
Exposure Scenarios in Toxicology

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Abstract

Exposure is defined as the “concentration or the amount of a particular agent that reaches a target organism, system, or (sub)population in a specific frequency for a defined duration” (WHO/IPCS 2004). Exposure is normally characterized by means of exposure scenarios. The information from the exposure scenario is used for building up an exposure model. Exposure models can be understood as a translation of an exposure scenario to a mathematical algorithm to yield

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a qualitative and a quantitative estimate of exposure. Exposure can be understood as dose estimation, by the oral, dermal, or inhalation route.

Exposure assessment is based on three basic elements: (i) the exposure scenario, (ii) the exposure model, and (iii) the exposure parameters (WHO/IPCS 2005). The basic characterization of the exposure is made by the exposure scenario (ES). The ES describes the circumstances of the exposure, covering all situations and corresponding information needed to perform an exposure estimate. The WHO (2004) defines the term exposure scenario as “a combination of facts, assumptions, and interferences that define a discrete situation where potential exposures may occur. These may include the source, the exposed population, the time frame of exposure, microenvironment(s), and the activities. Scenarios are often created to aid exposure assessors in estimating exposure.” This definition should be used as a basic concept for exposure estimation.

Since 2006, an additional definition of exposure scenario must be taken into consideration regarding to the European Chemicals Regulation (REACH; European Commission 2006). In the regulation, the exposure scenario is defined as “. . .the set of conditions that describe how the substance is manufactured or used during its life-cycle and how the manufacturer or importer controls, or recommends others to control, exposures of humans and the environment.”

This chapter is explaining the exposure scenario on the basis of the WHO definition, with hints of the particularities of the REACH regulation.

Similarly to drug treatment, an exposure estimate can be understood as the dose of a contaminant or hazardous substance that can be taken in by an individual or a population.

Structure of Exposure Scenarios

Exposure scenarios describe the complex characteristics of the external exposure from any substance that can be released from a variety of sources, e.g., the environment, consumer products, food, and other sources. This resulting external “dose” will be systemically absorbed and results in the toxicologically relevant “internal” exposure. The characterization of the exposure scenario describing external exposure should be divided into “subscenarios” to be combined with each other yielding the complete scenario.

In the REACH regulation (European Commission 2006), the scenario contains basically the same information. However, the exposure scenario also contains information about measures that reduce the exposure to an extent that will not exceed the DNEL. If, for example, in an exposure calculation, the DNEL is exceeded, the registrant must reduce it by risk management measures (Bruinen de Bruin et al. 2007) [Registrant: The company that prepares the chemical safety report for notification to ECHA (European Chemicals Agency)]. Examples for RMM are reduction of the concentration of a substance in a product, hindrance of migration of a substance from an article, or release reduction by special dispensers. Non-exceedance of the DNEL indicates that a product is safe.

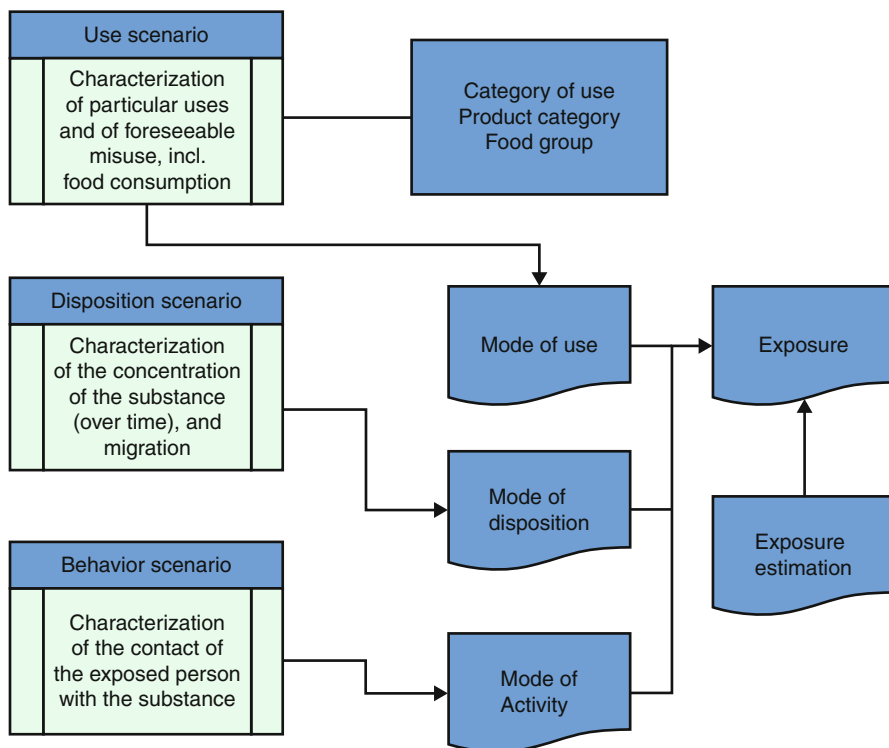


Fig. 1 The different types of exposure scenarios and their interaction

Three subscenarios (see Fig. 1) should be considered when describing an exposure scenario, as shown by the following simple example:

Use scenario: Characterization of the source in contact and amount of a substance that will be potentially released

Example

A certain household cleaner (use category) containing a substance in a particular concentration will be applied to a bigger area (e.g., the ground of a room). The amount of substance has the potential of release from that source.

Disposition scenario: Characterization of release, distribution, and disappearance of a substance in the environment

Example

The substance, due to its vapor pressure and molecular weight will be released and evaporated to room air to yield a certain concentration. The concentration will increase and continue over time and can be inhaled by persons in that room.

Due to air exchange, the concentrations in room air will decrease. Substances having low volatility will be distributed mostly via the house dust path.

Behavior scenario: Description of the exposed population and the characteristics of use of products and articles, consumption of food, etc.

Example

The exposed person stays in that room for a certain time and will inhale the air. The time an exposed person is spending in a room may account for, e.g., 4 h.

Use Scenario: Characterization of the Source and the Use of the Substance in a Product

This subscenario is used to characterize the source of the substance and the amount that is released during the use of the product. The limitations of these processes are determined by the product itself that contains the substance, its physicochemical properties, its concentration, and the mode of use.

Categories of Use

A substance may appear as an ingredient in many different products and product types (Heinemeyer and Hahn 2005). An approach that characterizes product use categories can therefore be very helpful to identify the sources of substances. Product categories have been used on the national and international level. Some of the documents became “official” due to their use in technical guidances (ECHA 2010) or from use and recommendations by international agencies (EFSA 2009) and organizations (WHO 2005). Therefore they have some standardizing character, although the details are differing. Major importance is due to the guidance documents and classifications used in international databases, such as the *industrial categories* and *product and article categories* described in the ECHA guidance R12 *use descriptor system* (ECHA 2010) (Table 1).

Other classification systems have been published by the EIS-Chemrisks framework developed by the EU-JRC (European Commission 2003). Also, poison centers around the world are using product use classification systems for documentation of cases and to prepare annual reports. In most of the classification systems, a differentiation is made according to the use of the products, e.g., paints, household cleaners, pesticides, cosmetics, and others. Due to these documentations, it can be checked how close exposure scenarios are close to reality (Heinemeyer and Hahn 2005). The identification of use of a substance and the description of manufacturing and the use process is an important part in defining exposure scenarios under REACH (van Engelen et al. 2007; Heinemeyer 2008).

Table 1 Important sources of information on classification systems to characterize exposure scenarios

Reference	Editor	Remarks
AUH report	Behörde für Arbeit, Gesundheit und Soziales, Hamburg. Ausschuss für Umwelthygiene der AGLMB	Food intake data from the national survey 1985–1989
Bundeslebensmittel-schlüssel	BVL (2012a) und Max-Rubner Institut (2012)	Nutrient database with food category system, national, Germany
Food contamination surveys	For example, BVL (2012), EFSA (2009)	
EFSA concise food consumption database	EFSA (2012)	A collection of national food consumption data due to harmonized food grouping
EFCOSUM report	Efcosum Consortium (2001), Brussard et al. (2002)	Report from an EU research project
LanguaL	Møller and Ireland (2010)	
EIS-Chemrisks	EU Commission, Joint Research Centre, Ispra	Project report and database EIS-Chemrisks
GEMS food	WHO (2012)	Worldwide classification system for foods
ECHA technical guidance document R12	European chemicals agency (2010)	Compilation of different product and article categories and product use classification for REACH
EU commission	Technical guidance document 2003	
General factsheet	RIVM; Bremmer et al. (2006)	Collection of exposure defaults and assumptions
Paint products factsheet	RIVM, Bremmer and van Engelen (2007)	Collection of model parameters for paints
Pest control products factsheet	RIVM, Bremmer et al. (2006a)	Collection of model parameters for pesticides
ECETOC TRA	European centre for ecotoxicology and toxicology of chemicals, several versions (2012)	Guidance document and tools for targeted exposure assessment
Annual reports of poisonings reported due to chemical law	Federal Institute for Risk Assessment (2011)	Product classification developed on national levels in cooperation with poison centers
INTOX	WHO (2012)	Classification developed for poison center annual reports

The development of classification systems available for foods is more advanced than the others mentioned above. Food classification is used since longer times for systematic characterization and for exposure assessments. National food consumption surveys normally are using food classifications. The EU the European Food Safety Agency has introduced a harmonized food classification characterization in its *Comprehensive Food Consumption Database* (EFSA 2012), which comprises data on food consumption from nearly all EU member states. In Germany the *Bundeslebensmittelschlüssel* (BVL 2012a; Max-Rubner-Institut 2012b) is used to

classify food. The Max-Rubner Institute is responsible to maintain this classification system up to date which is close to the *LanguaL* (Møller and Ireland 2010). The latter combines a fixed three-level thesaurus with relational and dynamic tables, so-called facets. Product/use categories can be transferred and expressed as subscenarios on different levels of aggregation to apply a standardized approach (use model) with respective model parameters (model variables/exposure factors).

Disposition Scenario: Release, Distribution, and Disappearance

As in pharmacokinetics, the disposition scenario describes the appearance, distribution, and disappearance of a substance in an environment. The disposition scenario includes:

1. A description of the concentration of a substance in the product and its release, by migration, evaporation, or emission.
2. The distribution of the substance in the environment of contacting it, as described in Fig. 2. Substances can be bound to particles, e.g., house dust, but also distributed in the gas phase.
3. The disappearance of the substance from the microenvironment

Source, (micro)environment, and substance characteristics are limiting the release of the substance. In combination with the use, the route of exposure will be oral, dermal, or by inhalation.

Route of Exposure: Inhalation

The scenario characterizing the exposure by inhalation normally describes the concentration – time course of a volatile substance in the indoor air, either in one or multiple rooms. The concentration can be used for comparison with toxic concentrations.

It is recommended to use the concentration in air to estimate the uptake of a substance via the lungs to systemic circulation. Internal exposure evaluation enables risk assessors to estimate total body burden, e.g., in children or other particular populations. To perform these estimates, the respiratory volumes per time and pulmonary absorption rates are needed.

In addition to inhalation of substances in its gas phase, the inhalation of small particles should be also taken into account. Dust is a vehicle for nonvolatile substances that can be adsorbed and desorbed from the particles, absorbed through the alveoles, and thus enter the human body.

Exposure factors needed to estimate exposure from inhalation

- Concentration of the substance in room air
- Concentration of the substance in fine dust particles
- Migration rates (release rate per time)
- Vapor pressure
- Molecular mass
- Density

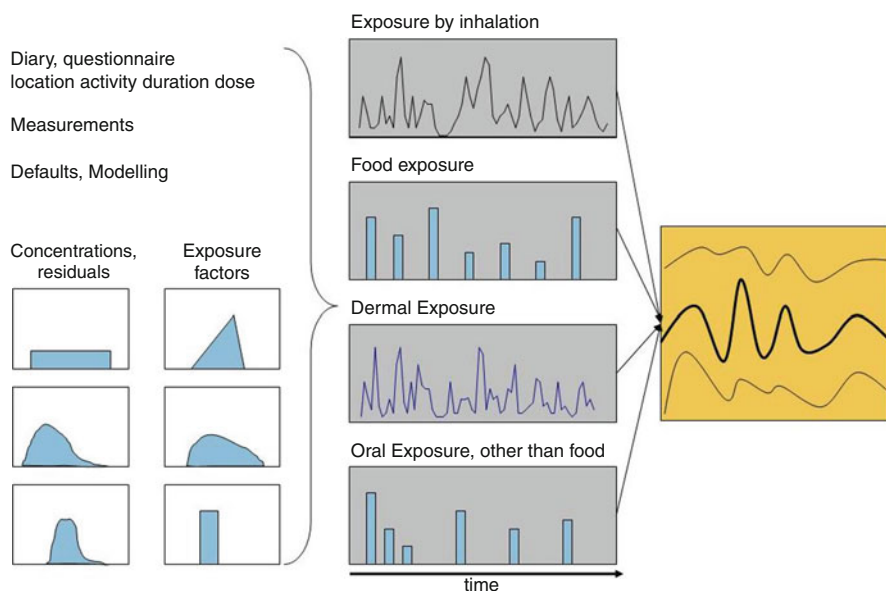


Fig. 2 Theoretical contribution of different paths to the total exposure

- Product amount used in the application
- Concentration of the substance in the product
- Duration of the application
- Room volume
- Air exchange rate

Typical Scenarios of Inhalation Exposure

1. Use of volatile substance, e.g., solvents in paints, laquers, or cleaners
 A certain amount of a product (e.g., a paint or cleaner) will be applied to a surface. A volatile substance will be evaporated and produces indoor room concentrations. The substance distributes in the room and disappears after some time, according to the air exchange rate. This type of scenario has been considered, e.g., in the computer tool ConsExpo (RIVM 2012) and the wall paint emission model published by the US EPA (2001).
2. Emission from solid bodies
 A constant amount will be evaporated over a longer time period from, e.g., furniture and textiles. This may lead to constant (steady state) concentrations of the substance in indoor air. The extent of this concentration depends on the air exchange rate, temperature, and other factors, e.g., whether the substance can be adsorbed to particles. This scenario may be applicable for exposures from inhalation due to solvent contaminated residual wastes.

3. Inhalation of dust

Dust inhalation represents a special form of exposure by inhalation, where the substance is adsorbed to inhalable fine particles in the microenvironment. By this pathway, they can enter the lungs and alveoles. After desorption from the particles, the substance can be absorbed to the systemic circulation. Sometimes, they will remain in the alveolar cells and lead to local effects. The concentrations in the dust cannot be estimated and have to be measured.

The example shown below represents a so-called *worst case* estimation of exposure for a child (bodyweight (BW) 10 kg). This estimate is characterized by its conservatism, taking low body weight (5th percentile), a respiratory volume (RV) that considers (partly) activity *and* rest, as well a maximal contact time (CT) and a high pulmonary absorption rate (RPA; 100 %).

Example “worst case” estimation of exposure by inhalation

- Concentration in room air (estimated or measured, C) – 10 µg/m³
- Body weight (BW) – 8.1 kg
- Respiratory volume per time (RV) – 2.9 m³/day
- Contact time (TC) – 1 day
- Pulmonary absorption rate (RPA) – 1
- inhalation exposure (absorbed amount) $[C \cdot RV \cdot RPA \cdot TC / BW]$ – 3.5 µg/kg/day

Route of Exposure: Dermal

The dermal exposure estimation characterizes the amount of a substance which is on the skin and can be absorbed through the skin.

Typical Scenarios: Dermal Exposure

1. Use of cosmetic products

A product will be applied to skin; one or more substances in the product can be absorbed through the skin. In dermal exposure assessment, products that can remain on skin (non-rinse) will be differentiated from those that will be removed by washing (rinse off).

2. Use of household cleaners

The hands will be shortly put into the water that contains the washing product. Substances in that diluted product can be adsorbed to and remain on skin and may be dermally absorbed. When taking a bath, the whole body surface will be exposed.

3. Dermal exposure via air

Volatile substances in the air can become into contact with the skin and are dermally absorbed. Normally, the extent of this exposure is small.

4. Wearing textiles and contact with leisure and hobby products

Direct contact of substances with the skin from textiles or leisure and hobby products is possible from migration to the skin. The exposure surface is the part of skin that is covered by the textile or contacting the leisure and hobby product.

5. Contact with pets

Ingredients from, e.g., pesticides used for domestic animals to treat against pest may lead to dermal contact when touching pets. Children may have oral exposure after licking hands (mouthing behavior) after touching the animals.

A basic rule for estimating dermal exposure has been described in the EU technical guidance document for existing chemicals and has been taken over by ECETOC (2005) as well as in the ECHA technical guidance document (2010). The amount (AM) that can lead to exposure can be estimated from the area (A) of exposure times an estimated *thickness of the layer* (TL) of 0.01 cm and from the concentration (C) of the substance in the product ($AM = A * TL * C$). In some documents, additional *absorption rates* given as percentages are used. However, it must be considered that dermal absorption is a time-dependent process. Taking percentages as rates can lead to errors and should only be applied as a default assumption, e.g., a *worst case concept* for 100 % of absorption. For short contact times (e.g., shortly applied cosmetics), correction factors have been introduced that reduces the absorption rate. In general, values from 1 – (10) – 50 % are used as default assumptions, with different justifications, depending on the purpose of the evaluation. For some substances, absorption constants and coefficients have been derived, due to lipid solubility (octanol/water coefficient) and molecular weight. Respective models have been established by Wilschut et al. (1995) and have been integrated into the ConsExpo tool.

Exposure factors needed to estimate dermal exposure

- Exposed skin area (e.g., 840 cm² for hands)
- (Theoretical) thickness of layer (0.01 cm; mixtures; 0.001: articles)
- Concentration of substance in the product
- Migration rates of the substance (measured)
- Absorption coefficient (derived by model evaluation), alternative: absorption rates (worst case, percentages)

Oral Path of Exposure

Oral exposure characterizes the oral intake of a substance by mouth and the amount that is absorbed in the gastrointestinal tract. Oral intake is possible with food, drinking water, house dust, the mouthing behavior, and some personal care products (e.g., tooth paste). House dust and related paths are particularly important in small children. In general oral exposure estimation requires knowledge of the concentration of the substance in and the amount of the medium that is taken in.

Typical Scenarios

1. Intake of food and drinking water

A number of different sources have to be distinguished to estimate the dietary exposure to contaminants in the food chain, food additives, process contaminants,

substances in food packaging, and bacterial toxins and metabolic products. Process contaminants, e.g., acrylamide or MCPD, (3-Chlor-1,2-propandiol) can be formed during heating of foods.

Dietary exposure estimation is normally performed by modeling concentration data in the food and the respective food consumption data. Concentrations in food can be obtained from, e.g., market control measurements. However, as these data are risk oriented (there is a reason for expecting high concentrations), systematic and representative evaluations of concentrations in food are more adequate to study dietary exposure in a population. Such data are available from, e.g., the German food monitoring system (BVL 2012). The European Food Safety Agency is establishing a system to regularly collect data of concentrations of substances in food, collected from the member states (EFSA 2011). Due to the immense number of samples needed to describe concentrations in food, approaches have been developed to reduce numbers of sample by, e.g., pooling, for example, by the concept of total diet study (TDS).

The identification of food consumption data normally is performed by means of questionnaire studies. On the national levels, food consumption surveys have been performed in many countries, for example, the Nationale Verzehrsstudie II (Max-Rubner-Institut 2012a) in Germany. There are several methodological approaches by which consumption studies can be performed (24-h recall, dietary history, food frequency study, diary studies, with and without weighing the food). It should be mentioned that these study types have advantages and disadvantages for the particular questions asked in risk assessment, e.g., acute or chronic hazards.

Normally, to perform food consumption studies, foods will be characterized by a food basket that contains > 90 % of all foods eaten. The particular foods should be classified by a systematic food group classification system (see respective chapter).

Food exposure estimation is in general performed for the general population and normal food consumers (eaters), by taking concentration and consumption data describing a central tendency (means, medians). To describe high consumers, EFSA has proposed to identify those foods that have the highest contribution to exposure and exchange the means by 95th percentiles.

2. Ingestion of substances via the house dust and soil path

House dust and soil represent an important vehicle for nonvolatile substances. House dust consists of particles from several sources, e.g., soil dust, and from pollution. It contains a lot of different materials, e.g., plant pollen, mites, human and animal skin cells, fibers, soil, and vapors. Substances migrate from the different materials (textiles, floor coverings, furniture, etc.) and, after release due to mechanical or thermic influence, adsorb to house dust. Partly, bigger particles may become a part of dust themselves.

The daily intake of house dust is unknown. Extrapolations from soil dust intake studies are normally used to estimate exposure from house dust intake. The intake of soil has been identified by means of tracer studies, taking substances that are poorly absorbed in the gut and comparing the concentrations measured in the stool with those in the soil. The AUH report (1995) recommends to take an estimate of 16 mg (median) and 110 mg (95th percentile) as standard values for house dust intake. The US EPA (2009) employs 60 mg per day as an estimate for central

tendency. The extrapolation of soil to house dust may introduce uncertainties into the assessment; overestimation of exposure by house dust should be assumed.

Exposure factors needed to estimate oral exposure

- Concentrations of the substance in food and drinking water
- Consumption values for the food or drinking water, preferably related to individual body weight
- Weight
- Concentrations of substances in house dust
- Default – values of house dust intake

Behavior Scenario

Many exposed people are limiting their exposure by themselves and by their particular behavior. Studying the behavior in certain populations is essential and plays an increasing role in exposure assessment. While in the use scenario, the instructions of use will govern the scenario characterization, the behavior scenario influences the variability of the uses in a population. The behavior scenario characterizes how exposed persons act and handle the products. Two different types can be distinguished: (i) the active exposure where a person actively uses a product and (ii) the passive exposure where the exposed is a bystander. The major difference between active and passive exposure is that the active person may be closer to the source of exposure. An older version (3.0) of the ConsExpo tool is using a fictive room volume that is considerably smaller than the room to consider that situation. The indirect exposure via the environment is a particular form of passive exposure. From this perspective, eating food is passive exposure as well as being in a room and inhaling a substance that is released from furniture, while painting that furniture is active exposure.

Active and passive exposure can also be differentiated in terms of the degree of activity having impact for, e.g., exposure by inhalation. For example, the respiratory volume over time can vary from 15 m³/day (at rest) up to 100 m³/day (heavy work). This may lead to considerable variability in the exposure estimate and thus having impact for the risk characterization. When estimating exposure from inhalation, it is appropriate to assume a well-balanced ratio of activity and resting times.

Time Budgets

As an important element of behavior scenarios, time budgets characterize the contact times of an exposed person. In case of exposure by inhalation, this is the time a person is staying in the room where the exposure takes place. Small children have normally longer contact times as adults because they may stay at home for longer time while adults are at work, outside, or at other business. This will change with school age. It is therefore of great importance to relate the time budgets to age. Data sources for time budget are, e.g., the US-EPA exposure factors handbook, the AUH (1995) report, and the RIVM general factsheet (Bremmer et al. 2006).

Particular Age-Related Behaviors

Behavior scenarios can be used to characterize important differences between adults and children. For example, the ingestion of soil and house dust may account for an important amount of oral exposure in small children. This occurs primarily in the toddlers, by crawling on the ground, as well as in the kindergarten, becoming less importance in the school age. Children frequently put their hand into the mouth, which is called the *mouthing behavior*. The latter has particular importance for exposure from insecticides after treatment of pets against insects (lies, flies). Migrating substances from toys may also be relevant for mouthing. Therefore, migration rates are very important to estimate exposure. The mouthing time may vary over a big range (Groot et al. 1998; Juberg et al. 2001; Smith and Norris 2003). House dust evaluations represent an essential part of exposure assessment in children.

Exposure factors needed to characterize a behavior scenario

- Duration of stay
- Frequency of staying
- Air ventilation
- Activities of “daily life”
- Exposure as active user or bystander
- Hand to mouth activities

Anthropometric Data

Exposure estimation needs anthropometric data that characterize the exposed person or population. Estimation of exposure by inhalation needs, according to the exposure scenario and the respective model, data about respiration rates and the lung surface. Dermal exposure evaluation requires information about body surfaces. However, estimation results are normally related to body weight. Relation to body surface is more appropriate, because body surface is correlating better with the extracellular fluid. Many substances distribute into body water, and there is also correlation between body surface and the basic metabolic rate. This is in particular of relevance when comparing results in children and adults.

Most important anthropometric data

- Body surface and parts of body surface, e.g., hands and arms
- Body height
- Body weight
- Respiration time volume and related to activity
- Lung surface

Combination of Scenarios

The scheme in Fig. 2 shows how use and disposition scenarios can be combined to yield the entire exposure. All possible sources and paths have to be taken into account which may result in very complex scenarios. The estimation is performed

by separated estimations of the particular pathways with subsequent summation. Possible correlations of exposure paths must be taken into account. Also, summarizing exposure results should only be made for central tendency estimations. Results from individual conservative estimations, e.g., by using 95th percentiles, should not be summarized. Consideration of worst case estimates must be performed very carefully, possibly by addition of one conservative estimate with other averages. The European Food Safety Agency has proposed to take the 95th percentiles of exposures contributing most to exposure, exchange them with the averages, and sum all up.

Distribution-Based (Probabilistic) Exposure Assessment

Exposure factors can be characterized as single and fixed values (deterministic approach) or as distributions (probabilistic approach). Therefore, every deterministic value represents a certain value from the distribution. The bounds of the distribution may represent conservative estimations. In many exposure calculations, arbitrary high values are used, in order to end up with an overestimation, without knowing the real situation. Such approaches are often lacking from reality and cannot be called *worst case*. From this reason, it is appropriate to use distributions and their statistical descriptors as a basis for exposure estimations. It is therefore recommended to check whether or not the used value can be matched with other representative values. Well characterized distributions should be used for exposure estimations. This approach will be facilitated considerably by use of modern computer tools. The total range and variability of the individual distributions will be weighted out and ends up with a distribution as result.

Probabilistic exposure modeling can be used as an alternative that considers the variability and uncertainty of the assessment. Distributions are characterized by (i) variability and (ii) uncertainty. Variability is characterizing the natural variation of parameters, while the uncertainty is determined by the lack of knowledge, which is often depending on data quality. For example, the body weight in the population participating in, e.g., the German food consumption study is described mostly by variability, because it is based on a representative sample from the entire population. On the other hand, the basis of data characterizing, e.g., concentrations of substances in products or food is often very poor. Therefore, these data must be considered uncertain.

Probabilistic models are formed by taking a similar general algorithm in the model but characterizing the model variables (parameters) as distributions. If the distributions are appropriately formed, i.e., the data basis is sufficient large and the values are representative for a population, the probabilistic distributions are describing the variability of the parameters. The less the number of data is and their representativeness, the more will distributions represent a mixture of variability and increasing degree of uncertainty.

Importance of Exposure Assessment

Exposure assessment represents, besides hazard identification, the second pillar that is needed for risk characterization. The margin between the quantitative estimate exposure and the N(L)O_{AEL} is characterizing the risk (risk characterization). It is called the margin of exposure (MOE), in earlier times the **m**argin of safety (MOS), but both are meaning the same. The larger the MOS/MOE is, the more can the probability of risk be denied. A concern for risk is assumed if the exposure is exceeding the NOAEL. Risk can also expressed as a ratio of the exposure dose and the NOAEL, which should be lower than 1. Uncertainty factors are used in this formula to consider uncertainties, e.g., the lack of knowledge of the intraindividual and interindividual variation between animals and humans.

In the REACH regulation, the DNEL will be used instead of the NOAEL (compare the resp. chapter).

For these reasons it is of great importance to estimate the exposure as exact as possible. Estimates taking exposure scenarios and models are having sometimes considerable uncertainties, leading to partly extreme ranges of the exposure estimates which depend on the exactness of the description of the exposure scenario. It is essential to describe the exposure parameters as exactly as possible. The approach of using worst case scenarios is leading to overestimations, resulting from rough models or taking defaults or other conservative values as model parameters. Due to the precautional principle, there is an intention to overestimate the exposure; it should, however, not result in unrealistic results. Distribution-based (probabilistic) modeling can be taken as an appropriate alternative because it considers the range of exposure parameters and reveals a distribution of exposure. Taking distribution allows to consider extremes that characterize the skewness of a distribution. 95th and higher percentiles are therefore appropriate descriptors of *reasonable worst case* assumptions and estimates and thus reflect “reality.”

Measurements can be taken into account for exposure estimations, if they are representative for the population of interest. On the other hand, they are showing a *shot* of a particular event or situation which can hardly be transferred to a general scenario. Measurements available for, e.g., contaminants in food, in house dust, and indoor air should therefore be given attention, but they are not necessarily representative for the scenario of interest. Although there is a lot of data available for some substances, they often lack from representativity and thus can be used for risk assessment only with great caution.

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