART) provides a relative ranking of exposure levels from different scenarios ([40]; [41]). These relative ranking scores have subsequently been calibrated:

- to study whether the mechanistic model scores are accurately ranked in relation to exposure measurements;
- to enable the mechanistic model to estimate actual exposure levels rather than relative scores; and
- to provide a method of quantifying model uncertainty. Stringent data quality guidelines were applied to the collated data.

Linear mixed effects models were used to evaluate the association between relative ART model scores and measurements. A random scenario and company component of variance were introduced to reflect the model uncertainty. Stratified analyses were conducted for different forms of exposure (abrasive dust, dust, vapours and mists). In total more than 2000 good quality measurements were available for the calibration of the mechanistic model [42]. In addition, the inhalable dust algorithm of the Advanced REACH Tool (ART) has been refined and validated to predict airborne exposure of workers in the pharmaceutical industry [43]. For 75% of the scenarios the exposure estimates were within the 90% uncertainty factor of 4.4, as reported for the original calibration study, which may indicate more uncertainty in the ART estimates in this industry. Furthermore, the reliability of the Advanced REACH Tool (ART) was assessed by:

studying inter-assessor agreement of the resulting exposure estimates generated by the ART mechanistic model,

- studying inter-assessor agreement per model parameters of the ART mechanistic model,
- investigating assessor characteristics resulting in reliable estimates, and
- estimating the effect of training on assessor agreement.

The correlation showed good agreement before and almost perfect agreement after training. However, substantial variability was observed between individual assessors' estimates for an individual scenario ([44]).

Recently, an exposure database has been added to the Advanced REACH Tool (ART; version 1.5). The incorporation of the exposure database into ART allows users who do not have their own measurement data for their exposure scenario, to update the exposure estimates produced by the mechanistic model using analogous measurement series selected from the ART exposure measurement database [45]. After selecting one or more analogous data sets, the data are used by the Bayesian module of the ART system to update the mechanistically modelled exposure estimates [46].

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