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Guidance on Information Requirements and Chemical Safety Assessment

Chapter R.15: Consumer exposure estimation

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European Chemicals Agency

Mailing address: P.O. Box 400, FI-00121 Helsinki, Finland
Visiting address: Annankatu 18, Helsinki, Finland

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].

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, p.1; corrected by OJ L 136, 29.5.2007, p.3).

Document History

Version	Comment	Date
Version 1	First edition	May 2008
Version 1.1	Footnotes added	July 2008
Version 2	The information on exposure models in Part D of IR&CSA was integrated into Chapter 15.4.	April 2010
Version 2	Chapter R.15.4 on the ECETOC TRA consumer tool for exposure estimation at Tier 1 was subjected to a major revision and update, with the inclusion of a new version of the ECETOC TRA consumer model.	April 2010
Version 2	The order of chapters on i) the agreed standard algorithms for calculation of consumer exposure (presently R.15.3) and ii) on the ECETOC TRA consumer tool for exposure estimation at tier 1 (R.15.4) was switched.	April 2010
Version 2	All presentations on higher tiers were moved into a single chapter R.15.6 and an additional Appendix R.15-4	April 2010
Version 2	A new chapter R.15.6 on risk characterisation was introduced and all relevant texts from other parts were moved into it.	April 2010
Version 2	The introduction was updated	April 2010
Version 2	The chapter on RMMs (earlier R.15.3.2.1) was shortened, moved to Chapter R.15.2.7 and information which duplicated that in R.13 was deleted.	April 2010
Version 2	A new Appendix R.15-1 on consumer mixture and article categories that can be assessed with the ECETOC TRA was introduced	April 2010
Version 2	Text on JRC GExFRAME model and EIS-Chemrisks-toolbox in Chapter R.15.5.3 and Appendix R.15.3, including Table R.15-7, was updated.	April 2010

Version 2	The default units for the algorithms in R.15.3 were updated to be consistent with other guidance (Chapter R.8) and modelling tools.	April 2010
Version 2	Further minor technical and language corrections	April 2010
Version 2.1	Corrigendum to: (i) replace references to the DSD/DPD by references to CLP; (ii) implement minor recommendations concerning nanomaterials arising from RIP-oN3; (iii) make further minor editorial changes/corrections.	October 2012
Version 3.0	• The description of the workflow has been streamlined • New specification of how to deal with infrequent uses has been introduced • Have removed "migration from article" as a tier 1 algorithm for dermal exposure • Have updated the information on modelling tools • Have harmonized the text with the updated Chapter R.12 of the IR & CSA Guidance • Have integrated relevant parts from Chapter R.17 (to be obsoleted)	XXXX 201y

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Notes on the updates

Most of the changes in the current update provide additional tools and parameters to support consumer exposure assessment and exposure scenario building under REACH, or are of an explanatory or an editorial nature.

A registrant having already finalised the consumer exposure estimation based on Chapter R.15 as published in April 2010 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.

If the conclusion of the check is that neither is put into question, it is unlikely that the adaptation of the already existing Chemical Safety Report to this guidance update (version 2.1 to version 3.0) is of high priority. In this respect, it should be highlighted that previous version of the Tier I ECETOC TRA consumer tool (version 2, as described in the R15 Guidance, April 2010) is more conservative than the new ones developed more recently (Version 3.0 and 3.1, see Section R.15.4). Therefore an assessment carried out with version 2 of the TRA consumer tool without further refinement can still be considered valid.

This updated guidance (version 3.0) describes how to deal with infrequent uses, in this respect existing assessments based on averaging out the event exposure from infrequent events over a longer period of time may need revision.

Convention for citing the REACH regulation

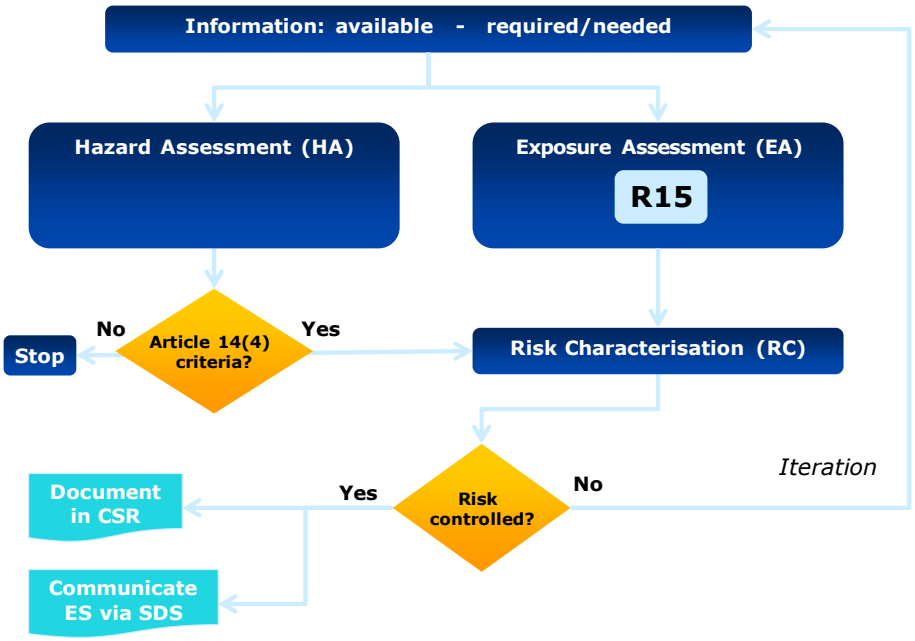
Where the REACH regulation is cited literally, this is indicated by text in italics between quotes.

Table of Terms and Abbreviations

See Chapter R.20

Pathfinder

The figure below indicates the location of chapter R.15 within the Guidance Document structure.



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R.15. Consumer exposure assessment

R.15.1. Introduction

R.15.1.1. Aim

This document provides guidance on how to carry out consumer exposure assessment in the context of 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 meets the criteria to be classified as hazardous.

The aim of this guidance chapter is to describe an efficient, step-wise and iterative procedure for consumer exposure assessment under REACH, related to substances on their own, in mixtures or in articles[2]. In this guidance substances on their own or mixtures or articles used by consumers are called consumer products.

It consists of the following sections:

- Introduction to consumer exposure assessment (Section R.15.1.2)
- Workflow for consumer exposure assessment (Section R.15.1.3)
- General principles related to assessment of consumer exposure (Section R.15.2)
- Calculation of consumer exposure at Tier 1 level (Section R.15.3)
- Tools for supporting exposure scenario building at Tier 1 level (Section R.15.4)
- Higher tier models and measured data (Section R.15.5),
- Risk characterisation (Section R.15.6),
- Overview on information sources and available tools (Section R.15.5 and Appendix R.15.2, Appendix R.15.3 and Appendix R.15.4)

This guidance does not address prevention of accidents for example ignition of flammable products or drinking of oxidising, very corrosive products or poisonous products.

R.15.1.2. Introduction to consumer exposure assessment

The consumer, i.e. a member of the general public who may be of any age, either sex, and in any state of health, may be exposed to a substance by **using** consumer products, or by being present when others (e.g. professionals) are using products. A consumer product (substance, mixture or article) is a product that can be purchased from retail outlets by members of the general public. This includes also chemicals and materials for construction works or car maintenance sold to both professionals and consumers (do it yourself products). The M/I of substances being part of do-it-yourself products sold at retailers should also ascertain that consumer use has been assessed and safe consumer use can be assured

For consumer exposure assessment under REACH, the addressee of exposure scenarios is the

[2] Article 3(3) of REACH provides that "*article: means an object which during production is given a special shape, surface or design which determines its function to a greater degree than does its chemical composition*"

formulator of the mixture or the producer of the article sold to the consumers. The means of controlling the exposure from consumer products are very limited and cannot normally be monitored, or enforced beyond the point of sale of the products.

Manufacturer/ importer (M/I) of substances may initially use a broad or general (conservative) exposure scenario, and he may, as a result, be unable to demonstrate control of risk at a generic, conservative approach. The producer of the mixture or the article may have specific information related to the formulation and end use of his product. By making this knowledge available to registrants (e.g. in the form of SCEDs), DU sectors can support registrants in developing more realistic exposure scenarios.

Consumers may be **directly** exposed to substances from the products they use, for example solvents in adhesives or dyes/finishing chemicals in textiles. Additionally, exposure should be considered that does not result from uses by the consumer itself but from uses by other actors in the public domain, for example:

- exposure to substances at home after use of decorating or cleaning products by professionals;
- exposure to substances in indoor air (residential air: e.g. household, schools, nurseries);

exposure to substances in public areas (e.g. swimming pools, recreational areas).

In REACH guidance, **indirect** exposure of humans via the environment is defined as the exposure of humans via consumption of food, drinking water and inhalation of air which in turn are directly influenced by the releases of the substance into the environmental compartments air, water and soil. Indirect exposure is not included in consumer exposure assessment in REACH. However, it should be reported in the 'man via the environment' section in the chemical safety report and is further detailed in *Chapter R.16 of the IR&CSA Guidance*.

Consumer exposure levels may need to be estimated for long-term (repeated or continuous) exposure, and /or for acute/short term exposure (single event, peak exposure), depending on the properties of the substance and the nature of the use (see also Section R.15.2.3).

The way in which consumers are exposed to substances can generally be characterised by:

- the different routes of exposure, separately or in combination;
- the identification of the different phases of activity in handling the consumer product or article;
- the duration and frequency of exposure.

The consumer exposure estimation should normally address the intended uses of the products that contain the substances under investigation. However, since consumers may not accurately follow instructions for use of products, the exposure estimation should cover the reasonably foreseeable uses or use conditions. For example, consumers may over-dose (e.g. by increasing the amount of dishwasher detergent in relation to the doses recommended on the product), fail to take recommended actions that are designed to minimize the potential for contamination (e.g. they may leave containers open after having used the product which can give rise to potential inhalation exposure to substances) or use the product for foreseeable other uses (e.g. dishwashing product used to wash hands). Consideration of deliberate abuse is not part of the exposure assessment process under REACH.

If a substance is used in a consumer product type that has different ways of application (e.g. brush painting and spray painting) two options exist:

- define one contributing scenario covering both types of application: all conditions of us are the same and highest exposure estimate is carried forward to risk characterisation.

- define two contributing scenarios addressing the differences in the conditions of use and generate corresponding exposure estimates for both.
  Exposure scenarios can be developed for each use if the operational conditions and risk management measures are different between these use;

If the same substance (for a single registration) occurs in different consumer products that could reasonably be expected to be used jointly and frequently by an average consumer, the risk from aggregated exposure across these products should be considered, (see Section R.15.6).

Certain sub-populations may be exposed differently from others. If, for instance, exposure of young children is anticipated, their crawling behaviour and hand to mouth contact may bring them into contact with residues of products on the floor. In addition, the children's small ratio of body weight to surface area, compared to that of adults, will have an effect on the exposure estimates. Therefore, it has to be ensured that exposure scenarios chosen take into consideration exposure routes for the identified relevant consumer sub-populations, and the corresponding values for exposure determinants such as body weight and skin surface area should then be used in the estimation. Several tools and information sources are available for this (see Section R.15.4, Appendix R.15.2 and Appendix R.15.3).

R.15.1.3. Workflow for consumer exposure assessment

Chemicals safety assessment for consumers usually includes the steps outlined below. Note: The first two steps relate to hazard assessment and are not further explained in the current guidance. However, they are included in the workflow as the hazard assessment determines the scope of the exposure assessment and provides the references for the risk characterisation.

- Collect or generate information on the intrinsic properties of the substance (See *Part B and Chapters R7a and R.8 of the IR&CSA Guidance*) and take into account use patterns and routes of exposure.. This includes:
  - toxicological endpoints (e.g. irritation or corrosion, sensitisation, acute and repeated dose systemic toxicity, genetic toxicity, carcinogenicity, reproductive toxicity);
  - endpoints regarding physicochemical properties (e.g. vapour pressure, water solubility)
- Determine the type and the extent of hazards by comparing with classification and labelling criteria and by determining derived no-effect levels" (DNELs)[3] or derived minimal effect levels (DMELs) for all relevant exposure routes; different from hazard assessment for workers, this also includes a DNEL for systemic effects via the oral route. Determine the leading hazard for each exposure route. Th e conclusions at this step determine i) whether a substance should/must not be introduced to consumer uses at all (e.g. CMRs and acutely toxic substances) and ii) which hazards are to be addressed in the exposure assessment.
- Determine the scope of exposure assessment based on the outcome of the hazard assessment and the physicochemical properties of the substance:

[3] DNEL 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)

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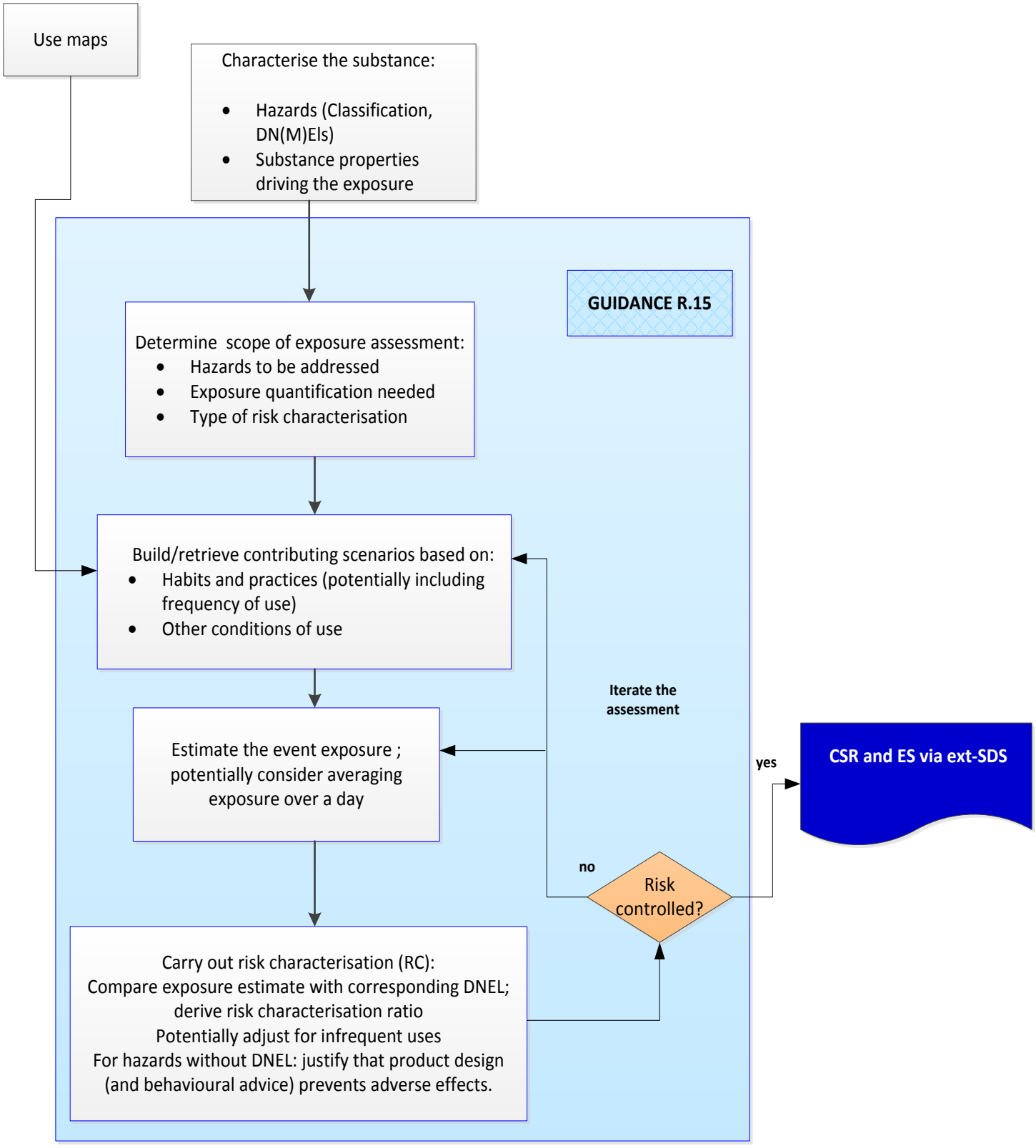
  - Determine whether serious local effects on skin and eyes may occur (e.g. due to irritation, corrosion or sensitisation) and therefore need to be addressed in the exposure assessment.
  - Determine routes and types of effects for which exposure quantification is required (i.e. where a DNEL can be derived based on effects seen in the corresponding study(ies). If systemic effects are observed, usually DNELs and corresponding exposure estimates for all three routes would be required.
- Build an exposure control strategy, taking into account that control of consumer exposure should largely be based on the design of the product itself (e.g. concentration limits, packaging avoiding overdosing; viscosity avoiding splashes). It is assumed that the number of consumers following behavioural advice or instructions (including correct use of personal protection equipment) is relatively low, and thus these measures are not sufficiently effective to control the risks to consumers. Special attention is needed for products where a single exposure to eyes and skin may cause serious effects. If the registrant nevertheless intends to support such consumer uses in his assessment, he needs to demonstrate that there is a negligible likelihood that such effects occur when used by consumers.
- Build/retrieve contributing scenarios for the product types (mixtures and articles) expected to contain the substance. Retrieve realistic information on the conditions of use from use maps and exposure assessment inputs (e.g. Specific Consumer Exposure Determinants [SCEDs], see Section R.15.2.6) if available from DU sector organisations or single representative customers (i.e. formulators or article producers); make use of published exposure studies and surveys on consumer habits and practices; ensure that the exposure scenarios sufficiently address local effects such as skin sensitisation, corrosion and irritation, if relevant. Consider whether habits and practices of adult-consumers may differ from the behaviour of child consumers and define the contributing scenarios accordingly.
- Derive exposure estimates for all contributing scenarios (i.e. product (sub) categories) where needed to support the risk characterisation.
  - Derive exposure estimate for one use event starting with a Tier 1 model, and for risk characterisation compare with the DNELs for repeated or continuous exposure (long-term DNEL). If the risk characterisation ratio is < 1, the use can be considered safe, independently of any considerations on frequency over a year or over a day.
  - If the risk characterisation is > 1, refine the exposure estimate (either option possible)
    - Refine exposure determinants to that given use (e.g. concentration, frequency, duration) for instance with the product-use information contained within the sector's SCEDs (if available). With regard to the frequency of use, there may be cases where the product is known to be used infrequently only and so the assessment may be further refined based on frequency of use (see boundaries and additional information in section R15.2.5).
    - Refine the event exposure estimate with higher tier models or measured data. If the risk characterisation ratio is <1, the use can be considered safe.
- Consider whether risks from combined exposure are to be addressed:
  - Risks via different routes of exposure are to be taken into account by summing the individual risk characterisation ratios under each contributing scenario
  - Risks resulting from exposure to the substance via simultaneous use of different products should, where relevant, also be taken into account through summing of risk characterisation ratios across exposure scenarios. For some general advice, refer to SectionR.15.6.
- Conclude whether further refinement of assessment is needed, and finalise the risk characterisation. Where DNELs are available the risk characterisation ratio (possibly supported by considerations on uncertainty) is sufficient. Where no DNEL is available (qualitative assessment), the registrant is expected to provide an argumentation why under the conditions described in the exposure scenarios it is unlikely that adverse effects occur on use.

- Document the assessment (including exposure calculations) in the CSR and communicate conditions/measures for safe use down the supply chain to the formulators of consumer mixtures and the producers of consumer articles.

The following flowchart (Figure R.15- 1) illustrates the steps described above.

Figure R.15- 1: Workflow for the consumers' exposure assessment



R.15.2. General exposure considerations related to consumers

R.15.2.1. Routes of exposure

In this chapter, the evaluation of exposure for consumers refers to external exposure. External exposure is characterised by the amount of a substance that is inhaled, lands on the skin or is ingested. The aim of this evaluation is to generate information that can be compared to DNELs, which are also expressed as external exposure values. Consumer exposure estimation will need to consider three separate exposure routes:

- inhalation exposure
- dermal exposure
- oral exposure

R.15.2.1.1 Inhalation exposure

Inhalation exposure may occur in the case of substances reaching the breathing zone of consumers. This may happen either during the actual use of the consumer product or article (e.g. as the result of vaporizing solutions or aerosol-forming mixtures or by use of dusty products) or as a result of volatilisation after the product has been used (e.g. evaporation of solvents from paints) or due to emissions from articles (by evaporation). Exposure by inhalation is expressed as the average concentration of the substance in the inhaled air, and is normally presented as an average concentration over a reference period of time (e.g. per day). If exposure is of intermittent short duration there may also be interest in exposure over shorter periods (e.g. per event). The assessment can also be based on exposure during specific tasks, which may be carried out over varying time periods. Some consumer products generate aerosols from the use of sprays. In this case the resultant exposure to the substance may be related to the characteristics of the droplets (e.g. particle size) which may need to be considered specifically in a higher tier exposure model.

Inhalation exposure is expressed in terms of external exposure, as a concentration, usually in mg/m^3. In specific cases, other metrics could also be relevant, for instance number concentration and surface area concentration (i.e. n/m^3 or cm^2/m^3) in the case of nanomaterials.

R.15.2.1.2 Dermal exposure

Dermal exposure is an estimate of the amount of substance contacting the exposed surfaces of the skin. It is the sum of the exposure estimates for the various parts of the exposed body surface. Dermal exposure can occur from splashes on the skin, from direct hand or body contact with the consumer product or article (e.g. jewellery, textiles, straps, belts, shoes), from deposition of particles or aerosols from an airborne substance on exposed skin or from skin contact with residues of the substance after product use (e.g. residues on clothing after laundering or dry cleaning). For heavy use of consumer products, the substances penetrating the clothing may represent an important exposure situation. The amount and concentration of the substance, the area of skin exposed and the duration and frequency of exposure can influence the actual dermal exposure to a substance. Dermal exposure is expressed in terms of the amount of substance per unit surface area of the skin exposed (mg/cm^2) or as dose (mg/kg body weight/day) on skin. Please note: DNELs derived under REACH refer to the external dose and should already take into account absorption through the skin. If data on absorption are not available, 100% absorption is assumed for DNEL derivation.

R.15.2.1.3 Oral exposure

This refers to substances occurring in mixtures that can be ingested resulting in exposure by the oral route. Examples are the exposure from residues of finger paints in the hands or inges-

tion of residues from dishwashing products remaining on dishes. Exposure by the oral route may also occur as a consequence of migration from articles through sucking, chewing or licking of toys, children's books, plastic articles or textiles, or by unintentional ingestion of the article itself or parts of the article. This is of particular relevance to children due to their hand to mouth and/or mouthing behaviour.

A specific type of oral exposure for children is from the uptake of dust and soil to which release of substances from consumer products have absorbed, especially due to release of substances from articles e.g. textiles, building materials or computers, TVs. The exposure to products and chemicals that are rarely accessible to children should not be considered.

Migration characteristics of the substance in the matrix, solubility and amounts typically used are important determinants to be considered. These parameters, together with concentration and contact parameters, are used to quantify the respective exposures.

Oral exposure is expressed as the amount of substance ingested per kg body weight, and is normally presented as an average daily external dose (mg/ kg body weight/day).

R.15.2.1.4 Other routes of exposure

Besides the three major routes of exposure mentioned previously, in special cases other routes of exposure must be considered, e.g. eyes (splashing) or in rare cases, intradermal routes. Intradermal exposure occurs when the integrity of the skin is disrupted by the use of consumer products (e.g. by earrings, piercings or tattoo inks). In these cases, the exposure is expressed as the total amount of the migrating substance and is normally presented as an average daily dose.

R.15.2.2. Phases of activity, including post-application

Consumer exposure can be characterised by looking at the different phases of activity in which the products are actually used. There are up to four phases of activity that are relevant to consumer exposure:

- preparatory activity, which includes tasks like handling and dilution of solid or liquid concentrates;
- application of product by the consumer, including handling of articles during their service life;
- post-use or post-application leading to exposure of the user (e.g. exposure to paints, cleaners etc. after use). It is possible that due to chemical reaction the exposure at this stage may be to the substance in a different physical state, or that exposure is to a different substance, e.g. reaction products of the substance;
- removal/cleaning leading to exposure of the user. This includes activities such as emptying and cleaning equipment, stripping coatings, etc.

Each phase of activity may require separate exposure estimation, given that the first phase reflects exposure to a concentrate, the second to a diluted solution, the third to a vapour or semi-dry residue and the fourth to "waste material" and different individuals may carry out each of the activities. If a consumer is exposed to a substance in a particular consumer product or article during different phases of activity including post-application phase, the contribution of each phase to the exposure may need be taken into account.

In addition to this, secondary exposure may occur at any stage to people that are not engaged in the activities, but happen to be exposed as well ('bystanders'). In practice however, the resulting exposure scenario for the different products should include some or all of these phases. The exposure scenario could focus on the phase with the highest risk associated with it, provided that the recommended operational conditions or risk management measures are also relevant and practicable for the other phases of activity. Additionally, it should be noted that very conservative assumptions (e.g., 100% substance release) could cover all the applica-

tion phases (See Section R.15.3: Calculation of exposure).

R.15.2.3. Frequency of use and duration of exposure

The large variety of consumer products corresponds to a large variety in the frequency and duration of use and exposure. Exposure may occur during use and sometimes it continues after use for a certain time. Duration of exposure can vary from seconds to hours per use event. The use events can take place regularly/frequently (e.g. every day) or infrequently/occasionally (e.g. less than monthly or only few times a year). Thus the product specific time pattern of use needa to be considered in the assessment. It will mostly be a distribution of consumer behaviour, and for many products the corresponding statistical information is not available. In this respect, the sector SCEDs can be helpful as they are targeted to provide additional information for refining the defaults in specific exposure scenarios (i.e. in this case the "daily use"). Moreover, for some products, it may be possible to exclude (even for the high-level user fraction within the general population) more frequent use due to the technical purpose of the product.

In general, consumer exposure assessment should match the relevant exposure duration and frequency with the corresponding DNELs.

The default approach in consumer exposure assessment is to assume that the products containing the substance are used on a daily basis, and that control of risk should be demonstrated for this use situation (to be described in the exposure scenario). The starting point for the assessment is therefore the exposure during one **use event**. All kinds of effects identified need to be addressed:

a) Effects occurring after **short (single)** exposure time (e.g. up to 1 hour):
   - For acute systemic effects leading to classification and labelling, an acute systemic DNEL should be derived. Risk for this scenario is characterised by comparing the event exposure (reference period of 15 minutes) to this DNEL.
   - No threshold may be available for dermal irritation, corrosion or sensitization. For these types of effects, the registrant would need to develop a qualitative argumentation under which conditions of use the risk is controlled; if for example the concentration of an irritant or corrosive substance in a mixture is below the classification limit the risk can be assumed to be adequately controlled.

b) For effects occurring after **repeated and/or continuous** exposure: Usually for these effects, a long-term (chronic) DNEL should be used (unless no threshold can be derived). The risk can be characterised by comparing the event exposure to this DNEL. The chronic DNEL corresponds to a concentration level present over life-time at which no effect is expected. It may be therefore appropriate to adjust the risk characterisation if the daily exposure occurs only for one or a few hours instead of 24 hours.

Adjustments for frequency and duration

If the registrant can provide supporting evidence that the use to be assessed only takes place infrequently or for only few days per year, he may want to carry out a particular assessment for the infrequent or short-term use. This may in particular be relevant for substances or use conditions where the assessment based on the long-term DNEL for organ toxicity (systemic toxicity) fails to demonstrate control of risk even after refinement of the event exposure estimates (e.g. modification of default input values, use of higher Tier exposure models or measured exposure data).

Based on the considerations in Appendix R.15.6 of this guidance, the risk characterisation for the daily exposure event (based on event exposure concentration and longterm DNEL) can be adjusted for infrequent or short term use. As a first step, or in case no toxicological support is

available, the RCR can be divided by a default adjustment factor: When a long-term DNEL is based on an oral study in rats, the factor is 10. When the long-term DNEL is based on an inhalation study, the factor 40. These factors consist of two elements.

- the adjustment for infrequency (Factor 6) corresponding to the assessment factor of 6 for duration in DNEL derivation
- the adjustment for the event duration if significantly shorter than 24h (Factor 2 to 8), depending on study from which the DNEL was derived (for details seeAppendix R.15.6)

For considering a use/exposure event "infrequent" it should occur no more than 12 times a year, which can be up to 12 single events distributed over the year or 12 consecutive days in one year. Note: Potential accumulation of the substance is already taken into account in the long-term DNEL, and thus the distribution of the 12 days over the year does not require particular considerations.

Study on which the long-term DNEL is based	Default adjustment factor for infrequent or short-term exposure	Adjustment for infrequency	Adjustment factor when exposure << 24 h
Rat, oral study	10	6	2 or 3
Rat, inhalation study	40	6	8

Based on **substance-specific** toxicological arguments the adjustment factor for infrequent uses can be increased up to 100 if it can be demonstrated that

- the systemic effects are driven by the accumulated dose rather than the actual exposure concentration
- local effects in the respiratory tract are unlikely to occur at the adjusted value.

The same approach can be applied for frequent uses where the daily exposure is significantly shorter than 24 hours (e.g. one hour). Depending on the substance characteristics (see above) an adjustment factor of up to 24 may be appropriate.

Information on frequency of use can be retrieved from published surveys on habits and practices, and/or from recognised other data sources (e.g. ECHA, RIVM fact sheets, ECETOC, industry peer-review initiatives such as HERA, Nordic Council, USEPA etc.) or published literature. Other types of information may also be considered. For example, the function of a product may inherently determine that it is normally not used for routine daily activity.. When available, additional supportive information may include aspects such as production volume, market volume, purchase frequency, etc. An example on how evidence for the infrequency of use for a consumer product can be demonstrated can be found at: https://www.concawe.eu/uploads/files/sced/Lubricant_liquids_with_base_oils_CONCAWE_SCED_24_1_a_v1-2014-02693-01-E.pdf.

R.15.2.4. Operational conditions and risk management

General information on the use of a substance in consumer products or articles is needed to identify the contributing scenarios to be assessed and the relevant exposure pathways. The brief general description of consumer uses should follow *Chapter R.12 of the IR&CSA Guidance.*

Direct exposure from product use will often be the main source of consumer exposure to a chemical present in that product. Characterisation of the direct consumer exposure requires knowledge of the nature of the products used and of the circumstances of their intended and reasonably foreseeable. A reasonably foreseeable use is in this respect the use dishwashing liquid for handwashing, but not using wall-paint as body paint.

The operational conditions and risk management measures of the exposure scenario have to reflect the driving parameters of the exposure estimation and its algorithm. Consumer exposure is related to the amount of substances in consumer products or articles. Therefore, the amount of the products used per event, the quantity of chemical in the product and the frequency and duration of the event are essential information needed to estimate consumer exposure. In particular:

- The duration of exposure for consumers should either be estimated as 24 hours per day as a worst case or by estimating the duration of the specific activities leading to exposure (e.g., cleaning of floor or manual dishwashing). For consumer products, and especially in indoor situations, the duration of use is not the same as duration of exposure (e.g. in the case of painting). In the exposure estimation, it should be taken into account that exposure to a substance may also occur after application.
- The applied amount of chemical is found by multiplying the handled weight of the product with the weight fraction of the substance in the mixture. For using a mixture after dilution (e.g., detergent concentrate), the handled weight of the diluted mixture is multiplied with the weight fraction in the diluted mixture. The realistic maximum amount of chemical in use by consumers varies not only between consumer products but also between individuals. For certain types of products it should be assumed that some consumers use more than the recommended amount, because they expect a better product performance. In these cases, individually packed amounts (e.g. tablets or separate sachets) will ensure a constant use amount.
- The size of the receiving compartments, normally a room in a flat or a house represents one of the most important parameters for the exposure assessment. This descriptor of exposure is needed for tier 1 assessments. Also a a standard ventilation rate for rooms with closed doors and windows can be considered in the exposure algorithms.

The exposure routes are related to the type of use and to substance properties. For example, inhalation may play a role for volatile substances but also for dust-forming conditions of use or conditions promoting mobility of a substance as such, in mixtures or in articles. Substances of low volatility can be released by mechanical abrasion (rubbing off), via leaching (e.g. during mouthing) or by migration (e.g. due to elevated temperatures or interaction between the substance and polymer-matrix) with subsequent release. The Tier 1 calculations for the different exposure routes are given in **Error! Reference source not found.**

Effective risk management measures for consumers are usually product-integrated measures. For quantitative exposure estimation, only those RMMs which can be controlled by the manufacturer of the product should be considered. This means that RMMs may be implemented by changing operational conditions or product composition, e.g.: maximum concentration used in the product, change of the product form (pellets or granules instead of powder), maximum amount of product used (package size), and type of packaging – many dishwasher tablets are now sold encased as gel capsules.

The use of consumer instructions as RMMs cannot be expected to be highly effective, unless

consumer behavioural data provide evidence that a sufficient degree of compliance can be assumed. The adherence to instructions is fundamentally different for consumers by comparison to that in occupational settings where the employer has the duty to ensure good operational conditions and use of RMMs.. For example, an RMM like "open windows to ensure a good ventilation" may be a useful advice to consumers but "good ventilation" should not be assumed when estimating the exposure. Increasing ventilation rates above default is not always a suitable option to iterate an exposure scenario for consumer uses, as adherence to the instructions cannot be guaranteed.

There are limited circumstances for consideration of personal protective equipment (PPE) in consumer exposure, because people will not necessarily use PPE even though recommended by the manufacturer. Even when PPE is provided with the product (e.g., gloves with a hair dye), it cannot be ensured that consumers will use it. The exposure estimation needs to consider the reasonable worst-case situation which indicates no use of gloves or other PPE. As an element of good practice and personal hygiene, the advice to use household gloves or other skin protection should be part of consumer instructions (e.g. for products that are irritating/corrosive to the skin, such as strongly acidic, alkaline or oxidising household detergents, and caustic oven cleaners).

R.15.2.5. Habits and practices of children

For children's products and for some consumer products for which the habits and practices of children significantly differ from those of adults (e.g. mouthing and crawling behaviour; handicrafts in school/kindergarten), the assessor needs to take these habits and practices into account and should derive contributing scenarios that are sufficiently protective for both children and adults. In addition, the anthropometric parameters (e.g. body weight, inhalation rate, body surface) of children and adults differ, which might lead to higher exposures in comparable exposure situations. This should, for example be taken into account for consumer products that are frequently used by children at school (e.g. universal glue) or during household activities (e.g. dishwashing products).

R.15.2.6. Specific Consumer Exposure Determinants SCEDs

The SCEDs (Specific Consumer Exposure Determinants) provide "information input" into the registrant's consumer exposure assessment. They document the typical conditions of use for a substance incorporated into a specific consumer product. This includes information related to consumer habits and practices (e.g. quantity of product used, frequency of use, place of use…) and information related to product characteristics (e.g. concentration of substance, transfer of substance from product to skin surface).

The SCED format has initially been designed to directly feed the information into ECETOC TRA v.3.1 and Chesar. However it is also possible to use the SCED information in other REACH consumer models (such as ConsExpo).

The SCEDs do not affect the algorithm inherent to the exposure model.

The SCEDs are developed by downstream sector organisations to transparently document the ways in which their products are commonly used by consumers. The first SCEDs were made publicly available in 2014, further SCEDs followed in 2015. See:

https://www.concawe.eu/reach/specific-consumer-exposure-determinants-sceds-documents

https://www.aise.eu/our-activities/product-safety-and-innovation/reach/consumer-safety-exposure-assessment.aspx

Each value within the SCEDs has to be substantiated by reference to suitable information sources that~~, ideally,~~ are open access and have been published and ideally are peer reviewed (the "rationale")[4]. Preferably this will refer to European data sources and/or be already used in regulatory processes (within the EU or beyond e.g. EPA, IPCS).

The SCEDs are designed so that the resulting exposure scenario as a whole represents conservative conditions of use. Where habits and practices significantly vary across European countries/regions, then the SCEDs will reflect those areas with the highest uses/exposure conditions.

The Guidance on SCED published by DUCC/Concawe can be downloaded from: http://www.ducc.eu/documents/20140424-Guidance%20documents%20on%20SCEDs-Final-V1.pdf

R.15.3. Calculation of exposure

This section summarises the Tier 1 principles and algorithms for consumer exposure estimation. The assessor may start the assessment by using tools that implement the Tier 1 algorithms. Tools for lower tiers of consumer exposure estimation are discussed in Section R.15.4 (ECETOC TRA) and Section R.15.5.1(some ConsExpo sub model), further tools are listed in Section R.15.5.2 and Appendix R.15.3.

As it explained later in this section, the tier 1 algorithms and the tools require values the calculations for anthropometric data (e.g. surface area of different body parts, body weight, and respiration volumes), room volumes and room ventilation etc. The default values used by each tool can be found in the tool documentation. Further information on default values for these parameters can be found at:

- RIVM Fact Sheets (room and anthropometric data, default for Consexpo): http://www.rivm.nl/dsresource?objectid=rivmp:266571&type=org&disposition=inline&ns_nc=1
- JRC ExpoFacts site (complete collection of EU data, no default proposed): http://expofacts.jrc.ec.europa.eu/
- US EPA Exposure factor handbook (containing also default for US): http://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252

The ECHA Biocides Human Exposure expert group (HEAdhoc), has agreed on harmonised values to be used for the exposure assessment from Biocidal products as available within the Biocides Human Health Exposure Methodology document within Section 2: Default parameters for Exposure Assessment" available at ECHA website. These include anthropometric parameters, activity patterns, room sizes and ventilations.

[4] Where a value has been copied from the ECETOC TRA defaults and where the original source of information is clearly referenced in the TRA documentation a reference to the corresponding ECETOC Technical Report may be sufficient.

Consumer exposure assessment on the Tier 1 level is rather a decision criterion on a screening level than a realistic exposure estimation. In contrast to higher tier assessments, it assumes instant and complete release of the substance from the product or from a thin product layer. In consequence of this complete release assumption, Tier 1 exposure estimates for the application phase also represent the exposure during other phases of activity like the post application period. The Tier 1 equations are simple and include few and highly conservative parameters which represent worst case situations. Depending on the substance properties and the use situation, Tier 1 assessments may already be sufficient to demonstrate safe use. Otherwise the assessment needs iteration by modifying the assumed conditions of use and the assessment models. In these refined consumer exposure estimations, the use conditions of the exposure scenarios are more realistic while the scope of the exposure scenarios is smaller (e.g. covers a more specific sub product or article).

Exposure quantification may be relevant for three routes:

Inhalation: A substance may be released into a room as a gas, vapour or airborne particulate (e.g. a carrier/solvent in a cosmetic formulation, a powder detergent, dust), or by evaporation from liquid or solid matrices, like articles (e.g. wall wooden panels, PVC flooring). Tier 1 algorithms assume that all substance is released at once into a standard room (instantaneous release) with immediate mixing, and no removal takes place due to ventilation. The main input parameter to be determined by the assessor is the amount of substance available for release in the standard room and the number of use events per unit of time. The amount results from the product/article amount per use event and the concentration of the substance in it. Some lower tier tools enable release modification based on vapour pressure of the substance. The estimated exposure is expressed in mg/m^3, averaged over the exposure event or over the day (24 h). Note: In order to support the assessment of outdoor uses some lower tier tools define a "virtual standard room" to generate an exposure concentration based on instantaneous release.

Dermal A: The substance is contained in a mixture. This option is applicable when, for example, hands are dipped into a solution containing the substance under evaluation, or splashes occur (painting). Tier 1 assessment assumes that all the substance contained in a contact layer of 0.01 cm thickness will be available to form the dermal load on the skin surface. Note that this Tier 1 assumption may not be valid for continuous immersion of body parts

The main input parameters to be determined by the assessor are the fraction of the substance in the mixture, the exposed skin contact area and the number of use events per unit of time.

The estimated exposure is expressed as dermal load per use event, calculated as the amount of substance per unit surface area of skin or as an external dose in mg/kg of bodyweight (per use event or per 24 h)

Dermal B: The substance is contained in an article matrix and migrates to the skin surface. This option is for example applicable when residual dyes in clothing or additives in plastic articles are in contact with skin. Tier 1 assessment assumes that all the substance contained in a contact layer of 0.001-0.01 cm thickness (depending on the article) will be available to form the dermal load on the skin surface.

The main input parameters to be determined by the assessor are the fraction of the substance in the article, the exposed skin contact area and the number of use events per unit time.

The estimated exposure is expressed as dermal load per use event, calculated as the amount of substance per unit surface area of skin or as an external dose in mg/kg of bodyweight (per use event or per 24 h).

Oral A: The substance is contained in a mixture or in an article and a part of the product/ article is unintentionally swallowed during normal use. This option is for example applicable for the use of finger paints or for residues from dishwashing on the dishes. The main input parameters

to be determined by the assessor are concentration of the substance in product when swallowed, the amount ingested per event and the number of use events per time. Oral exposure is expressed as external dose (mg/kg bw).

Oral B: The substance is contained in an article and migrates to the surface. Licking and sucking (e.g. by children) may promote leaching of the substance from the article matrix. This option is applicable for example when a substance migrates from a pen, cutlery or textiles. The main input parameters to be determined by the assessor are the fraction of the substance in the article, the area subject to sucking or licking and the number of use events per unit time. Oral exposure is expressed as external dose (mg/kg bw).

R.15.3.1. Inhalation exposure

. The **Error! Reference source not found.** represents a worst-case situation by assuming hat the substance is directly available as a gas or vapour. The equation applies to both volatile substances and airborne particulates. For inhalation exposure, the concentration of the substance in the room air (e.g. mg/m³) must be estimated; the inhalatory dose (mg/kg body weight/day) can then be also estimated. The event duration is assumed to be 24 hours in the worst case. For a Tier 1 evaluation, it is assumed that 100% of the substance in the consumer product or article will be released at once into the room and there is no ventilation. There should be a clear description in the CSR of the uncertainties associated with the estimated values and the consequences for the risk characterisation. The two essential parameters used that the assessor should know are:

- Amount of product used or article weight
- Fraction of substance in the product or in the article (concentration)

The concentration in air after using an amount Q_{prod} of the product becomes:

$$C_{inh} = \frac{Q_{prod} \cdot Fc_{prod}}{V_{room}} \cdot 1000 \quad \textbf{(Equation R.15- 1)}$$

When the inhalable and/or respirable fraction is known, it should be taken into account. If the product contains releasable nanomaterials then the assumption should be made that it is entirely within the respirable fraction if not otherwise known. The non-respirable fraction can be swallowed and oral exposure may also need to be considered (see Equation R.15- 8 and Equation R.15- 9). For the purpose of calculating overall systemic exposure via different exposure pathways, see Section R.15.6.

The air concentration C_{inh} results in an inhalatory dose D_{inh} of:

$$D_{inh} = \frac{F_{resp} \cdot C_{inh} IH_{air} T_{contact}}{BW} \cdot n \quad \textbf{(Equation R.15- 2)}$$

Table R.15- 1: Explanation of symbols for inhalation exposure

Input parameter	Description	Unit

Q_{prod}	Amount of product/article used	[g]
Fc_{prod}	Weight fraction of substance in product/article	$[g \cdot g_{prod}^{-1}]$
V_{room}	Room size (default 20 m^3)	$[m^3]$
F_{resp}	Respirable fraction of inhaled substance (default 1)	[-]
IH_{air}	Ventilation rate of person	$[m^3 \cdot d^{-1}]$
$T_{contact}$	Duration of contact per event (default 1 day)	[d]
BW	Body weight	[kg]
N	Mean number of events per day	$[d^{-1}]$

Output parameter	Description	Unit
C_{inh}	Concentration of substance in air of room	$[mg \cdot m^{-3}]$
D_{inh}	Inhalatory dose (intake) of substance per day and body weight	$[mg \cdot kg_{bw}^{-1} \cdot d^{-1}]$

It should be noted that for Tier 1 assessment for short-term local exposure, the value for V_{room} could be reduced (e.g. to 2 m^3) to represent the volume of air immediately surrounding the user ('breathing zone'). If this is not sufficient, higher tier models may be more appropriate. Inhalation exposure can occur to a substance that is released relatively slowly from a solid or liquid matrix (e.g. solvent in paint, plasticizer or monomer in a polymer, fragrance in furniture polish). In these cases, a simple Tier 1 screening model will usually overestimate exposure. Improved estimation models are further described in Section R.15.5.

R.15.3.2. Dermal exposure

Dermal scenario A: Instant application of a substance contained in a mixture

The model is used as a first Tier worst case approach or if details on how the skin is exposed to the compound are not known. If more precise information is available, the amount of product can be changed to reflect the actual use. The exposure expressed as dermal load L_{der} is calculated as the amount of product per unit surface area of skin or as external dose in mg/kg of bodyweight. The essential parameters used for this model are:

Weight fraction compound: the fraction of the compound in the total product
Amount of product: the amount of total product applied to the skin
The surface area of the exposed skin

The dermal load is calculated as:

$$L_{der} = \frac{Q_{prod} \cdot Fc_{prod}}{A_{skin}} \cdot 1000 \quad \textbf{(Equation R.15- 3)}$$

and the external dose Dder as:

$$D_{der} = \frac{Q_{prod} \cdot FC_{prod} \cdot n}{BW} \cdot 1000 \quad \textbf{(Equation R.15- 4)}$$

In cases where the substance is contained in a liquid into which certain parts of the body are dipped, the equation is not based on the mass of the substance applied to a certain area of skin, but rather on the concentration of the substance in the mixture that is in contact with the skin. First, the concentration C_{der} of a substance in contact with skin is calculated. Depending on how the parameters are provided, three analogous calculations are used:

$$C_{der} = = \frac{C_{prod} \cdot 1000}{D} = \frac{RHO_{prod} \cdot Fc_{prod} \cdot 1000}{D} = \frac{Q_{prod} \cdot Fc_{prod} \cdot 1000}{V_{prod} \cdot D} \quad \textbf{(Equation R.15- 5)}$$

The total dermal load L_{der} is then calculated using:

$$L_{der} = C_{der} \cdot TH_{der} \quad \textbf{(Equation R.15- 6)}$$

The dermal dose is then derived as:

$$D_{der} = \frac{L_{der} \cdot A_{skin} \cdot n}{BW} \quad \textbf{(Equation R.15- 7)}$$

Table R.15- 2: Explanation of symbols for dermal scenario A

Input parame-ter	Description	Unit
C_{prod}	Concentration of substance in product before dilution	[g·cm^{-3}]
D	Dilution factor (If not diluted, D =1)	[-]
RHO_{prod}	Density of product before dilution	[g·cm^{-3}]]
Q_{prod}	Amount of product used	[g]

Fc_{prod}	Weight fraction of substance in product before dilution	[-]
V_{prod}	Volume of product used before dilution	[cm^3]
V_{appl}	Volume of diluted product actually contacting the skin	[cm^3]
TH_{der}	Thickness of product layer on skin (default 0.01 cm)	[cm]
A_{skin}	Surface area of the exposed skin	[cm^2]
BW	Body weight	[kg]
N	Mean number of events per day	[d^{-1}]
Output	**Description**	**Unit**
C_{der}	Dermal concentration of substance on skin	[$mg \cdot cm^{-3}$]
L_{der}	Amount of substance on skin area per event	[$mg.cm^{-2}$]
D_{der}	Amount of substance (external dose) that can potentially be taken up (account later for actual dermal absorption) per body weight	[$mg \cdot kg_{bw}^{-1} \cdot d^{-1}$]
Further applications	**Description (see the text below)**	
V^*_{appl}	Volume of diluted product actually remaining on the skin	[cm^3]
Fc_{der}	Fraction of the applied product remaining on the skin	[-]

The above dermal equations also apply to:

a non-volatile substance in a medium used without further dilution. In this case the dilution factor (D) is set to 1;

a non-volatile substance contained in an undiluted medium removed from the skin by, for example, wiping or rinsing and drying (e.g., liquid soap). Recalculate the V^*_{appl} "real" volume of application based on volume of application ($V_{appl)}$ as $V^*_{appl}=V_{appl} \cdot Fc_{der}$; where Fc_{der} is the fraction of the product remaining on the skin;

Example R.15- 1: Calculating dermal exposure to a substance in a solution

The identified use is a waterborne "Washing and cleaning products"

In this example, the undiluted cleaning product is a surfactant-water mixture, where the weight fraction of the surfactant (Fc_{prod} in **Error! Reference source not found.**) is 0.1 =10%). It is assumed that the density of the product can be set to 1 (RHO = 1 in Equation R.15-5) and thus the concentration of the substance in the undiluted product is 0.1 g/cm^3 or 100 g/L (C*prod* = 0.1 in Equation R.15- 5).

Exposure is calculated for a situation in which the hands are dipped into the diluted product. The concentration of the substance after dilution (dilution factor D = 40) is 0.0025 g/cm^3. The dermal concentration of substance on skin (C_{der}) is 2.5 mg/cm^3.

Error! Reference source not found. is applied to derive the dermal load to skin (L_{der}) by ultiplication of C_{der} with the thickness of layer (TH_{der}). The thickness of the layer in direct exchange with the skin is assumed to be 0.01 cm by default **Error! Reference source not ound.**).

$L_{der} = C_{der} \cdot TH_{der}$ = 2,5 mg/cm^3 * 0.01 cm = 0.025 mg/cm^2.

In a Tier 1 scenario, default parameters leading to worst-case assessment are applied. Accordingly, the body surface area of males is assumed, but the body weight of women (60 kg) is applied. The surface area of the exposed skin(A_{skin}) for hands (fronts and backs) for males is 840 cm².

Using the **Error! Reference source not found.**, the external dermal dose (in mg per kg body eight can be calculated.

$$D_{der} = \frac{L_{der} \cdot A_{skin} \cdot n}{BW}$$ = 0.025 mg/cm^2 *840 cm²* 1/60 kg = 0.35 mg/kg bw

RMMs are not considered in the quantitative exposure estimation because consumer compliance to the advice 'wear gloves while cleaning' cannot be ascertained. However, it is considered a good practice to add this as a labelling instruction for consumer use. In Tier 1 assessments, exposure times are not taken into account.

Dermal scenario B: a substance migrating from an article

The Tier I algorithm to calculate dermal exposure (e.g. dermal dose) to substance migrating from an article is similar to the equation presented in the previous paragraph for mixtures (e.g.) where:

- C_{der}, A_{skin}, n is referred to the article (i.e. concentration C of the substance in the article, skin surface A in contact with the article)
- TH (Thickness of product layer on skin) is generally set to 0.001 for article (instead of 0.01 for mixtures)

This algorithm is used in ECETOC TRA consumer tool (see section R.15.4)

R.15.3.3. Oral Exposure

Oral exposure is expressed as external dose (mg/kg bw). The parameters used are:

Weight fraction compound: the fraction of the compound in the product
Amount ingested: the total amount of product swallowed

Oral scenario A: exposure of a substance in a product during normal use

The concentration in the product as swallowed is calculated from:

$$C_{oral} = = \frac{C_{prod} \cdot 1000}{D} = \frac{RHO_{prod} \cdot Fc_{prod} \cdot 1000}{D} = \frac{Q_{prod} \cdot Fc_{prod} \cdot 1000}{V_{prod} \cdot D}$$ **Equation R.15- 8**

and the oral dose is then given by:

$$D_{oral} = \frac{F_{oral} \cdot V_{appl} \cdot C_{oral} \cdot n \cdot 1000}{BW} = \frac{Q_{prod} \cdot Fc_{prod} \cdot n \cdot 1000}{BW}$$ **Equation R.15- 9**

If an undiluted product is swallowed, D = 1.

Table R.15- 3: Explanation of symbols for oral scenario A

Input parameter	Description	Unit
C_{prod}	Concentration of substance in product before dilution	[g·cm^{-3}]
D	Dilution factor	[-]
RHO_{prod}	Density of product before dilution	[g·cm^{-3}]
Q_{prod}	Amount of product before dilution	[g]
Fc_{prod}	Weight fraction of substance in product before dilution	[g·g$_{prod}^{-1}$]
V_{prod}	Volume of product before dilution	[cm^3]
V_{appl}	Volume of diluted product per event in contact with mouth	[cm^3]
F_{oral}	Fraction of V_{appl} that is ingested (default = 1)	[-]
BW	Body weight	[kg]
N	Mean number of events per day	[d^{-1}]
Output	**Description**	**Unit**
C_{oral}	Concentration in ingested product	[mg.m^{-3}]

D_{oral}	Intake per day and body weight	[$mg.kg_{bw}^{-1}.d^{-1}$]

These equations may also be used to estimate exposures arising from ingestion of the non-respirable fraction of inhaled airborne particulates.

For some products, exposure due to hand mouth contact can be calculated (e.g. finger paints). The volume of product swallowed is related to the oral contact area A_{skin} and the thickness of product layer TH on that part of the hand (default 0.01 cm). It is assumed that 100% of substance present on the hand is transferred and available for ingestion.

Oral scenario B: exposure of a substance in an article during normal use

The Tier I algorithm for oral exposure to substance in an article is similar to those presented for a product. The only difference is how the amount (or volume) of product migrating from article and being ingested (Q_{prod} or V_{prod} in the previous algorithms) is calculated.

The volume of product swallowed is calculated based on the article area in contact with the mouth A_{skin} (default 10 cm2) and the thickness of article layer TH assumed to be in contact during mouthing (default 0.01 or 0.001 cm). It is assumed that 100% of substance present in the contact layer is transferred and available for ingestion.

V_{prod} (volume product swallowed) = A_{skin} x TH Equation R.15- 10

R.15.3.4. Exposure to non-volatile substances

Non-volatile substances (i.e. substances having low vapour pressure) can be released from products via migration (e.g. softeners) or by mechanical abrasion (e.g. pesticides, flame retardants), or by heating (e.g. soldering and welding, articles used at elevated temperature like candlewick or cake pan).

Because some of these substances can be found in house dust, house dust may present an important path for exposure to non-volatiles. In small children, exposure via house dust can account for about 50% of the total exposure (Wormuth, et al., 2006). Therefore, exposure via house dust may need to be considered when preparing a chemical safety assessment for REACH.

It is anticipated that non-volatiles occurring in any products used in private households may contribute to accumulation in house dust. For example, the substance in articles may become available for inhalation due to rubbing or while handling or working with the article (e.g. building materials, hobby materials etc.). The resulting dust can be inhaled. Therefore, use specific exposure via house dust is difficult to predict. House dust itself may lead to dermal exposure and in small children to oral exposure due to mouthing behaviour. A conservative estimate of 100 mg/day has been proposed for house dust intake for children (Oomen, et al., 2008).

In standard lower tier assessments using TRA consumer model with default values provided by the tool, ECETOC assumes that exposure to non-volatile substances via house dust is covered by the model exposure estimate (see discussion in Section R.15.4.2.). For higher tiers, the concentration of the substance of concern can be evaluated or measured in house dust and multiplied with the intake value mentioned above. For example, if the concentration of a substance in house dust is 1 µg/g, then the intake of the substance would be 0.1 µg/day.

R.15.4. The ECETOC TRA consumer tool for exposure estimation

ECETOC has released different versions of the TRA Consumer tool during recent years to better capture exposure refinement options, while maintaining algorithms for exposure estimation, which are largely based on Tier 1 algorithms documented in Section R.15.3 . Three recent versions of TRA are briefly described and compared with each other and to Tier 1 algorithms in Appendix R.15.4

References to be consulted for better comprehension of the TRA consumer tool are:

- "Addendum to ECETOC Targeted Risk Assessment Report No. 93 - Technical Report No. 107" - (ECETOC, 2009);
- "ECETOC TRA version 3: Background and Rationale for the Improvements - Technical Report No. 114" – (ECETOC, 2012)
- "Addendum to TR114: Technical Basis for the TRA v3.1 - Technical Report No. 124" (ECETOC, 2014)

The above mentioned documentation is freely available at http://www.ecetoc.org/tra. The description in the following paragraphs always refers to the latest version of TRA tool, ECETOC TRA Consumer v.3.1.

ECETOCTRA is the main consumer tool that allows batch processing of exposure calculations and risk characterisations for many product and article categories. The ECETOC TRA consumer tool Vs 3.1 is integrated in the CHEmical Safety Assessment and Reporting tool (CHESAR) developed by ECHA. Therefore, main features of the tool are presented in this guidance. However, the assessor will have to decide whether the assumptions that are integrated into the tool are suitable for the consumer uses and risks that he has to assess.

R.15.4.1. Consumer Product and Article Categories

The core concept of the TRA tool is to provide a setting of defaults for 46 specific product and article types relevant for consumer use. The product and article types driving the exposure estimate in the TRA are referenced to the broader product and article categories in the use descriptor system as presented in *Chapter R.12 of the IR&CSA guidance*.

In the initial assessment the TRA enables derivation of worst case exposure estimates for broad product categories (so called sentinels) which contain more specific product subcategories. If it turns out that adequate control of risk cannot be demonstrated on this basis, an assessment of the more specific product type can be launched. More than one sentinel product/article and/or product subcategory can be evaluated simultaneously, but the tool will not aggregate the exposure estimates. The product/article categories and subcategories for which a TRA exposure estimate can be derived are listed in Appendix R.15.1.

This list does not include all types of consumer products. A registrant under REACH cannot rely on this list as giving the complete overview on which consumer uses of the substance he potentially has to assess. If a category of interest is not addressed by the TRA, then the registrant could check whether his products and use conditions can be approximated by some TRA categories, and if so make use of the TRA with appropriate justification of any deviations and adaptations. The registrant could also consider assessing the exposure by Tier 1 algorithm calculations (Section R.15.3) or by other tools like ConsExpo.

Moreover, ECETOC TRA enables the user to define a new (sub)product or article type, e.g. one not covered by the list in Appendix R.15.1 or being a specific product for which habits and practices and related input parameters are defined at the sector organisation level (so called SCED, see Chapter R.15.4.5). Single registrants are advised to select this functionality only when they use the products type and related input parameters as contained in the SCED proposed by sector organisations.

The user of the ECETOC TRA tool is advised always to check:

- If the use he wants to cover fits the (sub)category of product or article chosen
- If the scenario (e.g. target population covered, input parameters) described by the selected (sub) product or article category fits the use he wants to cover.

R.15.4.2. Input and output parameters

One algorithm per exposure route (dermal, oral, inhalation) is used to calculate the exposure for all consumer product and article categories. For the sentinel product/article, the exposure estimates for each route corresponds to the highest exposure estimate of the individual product/article subcategories within the sentinel. The algorithms for each exposure route are fully described in ECETOC Technical Reports TR 114 and TR 124. In the following text only input and output parameters are described.

Inhalation route

Output parameters

The ECETOC TRA calculates the inhalation exposure as

- concentration in room air (mg/m^3), resulting from one or more events of product/article application on the day of exposure;

Or as

- dose (amount per kg bodyweight) inhaled over the duration of the event (depending on the product category 20 min to 8h).

Input parameters – Lower tier standard calculation

- Product ingredient (g/g): ECETOC TRA provides a default for each product or article type; this can normally be overwritten by the user;
- Amount of product used per application (g/event): ECETOC TRA provides a default for each product or article type; this can be overwritten by the user, who has to support his choice with proper justification;
- Spray application: ECETOC TRA provides a default for each product type (whether the product is intended to be sprayed or not); for some "not spray" products, the default setting can be modified by the user (from "not spray" to "spray");
- Frequency of use (events/day): the default value is assigned for each product type (normally 1 event/day) and is not modifiable by the user;
- Exposure time (hr): the default value is assigned for each product type and is not modifiable, unless a new (sub)product category is defined by the user;

The chemical physical parameters needed to run the exposure assessment are reported below:

- Molecular weight (g/mol), which enables the calculation of the saturated vapour concentration
- Vapour pressure (Pa), which enables the calculation of the saturated vapour concentration and fraction released to air (see table below).

For substances with a vapour pressure < 10 Pa in non-spray application, only a fraction of the substance in the products or article is assumed to be transferred to air (vapour pressure bands

A to D, see Table R.15- 4).

Table R.15- 4: Vapour pressure bands

Vapour pressure of compound of interest	Released % of the amount available for instantaneous release	Band
≥ 10 Pa	all compound	A
between 1 and 10 Pa	10 % of the compound	B
between 0.1 and 1 Pa	1 % of the compound	C
< 0.1 Pa	0.1 % of the compound	D

Any substance with a vapour pressure higher than 10 Pa is assumed to be completely released into air instantly. For a substance with low volatility only a fraction of it is assumed to be released into the air. However, for all spray products it is assumed that substances are released fully and instantly into the air.

Note: for activities taking place at a temperature different from ambient temperature (e.g. dishwashing products), the vapour pressure of the substance should be adapted to the process temperature; in such a case, the operating temperature should be reported in the exposure scenario as well.

ECETOC TRA algorithm does not address exposure to house dust, since releases from a product or an article are driven by the substance's vapour pressure. However, ECETOC assumes that the TRA tool covers also the exposure of non volatile compounds, such as flame retardants and plasticizers in house dust. This because the tool assumes that 0.1 % of the non volatile compound evaporates immediately and is inhaled in the standard room with standard ventilation. Therefore, ECETOC assumes also that this exposure covers not only the inhalation exposure, but also the dermal and oral exposure to this substance via house dust.

Note: the tool does not cover exposure arising from dusty materials or from dust-generating consumers' activities, since releases from a product are driven by the substance's vapour pressure.

Dermal route – Lower tier standard calculation

Output parameter

External dermal dose (expressed in mg/kg bw / day) over the day of exposure, resulting from one or more events of product/article application.

Input parameter

- Product ingredient (g/g): ECETOC TRA provides a default for each product and article type; this can be normally overwritten by the user
- Skin contact areas: ECETOC TRA provides a default for each product and article type according to one of eight categories (see below), each one is characterized by a default surface area for adults and children. This can be overwritten by the user, who has to support his choice with proper justification; if the selected target group is children, then the dose is adjusted to the child body weight.

- Frequency of use (events/days): the default value is assigned for each product type (normally 1 event/day) and is not modifiable by the user
- Thickness layer (cm): represents the thickness of the layer in contact with the skin and it is set to 0,01 for mixtures and 0,001 for articles; it is not modifiable by the user

Note: the dermal model only covers direct contact with the product or article, which in most cases can be considered the predominant route for dermal exposure; indirect dermal contact (e.g. via vapours or spray clouds) is not covered by the tool. The skin contact areas linked to product/article subcategories can be expressed in one of ten categories each characterized by a default surface area for adults and children:
1 – fingertips
2 – two fingerprints
3 – palm of one hand
4 - inside (palms) of both hands / one hand
5 - hands
6 - hands and forearms
7 - upper part of the body
8 - lower part of the body
9 - whole body except feet, hands and head
10 - whole body

Oral route – Lower tier standard calculation

Output parameter

External oral dose (expressed in mg/kg bw /day) over the day of exposure, resulting from one or more events of product/article application

Input parameter

- Product ingredient (g/g): ECETOC TRA a provides default for each product type; this can be normally overwritten by the user
- Volume of product swallowed: ECETOC TRA provides a default for each product or article type. The volume for some product or article categories depend on the contact surface area and thickness of the layer (see discussion in **Error! Reference source not ound.**– Oral route – Scenario B). In such cases, the user can overwrite default surface area, providing proper justification.
- Frequency of use (events/days): the default value is assigned for each product type (normally 1 event/day) and is not modifiable by the user

REACH does not deal with accidents or assessment of consumer exposure to food, food-related or pharmaceutical products. This limits the relevance of consumer oral exposure to situations where: i) substances as such or in mixtures are unintentionally swallowed (e.g. ingestion through hand-mouth contact) or ii) where articles are mouthed by small children.

Higher tier option in ECETOC tool

ECETOC TRA offers the option to perform additional refinement calculations which are beyond the first tier approach. Therefore, they need careful considerations by the assessor, including the issues discussed under 15.2.5 and 15.3. These refinement calculations are based on the following additional input parameters:

- **Transfer factor (Inhalation, Dermal, Oral)**. For the inhalation route this factor may be used to reduce the amount of substance (as such or in a mixture) to the amount actually available for instant release. For example, during tank filling with 70 l of gasoline, not all these 70 l are available to be released into air. The inhalation transfer factor (amount of the substance actually available for being released into the air) should not be confused with the fraction releases to air (driven by vapour pressure). For the dermal route the factor may be used if there is evidence that the dermal load on skin in

the dermal contact area is smaller than the load resulting from instantaneous release of all substance present in 0.01 cm (respectively 0.001 cm) contact layer. If the transfer factors are set to a value different from default (100%), a scientifically sound and robust argumentation should be provided by the registrant to justify the proposed value. If he cannot rely on peer-reviewed scientific exposure studies, it is highly unlikely that the necessary knowledge to justify transfer factors would be available at the level of a single registrant; therefore the advice is to use the transfer factors only in the context of SCEDs developed at the sector organization level (e.g. consumer product formulators or article producers or importers, see Section R.15.2.6).

- **Frequency over the year**. Only when a new (sub)product category is defined, the user can chose to set the frequency band (frequent, occasional, infrequent, very infrequent) over the year. Compared to the frequent (daily) exposure, the exposure would be reduced up to a factor of 100 by this procedure. However, following the considerations in Section R.15.2.3 of this guidance, it cannot be advised to use this function as it is. If the conditions for occasional use set under R.15.2.3 are met, a standard factor of 0.2 can be applied to the risk characterization for long-term effects instead.

- **Outdoor/Indoor use**. Only when a new (sub)product category is defined, the user can select an outdoor instead of an indoor use in order to refine the calculation for the inhalation route. The registrant should consider that due to the many influences on outdoor air dispersion in a housing environment, the assumption of equal distribution of the substance in outdoor air may not be valid. Especially for spray products, a peak exposure in a smaller space has to be assumed and this function should not be used.

R.15.4.3. Default values

Default values associated with subcategories, such as amount of product used per application and exposure time (for the inhalation route), were obtained from the RIVM (The National Institute for Public Health and the Environment, Netherlands) fact sheets for specific products, in order to build consistency with ConsExpo. When product-specific fact sheets were unavailable, values were derived using expert judgment. The supporting reference for the default values used to calculate exposure can be viewed for each subcategory in the 'defaults' table. Only potentially significant exposure routes are 'flagged' for exposure assessment. A qualitative justification of why a particular route is not relevant for a particular product is provided in the documentation of the tool.

In some cases one route is more dominant than others. Then only the most dominant route is described, for instance dermal exposure for grease pastes (PC24), the inhalation exposure for spray application of aircare products (PC3) and dermal exposure for fertilizers (PC12). This is important to realize, especially for situations where the most dominant route can be excluded, e.g. due to product characteristics. Exposure for the other route(s) should then still be considered. This means that it needs to be checked, whether the contribution of the second route becomes significant if exposure for the primary route is reduced to a large extent.

Use scenarios have been defined for all product and article subcategories according to the potential exposure of consumers to these (sub)categories. The defaults used are presented in the "defaults" table of the tool. The references for the defaults (RIVM reports, conservative expert estimates) are specified in Appendix E of the ECETOC Technical report 107 (ECETOC 2009). Default values such as body weight, surface area, room volume and ventilation rate were obtained from the RIVM general fact sheet (Bremmer, et al., 2006).

R.15.5. Advanced refinements, higher tier models and measurements

More advanced refinement of exposure calculation and higher tier models may include, for example, the consideration of time-dependent processes of migration and release of the substance from a matrix, the deposition (adsorption) to other matrices (e.g. dust) and its release (desorption) as well as the disappearance from the medium (e.g. by decrease of room air concentrations due to ventilation or degradation). Expert assessors should normally conduct these assessments.

Higher tier consumer exposure estimation uses more sophisticated and detailed and more realistic parameters than Tier 1 tools. Therefore, a detailed description of the scenario and reference to the models used for calculations, including all assumptions and results should be reported in the CSR.

R.15.5.1. ConsExpo

The ConsExpo (version 4.1) computer tool (downloadable from www.consexpo.nl) is a well-known higher Tier tool for expert consumer exposure assessment. All the equations used are published in the ConsExpo manual (Delmaar, et al., 2005). An evaluation of the higher tier models showed that ConsExpo has a reasonable coverage of many other available higher tier models (Park MVDZ, 2006). If parameters are specified as distributions, ConsExpo can perform a distributed (Monte Carlo) calculation. The program will draw a set of random numbers from the specified distributions (uniform, normal, lognormal, triangular) for distributed parameters and calculate the endpoint of choice with this set. For the non-distributed parameters the specified point value is taken. Exposure and dose distributions reflect stochastic parameters and these distributions can be depicted and percentiles can be quantified. The program can provide sensitivity analyses for each stochastic parameter, where mean exposures or doses as a function of the value of a selected stochastic parameter are depicted and analysed. The ConsExpo model contains an associated database reflecting the RIVM factsheets, which contains default parameters for a large number of consumer products and scenarios (higher tier, see www.consexpo.nl).

Inhalation exposure

The concentration of a chemical in room air will depend on the amount of chemical present in the room, the room size, ventilation of the room, vapour pressure of the compound and the rate at which the compound is released into the air. A refined estimation should consider time. Modelling exposure therefore requires data that describe the duration of use and the duration of primary and secondary exposure. For instance, 1 kg of paint may be used over a period of 2 hours, followed by secondary exposure of 10 hours, which must be considered by the model chosen for estimating this exposure. As a further additional variable, room ventilation has to be taken into account for inhalation exposure. Depending on the information available on physicochemical properties of the compound and the use of the product, different models are available in ConsExpo.

The instantaneous release model. The model assumes that all compound is released from the product at once into the room. When the ventilation rate is set at 0, this will result in the Tier 1 algorithms as described in **Error! Reference source not found.**. The model is comparable to he ECETOC TRA inhalation model when the ventilation rate is set to 0.6 exchange per hours and the volume of the room is set to 20 m^3.

The constant rate model describes the release of a compound with a constant rate of release over a certain period of time. During this time, the compound is simultaneously removed from the air by ventilation of the room. In addition to the parameters used in the Tier 1 inhalation model, the constant rate model also uses the emission duration, i.e. the time during which the compound is released.

The evaporation model describes the release of the compound from the surface of the product

by evaporation, and can be used if information on the application duration, the release area and the release rate of the compound from the product is available. The release rate is estimated from the temperature, the molecular weight, vapour pressure, and the mass transfer rate (the coefficient, which describes the transport conditions from the boundary layer immediately above the liquid surface). The tool is suitable to estimate releases from mixtures, not from articles; for the latter, a more targeted model (Section R.15.5.2.1) has been developed by RIVM.

The spray model describes the indoor inhalation exposure to slowly evaporating or non-volatile compounds in droplets that are released from a spray can. For volatile substances released from a spray can, the evaporation model should be used to calculate exposure to the volatiles. Inhalation is influenced by many factors such as the size of the droplets, the breathing pattern and human physiology. Only droplets that penetrate to the alveolar region will reach the lung-blood barrier and give rise to inhalation exposure.

General exposure parameters needed for this model are spray duration, exposure duration, room volume, room height, ventilation rate and spray direction. The specific spray parameters are the mass generation rate, the airborne fraction, the weight fraction of non-volatiles, the mass density of the total of non-volatile compounds, the weight fraction of the substance in the mixture, and the initial particle distribution.

Dermal exposure

For higher tier assessments, extractability of substances from articles e.g. textiles should be considered. For migrating substances, only the part of the total amount available to/in contact with the skin is able to penetrate the skin. The models estimating dermal exposure in ConsExpo are described here below.

The instant application model describes a low tier estimate. The model does not include the product layer thickness that is included in Tier I algorithms in **Error! Reference source not ound.** and ECETOC TRA.

Constant Rate model. Similarly to the Tier 1 'dermal scenario A' model, the constant rate model assumes that any compound in the product is directly applied to the skin. The model calculates the amount of product per unit surface area of skin or per kg of body weight over a period of time. Therefore, if a good estimate can be made of the time during which the compound is applied, this mode can be used instead of the instant application mode. Two additional parameters are required for this mode: the release duration and the rate at which the product is applied to the skin.

Rubbing Off model. This describes a secondary exposure situation in which a surface (table top, floor) is treated with a product and dermal exposure arises from contact with the treated surface. The additional parameters used in this model are the transfer coefficient (treated surface area in contact with skin/ time), the dislodgeable amount, the contact time and the rubbed surface.

Diffusion model. This describes the diffusion of substance into skin due to direct application of a product to the skin. After application, the compound diffuses through the product to the skin. The diffusion model can be used if the diffusion coefficient of the compound in the product is known or can be estimated. The model requires the following additional parameters: the diffusion coefficient, the layer thickness of the applied product and the exposure time.

Migration model. This describes the migration of a compound from a material to the skin when dermal contact with the material occurs. The migration is specified as a 'leachable fraction': the amount of substance that migrates to the skin per unit amount of product. Typically, this fraction has to be determined in extraction experiments with sweat simulant. This model can be used, for instance, to estimate exposure to dyes leaching from clothing to the skin.

Oral exposure

The models estimating oral exposure in ConsExpo are described here below.

The direct intake model describes a low tier estimate, and is comparable to the algorithm described in **Error! Reference source not found.** and in Section R.15.4 (ECETOC TRA tool).

Constant Rate model. This describes a scenario in which the compound is taken in over a certain period of time, e.g. to estimate (secondary) exposure originating from dermal exposure on the hands and subsequent hand-mouth contact. The additional parameters used in this model are ingestion rate and exposure time.

Oral Migration from Packaging Material. This secondary exposure model calculates the exposure to compounds from packaging material via food[5]. The migration of the compound into the food is calculated from the concentration of the compound in the packaging material, the contact area of the packaging and the food and the initial migration rate. The oral exposure resulting from food consumption is subsequently calculated by assuming that the migrated compound is homogeneously distributed over the food and that the intake of the compound is therefore proportional to the fraction of packaged food consumed.

R.15.5.2. Other tools

There are sector specific tools, largely based on Tier I algorithms, where habits and practices from sector organizations are specified and used as input parameters. Two models need to be mentioned:

- AISE (International Association for Soaps, Detergents and Maintenance Products) has developed a model, REACT Consumer Tool, which allows quantitative estimation of exposure to substances that are present in products (washing and cleaning - PC 35, air freshener – PC3 and polishes and wax – PC31) used by consumers. The tool calculates exposure via inhalation, dermal, and oral routes separately and also provides a summation of all the relevant exposure routes. The model uses as input parameter habits and practices coming from HERA Project (see Appendix R.15.2). It should be noted that the tool does not cover the evaporation of volatile substances from the product, since it considers the inhalation route relevant for spray applications only. The tool is freely available on the AISE website (www.aise.eu).
- ESIG (European Solvent Industry Group) has developed the EGRET consumer tool (2010). The tool takes the default assumptions and algorithms (equations) described in the ECETOC TRA, but it introduces refined default values for those product categories relevant to solvents. Since the tool addresses all Product Categories (PC) potentially applicable to solvents, additional PCs (not assessed by ECETOC TRA) are covered by the ESIG tool (e.g. anti-freezing and de-icing products – PC4, different fuel products – PC13, functional fluids – PC17). Relevant characteristics of the tool are presented hereafter. First, the tool suggest refined default values for product and article subcategories which are not fully justified and agreed among stakeholder (as is the case for the ECETOC TRA tool). Second, the model introduces automatic refinement if the event exposure exceed the long term DNEL. Some of these refinements consist in additional measures on the part of the consumer and may not be easy to communicate or implement (e.g. "open windows"); or linear averaging of the event exposure over the day and over the year, which might be in contradiction with provisions reported in Section

[5] ConsExpo model covers consumer exposure situations beyond the scope of REACH. Please note that. exposure from food or food-related products is outside the scope of REACH.

R.15.2.3. The tool is freely available at ESIG website (www.esig.org)[6].

Several previous route-specific models and general consumer exposure models are now integrated into the US EPA E-Fast model (US EPA, 2015) (see Computer tools for estimation of consumer exposure, Appendix R.15.3).

Other potentially relevant tools are also described in Appendix R.15.3.

R.15.5.2.1 Substances in articles

Regarding the exposure to substance in articles, RIVM has developed (2010) the Emission Model to specifically estimate the inhalation exposure after release of chemicals from solid materials (Delmaar, 2010). The model takes into account the diffusion of a substance in a material, the mass transfer from material into air and removal of the substance from residential air by ventilation. The tool simulates time profiles of the air concentration and mean air concentrations arising from emission. The model is based on well-established modelling of emissions from building materials, and is designed for specific shapes (e.g. slab like articles like panels, flooring, etc.); extrapolation to other shapes may introduce an unknown degree of uncertainty. The model, its underlying assumptions and an overview of available input data and methods to estimate key input parameters are described in (Delmaar, 2010). The program is freely available for download from www.consexpo.com.

R.15.5.3. Overview of the consumer estimation tools

Table R.15- 5 below shows an overview of the modelling tools mentioned in Sections R.15.4 and R.15.5. It includes a brief description of the tools, the main characteristics and the tool boundaries.

[6] Following feedback from users and stakeholders, notably discussions at ENES and experiences arising from the (mis) application of EGRET in some 2010 chemical safety assessments, ESIG initiated a revision of EGRET in 2014. The most recent version of EGRET (v.2) now accommodates improved functionalities to address this feedback and in particular to minimize potential misuse of the model in the future. The updated tool will be available in 2016.

Table R.15- 5: Overview of the consumer exposure estimation tools

Model	Summary	Main characteristics	Boundaries
ECETOC TRA v.3.1	Partially based Tier 1 algorithms (inhalation/dermal/oral) Allows batch processing of exposure calculations a for many PCs/ACs Default values provided for all PCs/ACs covered by the tool Possible to define a new product/article subcategory It is integrated in Chesar	It allows lower tier assessment as well as higher tier assessment when transfer factors, frequency bands and outdoor/indoor use are set by the user	The tool does not cover exposure arising from dusty materials or from dust-generating activities Indirect dermal contact (e.g. via vapours or spray clouds) is not covered by the tool
Consexpo	Higher tier model which contains 4 sub models for inhalation, 5 for dermal and 3 for oral exposure Possible to perform Montecarlo distribution (uncertainty analysis) Contains an associated database reflecting the RIVM factsheets, which contains default parameters for a large number of consumer products and scenarios	Consexpo contains mainly higher tier sub models, for which relevant number of input parameters is needed. If the scenario is not supported by RIVM factsheet, the registrant needs to estimate those parameter's values by himself	Evaporation model (inhalation) is not suitable to estimates exposure from solid material Spray model not suitable for estimate exposure from volatile substances in the sprayed product

Model	Summary	Main characteristics	Boundaries
EGRET	Based on the same principle of TRA v.3.1 (inhalation/dermal/oral). New products are added and default provided to cover solvent sector. New refined default are proposed for all the PCs covered by the tool	It allows lower tier assessment (as for TRA) as well as higher tier assessment when refined default values are proposed, transfer factors introduced, frequency over the day/year assumed (linear averaging), outdoor activities or extra ventilation assumed.	Same as TRA v. 3.1
REACT	Based largely on Tier 1algorithms (inhalation/dermal/oral). It contains several sub products within PC3, PC31, PC35. For all sub products default values coming from HERA project are given	Can be considered as Tier 1 tool with refined sub product categorisation (PC3, PC31, PC35) and refined default values assigned to them	The tool does not cover the evaporation of volatile substances from the product. It covers the inhalation route in case of spray products only
RIVM emission model	It estimates releases from solid materials to indoor air and subsequent inhalation exposure concentration in a room. It is based on Tier 2 algorithms which take diffusion and mass transfer mechanism from solid material to indoor air into account. Exposure are represented by profile concentration in indoor air for selected time	As Tier 2 tool, it requires input parameters such as diffusion, partitioning coefficient and mass transfer coefficients. Values and equation on how to derive them are reported for number of materials and substance's types in the tool supporting guidance	The tools does not cover releases from liquid mixture. It does cover slab like articles (e.g. panels, flooring) only

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R.15.5.4. Measurements

In general measured data are preferred over modelled data, provided that they are reliable and representative for the situation that needs to be assessed. For most consumer exposure scenarios, measurements of the actual exposure of consumers will not be available. However, it may be possible that for one or more of the parameters used in the estimations measurements are available and can be used to override the default values (see Appendix R.15.4 for room volumes, air exchange rates, migration rates, ad- and desorption as well as absorption rates). If needed, reasonable worst-case assumptions can be replaced by considering measured parameter values and their variability.

Exposure data, including releases from articles and room concentrations, might be generated within other legislation frameworks, such as the product safety legislation. The latter could be very interesting for an assessor under REACH since they may be already available for a representative range of conservative scenarios. For example, the Construction Products Regulation (CPR) might be a source of information to support the assessment under the REACH of some mixture or article used as building materials. Under this framework, some Member States (Belgium, France, Germany) require the testing of some construction products (e.g. floorings, adhesives) to measure the emissions to indoor air of some substances and simulates the indoor concentration arising from such releases. This testing is done in a standardised default "chamber test" (relative humidity 50% and temperature 23 C) according to the project European Standard prEN 16516.

There may be measurements of external exposure (i.e. concentrations in the environment in which the contact takes place) as well as measurements of internal exposure (e.g. in blood or tissues) available. Non-volatile substances may accumulate in house dust. For such substances, release from consumer articles e.g. furniture, textiles, and building material may be monitored by measurements performed in house dust. The uptake is then calculated by multiplying the concentrations with dust uptake defaults. Measurements of concentrations in house dust yield 'aggregate' values, including possibly the contribution of environmental sources or products not regulated under REACH, such as cosmetics. Such measurements are then to be regarded as upper limits of exposure. Monitoring data may be available e.g. on substances with a (potential) PBT or vPvB profile. Measured data have to be representative of the Exposure Scenario to be assessed, i.e. they reflect the conditions of use set in the ES.

Data from biomonitoring or occupational exposure programmes may be valuable for consumer exposure estimations, although their number, representativeness and quality will often vary widely. Measured data from surrogate substances or analogues and surrogate scenarios (e.g. chamber measurements) may also be useful when estimating exposure levels.

Several sources of measured data are reported in in Appendix R.15.2.

R.15.6. Risk Characterisation

Risk characterisation is expected to address both qualitative assessment (for hazards with no DNELs available) and quantitative assessment (hazards where DNELs are available) for each use and its contributing scenario.

- **Qualitative risk characterisation**: Provide the arguments that the conditions of use as described in the exposure scenario will make it unlikely that adverse effects occur. Most often this refers to hazards like irritation, corrosion and sensitisation. For the inhalation route exposure estimates may be helpful to demonstrate that exposure concentration is indeed limited to the minimum or absent. Where CMR substances with no threshold are to be assessed for consumer uses (potentially relevant for substances in article), the risk characterisation can additionally be referred to a Derived Minimum Effect Level (DMEL). If the estimated exposure is lower than the DMEL, the measures described to prevent exposure can be considered appropriate.
- **Quantitative risk characterisation**: Compare the estimated exposure on the relevant routes with the DNELs and derive risk characterisation ratios (RCR). The Tier 1 exposure estimation and/or information from higher tier tools/models and/ore measured data (if deemed necessary) can be used in the quantitative risk characterisation (see *Part E of the IR&CSA guidance*). If the exposure is below the DNEL, the risk is considered controlled (RCR < 1). For consumers regularly the risk is to be characterised against DNELs long-term systemic hazards. Depending on the duration and frequency of event and the substance properties (toxicity and half-life in body) a particular risk characterisation for acute or **short term single (infrequent)** exposure events may be appropriate. This may be based short-term DNELs or on long-term DNELs (using adjustment factors).

A risk characterisation is required for all uses and their contributing scenarios, differentiated according to routes of exposure. Risks from **combined exposure across the three routes** is to be characterised by building the sum of RCRs per contributing scenario.

For products designed for use by **children** or for consumer products for which the habits and practices of children significantly differ from those of adults (e.g. mouthing and crawling behaviour) particular risk characterisation for children should be provided. The assessment should be based on the specific body parameters of children.

According to REACH Annex I, the registrant should consider risks from **combined/(aggregated)[7] exposure across different uses** (products) relevant for his substance. He is, however, not obliged to carry out a risk characterisation related to uses of the substance not covered in his own registration."

Risks resulting from exposure to the substance via simultaneous use of different products can be taken into account (where relevant) through summing up of risk characterisation ratios for systemic effects across exposure scenarios. This may be relevant for instance when products are used routinely together (e.g. cleaning products) and the risk characterisation for the single product use is close to 1. Exposure to the substance via different products may be also relevant when averaging the event exposure over the day or when characterising the risk related to infrequent exposure. Exposure to the substances from other products might put into ques-

[7] Please note, that the REACH terminology is not fully aligned with the one used at OECD level with regard to the use "combined exposure or risk". Under REACH this always refers to one substance and not to combination of different substances.

tion the applicability of averaging over the day or assuming infrequent exposure only. For further information, see also (Karabelas, n.d.) and (von Goetz, n.d.).

In addition to direct exposure resulting from the use of products, the general population may be exposure to the substance **via the environment** (ambient air, drinking water and food). In the environmental assessment these routes are considered by default and the resulting risk characterisation for long-term systemic effects may need to be taken into account when assessing the overall exposure to a substance (see *Chapter R.16 of the IR&CSA Guidance explains* the assessment of exposure of man via the environment). I

The outcome of the risk characterisation is used to decide whether safe use can be demonstrated or if further iterations are needed. Once the final iteration has shown sufficient control of risks for consumers the assessment can be finalised. This is the case if i) the exposure estimates are below the DNEL and ii) the likelihood of effects due to irritation, corrosion and sensitisation or other non-threshold effects is negligible.

The RMMs and operational conditions ensuring control of risk for consumers (i.e. mainly the characteristics of a safe consumer product and the underlying assumption on habits and practices) should be documented in final exposure scenarios.

If certain consumer uses are not supported or are advised against due to health risks, this should be recorded in the CSR and communicated via the extended Safety Data Sheet (extended SDS).

In order to produce a meaningful risk characterisation it is important for the assessor to understand and take into account the uncertainties associated with the information/data that is provided (related to both hazard assessment and exposure assessment). The registrant is expected to include a reflection on the most significant uncertainties in his assessment into section 9.0 of the CSR. *Chapter R.19 of the Guidance on IR&CSA* contains more information on using uncertainty analysis.

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Appendix R.15.1 Consumer product and article categories

Chapter R.12 (on Use description) *of the Guidance on IR&CSA* provides lists of the Product Categories (PCs) and Article Categories (ACs). Table R.15- 6 and Table R.15- 7 list PCs and ACs which describe uses regulated by REACH and which are generally considered to potentially result in significant exposures of consumers. These PCs and ACs with specific subcategories can be assessed by using the ECETOC TRA consumer tool. The tables were agreed as a non exhaustive list of relevant consumer product and article categories upon by the ECHA consumer expert group comprised of representatives of ECHA, ECETOC, RIVM, BfR, INERIS and the Danish EPA during 2008-2009. The Table R.15- 7 also provides cross references between ACs as provided in Chapter R.12 and a list of AC subcategories proposed by ECETOC for the assessment. Please note that this list do not cover all the relevant consumer uses. (see Section R.15.4.1)

Table R.15- 6: Consumer products addressed in the consumer TRA

Descriptor	Product Subcategory
PC1:Adhesives, sealants	Glues, hobby use
	Glues DIY-use (carpet glue, tile glue, wood parquet glue)
	Glue from spray
	Sealants
PC3: Air care product	Air care, instant action (aerosol sprays)
	Air care, continuous action (solid & liquid)
PC9a:Coatings, paints , thinners, removers	Waterborne latex wall paint
	Solvent rich, high solid, water borne paint
	Aerosol spray can
	Removers (paint-, glue-, wall paper-, sealant-remover)
PC9b:Fillers, putties, plasters,	Fillers and putty

Descriptor	Product Subcategory
modelling clay	Plasters and floor equalizers
	Modelling clay
PC9c: Finger paints	Finger paints
PC12: Fertilizers	Lawn and garden preparations
PC13: Fuels	Liquids
PC24: Lubricants, greases, release products	Liquids
	Pastes
	Sprays
PC31: Polishes and wax blends	Polishes, wax / cream (floor, furniture, shoes)
	Polishes, spray (furniture, shoes)
PC35: Washing and cleaning products (including solvent based products)	Laundry and dish washing products
	Cleaners, liquids (all-purpose cleaners, sanitary products, floor cleaners, glass cleaners, carpet cleaners, metal cleaners)
	Cleaners, trigger sprays (all-purpose cleaners, sanitary products, glass cleaners)

Table R.15- 7: Article Categories addressed in the consumer TRA and cross reference to Article categories reported in *Chapter R.12*

Descriptor	Article subcategory (ECETOC)	Article category (Chapter R.12)
AC5:Fabrics,	Clothing (all kind of materials), towel	AC5f1:

Descriptor	Article subcategory (ECETOC)	Article category (Chapter R.12)
textiles and apparel		Fabrics, textiles and apparel : articles with intense direct dermal contact during normal use: clothing
	Bedding, mattress	AC5f2: Fabrics, textiles and apparel : articles with intense direct dermal contact during normal use: bedding and mattresses
	Toys (cuddly toy)	AC5b: Fabrics, textiles and apparel : toys intended for children's use (and child dedicated articles)
	Car seat, chair, flooring	AC5e: Fabrics, textiles and apparel : furniture & furnishing, including furniture coverings Or AC5a: Fabrics, textiles and apparel : large surface area articles
AC6: Leather articles	Purse, wallet, covering steering wheel (car)	AC6g: other leather articles
	Footwear (shoes, boots)	AC6f: Leather articles : article with intense direct dermal contact during normal use
	Furniture (sofa)	AC6e: Leather articles : furniture & furnishing, including furniture coverings
AC8:Paper articles	Diapers	AC8f1: Paper articles: articles with intense direct dermal contact during normal use: personal hygiene articles
	Sanitary towels	AC8f1: Paper articles: articles with intense direct dermal contact during normal use: personal hygiene articles
	Tissues, paper towels, wet tissues, toilet paper	AC8f1: Paper articles: articles with intense direct dermal contact during

Descriptor	Article subcategory (ECETOC)	Article category (Chapter R.12)
		normal use: personal hygiene articles
	Printed paper (papers, magazines, books)	AC8f2: Paper articles: articles with intense direct dermal contact during normal use: printed articles with dermal contact in normal conditions of use
AC10:Rubber articles	Rubber handles, tyres	AC10e: Rubber articles: furniture & furnishing, including furniture cover-ings Or AC10g: other rubber articles
	Flooring	AC10a: Rubber articles: large surface area articles
	Footwear (shoes, boots)	AC10f: Rubber articles: article with intense direct dermal contact during normal use
	Rubber toys	AC10b: Rubber articles: toys intend-ed for children's use (and child dedi-cated articles)
AC11:Wood articles	Furniture (chair)	AC11e: Wood articles: furniture & furnishings
	Walls and flooring (also applicable to non-wood materials)	AC11a: Wood articles: large surface area articles
	Small toys (car, train)	AC11b: Wood articles: toys intended for children's use (and child dedicated articles)
	Toys, outdoor equipment	AC11f: Wood articles: articles with intense direct dermal contact during normal use
AC13:Plastic articles	Plastic, larger articles (plastic chair, PVC-flooring, lawn mower, PC)	AC13a: Plastic articles: large surface area articles

Descriptor	Article subcategory (ECETOC)	Article category (Chapter R.12)
		Or AC13e: Plastic articles: furniture & furnishing, including furniture coverings Or AC13g: Other plastic articles
	Toys (doll, car, animals, teething rings)	AC13b: Plastic articles: toys intended for children's use (and child dedicated articles)
	Plastic, small articles (ball pen, mobile phone)	AC13f: Plastic articles: articles with intense direct dermal contact during normal use

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Appendix R.15.2 Valuable sources on exposure data

Main EU consumer exposure databases

BUMAC Database

The BUMAC database is a well-designed consumer product emission database created within the framework of the EPHECT Project. The EPHECT Project focuses its efforts on European use and use patterns of relevant consumer products and contributes to a better understanding of multiple exposures to air pollutants emitted by typical household products. The specific objective of the BUMAC database is the creation of a database on the state-of-the-art of emissions and health end points from consumer products. The primary purposes of the database development were to: a) Create an overview of the available consumer products emission data; b) Create an overview of the existing data gaps.

The BUMAC database is set-up as a compilation of data on the current state-of-the-art on consumer product compositions and emissions, on test chamber experimental results, exposures, risks and health end points. Qualitative data were assured by using only data outcomes from procedures derived from standardized emission test protocols. The key indoor air pollutants and emerging pollutants studied constitute of (1) compounds prioritized by relevant international concerted actions or international organizations, such as INDEX, BUMA and WHO and (2) compounds reported in open literature as (potential) hazardous and occurring in this type of consumer products. They include gaseous and particulate matter emissions, secondary reactions and degradations of coated surfaces. The database allows a clear view on current research gaps.

The database is accessible via the webpage of EPHECT Project:
https://esites.vito.be/sites/ephect/Pages/home.aspx

IPCheM Database

IPCheM - the Information Platform for Chemical Monitoring - is a single access point for locating and retrieving chemical monitoring data collections managed and available to 'European Commission, European Agencies, Member States, international and national organisations and researchers. The Platform aims to support a more coordinated approach to collecting, storing and accessing monitoring data on chemicals and chemical mixtures, in humans and in the environment. IPCheM is a de-centralised system, providing remote access to existing information systems and data providers. The database contains also a "Product and indoor air module" associated to exposure inside the buildings. Indoor and outdoor sources of air pollution include chemical emissions from construction and consumer products. The Joint Research Centre Institute for Health and Consumer Protection is responsible for this module.

The database is accessible via the link: https://ipchem.jrc.ec.europa.eu/ and it will be soon available to general public.

1 **Table R.15- 8: Further information**

Acro-nym	Full name	Country	Remarks	Contact
AIHC	American industrial health council (1994). Exposure factors handbook	US	Anthropometric data on adults and children, behaviour data, given as distributions	Update coordinator, Suite 760, 2001 Pennsylvania Ave. NW, Washington DC 20006-1807
BgVV-ZEBS	Zentralstelle zur Erfassung und Bewertung von Stoffen in Lebensmitteln	DE	Food monitoring, focus to Germany	Federal Institute for Health Protection of Consumers and Veterinary Medicine, Berlin, Germany 49 1888 412 0
BVL	Federal office for Consumer Protection and Food Safety Food monitoring, focus to Germany	DE	Food contamination data from market surveillance programs	BVL Dienstsitz Berlin-Mitte Mauerstr. 39 – 42 10117 Berlin www.bvl.bund.de
CEPA	Air toxic Hot Spots Program Risk Assessment Guidelines Californian Environmental Protection Agency.	US	Part IV Technical Support for Exposure Assessment and Stochastic Analysis	www.oehha.ca.gov/air/hot_spots/finalStoc.html
CH-PR	Swiss product register	CH	Product information, given on request	Contact: Dr P. Bormann, Swiss Federal Health Office, Bern, Switzerland
ECETOC	Exposure Factors Sourcebook for European Populations (with focus on UK data)	EU	Probability analysis Anthropometrics Time activity patterns	www.ecetoc.org
IFL	Industrieverband Farben und Lacke	DE	National industrial association, focus on paints, lacquers	www.farbeundlack.de

Acro-nym	Full name	Country	Remarks	Contact
IKW	Industrieverband Körperpflege und Waschmittel	DE	National industrial association, focus on household preparations (mixtures)	www.ikw.org
IVA	Industrieverband Agrar	DE	National industrial association, focus on agricultural preparations (mixtures)	http://www.iva.de
JRC-IHCP	European Exposure Factors (ExpoFacts) Sourcebook (based on CEFIC-LRI project)	30 European countries: EU member states in addition to Iceland, Norway and Switzerland	Database of statistics and reference factors affecting exposure to environmental contaminants	http://expofacts.jrc.ec.europa.eu
	The Danish EPA	DK	Study reports on chemicals in consumer products and articles	http://www.mst.dk/English/
ChEmiTecs	Swedish EPA	SWE	Research and studies on emission of organic chemicals from articles	http://www.chemitecs.se/
Kemikalieinspektionen	Kemi	SWE	Webpage on mass flow analysis of substances, statistics on use of chemicals in Sweden	http://www.kemi.se
PR-D	Product data base according to regulations of chemical law	DE	Product information	Federal Institute for Health Protection of Consumers and Veterinary Medicine, Berlin, Germany 49 1888 412 0
PR-FIN (KETU)	Finnish product register	FIN	Product information	www.valvira.fi

Acro-nym	Full name	Country	Remarks	Contact
	Climate and Pollution Agency	NO	Webpage on various substances found in articles	http://www.klif.no
	Finland's environmental administration	FIN	Information of substances in textiles can be found here	http://www.ymparisto.fi/
DTU	Food. National food institute	DK	Information on migration from food packet materials.	http://www.food.dtu.dk
OECD	OECD Task Force exposure assessment		Work on consumer exposure ongoing	http://www.oecd.org/chemicalsafety/assessmentofchemicals/oecdactivitiesonexposure-assessment.htm
EPHECT	VITO	BE	EU Project on consumer products to be potential sources of hazardous air pollutants in dwellings.	https://esites.vito.be/sites/ephect/Pages/home.aspx
RIVM	Emission tool report	NL	Information on emissions from articles related to consumer exposures	http://www.rivm.nl/dsresource?objectid=rivmp:24644&type=org&disposition=inline
PR-S	Swedish product register	SWE	Product information	www.kemi.se
PR-D	Danish product register	DK	Product information	http://www.at.dk/
SPIN	Nordic SPIN database	NO, SE, DK, FI, IS	Product information from the Nordic product registers	www.sft.no www.kemi.se http://www.at.dk/ www.valvira.fi www.vinnueftirlit.is

Acro-nym	Full name	Country	Remarks	Contact
RefXP	Exposure Factors Database Umweltbun-desamt	DE	Update of AUH data with proba-bilistic focus	http://www.umweltbundesamt.de/service-e/uba-datenbanken-e/index.htm
RIVM	(te Biesebeek, et al., 2014)	NL	General infor-mation, room volumes, room ventilation data	www.rivm.nl
RIVM-paint	Bremmer HJ, Van Engelen, JGM (2007) Factsheet paint	NL	Use data on paints, paint classification, characterisation of paint use, fo-cus on NL	www.rivm.nl
RIVM-DIY	Ter Burg W. et al. (2007) Factsheet Do It Yourself products	NL	Use data on do it yourself prod-ucts.	www.rivm.nl
US EPA	Environmental Protection Agency (1997). Exposure Factors Hand-book.	US	Substantial com-pilation of expo-sure factors	www.epa.gov
HERA	Human and Envi-ronmental Risk Assessments on ingredients of household clean-ing products	EU	Data on house-hold cleaning products, collect-ed by A.I.S.E and CEFIC	www.heraproject.com
VCI	Verband der chemischen In-dustrie	DE	National indus-trial association (all chemical in-dustries)	http://www.vci.de

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Appendix R.15.3 Computer tools for estimation of consumer exposure

INTRODUCTORY REMARKS

All the computer tools mentioned in this section can be helpful in performing exposure assessments. It has to be kept in mind while using them that they are designed to address different scenarios (e.g. routes, products or articles types) and thus reflect different scientific approaches. First of all, the assessor must be aware that the scenarios governing the model characterisation are different. For instance, the ConsExpo inhalation exposure scenarios (see Section R.15.5.1) are based on a one room lay-out, while the CEM program (US-EPA) considers exposure in a whole house with different rooms and differentiated scheme of times staying in the rooms throughout a day of users and non-users. It is clear that these differences in the scenario must lead to different results and the assessor has to document the reasons for favouring a specific model.

Note: This section does not discuss the models presented elsewhere in the guidance text, namely ECETOC TRA (Section R.15.4), ConsExpo (Section R.15.5.1) and other tools such as RIVM Emission tool (Section R.15.5.2).

US EPA Wall Paint Exposure Assessment Model (WPEM)

The Wall Paints Exposure Assessment Model (WPEM) estimates the potential exposure of consumers and workers to the chemicals emitted from wall paint which is applied using a roller or a brush. WPEM is a user-friendly, flexible software product that uses mathematical models developed from small chamber data to estimate the emissions of chemicals from oil-based (alkyd) and latex wall paint. This is then combined with detailed use, workload and occupancy data (e.g., amount of time spent in the painted room, etc.) to estimate exposure. The output of WPEM was evaluated in a home used by EPA for testing purposes and, in general, the results were within a factor of 2. The WPEM provides exposure estimates such as lifetime and average daily doses, lifetime and average daily concentrations, and peak concentrations.

Specific input parameters include: the type of paint (latex or alkyd) being assessed, density of the paint (default values available), and the chemical weight fraction, molecular weight, and vapour pressure. Occupancy and exposure data are provided by the model as default values but the model is designed to be flexible and the user may select other values for these inputs: activity patterns on weekdays/weekends for workers or occupants, and during the painting event; number of exposure events and years in lifetime; room size (volume); building type (e.g., office, single family home); number of rooms being painted; air exchange rates; etc. For those chemicals for which the mathematical emissions model does not apply, emissions data can be entered manually.

Status and availability

WPEM Version 3.2, a Windows-based tool is available. The model has been peer reviewed by experts outside EPA. This model was developed under contract for the EPA's Office of Pollution Prevention and Toxics, Economics, Exposure, and Technology Division, Exposure Assessment Branch. WPEM was developed under the Design for the Environment Program, Designing Wall Paints for the Indoor Environment. This project was accomplished in coordination and cooperation with the National Paint and Coatings Association (NPCA), in addition to paint manufacturers and chemical suppliers.

The model, user's guide and background document is available as a pdf file via http://www.epa.gov/oppt/exposure/.

Consumer Exposure Model (CEM)

The Economics, Exposure and Technology Division (EETD) of the Office of Pollution Prevention and Toxics (OPPT) of EPA is responsible for conducting specific activities in support of the Agency's risk assessment process. One of these responsibilities is to assess new and existing chemical substances under the Toxic Substances Control Act (TSCA). CEM, developed by Drewes and Peck (1999) is designed to provide EETD's Exposure Assessment Branch and Chemical Engineering Branch with an easy way to perform consumer inhalation and dermal exposure assessments for OPPT's new and existing chemical programs. The methods used to perform these assessments often involve generic screening-level techniques to allow exposures to be estimated rapidly. CEM has been programmed in C++/Windows and is designed to be run on a personal computer.

CEM is an interactive model which calculates conservative estimates of potential inhalation exposure and potential for absorption through dermal exposure to consumer products. Consumer inhalation exposures modelled in CEM use the same approach and calculations as the Multi-Chamber Concentration and Exposure Model (MCCEM), as well as scenarios depicted in the Screening -Level Consumer Inhalation Exposure Software (SCIES). Dermal exposures are modelled using the same approach and equations as the DERMAL Exposure Model. CEM allows for screening-level estimates of acute potential dose rates, and estimation of average and lifetime average daily dose rates. Because the model incorporates upper percentile and mean input values for various exposure factors in the calculation of potential exposures / doses, the exposure / dose estimates are considered “high end” to “bounding” estimates.

The dermal portion of CEM uses a film-thickness approach which assumes that exposure occurs from a thin layer of the consumer product on a defined skin surface area to determine potential exposure. Few data exist on the actual thickness of films of various products on human skin. Therefore, due to the uncertainty associated with the amount of product forming a film on the skin the dermal exposure estimates are considered less certain than those calculated in the inhalation portion of CEM. Absorbed dermal dose rates can be calculated using a permeability coefficient or a log octanol water coefficient, but these values and their use in calculating exposure also involves uncertainty. Absorbed exposure can only be calculated for the User-Defined Scenario in CEM.

The consumer exposure scenarios were selected for inclusion in the model by EETD because they are products or processes for which exposure assessments are most frequently performed during the new chemical review process. In addition to these scenarios, users are able to create their own scenario. CEM is user friendly and provides on-line help to assist the user in optimizing model use.

The CEM programme covers most of the scenarios needed for consumer exposure modelling. It should be noted that input data are needed for 50th and 95th percentiles.

CEM is now integrated in the E-Fast program, available via
http://www.epa.gov/oppt/exposure/pubs/efastdl.htm

US EPA Multi-Chamber Concentration and Exposure Model (MCCEM)

Features

The Multi-Chamber Concentration and Exposure Model (MCCEM) Version 1.2 (GEOMET, 1995) was developed for the US EPA Office of Pollution Prevention and Toxics to estimate indoor concentrations for chemicals released in residences). The features of MCCEM include:

MCCEM needs time-varying emission rates for a chemical in each zone of the residence and outdoor concentrations. The emission rates of pollutants can be entered into the model either as numbers or as formulas;
inhalation exposure levels are calculated from the estimated concentration if the user specifies the zone where an individual is located in a spreadsheet environment;
MCCEM has data sets containing infiltration and inter-zonal airflow rates for different types of residences in various geographic areas. The user can select from the data sets, or can input zone descriptions, volumes and airflow rates;
concentrations can be modelled in as many as four zones (chambers) of a residence;
the programme is capable of performing Monte Carlo simulation on several input parameters (i.e., infiltration rate, emission rate, decay rate, and outdoor concentration) for developing a range of estimates for zone-specific concentrations or inhalation exposures;
the programme has an option to conduct sensitivity analyses of the model results to a change in one or more of the input parameters;
the percentage of cases for which modelled contaminant concentrations are at or above a user-specified level of possible concern or interest is determined.

Theoretical

This multi-chamber mass-balance model has been developed by using air infiltration rates and corresponding inter-zonal air flows for a user-selected residence or a user-defined residence. This model provides a spreadsheet to the user for entering time-service data for emission rates in one or more zones, the zone of exposure, and concentration values of the contaminant outdoors.

Information assembled by Brookhaven National Laboratory concerning measured infiltration or exfiltration airflow, inter-zonal airflow, and the volume and description of each zone for different types of structures in various geographic areas has been incorporated in the software for access by users. Two generic houses represent average volume (408 m^3) and flow information in summer or fall/spring that has been compiled from a large number of residences. One generic house has a bedroom as the first zone and the remainder of the house as the second zone. The other, with the same total volume as the first, has a kitchen as the first zone and the remainder of the house as the second zone. The features of the generic houses are noted in the Exposure Factors Handbook (US EPA, 1997).

Remarks

The user's guideline listing good examples enable risk assessors to conduct the exposure assessment quite easily within MCCEM. In addition, MCCEM contains a database of various default house data that are needed to complete each calculation such as air-exchange rates, geographically based inter-room air flows, and house/room volumes. However, the so many data parameters might cause a confusion to risk assessors who aim to evaluate exposure for a typical population at the first Tier approach.

The MCCEM model is available via http://www.epa.gov/oppt/exposure/pubs/mccem.htm

INTERA – Cefic LRI Program

The INTERA computational platform is a web-based computer program that was developed in the framework of the CEFIC Long-range Research Initiative (LRI) funded INTERA project. It was developed to enable the exposure assessment of compounds in indoor settings over the "full-chain". The program offers a number of exposure models and a database containing several types of data. The data includes human physiological parameters, emission data from consumer products and from indoor concentration levels, and building characteristics. An exposure assessment in INTERA is a step-by-step process, starting with the basic information on chemical, products and the exposed population. Subsequently, suitable models are selected per exposure route, according to the product usage scenario.

All models for oral, dermal and inhalation route can be considered as higher tier models where for example release rates from products or sources is a requested input in the models. Moreover, most of the equations have been set in such way that they describe the internal exposure all as a function of time.

The model needs information on the substance of interest, the exposed subjects and residential settings and on the specific scenario. A scenario does not necessarily involve a consumer product or article and therefore the information requested is dependent on the scenario, following a step-wise approach. The input requested and not included in the database are substance-material specific release factors, such as the migration/release rates from products (oral and dermal), emission rates (inhalation), and concentrations in matrices (dermal and oral), this means that no default values are available for these parameters. Fraction absorbed from ingested quantities may also be requested from the user. Data included in the databases are human physiological data, residential settings and certain scenario parameters such as exposure durations, frequencies of use and skin areas contacted. For a number of substances, exposure information, e.g. indoor air concentrations of volatile substances are included in the database.

The output is given in amount of chemical taken up by the body as a function of time (µg/h or in mg/kg bw/d). Input and output can be presented as distributions. The user has the option to generate graphical representations of the exposure.

The driving factors for exposure are the concentrations in the matrices, the migration from the matrices and the duration of contact. If the internal exposure is calculated using a fraction, e.g. in case of ingestion where not all substance ingested will be taken up, then the fraction also is considered a driving factor for exposure. One of the basic assumptions is that the release from the matrices is constant over time, once contacted. In other words, the release of a substance is considered independent of its concentration in the matrix and no depletion of substance takes place (oral and dermal exposure). Diffusion process in materials is not taken into account. Regarding the air concentration, it is assumed that equilibrium will be reached immediately.

Uncertainty analyses are possible, since the use of distributions and Monte-Carlo Markov chain technique.

The INTERA computational platform is currently online at: http://www.intera.cperi.certh.gr/
The platform contains a user guide from which information can be obtained about the platform itself and the data and models that are included.

BAMA/FEA Indoor Air model

The BAMA Indoor Air Model is a simple but powerful tool, developed by British Aerosol Manufactures Association (BAMA) and European Aerosol Federation (FEA) that can be used to predict the concentration of aerosol components within a room after a suitable time interval after spraying. The Model can be used to rapidly generate predicted air concentrations for a wide range of use conditions for spray products. The model is particularly useful for generating time weighted values for estimating longer term exposure, for example longer than 90 minutes. Validation work shows that by that time, the volatile ingredients and aerodynamically stable particle (less than 10 μm) are well mixed in modelled volume (i.e. room) and larger particle have dropped out. Therefore, the model can be used to generate reliable estimates for exposure lasting more than 2 hours.

On the other hand, the tool has an important limitation when applied to the assessment of short term exposure, for example during the application of the spray product, since the model assumes an immediate and perfect mixing within the modelled room volume; in particular, for products sprayed away from the body or on horizontal surfaces, BAMA model is likely to overpredict short term exposure because the breathing zone will be outside the spray clouds. On the contrary, for products sprayed at the body or on vertical surfaces, the breathing zone will be in the spray cloud and the model will lead to an underestimation of the short term exposure.

Key parameters to run the model are: room volume, ventilation rate, ingredient fraction, discharge rate of the spray, duration of the spray.

The output parameters are different averaged air concentrations: 15 minutes, 4, 8, 16 and 24 hours averaged air concentrations in the room. Also exposure profile of the air concentration is given by the tool; it is also possible to model multiple spray events during one day.

The model is freely available at: http://www.bama.co.uk

Appendix R.15.4 Development of ECETOC TRA Consumer tool and comparison with Tier 1 Algorithms

ECETOC TRA Consumer tool version 2 (ECETOC, 2009) was the result of a substantial revision of the previous version TR 93 (ECETOC, 2004). TRA version 2 combined the conservatism of first Tier assessment tool with the expert knowledge documented in the RIVM fact sheets (see RIVM, http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp#Fact_sheets and Section R.15.4.3). It used default values taken from the RIVM fact sheets (except for the cases when no such value is available); main differences between ECETOC TRA consumer version 2 and the Tier 1 algorithms documented in Section R.15.3 can be summarised as follow:

- For the inhalation route the ECETOC algorithm includes a parameter for modifying the fraction of substance released to air for substances with a vapour pressure < 10 Pa in non-spray applications.
- For exposure from articles via the dermal route, the assumed thickness of layer in contact with skin is reduced from 0.01 cm (widely accepted default for mixtures and used already in EU existing chemicals risk assessment procedures) to 0.001 cm in order to take account of the reduced mobility of substances in an article matrix. The figure 0.001 cm was chosen based on expert judgement, as no scientific data was available.

The ECETOC TRA Consumer tool version 2 aimed to balance the Tier 1 assumptions and the generic applicability to a wide range of product categories in order to deliver reasonably plausible outcomes. For each product use category a rationale is available that justifies the basis of the default values and assumptions.

In 2012 ECETOC released the TRA Consumer version 3.0 where some refinement of the exposure have been made possible, while keeping the same structure (based on product or article category and subcategories) and algorithm of the version 2; these refinements are summarised here below:

- The calculation of saturated vapour concentration as the upper bound value of concentration of substance in air of the room is applied to all of the inhalation scenarios for non-spray products.
- Inhalation exposure estimates account for basic ventilation (default value of 0.6 air exchange per hour) in the standard room (20 m^3).
- Dermal and oral transfer factors have been introduced to potentially reduce dermal and oral exposure. By default both transfer factors are set to 1, assuming 100% of the substance is available for oral and dermal exposure; users with relevant, specific information or knowledge on the pattern of transfer of a substance from a product or article matrix to skin or mouth might reduce oral or dermal exposure by means of transfer factors.

In 2014 ECETOC released the TRA Consumer version 3.1, which incorporates all the changes mentioned above, with the possibility (already present in version 3.0, but now revised) for the user to create a new (sub)product or article category, setting all input parameters. This option has been introduced to support the creation of SCED (Specific Consumer Exposure Determinants) which are described in detail in Section R.15.2.6. The user, only while creating a new (sub)category, can also set the following new input parameters having an impact on the calculation of consumer exposure:

- The inhalation transfer factor (by default set to 1) in order to reduce the amount released to air during the use of the product or article; the user is advised to deviate from the default only when specific information supporting the choice is available.
- Select the outdoor scenario for consumer exposure; if selected, the "room" volume (100 m^3) and ventilation (2.5 air exchanges per hour) are increased compared to the indoor scenario, reducing the estimated air concentration.

- For short term and infrequent uses, is now possible to introduce a frequency over the year less than once per day, reducing the exposure estimation according to a factor depending on bands set by ECETOC. These bands are defined as follow: frequent uses (at least once a week, no reduction of exposure), occasional uses (between once a week and once a month), infrequent uses (between once a month and once every six month) and very infrequent uses (no more than once every six month).

The differences between generic Tier I algorithms (Section R.15.3) and ECETOC TRA Consumer tool (v.2, v.3.0 and v.3.1) are summarised in the table below.

Table R.15- 9: Differences between Tier I algorithms and ECETOC TRA consumer

Route of exposure	ECETOC TRA v. 2	ECETOC TRA v. 3.0	ECETOC TRA v. 3.1
Inhalation	Modifying factor for inhalation according to VP bands for VP <10 Pa	Modifying factor for inhalation according to VP bands for VP <10 Pa	Modifying factor for inhalation according to VP bands for VP <10 Pa
		Basic ventilation rate taken into account to reduce air concentration in standard room	Basic ventilation rate taken into account to reduce air concentration in standard room
		Upper bound for air concentration based on saturated Vapour concentration	Upper bound for air concentration based on saturated Vapour concentration
			Inhalation transfer factor introduced. Unless default is used (=1), this reduces air concentration*
			Possible to select that use takes place outdoor, which reduces air concentration compared to indoor uses*
			Reduction of the exposure by frequency over the year according to frequency bands (occasional, infrequent, very infrequent)*

Dermal	For exposure to article, the thickness of layer is set to 0.001 instead to 0.01	For exposure to article, the thickness of layer is set to 0.001 instead to 0.01	For exposure to article, the thickness of layer is set to 0.001 instead to 0.01
		Dermal transfer factor introduced. Unless default is used (=1), this reduces dermal dose	Dermal transfer factor introduced. Unless default is used (=1), this reduces dermal dose
			Reduction of the dose by frequency over the year according to frequency bands (occasional, infrequent, very infrequent)*
Oral		Oral transfer factor introduced. Unless default is used (=1), this reduces oral dose	Oral transfer factor introduced. Unless default is used (=1), this reduces dermal dose
			Reduction of the dose by frequency over the year according to frequency bands (occasional, infrequent, very infrequent)*

* Only possible when creating new (sub)product or article category

Appendix R.15.5 Demonstration of control of risks for Articles

Tier 1 algorithms to calculate exposure to substances in articles via all routes are reported and analysed in Section R.15.3, while more refined exposure estimation models are reported in Section 15.5. The aim of this appendix is to complete the information on exposure estimation already provided in the main text.

Dermal exposure to a substance migrating from an article

The exposure calculation will involve estimating the amount of substance which will migrate from the area of the article in contact with skin during the time of contact (for a screening assumption, consider 24 hrs). The essential parameters used for this model are:

Weight fraction compound: the fraction of the compound in the total product

Amount of product: the total amount of product applied to the skin

The surface area of the exposed skin

The migration rate of the substance

The contact time of the substance

Skin contact factor (set at 1 for default), a factor that can be used to account for the fact that the product is only partially in contact with the skin.

Examples of such potential exposure situations are skin contact with substances in textiles see (Krätke & Platzek, 2004) for details or printing ink from a newspaper or magazine. For migrating substances, only a fraction of the total amount of substance on the skin is able to reach the skin. It should be noted that it should be checked whether the estimated daily uptake exceeds the theoretical maximum. This maximum can be derived from the amount of product used (g), the concentration of the substance ($g.g^{-1}$) in the product, and the use frequency (d^{-1}). Extractability in simulated body fluids for several classes of dyestuffs and different fabric types has been evaluated by (ETAD, 1983)).

The dermal load is calculated as:

$$L_{der} = \frac{Q_{prod} \cdot Fc_{prod} \cdot Fc_{migr} \cdot F_{contact} \cdot T_{contact} \cdot 1000}{A_{skin}}$$

In case a surface density Sd_{prod} for an article is available (in mass per unit area), the equation reverts to:

$$L_{der} = SD_{prod} \cdot Fc_{prod} \cdot Fc_{migr} \cdot F_{contact} \cdot T_{contact}$$ **(Equation R.15- 11)**

The external dermal dose in mg per kg of bodyweight is then calculated as $\boldsymbol{D_{der} = \frac{L_{der} \cdot A_{skin} \cdot n}{BW}}$ (Equation R.15- 7):

$$D_{der} = \frac{L_{der} \cdot A_{skin} \cdot n}{BW}$$ **(Equation R.15- 12)**

Table R.15- 10: Explanation of symbols for dermal scenario B

Input parameter	Description	Unit
Q_{prod}	Amount of product used	[g]
Fc_{prod}	Weight fraction of substance in product	[$g \cdot g_{prod}^{-1}$]
Fc_{migr}	Rate (fraction) of substance migrating to skin per unit time	[$g \cdot g^{-1}.t^{-1}$]
$F_{contact}$	Fraction of contact area for skin, to account for the fact that the product is only partially in contact with the skin (default = 1)	[$cm^2.cm^{-2}$]
$T_{contact}$	Contact duration between article and skin	[d]
SD_{prod}	Surface density (mass per unit area)	[$mg \cdot cm^{-2}$]
A_{skin}	Area of contact between product and skin	[cm^2]
C_{der}	Dermal concentration of substance on skin	[$mg \cdot cm^{-3}$]
BW	Body weight	[kg]
n	Mean number of events per day	[d^{-1}]
Output	**Description**	**Unit**
L_{der}	Dermal load on the skin that is expected due to migration	[$mg.cm^{-2}$]

D_{der}	Dermal dose per day and body weight	$[mg \cdot kg_{bw}^{-1} \cdot d^{-1}]$

Other sources of information

For some classes of articles, release from articles during their service life is given in relevant OECD emission scenario documents (e.g., on plastic additives; OECD 2004). Although developed to estimate release rates to the environment, they can also serve as source of information to estimate consumer exposure (e.g. to estimate releases to indoor air).

ECHA has recently published an illustrative example on consumer exposure to substances in article[8]. While the example focuses on a specific semivolatile substance in building material, a general framework guiding the assessor to build exposure scenario and performing consumer exposure estimation for substances in articles is also provided.

[8] http://echa.europa.eu/documents/10162/13632/csr_sia_exposure_examples_en.pdf

Appendix R.15.6 Assessment of infrequent and short term exposure of consumers

Infrequent exposures are defined as exposures which do not occur regularly, but only occasionally and with rather wide intervals. It is assumed that such exposure occurs only for brief periods of up to a few hours. But there may be also infrequent uses with exposure for a few days in the row.

For the assessment of infrequent and short-term exposures of the general population (consumer), a risk characterisation is performed by comparing (calculated) exposure concentrations with a long-term DNEL, most often based on systemic effects specifically for the general population. This long-term DNEL is intended to reflect a continuous exposure to a substance for 24 h exposure per day, 365 days per year for a 70 years lifetime.

This long-term DNEL is usually derived from a no-observed adverse effect level (NOAEL) or a no-observed adverse effect concentration (NOAEC) arising from a toxicity study in experimental animals. This is achieved by adjusting the NOAEL(C) to human inhalation conditions, and by applying assessment factors for inter- and intra-species differences and duration (see ECHA Guidance R.8). In rare cases, the long-term DNEL is derived from human information.

In ECHA Guidance R.8 it is recommended to use the long-term DNEL to assess long-term as well as acute or short-term exposures.

However, it is recognised that for specific short-term uses, the long-term DNEL might be too conservative.

One alternative would be to use an acute DNEL for the risk characterisation. ECHA Guidance R.8, Appendix R.8.8 advises that an acute DNEL is required in case an acute toxicity hazard (leading to C&L) has been identified. Such acute DNEL is only established for the inhalation route and for effects of peak exposures. It could be set for a reference period of 15 minutes at 1-5 times the value (default 3) of the long-term DNEL depending on the specific conditions that apply. However, an acute DNEL focuses on acute effects following 15 minutes of exposure. Since infrequent or short-term consumer uses may be longer than 15 minutes per day, an acute DNEL might not be suitable to evaluate this type of exposure.

This appendix is intended to provide guidance on how to address infrequent and short-term exposures of consumers to make the risk characterisation more realistic. It focuses on human inhalation exposures only and on substances which are not classified for acute toxicity hazard.

To address infrequent and short-term oral and dermal human exposures, similar considerations could be applied as mentioned below, adjusted to the specific routes.

Studies that can be used to adjust the risk characterisation for short-term exposure

Acute toxicity study

To address short-term exposure, an acute toxicity study with a single exposure might appear the most appropriate starting point. However, acute toxicity studies performed according to OECD or EU test methods are usually not suitable to derive a robust NOAEL(C) for systemic effects because, e.g., the investigation focuses mainly on mortality and/or severe effects.

28-day sub-acute toxicity study

The study with the shortest duration that allows derivation of a NOAEL(C) or of a lowest observed adverse effect level/concentration (LOAEL(C)) is the 28-day sub-acute toxicity study (28-day study) performed with rats. This study does not investigate single exposure, but a continuous daily exposure over a defined period of about 4% of the lifetime of a rat. The test methods for sub-acute toxicity studies, which are OECD TG 407 for oral route, OECD TG 412 for inhalation and OECD TG 410 for dermal route, comprise an appropriate histopathological evaluation of the organs, the use of several dose groups (for low-toxicity substances with only one high (limit) dose group) and a minimum number of 5 animals per sex and dose group. Hence, LOAEL(C)s and NOAEL(C)s can be derived from those studies. Furthermore, a sub-acute toxicity study is a standard information requirement for REACH substances registered in quantities of 10 tonnes or more per year. Therefore, information on a sub-acute toxicity study should be available in most registrations. These studies offer an appropriate starting point to derive a concentration adjusted to short-term conditions that can be used for risk characterisation of infrequent consumer uses.

OECD 422 screening study

The OECD 422 screening study is a combination of a screening for reproductive toxicity and a short-term toxicity study. Male rats are exposed, usually orally, for 28 days, females for about 50 days. Since this study uses twice the number of animals compared to the 28-day study, the result (e.g., NOAEL or LOAEL) is more robust than that of the 28-day study. Within REACH, the OECD screening study can be used to cover the requirement for the 28-day study. Hence, the NOAEL of an OECD 422 screening study can be used like the NOAEL of 28-day toxicity study to derive a concentration adjusted to short-term conditions.

90-day sub-chronic toxicity study

A 90-day sub-chronic toxicity study (90-day study) in rats is most often the basis to derive the long-term DNEL. This study is required for REACH substances registered in quantities of 100 tonnes per year and more. In the rare case a chronic toxicity and/or carcinogenicity study is available this study might be used instead of the 90-day study to derive the DNEL. To derive a concentration adjusted to short-term conditions, a NOAEL(C) of a 28-day study is considered the best basis. However, based on availability and quality of the 28-day study (e.g., the study was not performed according to a test guideline or no NOAEL/(C) could be derived), the use of the NOAEL of a 90-day study might be more appropriate. In case it can be demonstrated that the toxicity of a substance is more dose dependant rather than concentration dependant, the NOAEL of a 90-day study can be extrapolated to short-term conditions, e.g., by multiplying the NOAEL of the 90-day study with a default value of 3.

Reproductive toxicity studies

There are further studies on which the long-term DNEL might be based and which could also be considered as starting point to derive a concentration adjusted to short-term conditions. Those are the pre-natal developmental toxicity study (OECD TG 414), the two generation reproductive toxicity study (OECD TG 416) or the extended one-generation reproductive toxicity study (OECD 443). Studies on reproductive toxicity are performed preferably by the oral route. The extended one-generation reproductive toxicity study and the two-generation reproductive toxicity studies cover sub-acute to sub-

chronic exposure durations and provide also NOAELs and LOAELs for systemic effects (in addition to N(L)OAELs for developmental or reproductive toxicity). Hence, NOAELs of those reproductive toxicity studies can be used like the respective NOAELs of the 28-day or 90-day studies. The NOAEL of a pre-natal developmental toxicity study is used for DNEL derivation only if this study provides the lowest relevant NOAEL. It is to be noted that in a pre-natal developmental toxicity study the investigation of maternal toxicity is very limited and is focussed mainly on mortality and body weight changes. In case a long-term DNEL is based on such a study, adjustment to short-term conditions need to be justified dependent on the effect (maternal toxicity or developmental toxicity) and taking into account the exposure duration of this study (usually 10 or 21 days).

Human studies

For some substances, human information might be available on which to base the long-term DNEL. Expert judgement is required when considering the type of information on which the long-term DNEL is based, and if this information provides a case-specific basis to scientifically adjust the long-term DNEL for short-term conditions.

Summary

To adjust for short-term exposure, the preferred approach is to use the information (NOAEL(C)) from a 28-day study or an OECD 422 screening study in rats. However, based on availability and quality of the 28-day study, the use of the results of a toxicity study with longer duration (like a 90-day study) might be appropriate. In case where the long-term DNEL is derived from a pre-natal developmental toxicity study, this study could also be the starting point to adjust for short-term conditions.

The default approach presented below to adjust for short-term conditions is only applicable in cases where the animal species tested was the rat and the studies were performed according to OECD or EU test methods. Deviation from this default situation requires toxicological expertise to adjust appropriately to short-term conditions.

Furthermore, animal studies performed by the same route as the human exposure (e.g., inhalation exposure) should be preferred over studies for which route-to-route extrapolation is necessary.

In the very rare case a long-term DNEL for inhalation is based on a dermal study, any adjustment for short-term conditions requires specific toxicological argument and cannot be covered by a default approach.

Adjustment for short-term exposure based on a 28-day study

To adjust for short-term conditions, the NOAEL(C) from a 28-day study is considered the most appropriate starting point. The following adjustments are to be made when comparing with the long-term DNEL:

- adjustment for daily exposure duration;
- adjustment for exposure duration over lifetime; and
- adjustment for annual frequency of exposure.

Daily exposure duration

The following considerations on daily exposure duration are worst case assumptions. It is assumed that the toxicity of the substance is mainly driven by the exposure concentration (or highest dose) and less by the total accumulated dose.

If substance-specific data are available that demonstrates that the toxicity of a substance is more dose dependant rather than concentration dependant, a substance-

specific time-scaling could be applied. However, this requires an appropriate justification e.g., by comparing the results of toxicity studies with different durations performed using the substance under consideration or with structurally similar substances. In this respect, an appropriately reported dose-range finding study might also provide useful information on adverse effects at doses/concentrations which are higher than that in the main study.

It is to be noted that the mode and duration of administration of the test-substance differs between the test methods and might also differ within one test method. Therefore, the studies are considered individually.

28-day inhalation study (OECD TG 412)

The usual exposure regime for a 28-day inhalation study, according to OECD 412, is a 6 h exposure each day for 28 consecutive days.

To consider a default extrapolation to a daily exposure duration shorter than 6 h, a worst case scenario is used. This scenario assumes that the systemic toxicity is driven by the exposure concentration rather than by the cumulative dose and that the NOAEC of the 28-day study is 1 x Y mg/m^3 and the LOAEC three times the NOAEC (i.e. 3 x Y mg/m^3). For such a worst case scenario extrapolation from 6 h daily exposure (1 x Y mg/m^3) to 2 h daily exposure (3 x Y mg/m^3) would already lead to adverse systemic effects. Extrapolation to 3 h (2 x Y mg/m^3) might be acceptable considering that this is a worst case scenario and that for systemic effects often the cumulative dose is determining the toxicity.

Default: The default is to adjust from the 28-day inhalation study in rats with 6 h daily exposure to 3 h inhalation exposure per day. 3 h of daily inhalation differ from a 24 h daily inhalation (which is used to derive the long-term DNEL) by a factor 8.

Substance-specific adjustment: In the case where it can be demonstrated that the toxicity of the substance is driven more by the total accumulated dose, rather than by the exposure concentration, adjustment to an even shorter daily exposure (e.g., 1 h) is possible. An appropriate justification needs to be provided. However, the concentration used for risk characterisation that is adjusted to short-term conditions should not be higher than 100 times the long-term DNEL.

28-day oral study (OECD TG 407)

The usual exposure profile for a 28-day oral study according to OECD 407 is dependent on the mode of administration. This would either be a continuous administration via diet or drinking water, or a daily bolus administration.

To address short-term human exposure by inhalation, route-to-route extrapolation from oral administration to rats to inhalation exposure to humans is needed. Since the conditions of the gastrointestinal tract and the respiratory tract are different and the respiratory tract usually reacts more sensitively than the gastrointestinal tract, there is uncertainty that inhalation-specific effects in the respiratory tract might occur even if no effects in the gastrointestinal tract were observed. For example, the substance could be metabolised in the respiratory tract to reactive metabolites (e.g. esters). Furthermore, unspecific effects of solvents or dusts could occur in the respiratory tract that are not detected in the gastrointestinal tract. Hence, by performing oral-to-inhalation extrapolation it should be considered if at the exposure concentration that is extrapolated from oral conditions, effects in the respiratory tract might reasonably be expected or not.

Administration via diet or drinking water

For administration of the substance via diet or drinking water, the default assumption is

a continuous uptake of the substance (24 h per day) over 28 days. It is to be noted that this is a worst case assumption that does not take into consideration of the time when the animals are sleeping and, consequently, are not eating or drinking.

To consider a default extrapolation for daily exposure, a worst case scenario is used assuming that the systemic toxicity is driven by the exposure concentration rather than by the cumulative dose and that the NOAEL of the 28-day study was 1 x Y mg/kg bw/d and the LOAEL 3 x Y mg/kg bw/d. For such a worst case scenario extrapolation from 24 h exposure (1 x Y mg/m^3) to 8 h exposure (3 x Y mg/m^3) would lead to adverse systemic effects. Extrapolation to 12 h (2 x Y mg/m^3) might be acceptable considering that this is a worst case scenario and that for systemic effects most often the cumulative dose is determining the toxicity.

Default: The default is to adjust from the animal experiment with 24 h daily exposure to 12 h daily inhalation exposure. 12 h of daily inhalation differ from 24 h daily inhalation (which is used to derive the long-term DNEL) by factor 2.

Substance-specific adjustment: In the case where it can be demonstrated that the toxicity of the substance is driven more by the total accumulated dose than by the exposure concentration.

n, adjustment to an even shorter daily exposure (e.g., 1 h) is possible. However, it needs to be demonstrated that effects in the respiratory tract are not to be expected at the extrapolated exposure concentration. An appropriate justification needs to be provided. However, the concentration used for risk characterisation that is adjusted to short-term conditions should not be higher than 100 times the long-term DNEL.

Administration via daily bolus

For bolus administration, the default assumption is a single bolus once each day for 28 consecutive days. Hence, this scenario is already worst case considering one bolus per day. When deriving a long-term DNEL for the general population, the oral bolus dose is extrapolated to a 24 h daily exposure. Therefore, extrapolation to about 1 h daily exposure might be possible.

However, considering that route-to-route extrapolation from the oral route to inhalation is required, and that the respiratory tract may react more sensitively than the gastrointestinal tract, such an extrapolation performed as default without considering the toxicity profile of the substance contains too much uncertainty. ECHA Guidance R.8. allows extrapolation from oral administration to 8 h inhalation for workers. Hence, to adjust the long-term DNEL for the general population to short-term conditions, no higher default uncertainty should be accepted than for workers. Therefore, the default is to extrapolate for short-term consumer use to 8 h exposure per day.

Default: The default is to adjust from the animal experiment with bolus administration to 8 h inhalation exposure per day. 8 h of daily inhalation differ from a 24 h daily inhalation (which is used to derive the long-term DNEL) by factor 3.

Substance-specific adjustment: In case it can be demonstrated that the toxicity of the substance is driven more by the total accumulated dose rather than by the exposure concentration, adjustment to an even shorter daily exposure (e.g., 1 h) is possible. However, it needs to be demonstrated that effects in the respiratory tract are not to be expected. An appropriate justification needs to be provided. However, the concentration used for risk characterisation that is adjusted to short-term conditions should not be higher than 100 times the long-term DNEL.

Exposure duration over lifetime

To account for differences between sub-acute and chronic exposure duration, ECHA Guidance R.8., Table R.8-6 requires an assessment factor of 6 to be applied.

Considering a sub-acute exposure duration (reflecting the exposure duration of a 28-day study), a default value of 1 can be applied for exposure duration. The application of a lower default value to account for even shorter human exposure duration (e.g. acute) would require sound substance-specific justification following ECHA Guidance R.8-8 on acute toxicity.

Default: The default is to apply a value of 1 for duration to a 28-day study. The default value 1 differs from the assessment factor 6 for duration (which is used to derive the long-term DNEL based on a 28-day study) by factor 6.

Substance-specific adjustment: The application of a lower default value than 1 to account for shorter than sub-acute human exposure duration (e.g. acute) would require sound substance-specific justification following ECHA Guidance R.8-8 on acute toxicity.

Annual frequency

Long-term DNELs for the general population assume exposure for 365 days per year over a life-time, usually assumed to be 70 years. A 28-day study covers about 1 month in the life of a test animal. Assuming a life expectance of 2 years for rats, the exposure duration corresponds to about 4% of the life-time of a rat. For the human condition, this would reflect in total 1022 days, i.e. about 3 years of human lifetime exposure.

An annual exposure frequency that would reflect sub-acute exposure conditions, are about 15 days per year; this reflects about 4% of 365 days. As a precautionary default, the maximum annual frequency is set as 12 days per year.

The annual frequency can either be up to 12 single events distributed over the year or 12 consecutive days in one year. Note: Potential accumulation of the substance is already taken into account in the long-term DNEL and thus the distribution of the 12 days over the year does not require particular considerations.

Default: The default is to adjust for short-term consumer exposure only if consumer use is up to 12 events per year, either as single events distributed over the year or up to 12 consecutive days.

Substance-specific adjustment: It is not recommended to adjust this default annual frequency to more frequent uses.

Adjustment for short-term exposure based on a 90-day study

In case a reliable NOAEL/C from a 28-day study is not available, the NOAEL/C from a 90-day study can also be used to adjust for short-term conditions.

Daily exposure duration

The same considerations to adjust for daily exposure apply as for the 28-day study (see above).

Exposure duration over lifetime

Where the NOAEL from a 90-day toxicity study is used to adjust for short-term conditions, a default value of 1 can be applied for exposure duration. A substance-specific adjustment of the NOAEL from the 90-day study to reflect short-term exposure conditions is possible (e.g., by multiplication with a factor of 3) in case it can be demonstrated that the toxicity of the substance is driven more by the total accumulated dose rather than by the exposure concentration. An appropriate justification needs to be provided.

Default: The default is to apply a default value of 1 for duration to a 90-day study. The default value 1 differs from the assessment factor 2 for duration (which is used to derive the long-term DNEL based on a 90-day study) by factor 2.

Substance-specific adjustment: A substance-specific adjustment of the NOAEL from the 90-day study to reflect short-term exposure conditions is possible (e.g., by multiplication with a factor of 3) in case it can be demonstrated that the toxicity of the substance is driven more by the total accumulated dose rather than by the exposure concentration. An appropriate justification needs to be provided. However, the concentration used for risk characterisation that is adjusted to short-term conditions should not be higher than 100 times compared to the long-term DNEL.

Annual frequency

The same considerations to adjust for annual frequency apply as for the 28-day study (see above).

How to calculate the value for short-term exposure

An example is provided of how to adjust for short-term conditions regarding inhalation exposure

In the first step the NOAEL(C) of a 28-day study is corrected to address short-term inhalation exposure of the general population. Example 1 is to be used if the 28-day study is an inhalation study (OECD 412); example 2 is to be used if the 28-day study is an oral study (OECD 407) with dietary or drinking water administration; example 3 is to be used if the 28-day study is an oral study (OECD 407) with gavage administration.

In the second step, assessment factors are applied.

Step 1: correct the dose descriptor based on the type of the 28-day study to address short-term **inhalation** exposure of the general population; for comparison reasons, the calculation for a long-term DNEL is also provided.

Example 1: Rat 28-day inhalation study (6 h/d)	Adjustment for short-term use	Derivation of a long-term DNEL
NOAEC (mg/m^3)	Y	Y
Adjust for exposure duration (rat 6 h/d) 3 h/d general population short-term 24 h/d general population long-term	x 6 ÷ 3	x 6 ÷ 24
Corrected human exposure (mg/m^3)	Y x 2	Y x 0.25

Example 2: Rat 28-day oral dietary or drinking water study	Adjustment for short-term use	Derivation of a long-term DNEL
NOAEL (mg/kg bw/d)	Y	Y
Extrapolation oral rat to inhalation human (0.8 l/min) [1 h: 0.048 m^3/kg bw general population short-term] 12 h: 0.575 m^3/kg bw general population short-term 24 h: 1.150 m^3/kg bw general population	÷ 0.575	÷ 1.150

long-term		
Route-specific bioavailability; default: 50% oral, 100% inhalation	x 50 ÷ 100	x 50 ÷ 100
Corrected human exposure (mg/m^3)	Y x 0.870	Y x 0.435

Example 3: Rat 28-day oral gavage study	Adjustment for short-term use	Derivation of a long-term DNEL
NOAEL (mg/kg bw/d)	Y	Y
Extrapolation oral rat to inhalation human (0.8 l/min) [1 h: 0.048 m^3/kg bw general population short-term] 8 h: 0.384 m^3/kg bw general population short-term 24 h: 1.150 m^3/kg bw general population long-term	÷ 0.384	÷ 1.150
Route-specific bioavailability; default: 50% oral, 100% inhalation	x 50 ÷ 100	x 50 ÷ 100
Corrected human exposure (mg/m^3)	Y x 1.302	Y x 0.435

Step 2: Apply assessment factors (AF)

Type of default AF	Adjustment for short-term use	Derivation of a long-term DNEL
Interspecies differences: - Toxicokinetics - Toxicodynamics	 - ÷ 2.5	 - ÷ 2.5
Intraspecies	÷ 10	÷ 10
Duration	(1)	÷ 6
Dose-response	(1[1)])	(1[1)])
Quality of database	(1[1)])	(1[1)])
Remaining	(1[1)])	(1[1)])

[1)] see ECHA Guidance R.8., section R.8.4.3.1 for the conditions that require a larger AF than 1

Summary

By using the NOAEL(C) of a 28-day study to account for short-term exposure and the default approach as explained above, the concentration adjusted for short-term conditions are:

- 12-times higher compared to the long-term DNEL if an oral dietary or drinking water study has been used;

- 18-times higher if an oral gavage study has been used; and
- 48-times higher if an inhalation study with 6 h exposure per day has been used.

Study on which the 28-day study is based	Differences of concentrations adjusted to short-term condition compared to long-term DNEL
Rat, oral dietary or drinking water study	2 x 6 = 12
Rat, oral gavage study	3 x 6 = 18
Rat, inhalation study (6 h/d)	8 x 6 = 48

Adjustment factors for short-term exposure based on a long-term DNEL

The approach as explained above requires basic toxicological knowledge to apply default factors to adjust for short-term conditions and even more toxicological knowledge to adjust for short-term conditions exceeding the default values.

As a first step, or in case no toxicological support is available, the long-term DNEL can be multiplied with a general default adjustment factor which a slightly more conservative than adjustment starting from a 28-day study. In the case where a long-term DNEL is based on an oral study in rats, the long-term DNEL can be multiplied by factor 10. In the case where the long-term DNEL is based on an inhalation study, the long-term DNEL can be multiplied by factor 40.

Study on which the long-term DNEL is based	General default adjustment factor for short-term exposure to multiply with long-term DNEL
Rat, oral study	10
Rat, inhalation study	40

Based on substance-specific toxicological considerations the adjustment factor can be increased up to 100 if it can be demonstrated that

- the systemic effects are driven by the dose rather than the concentration and
- local effects in the respiratory tract are unlikely to occur at the adjusted value.