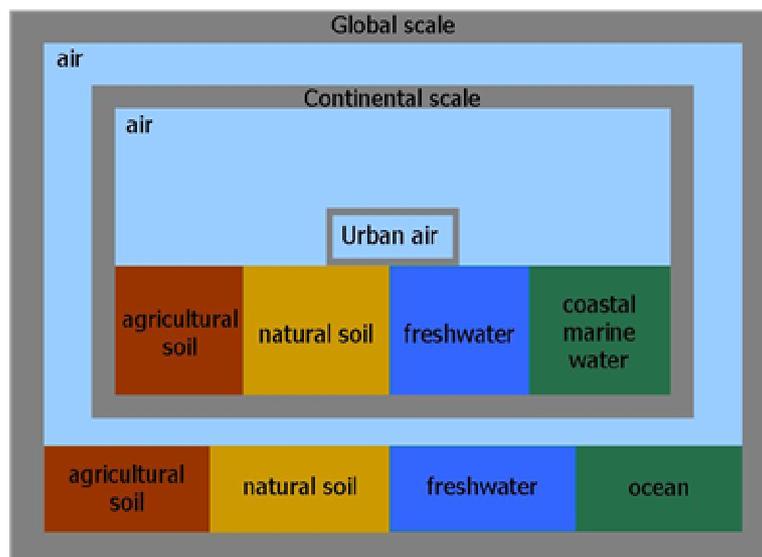# USEtox™

- User manual -

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Colophon

Title: USEtox^{TM} User manual

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Content

1. Background and objective

This user manual provides basic information needed to understand and apply the USEtox^{TM} model, i.e. to calculate midpoint characterisation factors for human toxicity and freshwater ecotoxicity.

The USEtox^{TM} model is an environmental model for characterisation of human and ecotoxicological impacts in Life Cycle Impact Assessment (LCIA) and Comparative Risk Assessment (CRA). It has been developed by a team of researchers from the Task Force on Toxic Impacts under the UNEP-SETAC Life Cycle Initiative. USEtox^{TM} is designed to describe the fate, exposure and effects of chemicals. The UNEP-SETAC Initiative supports the development, evaluation, application, and dissemination of USEtox^{TM} to improve understanding and management of chemicals in the global environment.

The goal of LCIA is to translate (characterize) the emissions that occur in the life cycle of a product into their potential impacts on the environment ranging from local impacts from land use over regional impacts due to e.g. toxic substances, acidification or photochemical oxidants to global climate change. For each category of impact (such as global warming or photochemical ozone formation), the impact assessment applies substance-specific characterization factors (CFs) that represent the substance's potency. An emission inventory for the life cycle of a product often contains hundreds of substances. It is thus estimated that 10 to 20,000 different chemicals are used in the life cycle of products marketed. When released to the environment, many of these substances have the potential to damage humans or ecosystems. These potential damages are quantified using characterization factors for the human and ecotoxicity categories of impact. A number of different models have been developed for this purpose around the world over the last 15 years varying in their scope, applied modelling principles and not least in terms of the characterisation factors they produce. These characterisation models all cover a limited number of substances, and the current situation for the LCA practitioner who wishes to include the chemical-related impacts in the impact assessment is that: (a) there will probably be many substances in the life cycle inventory for which no characterization factor is available from any of the models, (b) for some substances several of the models may have published characterization factors, but these often vary substantially among the models.

This unsatisfactory situation was the background on which a Task Force on Toxic Impacts under the UNEP-SETAC Life Cycle Initiative launched a comparison and harmonization of existing characterization models in order to (Hauschild et al., 2008):
1. Identify which differences in the old characterization models cause the observed differences in their characterization factors;
2. Develop a scientific consensus about good modelling practice based on the identified influential differences;
3. Harmonise the old characterisation models removing unintended differences; and
4. Develop a scientific consensus model based on the learnings from the comparison of the characterization models with the following characteristics:
   a. parsimonious (as simple a s possible, as complex as needed) containing only the model elements which were identified as the most influential in the comparison of the existing characterisation models;
   b. transparent and well documented;
   c. falling within the range of the existing characterisation models, i.e. not differing more from the old characterisation models than these differ among themselves;
   d. endorsed by the modellers behind all participating models.

The result of the scientific consensus model development is the USEtox™ model implemented in Microsoft Excel®. <u>Note that due to Microsoft Excel compatibility issues, the user that uses Excel 2007 may have to click on "view, New windows" to access the USEtox worksheets.</u>

2. Concept and model set up

2.1 Life cycle impact assessment

Life cycle impact assessment (LCIA) aims to improve the understanding of the relative importance of the individual emissions in life-cycle inventories. This is done using a weighted summation of the releases of pollutants of a product system with help of characterisation factors:

$$IS = \sum_i \sum_x CF_{x,i} \cdot M_{x,i}$$

where *IS* is the impact score for e.g. human toxicity (cases); $CF_{x,i}$ the characterisation of substance *x* released to compartment i (cases/kg) and $M_{x,i}$ the emission of *x* to compartment *i* (kg). The summation holds for substances and emission compartments.

The USEtox[TM] model calculates characterisation factors for carcinogenic impacts, non-carcinogenic impacts, and total impacts (Carc + non-carc) for chemical emissions to urban air, rural air, freshwater, sea water, agricultural soil and/or naturall soil. The unit of the characterisation factor for freshwater aquatic ectoxicity is $PAF.m^3.day/kg_{emission}$ and for human toxicity $cases/kg_{emission}$ both summarised as Comparative Toxic Unit (CTU) to stress the comparative nature of the characterisation factors.
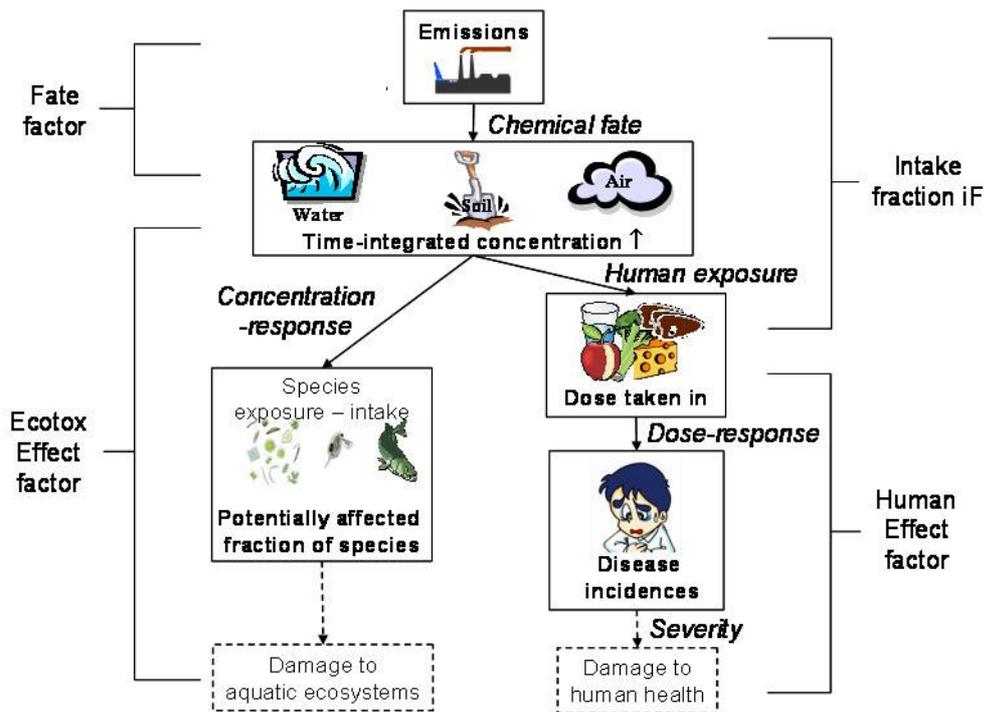
2.2 Ecotoxicity

In USEtox[TM], the ecotoxicological characterisation factor of chemicals includes a fate factor (FF), an exposure factor (XF) and an effect factor (EF) (Figure 1):

$$CF = FF \cdot XF \cdot EF$$

Multimedia fate models are commonly used for predicting environmental fate factors and exposure factors of a pollutant. In this type of model the study area is represented by a number of homogeneous compartments, each representing a specific part of the environment (i.e. atmosphere, water, soil). The fate factor and exposure factor of a chemical in a certain compartment can be calculated by solving a set of mass balance equations that describe processes such as degradation and inter-compartment transfer. The fate factor represents the persistence of a chemical in the environment (e.g. in days) and the exposure factor the bioavailability of a chemical, represented by the fraction of the chemical dissolved. For different chemicals, different processes are important. Which processes are the most important for a certain compound depends on the physical-chemical properties of the compound. Also the environmental conditions (temperature, rain intensity etc.) influence the model predictions.

Apart from the fate factors and exposure factors, effect factors are also required in the calculation of ecotoxicological characterisation factors. The ecotoxicological effect factor (EF) reflects the change in the Potentially Affected Fraction (PAF) of species due to change in concentration ($PAF.m^3.kg^{-1}$).

Characterisation factors are reported for freshwater aquatic ecotoxicological effects and include impacts for emissions to urban air, rural air, freshwater and/or agricultural soil.

Figure 1: Main Steps of the USEtox^TM assessment

2.3 Human toxicity

In USEtox^TM, chemicals that have a potential to increase human disease have a characterization factor that includes a fate factor (FF), an exposure factor (XF) and an effect factor (EF) (Figure 1):

$$CF = FF \cdot XF \cdot EF$$

The fate factor and exposure factor are combined to reflect the intake fraction (iF) of a chemical, representing the fraction of the emitted mass that enters the human population:

$$iF = FF \cdot XF$$

Intake through inhalation and ingestion is commonly considered in iF calculations.

The fate part (FF) is the same for ecotoxicity and human toxicity. A human exposure model is put on top of this to describe the transport from environmental compartments to the human via inhalation and ingestion (XF). Apart from the fate factors and exposure factors, effect factors are also required in the calculation of human-toxicological characterisation factors. The effect factor (EF) reflects the change in life time disease probability due to change in life time intake of a pollutant (cases/kg). USEtox^TM determines effect factors for carcinogenic and non-carcinogenic chemicals separately. Data for effects after inhalation and oral exposure are also determined separately.

2.4 Worksheets

USEtox^{TM} includes a number of interlinked worksheets. These are explained briefly in Table 1. To work with the consensus model in practice, substance-specific information for the chemical under consideration need to be gathered and stored in the sheet 'Substance data'. The sheet 'Results' provides the characterisation factors, fate factors, intake fractions and effect factors for the chemical considered.

Table 1: Explanation of the worksheets

Worksheet	Explanation
Version	Background information on the USEtox^{TM} model and its developers
Agreement	Text of the license/collaboration agreement for using USEtox^{TM}
Instructions	Instructions how to perform single substance calculations and series calculation for a list of chemicals
Run	Specification of the model runs and calculation routines for fate factors, exposure factors, intake fractions, effect factors and characterisation factors for human toxicity and freshwater aquatic ecotoxicity
Results	Presentation of the relevant outcomes of USEtox^{TM}
Substance data	Substance-specific information required to calculate characterisation factors with USEtox^{TM}. Important sheet for the user
Landscape data	Default landscape data applied in USEtox^{TM}
Fate	Background data and equations required for the calculation of fate factors and environmental exposure factors
Human exposure	Background data and equations required for the calculation of human exposure factors
Ecotox effect	Background data and equations required for the calculation of ecotoxicological effect factors
Human tox effect	Background data and equations required for the calculation of human effect factors (carcinogenic and non-carcinogenic)

More detailed information on the model results can be found in the sheet 'Run'. Both the human and ecotoxicity characterization factors are calculated using standard matrix algebra. This means that each of the above mentioned factors (e.g. fate, exposure, and effect factors) are represented as matrices which are multiplied to obtain a characterization factor matrix, as the final result. This optimises calculation efficiency (i.e. only one model run for all emission scenarios), transparency, and interpretability of results. On the left side (top to bottom) of the worksheet 'Run' the main matrices with fate, exposure, intake fraction and effect factors, followed by the characterization factor matrices can be found. In detail, the following matrices containing the respective intermediate/final results are given:

- Loss processes – (d^{-1})
- Mass balance rate constants – k (d^{-1})
- Fate factors – FF (d)
- Available fraction – XF_{eco} (-)
- Human exposure factors – XF_{hum} (d^{-1})
- Human intake fractions – iF $(kg_{intake}.kg_{emitted}^{-1})$
- Human health Effect Factors – EF_{hum} $(cases.kg_{intake}^{-1})$
- Human Toxicity Potential expressed $(CTU_h = cases.kg_{emitted}^{-1})$
- Ecotoxicity Effect Factors – EF_{eco} $(PAF.m^3.kg^{-1})$
- Ecotoxicity Potentials $(CTU_e = PAF.m^3.d.kg_{emitted}^{-1})$

On the right side (top to bottom) of the same worksheet, the following interpretations of these intermediate results can be found:

- *Mass* of chemical emission per compartment (kg), *relative mass* (i.e. distribution of the emitted quantity between compartments), and *concentration* in each compartment (kg.m^{-3}) – although, the CF calculations are entirely independent from emitted quantities, this table provides the possibility to define an emission (kg.d^{-1}) into one or several compartments in the column "emission" and to calculate the above mentioned results mass, relative mass and concentration which do depend on the amount emitted;
- *Direct removal pathways* – the contribution of each removal pathway (i.e. diffusion/advection to another compartment, advection to another spatial scale, or degradation within the same compartment—diagonal element) to the total removal from each emission compartment (column);
- *Feedback fraction* – the fraction of an emission that returns to the medium of release after transfer to other media providing a measure of the level of coupling between media;
- *Residence time* in the environment (d) – the effective residence time in the respective compartment;
- *Mass fraction* in the receiving environment for an emission to the column;
- *Overall transferred fractions* from emission (columns) to receiving (row) compartment – the transferred fractions already include the sum of all possible transfer pathways through a third media;
- *Fraction of ingestion per intake pathway* – contribution of each exposure pathway (row) to overall exposure via ingestion for an emission to the respective compartment (row).

More in-depth explanations and the basis for this matrix-algebra framework can be found in Rosenbaum et al. (2007).

2.5 Recommended and Interim characterisation factors

An outcome of the work in the USEtox^{TM} team, apart from the USEtox™ model itself, is the provision of characterisation factors for several thousand chemicals to be applied by the LCA practitioner. The provided characterisation factors have been classified as "recommended" or "interim". Recommended factors are given for substances where the USEtox™ model is considered fully appropriate and the underlying substance data is of sufficient quality to support a recommendation. In cases where relatively high uncertainty in addressing fate, exposure and/or effects of a chemical is expected, we label the characterisation factor as 'interim'. In practice, we give this recommendation in cases where the substance is a metal or an inorganic chemical, an organometallic chemical, an amphiphilic chemical (e.g. detergents) or dissociating under environmental conditions. We also recommend that aquatic ecotoxicological characterisation factors be specified as interim, if effect factors are based on species toxicity data covering less than three different trophic levels. This is to ensure a minimum variability of biological responses.

For human health effects, we recommend that characterisation factors be specified as interim if, effect factors are based on sub-acute data. Furthermore, if route-to-route extrapolation is applied to obtain ingestion or inhalation human health effect factors, a subdivision should be made between recommended and interim characterisation factors. First, human health characterisation factors based on route-to-route extrapolation should be considered interim when the primary target site is specifically related to the route of entry. In addition, characterisation factors based on extrapolation from the ingestion to inhalation route of entry should be considered interim if the expected fraction absorbed via inhalation is much higher than the fraction absorbed via ingestion, e.g. a factor of 1,000. This factor of 1,000 is rare but indicates that exposure by inhalation may be far more toxic than by ingestion. With the Kow-

based QSARs applied to calculate the expected fraction absorbed via inhalation, it appears that this factor of 1,000 applies for substances with Kow smaller than $2.5.10^{-2}$ or Kow larger than $4.5.10^{9}$. In these cases, the interim characterisation factor can underestimate the potential impact by inhalation.

3. Fate factor

In USEtox™, two geographical scales are specified:

- the continental scale with the following compartments: urban air, rural air, freshwater, sea, natural soil and agricultural soil;
- the global scale with the following compartments, air, freshwater, ocean, natural soil and agricultural soil.

The continental scale is nested in the global scale (see Figure 2). "Nested" means that chemicals can be transported from one scale to a higher scale and vice versa.
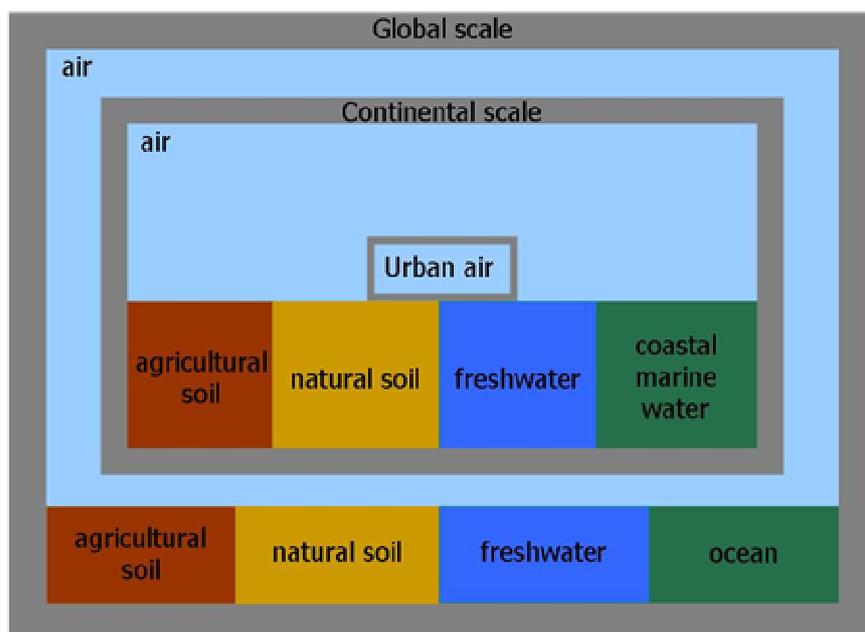
Figure 2: Nested structure of the USEtox™ (Rosenbaum et al., 2008)

The fate factor is equal to the compartment-specific residence time (in days) of a chemical. The longer the residence time, the longer a chemical remains in the environment. Within the consensus model, the residence time of a chemical depends on (i) the properties of the chemical, (ii) the selected emission compartment (e.g. urban air), and (iii) the selected receiving compartment (e.g. fresh water at the continental scale). For instance, USEtox™ calculates a residence time for dioxin of 136 days in agricultural continental soil after emission to rural continental air.

The fate component of USEtox™ accounts for removal processes and intermedia transport processes of chemicals in the environment. Examples of removal processes are (bio)degradation by micro-organisms, transport of the chemical to the sediment, leaching to the groundwater and escape to the stratosphere. Intermedia transport processes account for movement of chemicals from one compartment to the other (and back). Two types of intermedia transport processes exist: advective and diffusive transport. In the case of advective transport, the chemical moves with an environmental medium from one compartment to the other (one-way transport). For example, rivers transport a chemical from freshwater to seawater and rain transports a chemical from air to the earth's surface. Diffusive transport between two compartments, on the other hand, is passive two-way transport, i.e. the chemical can move from one compartment to another and back. Diffusive transport from air to water is called gas absorption, while diffusive transport from water to air is called volatilisation.

An important characteristic of intermedia transfer rates and removal rates is that they depend strongly on the properties of a chemical. To give a few examples:

- chemicals that are easily transformed by micro-organisms have high degradation rates in soil, water and sediment, while chemicals that are not susceptible to biodegradation will be persistent in these compartments.
- chemicals that tend to bind strongly to particles (hydrophobic chemicals) have a relative high removal from water to sediment via sedimentation of suspended particles.
- chemicals with a high vapour pressure (and low solubility) will have a relatively high tendency for passive transport from water to air.

The fate model part of USEtox[TM] calculates the residence time of a chemical, based on the quantification of all these environmental processes. This is done by solving the mass balance under steady state conditions with the help of linear algebra calculation rules. Steady state means that concentrations do not change over time in the compartments considered, when there is a constant emission rate. To run the fate model for organic chemicals a set of substance-specific input parameters must be provided in the worksheet 'substance data' of USEtox[TM] (Table 2). For inorganic chemicals, including metals, Table 3 shows the data required. We recommend that preference be given to experimental data over parameter estimates in building the substance data lists. Furthermore, we recommend specific and careful attention to units of the data, since many errors are made in units translation. Inputs should match exactly the units specified in Tables 2 and 3 (and the substance data worksheet).

Table 2: List of substance-specific input parameters required for the fate calculation in USEtox[TM] for organics

Input parameter	Abbreviation	Unit	Column in substance data sheet	Necessary?[a]
Molecular weight	MW	$g.mol^{-1}$	4	Yes
Partitioning coefficient between octanol and water	K_{OW}	-	5	Yes
Partitioning coefficient between organic carbon and water	K_{oc}	$L.kg^{-1}$	6	No
Henry law coefficient (at 25˚C)	K_H25C	$Pa.m^3.mol^{-1}$	7	No
Vapour pressure (at 25˚C)	Pvap25	Pa	8	Yes
Solubility (at 25˚C)	Sol25	$mg.L^{-1}$	9	Yes
Partitioning coefficient between dissolved organic carbon and water	K_{DOC}	$L.kg^{-1}$	10	No
Degradation rate in air	$kdeg_A$	s^{-1}	16	Yes
Degradation rate in water	$kdeg_W$	s^{-1}	17	Yes
Degradation rate in sediment	$kdeg_{Sd}$	s^{-1}	18	Yes
Degradation rate in soil	$kdeg_{Sl}$	s^{-1}	19	Yes
Bioaccumulation factor in fish/biota	BAF_{fish}	l/kg	30	No

[a] in case no experimental data is available, default QSAR-models in USEtox[TM] are applied to estimate input parameters, $K_{oc} = 1.26 \times K_{ow}^{0.81}$; $K_H25C = Pvap25 \times MW/Sol25$; $K_{DOC} = 0.08 \times K_{ow}$; $BAF_{fish} = 0.05 \times K_{ow}$.

Table 3: List of substance-specific input parameters required for the fate calculation in USEtox^{TM} for metals

Input parameter	Abbreviation	Unit	Column in substance data sheet	Necessary?
Molecular weight;	MW	g.mol^{-1}	4	Yes
Henry law coefficient	K$_H$25C	Pa.m^3.mol^{-1}	7	No (set at 1E-20)
Partitioning coefficient between dissolved organic carbon and water	K$_{DOC}$	L.kg^{-1}	10	Yes
Partitioning coefficient between suspended solids and water	Kp$_{SS}$	l/kg	11	Yes
Partitioning coefficient between sediment particles and water	Kp$_{Sd}$	l/kg	12	Yes
Partitioning coefficient between soil particles and water	Kp$_{Sl}$	l/kg	13	Yes
Degration rate in air	kdeg$_A$	s^{-1}	16	No (set at 1E-20)
Degration rate in water	kdeg$_W$	s^{-1}	17	No (set at 1E-20)
Degration rate in sediment	kdeg$_{Sd}$	s^{-1}	18	No (set at 1E-20)
Degration rate in soil	kdeg$_{Sl}$	s^{-1}	19	No (set at 1E-20)
Bioaccumulation factor in fish/biota	BAF$_{fish}$	l/kg	30	Yes

The fate factor results (in days) can be found in columns 20-55 of the 'Results' worksheet. Explanation of the abbreviations used in these columns is given in Table 4.

Table 4: Explanation of the abbreviations used in the fate factor results of USEtox^{TM}

Abbreviation	Explanation
airU	Urban air at the continental scale
airC	Rural air at the continental scale
fr.waterC	Freshwater at the continental scale
seawaterC	Coastal sea water at the continental scale
nat.soilC	Natural soil at the continental scale
agr.soilC	Agricultural soil at the continental scale
airG	Rural air at the global scale
fr.waterG	Freshwater at the global scale
oceanG	Ocean at the global scale
nat.soilG	Natural soil at the global scale
agr.soilG	Agricultural soil at the global scale

4. Exposure factors

4.1 Environment

In USEtox^{TM}, The environmental exposure factor for freshwater ecotoxicity is the fraction of a chemical dissolved in freshwater (FR$_{w.w}$). It is calculated by

$$FR_{w.w} = \frac{1}{1 + (Kp \cdot SUSP + K_{doc} \cdot DOC + BCF_{fish} \cdot BIOmass)/1 \cdot 10^6}$$

where Kp is the partition coefficient between water and suspended solids (l/kg), SUSP the suspended matter concentration in freshwater (= 15 mg/l in USEtox^{TM}), K$_{doc}$ the partitioning coefficient between dissolved organic carbon and water, DOC the dissolved organic carbon concentration in freshwater (= 5 mg/l in USEtox^{TM}), BCF$_{fish}$ the bioconcentration factor in fish (l/kg) and BIOmass the concentration of biota in water (= 1 mg/l in USEtox^{TM}).

The chemical-specific data required for calculating the environmental exposure factor is already gathered for the fate factor analysis. No extra chemical-specific data is required in this step.

The environmental exposure factor results for freshwater, i.e. the dissolved fraction (dimensionless) can be found in column 88 of the 'Results' worksheet.

4.2 Humans

Human exposure factors reflect the rate at which a pollutant is able to transfer from a receiving compartment into the human population through a series of exposure pathways. In USEtox^{TM} the following human exposure pathways are modelled:

- Air (inhalation);
- Drinking water;
- Exposed produce (= above-ground leaf crops, including fruit and cereals);
- Unexposed produce (= below-ground root crops);
- Meat;
- Dairy products;
- Fish.

The human exposure factor of a chemical depends on (i) the properties of the chemical, (ii) the selected receiving compartment (e.g. fresh water at the continental scale) and (iii) the exposure pathway (e.g. drinking water).

For exposure via inhalation of air, the exposure factor (XF$_{inh}$) is calculated by

$$XF_{inh} = INH \cdot POP / VOLUME_{air}$$

where INH is the average inhalation rate of a person (13 m^3/day), POP is the population number (e.g. 900 million on the continental scale) and VOLUME$_{air}$ the volume of the air compartment (e.g. 5.76x10^{10} m^3 at the urban scale).

The exposure factor (days^{-1}) for a specific food item or drinking water at a specific scale (e.g. continent) equals

$$XF_{i,r} = BAF_{i,r} \cdot PROD_i \cdot POP / MASS_r$$

where $BAF_{i,r}$ is the bioaccumulation factor of the chemical of exposure pathway i (e.g. fish) via compartment r (e.g. freshwater) in kg/kg, $PROD_i$ is the production per person of item i in the exposure pathway (e.g. 0.04 kg/day/person for freshwater fish), and $MASS_r$ is the mass of compartment r (e.g. $6.8 \cdot 10^{14}$ kg for continental freshwater)

Substance-specific bioaccumulation factors (BAF) are required in the human exposure factor calculation (Table 5). For most chemicals, experimental data are lacking for the BAF. In these cases, Quantitative Structure Activity Relationships (QSARs) can be applied to estimate the BAF on chemical properties that are well-known. In USEtox^{TM}, most BAFs are estimated on the basis of the Kow. Additionally, for the BAF of crops, the vapour pressure and solubility of a chemical play a role.

Table 5: List of substance-specific input parameters of organics additionally required for the human exposure calculation in USEtox^{TM}

Input parameter	Abbreviation	Unit	Column in substance data sheet	Necessary?
Degration rates in above-ground plant tissues	kdeg$_P$	s^{-1}	15	No
Bioaccumulation factor in root crops	BAF$_{root}$	kgveg.kgsoil^{-1}	26	No
Bioaccumulation factor in leaf crops	BAF$_{leaf}$	kgveg.kgsoil^{-1}	27	No
Biotransfer factor for meat	BTF$_{meat}$	d.kgmeat^{-1}	28	No
Biotransfer factor for milk	BTF$_{milk}$	d.kgmilk^{-1}	29	No
Bioaccumulation factor in fish	BAF$_{fish}$	Kgfish.kgwater^{-1}	30	No

Data requirements for metals are the same as listed for organics in Table 5. The difference is that experimental values are required to run the model ('Necessary?' is 'yes' for metals for all five BAF or BTF input parameters).

The combined fate factor and human exposure factor results, i.e the intake fractions of a chemical can be found in the columns 56-83 of the 'Results' worksheet.

5. Ecotoxicological effect factor

In USEtox[TM], the ecotoxicological effect factor is calculated by determining the linear slope along the concentration–response relationship up to the point where the fraction of effected species is 0.5 (Figure 3). The ecotoxicological effect factor of a chemical equals:

$$EF = \frac{0.5}{HC50}$$

where the HC50, based on species-specific EC50 data, is defined as the hazardous concentration of chemical at which 50% of the species are exposed above their EC50. The EC50 is the water concentration at which 50% of a population displays an effect (e.g. mortality). Aquatic ecotoxicological effect factors have the dimension m^3/kg.

The log HC50, also called α, can be calculated as follows:

$$\log HC50 = \alpha = \frac{1}{n_s} \cdot \sum_s \log EC50_s$$

where n$_s$ is the number of species.
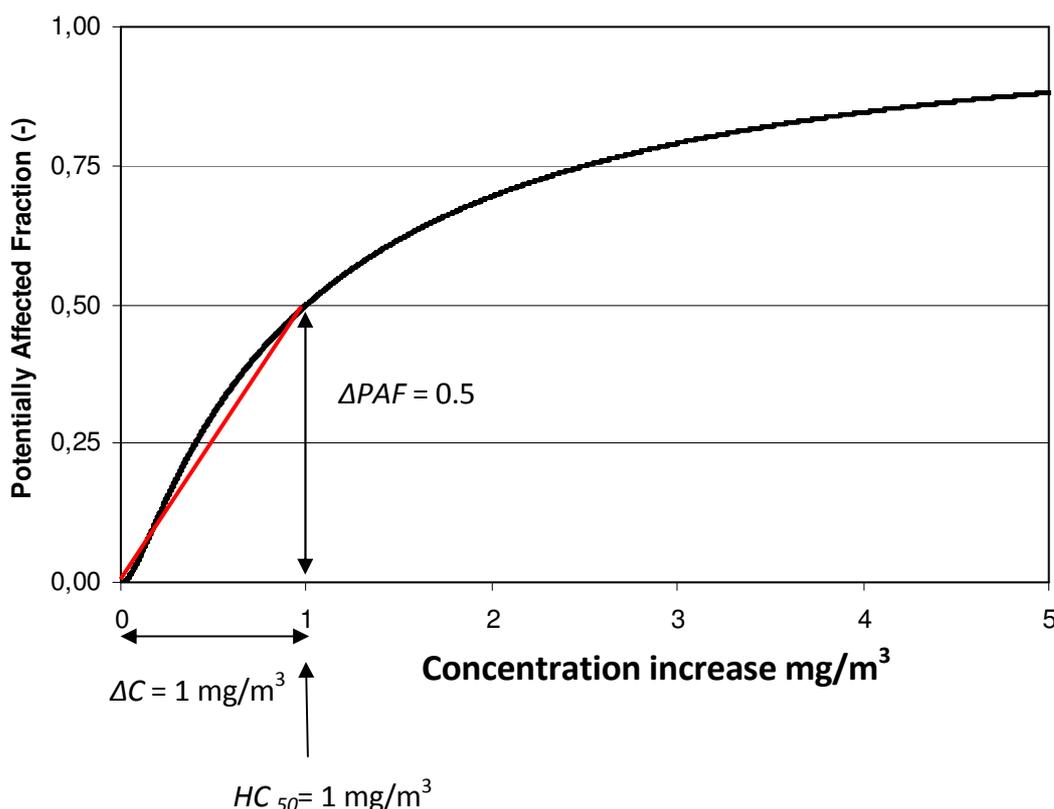
Figure 3: Example visualisation of the extrapolation procedure for the ecotoxicological effect factor in the consensus model.

In USEtox[TM], we calculate aquatic ecotoxicological effect factors based on geometric means of single species EC50 tests data. Chronic values have priority as long as they represent measured EC50 values. Note that chronic EC50 values are seldom reported. Second-order priority is given to acute data, applying an acute-to-chronic extrapolation factor that is set to a default factor of 2 (Rosenbaum et al., 2008).

The following calculation steps of the logHC50 can be identified:

1. Gather experimental or estimated EC50 data for the chemical of interest;
2. Specify for every EC50-value whether it is chronic or acute exposure;
3. Calculate the geometric mean chronic or acute EC50 (mg/l) for every individual species (this can e.g. be done with the function =GEOMEAN() in Excel).
4. In case of acute EC50-data, derive the chronic-equivalent EC50 per species by dividing by a factor of 2 (acute-to-chronic extrapolation factor)
5. Take the log of the geometric mean EC50s and calculate the average of the log-values. This average equals the logHC50 (log mg/l).
6. Implement this value in column 20 of the sheet "Substance data" of USEtox.xls.
7. Always be careful with the units!

6. Human effect factors

The human-toxicological effect factor (EF) reflects the change in life time disease probability due to change in life time intake of a pollutant (cases/kg$_{intake}$). In USEtox^{TM}, separate effect factors are derived for non-carcinogenic effects and carcinogenic effects. Furthermore, for each effect type (non-carcinogenic and carcinogenic) the two exposure routes, i.e. inhalation and ingestion are addressed separately. The human-toxicological effect factor is calculated under the assumption of linearity in concentration–response up to the point of at which the life time disease probability is 0.5 (Figure 4).
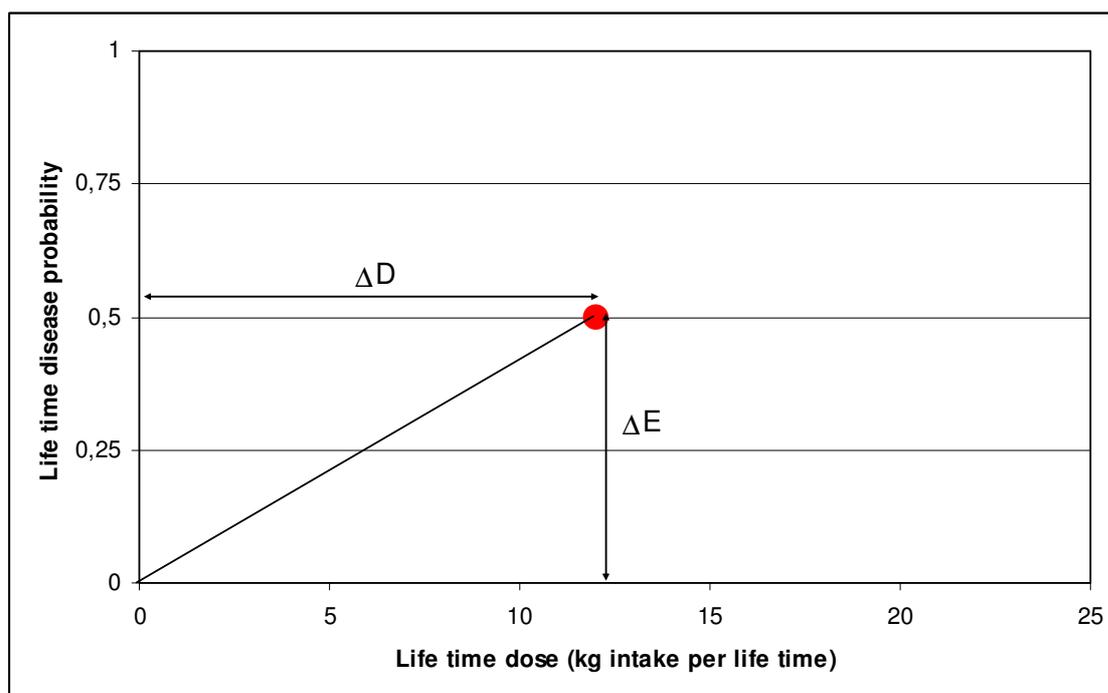
Figure 4: Visualisation of the extrapolation procedure for the human-toxicological effect factor in the USEtox^{TM} model.

The human-toxicological effect factor of a chemical equals:

$$EF = \frac{0.5}{ED50}$$

For carcinogenic and non-carcinogenic effects, the ED50$_{h,j}$ for humans related to inhalation or oral exposure (kg/person/lifetime) is calculated by:

$$ED50_{h,j} = \frac{ED50_{a,t,j} \cdot BW \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

where ED50$_{a,t,j}$ is the daily dose for animal a (e.g. rat) and time duration t (e.g. subchronic) per kg body weight that causes a disease probability of 50% for exposure route j (mg.kg^{-1}.day^{-1}), AF_a the extrapolation factor for interspecies differences (see Table 6), AF_t is the extrapolation factor for differences in time of exposure, i.e. a factor of 2 for subchronic to chronic exposure and a factor of 5 for subacute to chronic exposure (Huijbregts et al., 2005), BW is the average body weight of humans (70 kg), LT is the average lifetime of humans (70 years), N the number of days per year (365 days.year^{-1}).

If the inhalation ED50 is given as the concentration in air (mg.m^{-3}), the human-equivalent ED50 (kg/person/lifetime) can be estimated by

$$ED50_{h,inh} = \frac{ED50_{a,t,inh} \cdot INH \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

where INH is the average human inhalation rate (13 m^3.day^{-1}). Note that the AF_a, the extrapolation factor for interspecies differences, is by default 1 if the ED50 is given as concentration in the air. Metabolic activity and inhalation rate are assumed to have the same ratio for all species.

Table 6: Interspecies extrapolation factor ($AF_{interspecies}$) for various species i in case of body weight-based extrapolation (Huijbregts et al., 2005)

Type	$AF_{interspecies}$ (-)	Average bodyweight (kg)
human	1.0	70
pig	1.1	48
dog	1.5	15
monkey	1.9	5
cat	1.9	5
rabbit	2.4	2
hen	2.6	1.6
mink	2.9	1
guinea pig	3.1	0.750
rat	4.1	0.250
hamster	4.9	0.125
gerbil	5.5	0.075
mouse	7.3	0.025

For carcinogenic effects, the ED50 can also be estimated from the carcinogenic, low-dose, slope factor q* by the 1/q*-to-ED50 extrapolation factor:

$$ED50_{a,t,j} = \frac{1}{q_{a,t,j}} \cdot AF_q$$

where q*$_{a,t,j}$ is the carcinogenic, low-dose, slope factor for animal a (e.g. rat) and time duration t (e.g. chronic) for exposure route j (kg.day.mg^{-1} or m^3.mg^{-1}), and AF_q the extrapolation factor for 1/q* to ED50, which is a factor of 0.8 (Huijbregts et al. 2005).

For non-carcinogenic effects, the ED50 can also be estimated from the no-observed adverse effect level (NOAEL) by a NOAEL-to-ED50 extrapolation factor:

$$ED50_{a,t,j} = NOAEL_{a,t,j} \cdot AF_N$$

where NOAEL$_{a,t,j}$ is the daily dose per kg body weight or concentration for animal a (e.g. rat) and time duration t (e.g. chronic) that causes No Observed Adverse Effects for exposure route j (mg.kg^{-1}.day^{-1} or mg.m^{-3}), and AF_N the extrapolation factor for NOAEL to ED50, which is a factor of 9 (Huijbregts et al. 2005).

Finally, for some chemicals only the lowest observed adverse effect level (LOAEL) is available. In these cases, the NOAEL can be derived by a LOAEL-to-NOAEL extrapolation factor:

$$NOAEL_{a,t} = \frac{LOAEL_{a,t}}{AF_L}.$$

where AF_L is the extrapolation factor from LOAEL to NOAEL, which is a factor of 4 (Huijbregts et al, 2005).

To summarize:
1. Gather experimental (i) carcinogenic oral ED50 data, (ii) carcinogenic inhalatory ED50 data, (iii) non-carcinogenic oral ED50 data, and (iv) non-carcinogenic inhalatory ED50 data;
2. Specify for every ED50-value whether it is chronic, subchronic or subacute exposure;
3. In case of subchronic or subacute ED50-data, derive the chronic-equivalent ED50 by respectively dividing by a factor of 2 and a factor of 5 (subchronic-to-chronic extrapolation factor and subacute-to-chronic extrapolation factor);
4. In case of non-human ED50-data, derive the human-equivalent ED50 by dividing by an extrapolation factor for interspecies differences (see Table 6);
5. In case only carcinogenic, low-dose, slope factors are available, derive the carcinogenic ED50 via multiplication of 1/q* with the extrapolation factor for 1/q* to ED50, which is a factor of 0.8;
6. In case only NOAEL-data or NOAEC-data are available, derive the non-carcinogenic ED50 via multiplication with the extrapolation factor for NOAEL to ED50, which is a factor of 9;
7. In case only LOAEL-data or LOAEC-data are available, derive the non-carcinogenic ED50 via division by the extrapolation factor for LOAEL to NOAEL, which is a factor of 4, and multiply with the extrapolation factor for NOAEL to ED50, which is a factor of 9;
8. Implement the human-equivalent ED50-values (maximum 4 values) in columns 21-24 of the sheet "Substance data" of USEtox.xls.
9. Always be careful with the units!

7. Calculation of characterisation factors

Single substance calculation

1. On worksheet "Substance data"
   - Create input row by filling out columns 2 to 30 (B to AD) for the substance of interest. Do NOT use row 5 for this purpose, but always row 6 or further below.

2. On worksheet "Run"
   - Select a substance by entering the row no. in cell C5
   - Select a region by entering the row no. in cell J5 on which this region appears in sheet "landscape data" (presently, the only option is the USEtox default region)
   - Read from D111:I111 the Characterisation Factors for Human Toxicity emissions to urban air and to continental air, freshwater, seawater, natural soil and agricultural soil.
   - Read from D120:I120 the Characterisation Factors for Ecotoxicity emissions to urban air and to continental air, freshwater, seawater, natural soil and agricultural soil.

3. Or on worksheet "Results"
   - Read Characterisation Factors for Human Toxicity from D5:O5. For human toxicity, characterisation factors for carcinogenic and non-carcinogenic impacts are reported. In addition to that, carcinogenic and non-carcinogenic characterisation factors are summed as well, assuming equal weighting between cancer and non-cancer effects. This results in a single characterisation factor per emission compartment.
   - Read Characterisation Factors for Freshwater Aquatic Ecotoxicity from P5:S5

Series calculation

1. On worksheet "Substance data"
   - Create an input table by filling out columns 2 to 30 (B to AD), one row per substance. Do NOT use row 5 for this purpose, but always row 6 or further below.

2. On worksheet "Run"
   - Fill in the number of the first row and the final row of your chemical dataset in respectively cell C5 and G5.
   - Run series calculation macro by clicking the button 'Run Series'

3. On worksheet "Results"
   - Read Characterisation Factors for Human Toxicity from columns 5 to 15. For human toxicity, characterisation factors for carcinogenic and non-carcinogenic impacts are reported. In addition to that, carcinogenic and non-carcinogenic characterisation factors are summed as well, assuming equal weighting between cancer and non-cancer effects. This results in a single characterisation factor per emission compartment.
   - Read Characterisation Factors for Freshwater Aquatic Ecotoxicity from columns 16 to19

8. Use of characterisation factors

The toxicity impact score is calculated by multiplying the mass of a substance emitted in a given compartment with the corresponding toxicity characterisation factor. For example, benzene emissions of 0.1 kg to rural air and 0.2 kg to continental freshwater would be characterised with a human toxicity impact score in comparitive toxic units (CTU$_h$) of:

$$IS_{human\,tox} = CF_{h\,benzene,rural\,air} \cdot M_{benzene,rural\,air} + CF_{h\,benzene,freshwater} \cdot M_{benzene,freshwater}$$
$$= 6.9 \cdot 10^{-8}\,[CTU_h\,/\,kg] \cdot 0.1[kg] + 3.9 \cdot 10^{-7}\,[CTU_h\,/\,kg] \cdot 0.2[kg]$$
$$= 8.4 \cdot 10^{-8}\,[CTU_h]$$

As described by Rosenbaum et al. (2008), the characterisation factors must be used in a way that reflects the large variation, often orders of magnitude, between chemical characterisation factors as well as the three orders of magnitude uncertainty on the individual factors. This means that contributions of 1%, 5%, or 90% to the total human toxicity score are essentially equal but significantly larger than those of a chemical contributing to less than one per thousand or less than one per million of the total score. Disregarding this fact has been a major cause of complaints about the variability of these factors across impact assessment methods, whereas the most important chemicals were often the same within a factor 1,000 across methods. In practice, this means that for LCA practitioners, these toxicity factors are very useful to identify the 10 or 20 most important toxics pertinent for their applications. The life cycle toxicity scores thus enable the identification of all chemicals contributing more than, e.g. one thousandth to the total score. In most applications this will allow the practitioner to identify 10 to 30 chemicals to look at in priority and, perhaps more importantly, to disregard 400 other substances whose impacts are not significant for the considered application. Once these most important substances have been identified further analysis can be carried out on the life cycle phase, application components responsible for these emissions, and the respective importance of fate, exposure and effect in determining the impacts of this chemical.

Due to its simple and transparent matrix format, USEtox^{TM} will also allow identification of the main exposure pathways, (e.g. inhalation, water ingestion, various food ingestion) as well as the relative importance of potential carcinogenic and non-carcinogenic effects in the overall score. The inclusion of an urban area as a sub-compartment and emission scenario implies that the life cycle inventory should accommodate a distinction between air emissions in high- and low- population density areas. When air emissions are undifferentiated, a possible assumption is that emissions take place proportionally to population living in each area, leading to e.g. 50% emitted in urban air and 50% in rural air at world level.

9. Literature

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