10. Toxicity

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10.1 Areas of protection and environmental mechanisms covered

The impact assessment method for assessing human toxicity concerning the area of protection of human health and for assessing freshwater ecotoxicity, marine water ecotoxicity and terrestrial soil ecotoxicity concerning the area of protection of ecosystem quality is based on Rosenbaum et al. (2008), Rosenbaum et al. (2011), and Henderson et al. (2011).

Description of impact pathways

Chemicals can be emitted to the environment (air, water, soil, etc.) during all life cycle stages of products, services and systems. Emission inventories of different products may contain hundreds of chemicals, of which many will have the potential to cause toxic impacts on human beings and/or ecosystems. Hence, identifying and quantifying human health and ecosystem impacts associated with emissions of toxic chemicals are an important aspect for developing more sustainable products and technologies. The related impact pathway is covering the environmental fate of emitted toxic chemicals, human and ecosystem exposure to increased environmental concentrations of these chemicals, the associated toxicity-related effects due to chemical exposure in different environmental compartments, and finally the translation of these effects into damages on human health and ecosystem quality (Figure 10.1; Equations 10.1 and 10.2).

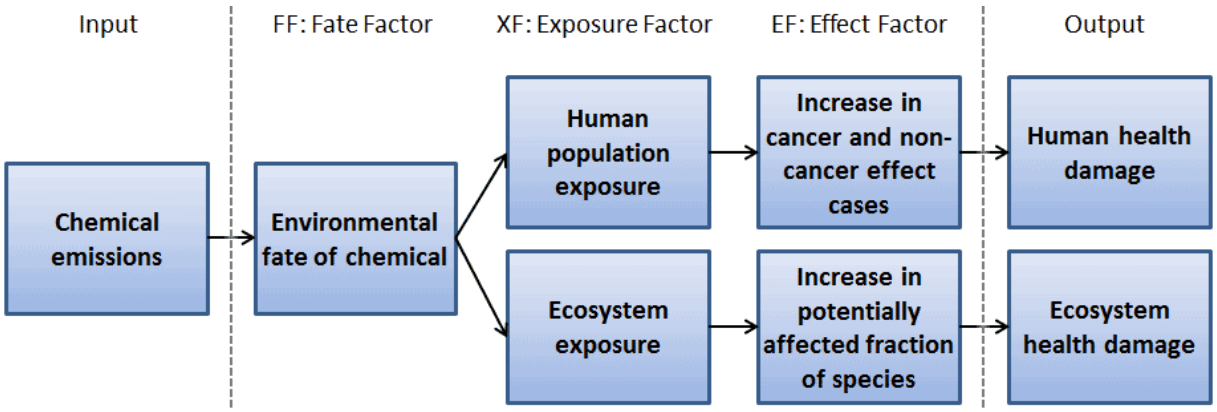

Figure 10.1: Cause-effect chain for damages on human health and ecosystem quality caused by chemical emissions. The interim steps of the impact pathways are depicted and the factors leading to them are described in Equation 10.1 for human toxicity and in Equation 10.2 for ecotoxicity.

The impact pathways for both human toxicity and ecotoxicity are consistently built from a set of multiplicative factors including (a) a fate factor accounting for the distribution and transformation of toxic chemicals in the environment, (b) an exposure factor relating environmental concentrations of toxic chemicals to human and ecosystem exposures, (c) an effect factor associating potential human toxicity and ecotoxicity effects per unit of chemical exposure, and (d) a damage factor relating toxicity effects to damages on human health and ecosystem quality. Chemicals thereby refer to organic chemical substances and metallic elements that exist in various chemical forms.

The toxicity-related human health characterization factor at endpoint level, CF^{h} [DALY/$kg_{emitted}$], representing the number of disability-adjusted life years (DALY) per kg of chemical emitted to an environmental compartment, is derived as follows:

$$CF^{\mathrm{h}} = \underbrace{FF \times XF^{\mathrm{h}}}_{iF} \times EF^{\mathrm{h}} \times DF^{\mathrm{h}} \qquad \textbf{Eq. 10.1}$$

where FF [$kg_{in\ compartment}$/($kg_{emitted}$/day)] is the fate factor relating the chemical mass in a given environmental compartment to the chemical mass emitted per day into an environmental compartment, XF^{h} [(kg_{intake}/day)/$kg_{in\ compartment}$] is the human exposure fator relating the chemical mass taken in per day by a human population to the chemical mass in a given environmental compartment, EF^{h} [disease cases/kg_{intake}] is the human toxicity effect factor relating the likelihood (or potential risk) of developing an adverse health effect expressed as number of cancer or non-cancer disease cases to the chemical mass taken in by a human population, and DF^{h} [DALY/disease cases] is the human damage factor relating the number of DALY to the number of cancer or non-cancer disease cases, respectively. Fate factor and human exposure factor can be combined into the population intake fraction, $iF = FF \times XF^{\mathrm{h}}$ [kg_{intake}/$kg_{emitted}$], directly relating the chemical mass taken in by a human population to the chemical mass emitted to a given environmental compartment or to the chemical mass applied (in case of exposure to pesticide residues in food crops). All factors in Equation 10.1 are further detailed in Equations 10.3 to 10.12.

The ecotoxicity-related ecosystem quality characterization factor at endpoint level, CF^{e} [PDF·$m^3_{exposure\ medium}$·day/$kg_{emitted}$], representing the potentially disappeared fraction of species (PDF) integrated over the volume of exposed compartment (e.g. freshwater) or medium (e.g. soil pore water) and time per kg of chemical emitted to an environmental compartment, is derived as follows:

$$CF^{\mathrm{e}} = FF \times XF^{\mathrm{e}} \times EF^{\mathrm{e}} \times DF^{\mathrm{e}} \qquad \textbf{Eq. 10.2}$$

where FF [$kg_{in\ compartment}$/($kg_{emitted}$/day)] is the fate factor relating the chemical mass in a given environmental compartment to the chemical mass emitted per day into the same or another environmental compartment, XF^{e} [$kg_{bioavailable}$/$kg_{in\ compartment}$] is the ecosystem exposure factor representing the bioavailability of chemicals to organisms in the environmental compartments considered for ecotoxicity, EF^{e} [PAF·$m^3_{exposure\ medium}$/$kg_{bioavailable}$] is the ecotoxicity effect factor relating the potential of the bioavailable fraction of a chemical to cause toxic effects to an exposed ecosystem expressed as potentially affected fraction of species in the exposed ecosystem integrated over the compartment or medium volume to the chemical mass in the environmental compartment surrounding the exposed ecosystem, and DF^{e} [PDF/PAF] is the ecosystem damage factor relating the potentially disappeared fraction of species to the potentially affected fraction of species. When the emission compartment is different from the compartment of the exposed ecosystem, the fate factor is interpreted as product of the residence time of a chemical in the receiving exposure compartment, FF_{i_2} [day], and the overall time-integrated chemical mass fraction transferred from the emission compartment i_1 to the exposure compartment i_2, $f_{i_2 \leftarrow i_1}$ [$kg_{in\ compartment}$/$kg_{emitted}$], i.e. $FF = f_{i_2 \leftarrow i_1} \times FF_{i_2}$. All factors in Equation 10.2 are further detailed in Equations 10.13 to 10.18.

Description of all related impact categories

This impact pathway affects the impact categories human health, freshwater ecosystem quality, marine ecosystem quality, and terrestrial ecosystem quality.

Methodological choice

For human toxicity and ecotoxicity impacts, global average CFs based on the assumption of linearity throughout the impact pathway are available to characterize potential human toxicity and ecotoxicity impacts associated with emissions of toxic chemicals into the environment.

Spatial detail

Global average CFs for human toxiciy and ecotoxicity are provided by default for different environmental emission compartments (local scale: indoor and urban air; continental and global scale: rural air, agricultural and natural soil, freshwater and marine water), where indoor, urban and continental parameters represent average residential and industrial buildings for indoor (Hellweg et al. 2009), an average city for urban air and a default continent (defined as average of all real-world continents) for the continental scale (Rosenbaum et al. 2008). The considered environmental compartments are shown in Figure 10.2.

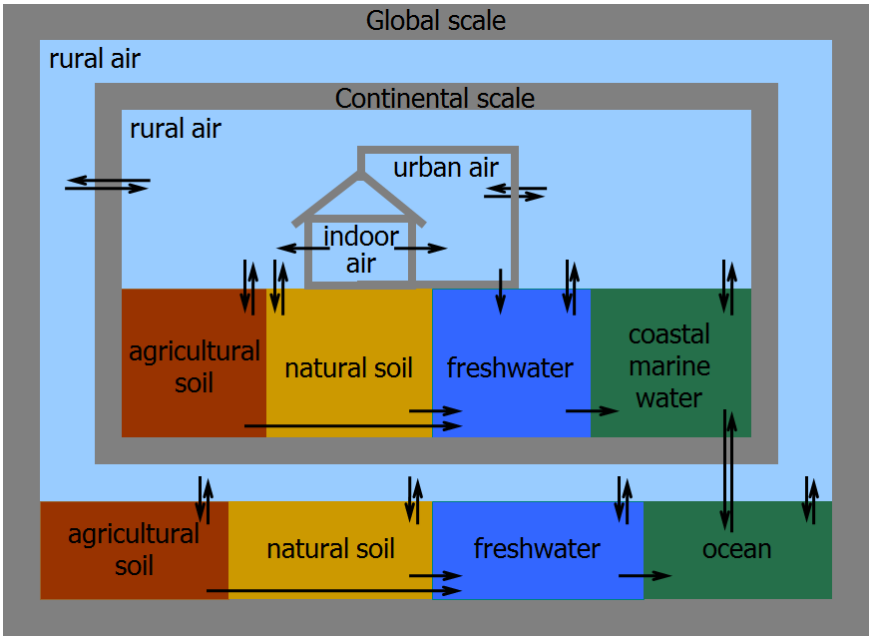

Figure 10.2: Nested compartment setup for human toxicity and ecotoxicity.

CFs for human toxicity and ecotoxicity are furthermore derived for 16 parameterized sub-continental zones[1] (Central Asia; Indochina; Northern Australia; Southern Australia and New Zealand; Southern Africa; North, West, East and Central Africa; Argentina+; Brazil+; Central America & Caribbean; USA and Southern Canada; Northern Europe and Northern Canada; Europe; East Indies and Pacific; India+; Eastern China; Japan and Korean Peninsula) and 8 parameterized continental zones (North America; Latin America; Europe; Africa and Middle East; Central Asia; Southeast Asia; Northern regions; Oceania) based on work by Kounina et al. (2014). Continental zones are either weighted averages of sub-continental zones (e.g. continental zone "Oceania" is the weighted average of the two sub-continental zones "Northern Australia" and "Southern Australia and New Zealand") or in specific cases equal to sub-continental zones (e.g. continental zone "Northern regions" equals the sub-continental zone "Northern Europe and Northern Canada"). CFs for continental and sub-continental regions can addietionally serve as sensitivity analysis of the default average global CFs (representing average continental emissions).

[1] The symbol "+" in the name of some sub-continental zones indicates that besides the country given in the zone name includes further, typically much smaller countries. Argentina+ includes Argentina, Chile, Falkland Islands (Malvinas), Paraguay, and Uruguay; Brazil+ includes Bolivia, Peru, most of Brazil, Colombia, and Southern Ecuador; India+ includes India, Bangladesh, Bhutan, Nepal, Pakistan, and Sri Lanka.

Global average CFs for freshwater ecotoxicity and marine water ecotoxicity for metals are based on, respectively, averaging CFs from 7 European freshwater archetypes representing the variation of freshwater chemistries in Europe mainland based on work by Gandhi et al. (2011) and Dong et al. (2014), and averaging CFs from 64 large marine ecosystems representing comparatively independent coastal seas, in total covering the global coastal zones, based on work by Dong et al. (2016). Global generic CFs for terrestrial soil ecotoxicity for metals are based on combining natural and agricultural soil compartments. Available properties (pH and organic carbon content) of these two soil compartments as originally defined by Rosenbaum et al. (2008) were matched with other relevant soil properties (e.g., content of clay, concentrations of dissolved base cations), equal to properties of soils which are the closest in terms of pH and organic carbon to properties of the natural or agricultural soil compartments. Details regarding the soil properties used for the matching are provided in (Owsianiak et al. 2013).

10.2 Calculation of the characterization factors at endpoint level

Human toxicity

The average toxicity-related characterization factor for human health is defined in terms of DALY per kg emitted chemical into a given environmental compartment as shown in Figure 10.1 and Equation 10.1. The specific factors are described below.

Fate factor: The fate factor, FF [$kg_{in\ compartment}$/($kg_{emitted}$/day)], relates the time-integrated chemical mass in a given environmental compartment to the chemical mass emitted per day into the environment. The fate factor thereby accounts for loss processes within environmental compartments (e.g. degradation) and multimedia transfer processes between different environmental compartments (e.g. diffusion and advection). The fate factor can be interpreted as the time-integrated chemical mass in a given environmental compartment due to an emission of the chemical in the same or another compartment. Fate factors for all considered environmental compartments can be expressed as elements of a square matrix, the fate matrix $\mathbf{FF} \in \mathbb{R}^{n\times n}$, whose columns denote $i \in \{1, \dots, n\}$ emission compartments and whose rows denote $j \in \{1, \dots, n\}$ receiving compartments, where the chemical is finally transferred to. The j^{th} main diagonal element of $\mathbf{FF}$ describes the effective residence time in the j^{th} environmental compartment. Each off-diagonal element of $\mathbf{FF}$ can be interpreted as the fraction transferred from an emission source compartment i to receiving compartment j with $i \neq j$ and $i, j \in \{1, \dots, n\}$ where all transfers through third compartments are already considered (Margni et al. 2004), multiplied by the effective residence time in compartment *j*. The fate matrix is determined from the square matrix of first order rate coefficients $\mathbf{K} \in \mathbb{R}^{\mathrm{n}\times\mathrm{n}}$ as (Rosenbaum et al. 2007):

$$\mathbf{FF} = -\mathbf{K}^{-1} \qquad \textbf{Eq. 10.3}$$

Elements of $\mathbf{K}$ are the first order rate coefficients $k_{ij}, i, j \in \{1, \dots, n\}$ [($kg_{emitted}$/day)/$kg_{in\ compartment}$]. Each main diagonal element of $\mathbf{K}$, i.e. k_{ij} with $i = j$ and $i, j \in \{1, \dots, n\}$, contains the bulk removal rate coefficient in compartment i, $k_{\mathrm{loss},i}$, plus the sum of transfer rate coefficients from compartment i to relevant adjacent compartments j, and off-diagonal elements of $\mathbf{K}$, i.e. k_{ij} with $i \neq j$ and $i, j \in \{1, \dots, n\}$ contain individual transfer rate coefficients from compartment j to compartment i. $\mathbf{K}$, hence, has the following structure (Fantke et al. 2013):

$$\mathbf{K} = \begin{pmatrix} k_{11} & \cdots & k_{1n} \\ \vdots & \ddots & \vdots \\ k_{n1} & \cdots & k_{nn} \end{pmatrix} \text{ with } k_{ij} = \begin{cases} k_{ij} & \text{for } i \neq j \\ -\left(k_{\mathrm{loss},j} + \sum_{l=1, l\neq i}^{n} k_{li}\right) & \text{for } i = j \end{cases} \qquad \textbf{Eq. 10.4}$$

with line and column indices for receiving and source compartments, respectively. Each element of $\mathbf{K}$ consists of one or more physical transport or removal process and, thus, describes a part of the fate of chemicals in the environment. These processes are futher described elsewhere (Rosenbaum et al. 2007, Rosenbaum et al. 2008, Henderson et al. 2011) and distinguish between neutral organic chemicals and ionized organic chemicals (bases, acids) according to the approach used by van Zelm et al. (2013) based on work by Franco and Trapp (2008) and Franco and Trapp (2010).

Human exposure factor: The human exposure factor, XF^{h} [(kg_{intake}/day)/$kg_{in\ compartment}$], relates the chemical mass taken in per day by a human population to the chemical mass in a given environmental compartment. Human exposure routes considered are inhalation and ingestion, where it can be distinguished between direct exposure (via inhalation of air and via ingestion of drinking water) and indirect exposure through bioaccumulation processes in animal tissues, such as meat, milk, and fish (Rosenbaum et al. 2011). Dermal exposure is currently not considered. Human exposure factors describing direct exposure, $XF^{\mathrm{h}}_{\mathrm{direct},x,i}$, are derived as:

$$XF^{\mathrm{h}}_{\mathrm{direct},x,i} = \frac{IR_{x,i} \times n_{\mathrm{pop}}}{\rho_i \times V_i} \qquad \textbf{Eq. 10.5}$$

where $IR_{x,i}$ [kg_{intake}/day/capita] is the individual human intake rate of environmental medium $i \in \{\mathrm{air}, \mathrm{freshwater}\}$ via exposure pathway $x \in \{\mathrm{inhalation\ of\ air}, \mathrm{ingestion\ of\ water}\}$, n_{pop} [capita] is the population head count in the exposure compartment, ρ_i $\left[\mathrm{kg_{compartment}/m^3_{compartment}}\right]$ is the bulk density of the i^{th} compartment, and V_i $\left[\mathrm{m^3_{compartment}}\right]$ is the volume of the i^{th} compartment. For inhalation exposure to chemicals in indoor air environments based on Wenger et al. (2012), an additional factor is included for calculating XF, namely a unitless mixing factor that accounts for incomplete mixing conditions (Hellweg et al. 2009). However, this mixing factor is currently set to 1, i.e. assuming complete mixing, and is therefore not considered in Equation 10.5. For indirect exposure, bioaccumulation in food substrates is additionally considered. Hence, human exposure factors describing indirect exposure, $XF^{\mathrm{h}}_{\mathrm{indirect},x,i}$, are derived as:

$$XF^{\mathrm{h}}_{\mathrm{indirect},x,i} = \frac{BAF_{x,i} \times IR_{x,i} \times n_{\mathrm{pop}}}{\rho_i \times V_i} \qquad \textbf{Eq. 10.6}$$

where $BAF_{x,i} = C_x / C_i$ [$kg_{in\ food\ substrate}$/$kg_{in\ compartment}$] is the bioaccumulation factor expressed as ratio between the steady-state concentration in the food substrate corresponding to the x^{th} exposure pathway (e.g. ingestion of meat), C_x [$kg_{in\ food\ substrate}$/$m^3_{food\ substrate}$], and the steady-state concentration in the i^{th} compartment, C_i $\left[\mathrm{kg_{in\ compartment}/m^3_{compartment}}\right]$. $IR_{x,i}$ [kg_{intake}/day/capita] refers for indirect exposure to the individual ingestion intake rate of food substrate related to the x^{th} exposure pathway. Each human exposure factor represents the increase in human exposure via the x^{th} exposure pathway due to an increase in chemical mass (or concentration) in the i^{th} compartment. The considered human exposure pathways are shown in Figure 10.3 and include inhalation of indoor, urban and rural air, ingestion of untreated surface freshwater, ingestion of leaf crops (exposed produce) and root crops (unexposed produce) grown on agricultural soil, ingestion of meat and milk, ingestion of fish from freshwater and marine water compartments (Rosenbaum et al. 2008, Rosenbaum et al. 2011), and ingestion of food crops grown on agricultural soil (wheat, paddy rice, tomato, apple, lettuce, potato) that are directly treated with pesticide chemicals (Fantke et al. 2011b, Fantke et al. 2012). In contrast, exposure pathways with negligible contribution to overall human exposure (e.g. ingestion of eggs) for most chemicals are not included following the principle of parsimony (Hauschild et al. 2008).

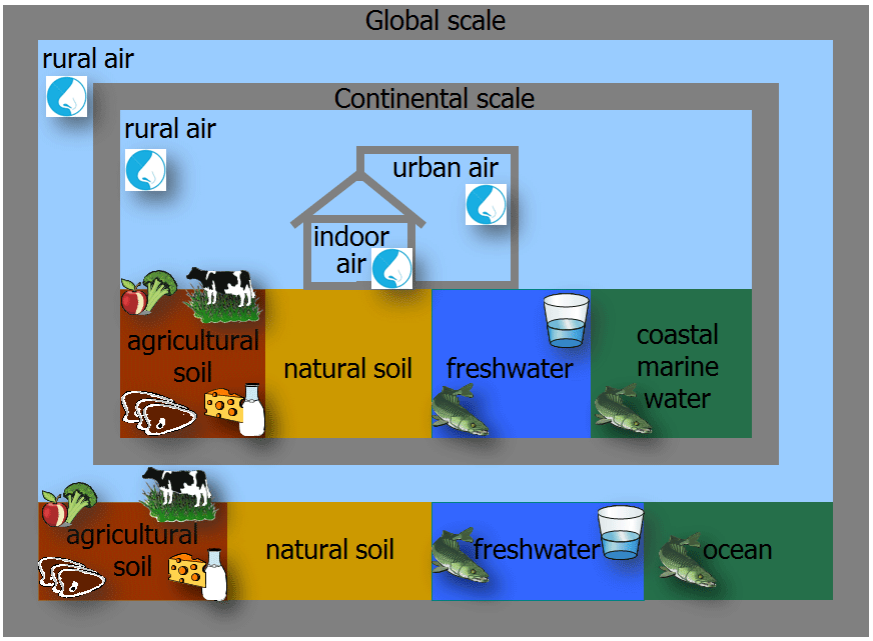

Figure 10.3: Exposure pathway setup for human toxicity.

Population intake fraction: The population intake fraction, iF [$kg_{intake}/kg_{emitted}$], directly relates the chemical mass that is eventually taken in by a human population via various exposure pathways to the chemical mass emitted to a given environmental compartment (Bennett et al. 2002a, Bennett et al. 2002b) or to the chemical mass applied (in case of exposure to pesticide residues in food crops, see Equations 10.8 and 10.9). The population intake fraction is the product of fate factor and human exposure factor (Rosenbaum et al. 2007, Rosenbaum et al. 2011):

$$iF = FF \times XF^{\mathrm{h}} \qquad \textbf{Eq. 10.7}$$

For human exposure to pesticide residues in food crops via ingestion of harvested crops, the corresponding population residue-related intake fraction directly relates the chemical mass that is eventually taken in by a human population via consumption of $c \in \{1, \ldots, n\}$ harvested food crop components to the chemical mass applied to the environment. Since transfer from the mass applied to the residual mass in the crop is not captured in the fate factors matrix, the corresponding intake fraction for crop residues, iF_{residue} [$kg_{intake}/kg_{applied}$], needs to directly relate the mass found as crop residues to the mass of chemical applied to the crop (Fantke et al. 2011b):

$$iF_{\mathrm{residue}} = \frac{\sum_p m_{\mathrm{residue},p}}{m_{\mathrm{applied}}} \times PF \qquad \textbf{Eq. 10.8}$$

where $m_{\mathrm{residue},p}$ [$kg_{\text{in crop harvest}}$] is the residual mass of chemical in the p^{th} harvested food crop component, m_{applied} [$kg_{applied}$] is the total chemical mass applied to the environment, and PF [$kg_{intake}/kg_{\text{in crop harvest}}$] is the residue reduction factor due to food processing (e.g. washing, cooking) relating chemical residues in processed food crop commodities, $kg_{\text{in processed food}}/kg_{\text{food product}}$, to chemical residues in harvested, unprocessed food crop components, $kg_{\text{in crop harvest}}/kg_{\text{harvested crop}}$ (Fantke et al. 2011a). The fractions of chemical mass applied that is emitted to the i^{th} compartment, f_i [$kg_{applied}/kg_{emitted}$], with $i \in$ {air, soil}, are further combined with the respective intake fractions for an emission to these compartments, iF_i. With that, we would arrive at the total population intake fraction from an application to any crop p:

$$iF^{\text{crop application}} = iF_{\mathrm{residue}} + \sum_i iF_i \times f_i \qquad \textbf{Eq. 10.9}$$

All CFs related to exposure to pesticide residues in food crops are by default normalized to the chemical mass applied (Fantke et al. 2011b), which means that in the life cycle inventories of food crop production, the mass applied to a crop needs to be given. Hence, CFs for food crop residues are given in impact/kg applied (instead of impact/kg emitted), and are provided for wheat as reference crop.

Human toxicity effect factor: The human toxicity effect factor, EF^{h} [disease cases/kg_{intake}], relates the likelihood (or potential risk) of developing an adverse health effect expressed as number of cancer or non-cancer mortality or morbidity disease cases to the chemical mass taken in by a human population. This factor is based on toxicity data for cancer and non-cancer effects derived from laboratory studies on different animal species, where differences in metabolic activation of chemicals between tested animals and humans are not considered. Other health endpoints, such as endocrine disruption, are currently not included. Relying on the assumption of linear dose-response curves for each disease endpoint and exposure pathway, the human dose-response slope factor for exposure route $x \in$ {inhalation, ingestion} and health endpoint $p \in$ {cancer, non-cancer} is derived as (Rosenbaum et al. 2011):

$$EF_{x,p}^{\mathrm{h}} = \frac{\alpha}{ED50_{x,p}^{\mathrm{h}}} \qquad \textbf{Eq. 10.10}$$

where α is the unitless response level corresponding to considered health effects that is set to $\alpha = 0.5$, i.e. 50% of the exposed population have a probability of getting cancer or non-cancer from taking in a chemical quantity equal to $ED50_{x,p}^{\mathrm{h}}$, and $ED50_{x,p}^{\mathrm{h}}$ [kg_{intake}/lifetime/person] is the estimated lifetime dose for humans related to the x^{th} exposure route that causes an increase in the probability of getting the p^{th} health effect.

For cancer effects, the lifetime $ED50_{x,\mathrm{cancer}}^{\mathrm{h}}$ is either derived in priority from human-based data for a few chemicals, for which such data are available, or as for most chemicals, extrapolated from cancer tests of the s^{th} animal species by using the chronic tumourigenic dose-rate, $TD50_x^s$ [mg_{intake}/$kg_{body\ weight}$/ $lifetime_{animal}$], expressed as mg of chemical taken in per kg animal body weight over the animal species standard lifetime (Rosenbaum et al. (2011):

$$ED50_{x,\mathrm{cancer}}^{\mathrm{h}} = \frac{TD50_x^s \times LT^{\mathrm{h}} \times BW^{\mathrm{h}} \times \frac{\mathrm{d}}{\mathrm{yr}}}{f^s \times f_{\mathrm{exposure}} \times \frac{\mathrm{mg}}{\mathrm{kg}}} \qquad \textbf{Eq. 10.11}$$

where $LT^{\mathrm{h}} = 70$ years is the average human life time (Rosenbaum et al. 2011), $BW^{\mathrm{h}} = 70$ kg is the average human body weight (Rosenbaum et al. 2011), f^s is the extrapolation factor correcting for differences between the s^{th} studied animal species and humans, i.e. $f^s = 4.1$ for rat, $f^s = 7.3$ for mouse, $f^s = 1.5$ for dog, $f^s = 2.4$ for rabbit and $f^s = 1.9$ for monkey (Vermeire et al. 2001), and f_{exposure} is the extrapolation factor correcting for differences between exposure duration of the study and chronic exposure, i.e. $f_{\mathrm{exposure}} = 5$ for subacute exposure and $f_{\mathrm{exposure}} = 2$ for subchronic exposure (Huijbregts et al. 2005). Finally, $\frac{\mathrm{d}}{\mathrm{yr}} = 365$ days/yr corrects for the number of days per year, and $\frac{\mathrm{mg}}{\mathrm{kg}} = 10^6$ mg/kg corrects for mg per kg.

For non-cancer effects, insufficient data are currently available for most substances to recalculate an $ED50_{x,\text{non-cancer}}^{\mathrm{h}}$ with dose-response models. In these cases, the $ED50_{x,\text{non-cancer}}^{\mathrm{h}}$ has been estimated from no-observed effect levels of the s^{th} exposed animal species, $NOEL^s$ [mg_{intake}/$kg_{body\ weight}$/day] or, if no-observed effect level data are not available, from lowest observable effect levels, $LOEL^s$ [mg_{intake}/$kg_{body\ weight}$/day]:

$$ED50^{\mathrm{h}}_{x,\text{non-cancer}} = \frac{NOEL^{S} \times f_{\text{NOEL-to-ED50}} \times LT^{\mathrm{h}} \times BW^{\mathrm{h}} \times \frac{\mathrm{d}}{\mathrm{yr}}}{f^{S} \times f_{\text{exposure}} \times \frac{\mathrm{mg}}{\mathrm{kg}}} = \frac{\overbrace{LOEL^{S} \times f_{\text{LOEL-to-NOEL}}}^{NOEL^{S}} \times f_{\text{NOEL-to-ED50}} \times LT^{\mathrm{h}} \times BW^{\mathrm{h}} \times \frac{\mathrm{d}}{\mathrm{yr}}}{f^{S} \times f_{\text{exposure}} \times \frac{\mathrm{mg}}{\mathrm{kg}}} \quad \textbf{Eq. 10.12}$$

where $f_{\text{NOEL-to-ED50}} = 9$ is the NOEL-to-ED50 extrapolation factor (Huijbregts et al. 2005), $f_{\text{LOEL-to-NOEL}} = 0.25$ is the LOEL-to-NOEL extrapolation factor in cases where $NOEL^{S}$ is not available (Huijbregts et al. 2005).

In case no data were available for a specific exposure route in Equations 10.11 and 10.12, an analysis of route-to-route extrapolation supports the assumption of equal potency or slope factor for systemic effects between inhalation and ingestion route for most chemicals (Rosenbaum et al. 2011).

Human damage factor: The human damage factor, DF^{h} [DALY/disease cases], relates the number of DALY to the number of cancer or non-cancer disease cases, respectively. Human damage factors of $DF^{\mathrm{h}}_{\text{cancer}} = 11.5$ and $DF^{\mathrm{h}}_{\text{non-cancer}} = 2.7$ DALY per cancer and non-cancer disease case, respectively, are used based on global human health statistics (Huijbregts et al. 2005). All DALY values are undiscounted and without age-weighting, i.e. future impacts are counted with similar weight as immediate impacts and health effects are weighted equally at all ages. This reflects an equal value of a life lived by children, young adults, and elderly for present and future generations as proposed by Arnesen and Nord (1999).

Ecotoxicity

The average ecotoxicity-related characterization factor for ecosystem quality is defined in terms of PDF integrated over time per kg emitted chemical to a given environmental compartment as shown in Figure 10.1 and Equation 10.2. The specific factors are described below.

Fate factor: The fate factor, FF [$\mathrm{kg}_{\text{in compartment}}/(\mathrm{kg}_{\text{emitted}}/\text{day})$], relates the time-integrated chemical mass in a given environmental compartment to the chemical mass emitted per day into the environment. The fate factor thereby accounts for loss processes within environmental compartments (e.g. degradation) and multimedia transfer processes between different environmental compartments (e.g. diffusion and advection). When the emission compartment is different from the compartment of the exposed ecosystem, the fate factor is interpreted as product of the residence time of a chemical in the receiving exposure compartment, FF_{i_2} [day], and the overall time-integrated chemical mass fraction transferred from the emission compartment i_1 to the exposure compartment i_2, $f_{i_2 \leftarrow i_1}$ [$\mathrm{kg}_{\text{in compartment}}/\mathrm{kg}_{\text{emitted}}$], i.e. $FF = f_{i_2 \leftarrow i_1} \times FF_{i_2}$. The fate factor is equal to the fate factor used for calculating human toxicity CFs and is, hence, described in more detail in the "Human toxicity" section (see text associated with Equations 10.3 and 10.4, and with Figure 10.2).

Ecosystem exposure factor: The ecosystem exposure factor, XF^{e} [$\mathrm{kg}_{\text{bioavailable}}/\mathrm{kg}_{\text{in compartment}}$], represents the bioavailability of chemicals to organisms in the environmental compartments considered for ecotoxicity. Several factors and processes may influence the amount of chemicals available for ecosystem exposure (e.g. sorption, dissolution, dissociation, chemical speciation), which can be expressed as bioavailability or bioaccessibility (Semple et al. 2004). For aquatic compartments, bioavailability is considered by calculating XF^{e} as the truly dissolved fraction of a chemical in freshwater (Henderson et al. 2011, Dong et al. 2014) and in marine water (Dong et al. 2016), respectively. The ecosystem exposure factor for aquatic ecosystems, i.e. for ecosystems in aquatic compartments $i_{\text{water}} \in$ {continental freshwater, continental marine water}, $XF^{\mathrm{e}}_{i_{\text{water}}}$, is derived as (Brandes et al. 1996, Huijbregts et al. 2010):

$$XF^{\mathrm{e}}_{i_{\text{water}}} = \frac{1}{1 + K_{\text{susp},i} \times C_{\text{susp},i} + K_{\text{doc},i} \times C_{\text{doc},i} + BCF_{\text{fish},i} \times C_{\text{biota},i}} \quad \textbf{Eq. 10.14}$$

where $K_{\mathrm{susp},i}$ [$L_{water}/kg_{suspended\ solids}$] is the equilibrium partition coefficient between suspended solids and (fresh-, marine) water, $C_{\mathrm{susp},i}$ [$kg_{suspended\ solids}/L_{water}$] is the concentration of suspended solids in (fresh-, marine) water and is assumed to be $C_{\mathrm{susp,freshwater}} = 15 \times 10^{-6}$ kg/L in freshwater (Brandes et al. 1996, Huijbregts et al. 2010) and $C_{\mathrm{susp,marine\ water}} = 5 \times 10^{-6}$ kg/L in marine water, $K_{\mathrm{doc},i}$ [L_{water}/kg_{DOC}] is the equilibrium partition coefficient between dissolved organic carbon (DOC) and (fresh-, marine) water, $C_{\mathrm{doc},i}$ [kg_{DOC}/L_{water}] is the concentration of dissolved organic carbon in water and is assumed to be $C_{\mathrm{doc,freshwater}} = 5 \times 10^{-6}$ kg/L (Huijbregts et al. 2010) and $C_{\mathrm{doc,marine\ water}} = 10^{-6}$ kg/L in marine water, $BCF_{\mathrm{fish},i}$ [L_{water}/kg_{fish}] is the bioconcentration factor of fish in (fresh-, marine) water, and $C_{\mathrm{biota},i}$ [kg_{biota}/L_{water}] is the concentration of biota in (fresh-, marine) water and is assumed to be $C_{\mathrm{biota,freshwater}} = C_{\mathrm{biota,marine\ water}} = 10^{-6}$ kg/L (Brandes et al. 1996, Huijbregts et al. 2010) in freshwater and marine water. Ecosystem species considered in calculation of ecosystem exposure and subsequent effects in freshwater ecosystems are schematially shown in Figure 10.4.

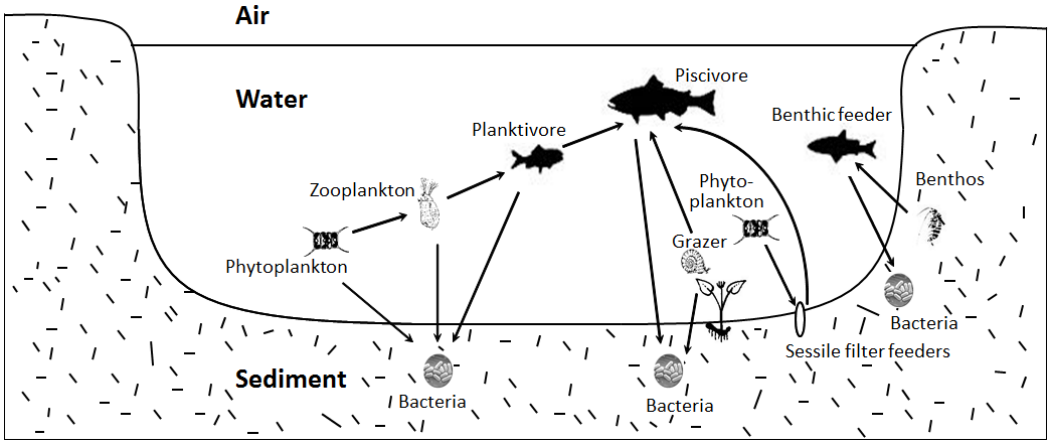

Figure 10.3: Simplified foodweb for freshwater/marine water ecosystems (Larsen & Hauschild 2007).

For terrestrial compartments (i.e. soil), the exposure factor, XF_i^{e} [$kg_{bioavailalbe}/kg_{in\ compartment}$], is calculated from the the ratio of the bioavailable concentration, i.e. the total dissolved concentration for organic substances and the reactive concentration for metallic elements, in the i^{th} terrestrial compartment, $C_{\mathrm{bioavailable},i}$ [$kg_{bioavailalbe}/kg_{compartment}$] with $i \in$ {continental agricultural soil, continental natural soil}, and the total chemical concentration in that compartment, $C_{\mathrm{total},i}$ [$kg_{in\ compartment}/kg_{compartment}$]:

$$XF_{i_{\mathrm{soil}}}^{\mathrm{e}} = \frac{C_{\mathrm{bioavailable},i}}{C_{\mathrm{total},i}} \qquad \textbf{Eq. 10.15}$$

For organic chemicals, this relies on equilibrium partitioning between bulk soil and soil pore water content. Bioavailability of metals in terrestrial compartments is considered by calculating $XF_{\mathrm{metal},i}^{\mathrm{e}}$ for compartment as the product of two factors, namely the accessibility factor in the i^{th} terrestrial compartment, ACF_i^{e} [$kg_{reactive}/kg_{in\ compartment}$], representing the reactive fraction of total metal, and the bioavailability factor in the i^{th} terrestrial compartment, BF_i^{e} [$kg_{bioavailable}/kg_{reactive}$], representing the bioavailable free ion fraction of reactive metal (Owsianiak et al. 2013). The ecosystem exposure factor of metals for terrestrial ecosystems, i.e. for ecosystems in terrestrial compartments, $XF_{\mathrm{metal},i_{\mathrm{soil}}}^{\mathrm{e}}$, is derived as:

$$XF_{\mathrm{metal},i}^{\mathrm{e}} = ACF_i^{\mathrm{e}} \times BF_i^{\mathrm{e}} = \underbrace{\left(\frac{\Delta C_{\mathrm{reactive},i}}{\Delta C_{\mathrm{total},i}}\right)}_{ACF_i^{\mathrm{e}}} \times \underbrace{\left(\frac{\Delta C_{\mathrm{bioavailable},i} \times \theta_i}{\Delta C_{\mathrm{reactive},i} \times \rho_i}\right)}_{BF_i^{\mathrm{e}}} \qquad \textbf{Eq. 10.16}$$

where $\Delta C_{\mathrm{reactive},i}$ [$kg_{reactive}/kg_{compartment}$] is the incremental change of reactive metal concentration in the i^{th} terrestrial compartment, $\Delta C_{\mathrm{total},i}$ [$kg_{in\ compartment}/kg_{compartment}$] is the incremental change of total metal concentration in the i^{th} terrestrial compartment, $\Delta C_{\mathrm{bioavailable},i}$ [$kg_{bioavailable}/m^3_{compartment}$] is the incremental change of bioavailable free ion metal concentration in the i^{th} terrestrial compartment, θ_i [$m^3_{compartment,\ water}/m^3_{compartment}$] is the volumetric water content of the i^{th} terrestrial compartment that is assumed to be $\theta_{\mathrm{soil,agri}} = 0.2$ m^3/m^3 for continental agricultural and natural soil, and ρ_i [$kg_{compartment}/m^3_{compartment}$] is the bulk density of the i^{th} terrestrial compartment that is assumed to be $\rho_{\mathrm{soil}} = 1500$ kg/m^3 for continental agricultural and natural soil. Reactive metal thereby refers to metal in the solid phase that equilibrates with the solution phase within a few days, i.e. metal which is accessible for leaching or uptake by biota. Bioavailable metal refers to metal in the liquid phase that is present in directly bioavailable, toxic metal forms (Owsianiak et al. 2015).

Ecotoxicity effect factor: The ecotoxicity effect factor, EF^{e} $\left[\mathrm{PAF} \times \mathrm{m}^3_{\mathrm{exposed\ medium}}/\mathrm{kg}_{\mathrm{bioavailable}}\right]$, relates the potential of a chemical to cause toxic effects to an exposed ecosystem expressed as potentially affected fraction of species in the exposed ecosystem (including continental freshwater and marine water, continental agricultural and natural soil) integrated over the compartment (e.g. freshwater) or exposure medium (e.g. soil pore water) volume to the chemical mass in the environmental compartment surrounding the exposed ecosystem. The ecosystem dose-response slope factor is calculated as (Henderson et al. 2011):

$$EF^{\mathrm{e}} = \frac{\alpha}{HC50^{\mathrm{e}}} \times \frac{SR_{\mathrm{continent}}}{SR_{\mathrm{global}}} \qquad \textbf{Eq. 10.17}$$

where α [PAF] is the response level, i.e. the potentially affected fraction of species, corresponding to considered toxic effects that is set to $\alpha = 0.5$ PAF, which means that 50% of the exposed ecosystem species have a chance of toxic effects from being exposed to a chemical quantity equal to $HC50^{\mathrm{e}}$, $HC50^{\mathrm{e}}$ [$kg_{in\ compartment}/m^3_{compartment}$] is the chronic hazardous concentration for 50% of the species included in the species sensitivity distribution (Henderson et al. 2011, Golsteijn et al. 2014) that expresses the ecotoxic potency of a chemical (Rosenbaum et al. 2008), and where $SR_{\mathrm{continent}}$ and SR_{global} [species count/m^3] is the relative species richness per unit area at the continental and global scale, respectively (Chaudhary et al. 2015, Verones et al. 2015). For freshwater ecotoxicity information on freshwater fish and for marine ecotoxicity information on lobsters, Chondrichtyes, Actinopoetygii and sea cucumbers has been used as based on data from IUCN (www.iucnredlist.org). For terrestrial ecotoxicity, vascular plants have been used as proxy (Kier et al. 2009). Species were counted per region ans then allocated to the respective USEtox regions. For marine ecotoxicity, USEtox regions bordering on the respective large marine ecosystems were used for allocating marine impacts to terrestrial regions, assuming that emissions take place on land. $HC50^{\mathrm{e}}$ is calculated as the geometric mean of the effective environmental concentration potentially leading to chronic (lethal) effects in 50% of all individuals of a single species, $L(E)C50^{\mathrm{e}}_s$ [$kg_{in\ compartment}/m^3_{compartment}$], with preference given to chronic test values:

$$\log HC50^{\mathrm{e}} = \frac{1}{n_s} \times \sum_s \log L(E)C50^{\mathrm{e}}_s \qquad \textbf{Eq. 10.18}$$

where n_s is the number of species for which toxicity tests have been performed for a given chemical (Golsteijn et al. 2013). If chronic test data are not available, an acute-to-chronic ratio of $ACR = 0.5$ is applied by default to relate chronic $HC50^{\mathrm{e}}$ to acute $HC50^{\mathrm{e}}_{\mathrm{acute}}$ via $HC50^{\mathrm{e}} = HC50^{\mathrm{e}}_{\mathrm{acute}} \times ACR$ based on an analysis by Payet (2004). Different ACR are used for metals based on Dong et al. (2014). Due to inconclusive evidence regarding the sensitivity of ecosystems in different environmental compartments (Hutchinson et al. 1998, Wheeler et al. 2002), ecotoxicity effect data are for organic chemicals by default set equal for freshwater, marine water, and terrestrial ecosystems. For metals, ecotoxicity effect data are kept separate based on work by Dong et al. (2014) and Dong et al. (2016).

More specifically, freshwater species data are used for freshwater ecosystem effects, marine species data are used in preference for marine ecosystem effects and if not available, freshwater species are are used as proxy. Freshwater species data are furthermore used for terrestrial soil ecosystem effects and are recalculated to be based on free ion metal concentration.

Ecosystem damage factor: The ecosystem damage factor, DF^{e} [PDF/PAF], relates the potentially disappeared fraction of species to the potentially affected fraction of species and is assumed to be for all considered environmental compartments $DF^{\mathrm{e}} = 2$ PDF/PAF based on the rationale that it has been shown that chronic effects (on freshwater ecosystems) can be predicted with PAF based on acute $L(E)C50_s^{\mathrm{e}}$ data (Posthuma & de Zwart 2006).

10.3 Uncertainties

Specific uncertainties in calculating human and/or ecotoxicity characterization factors include:

a) Current biotransfer models for meat and milk used in the impact pathway for human toxicity as these are very uncertain and provide unreliable results for highly hydrophobic chemicals (Rosenbaum et al. 2009),
b) Metals, for which relatively high characterization factors are obtained due to long residence times in the marine water compartments (Dong et al. 2016),
c) The assumption of homogeneously mixed compartment boxes for agricultural soil and for natural soil, while soils are complex media consisting of several multi-layered sub-compartments with distinct fate properties (Dubus et al. 2003),
d) Steady-state as assumed temporal condition (as compared to quasi-dynamic calculations up to 100 years for higher level of robustness factors), since for specific substance classes and exposure pathways, dynamics over time are driving substance distribution in the environment and subsequent exposure (Stroebe et al. 2004, Fantke et al. 2013),
e) A single compartment plant uptake module for the pathway associated with continuous environmental emissions, which might over- or underestimate the fate of substances in the agricultural crop-environment system with respect to crop residues (Fantke et al. 2012),
f) Assuming equal severity between human effects (within cancer and within non-cancer effects) as there might be significant differences when combining dose-response slope and severity of disability (Vos et al. 2012) and particularly high uncertainty for non-cancer effects (Huijbregts et al. 2005),
g) The extrapolation of species and compartments for ecosystem fate and toxicity effect factors as differences between exposed species (composition) and environmental compartments (characteristics) might be relevant for ecotoxicological effect assessments of both organic chemicals (Hutchinson et al. 1998, Wheeler et al. 2002) and metals (Wheeler et al. 2002, Owsianiak et al. 2014, Dong et al. 2016),
h) The extrapolation from acute ecotoxicity data to predict chronic effects as differences in species-specific and cross-species effect endpoints might be relevant for ecotoxicological effect assessment (Posthuma & de Zwart 2006),
i) Accessibility was not considered for all metals, resulting in overestimation of related terrestrial soil ecotoxicity characterization factors, and bioavailability was not considered for all relevant metals, resulting in either over or underestimation of terrestrial soil ecotoxicity characterization factors.

10.4 Value choices

Subjective value choices with respect to the level of robustness in the impact pathway are expressed as high level of robustness and low level of robustness as detailed in the following. To maintain consistency with other impact categories, a time horizon of 100 years is set for the high level of robustness scenarios. CF calculations for the 100 years time horizon are based on dynamically solving the mass balance equation underlying the fate factor. This computation is referred to as “quasi-

dynamic", where all model parameters except the chemical masses in the environmental compartments are assumed to remain constant over time. More information on the quasi-dynamic computation can be found in Brandes et al. (1996).

CFs with high level of robustness are available including factors for freshwater ecosystem toxicity effect factors based on data for ≥3 different species from ≥3 different trophic levels, and for human toxicity effect factors based on chronic and sub-chronic effect data for cancer effects. Other chemicals and fate, exposure and effect factors, however, only come with a lower level of robustness. In these cases, CFs are available with higher uncertainty including CFs based on human exposure route-to-route extrapolation, for ecotoxicity effect factors based on data for metals without available speciation calculations, marine and terrestrial soil ecotoxicity factors whenever based on freshwater species, for fate and exposure factors for amphoteric substances, and for effect factors based on sub-acute effect data.

Not all substances with a carcinogenic ED50 are necessarily known carcinogenics to humans. The International Agency for Research on Cancer (IARC), part of the World Health Organization (WHO), evaluated the carcinogenic risk of over 1,000 substances (mixtures) to humans by assigning a carcinogenicity class to each substance (IARC 2019). The classes reflect the strength of the evidence for carcinogenicity derived from studies in humans and in experimental animals and from other relevant data. This information can be readily used to define two scenarios. The certain impacts scenario only includes the substances with strong evidence of carcinogenicity (IARC-category 1, 2A and 2B). The all impacts scenario includes all substances for which ED50 information is available (IARC-category 1, 2A, 2B, 3 or no classification).

10.5 Characterization factors

Out of 3104 substances included in the characterization model, human toxicity CFs are available for 18 metal ions and 1255 organic substances (931 with non-zero CFs and with 324 CFs that equal zero based on being netatively tested for carcinogenicity effects), and ecotoxicity CFs for freshwater, marine water and terrestrial soil ecotoxicity are available for 27 metal ions and 2499 organic substances. Toxicity CFs for human health are shown in Figure 10.5, and ecotoxicity CFs for ecosystem quality are shown in Figure 10.6.

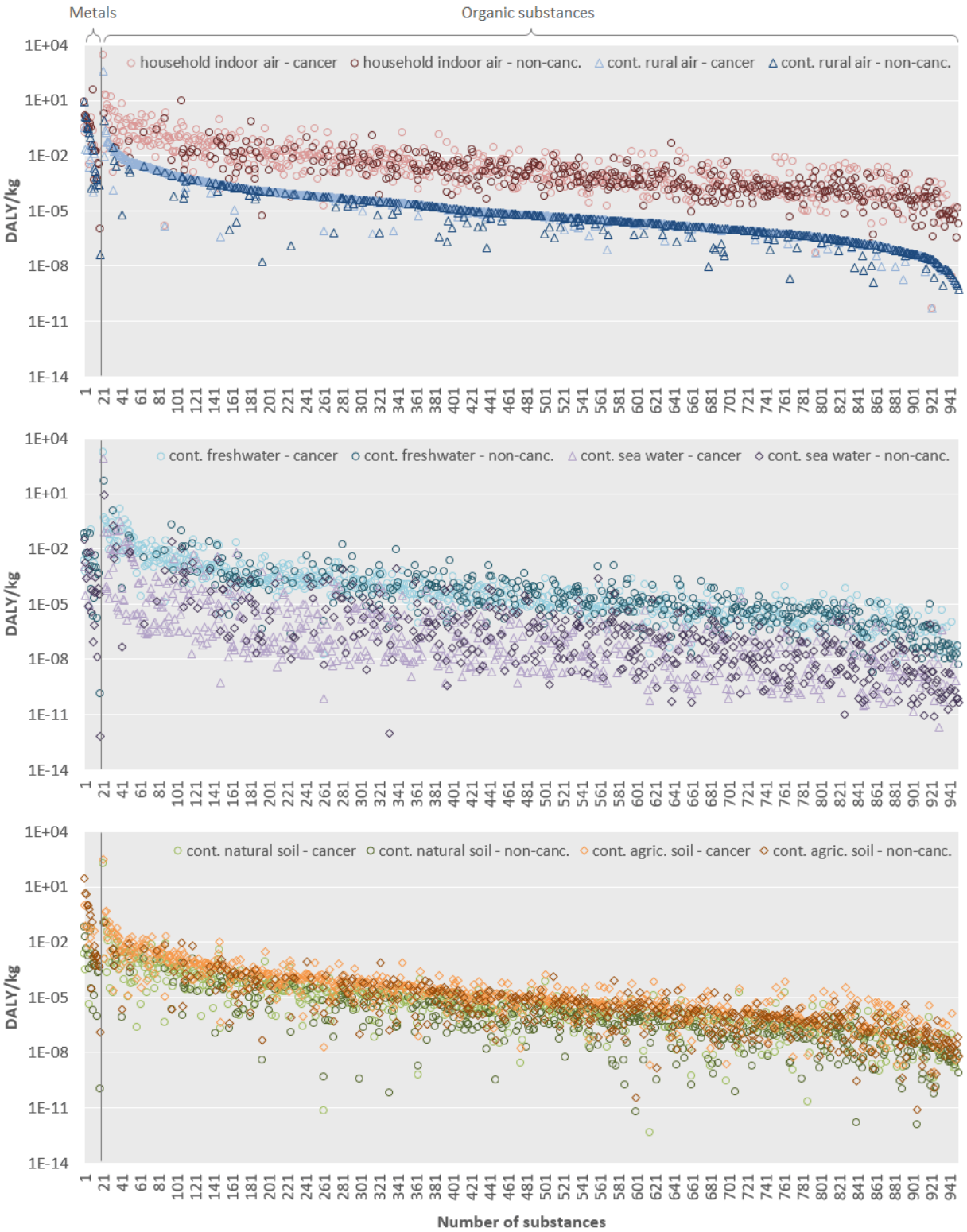

Figure 10.5: Characterization factors for human health impacts caused by emissions of toxic chemicals into the environment, expressed in disability-adjusted life years (DALY) per kg emitted.

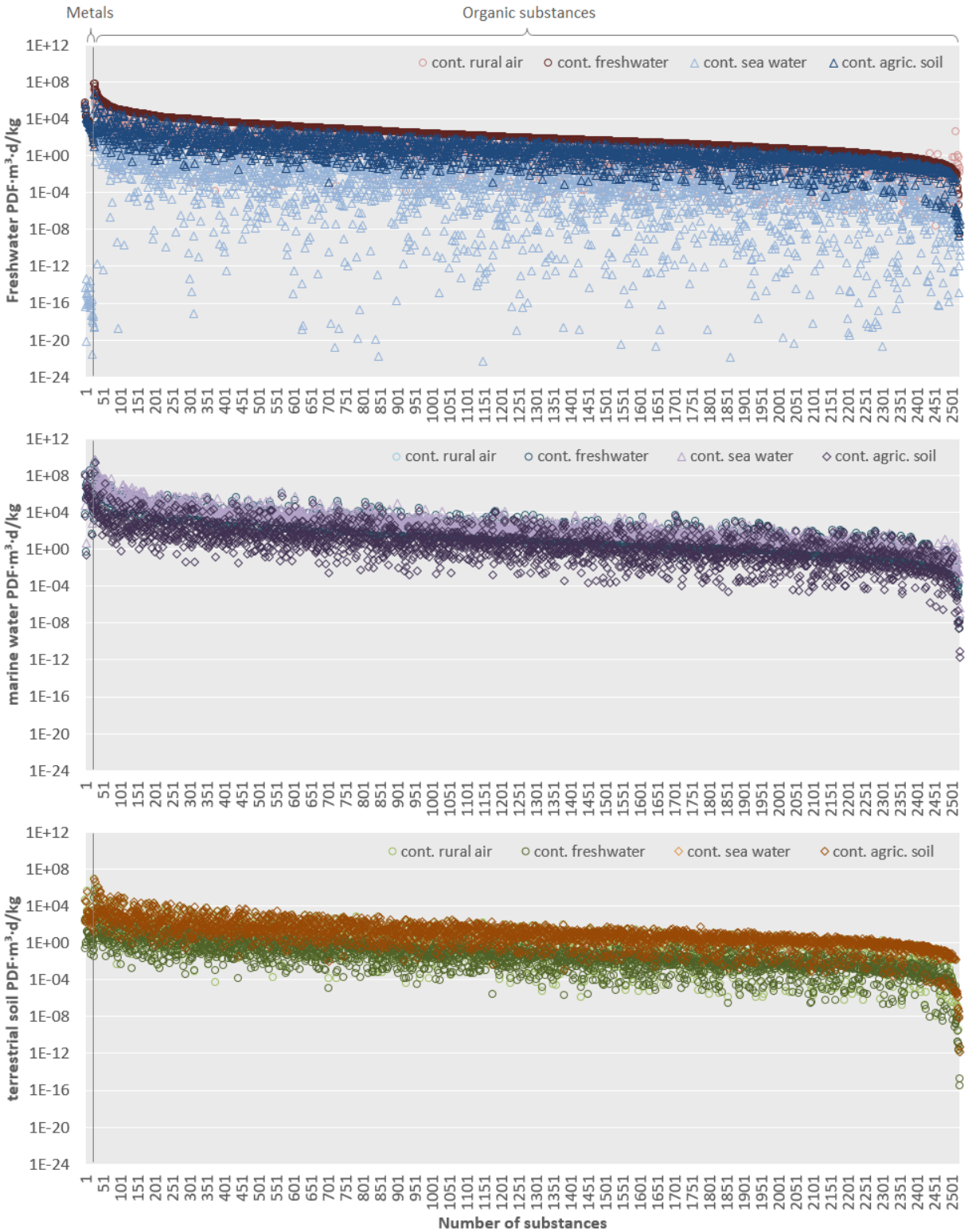

Figure 10.6: Characterization factors for freshwater, marine water and terrestrial (soil) ecosystem quality impacts caused by emissions of toxic chemicals into the environment, expressed as potentially disappeared fraction (PDF) of species integrated over exposed volume and time per kg emitted.

10.6 References

Arnesen T, Nord E (1999) The value of DALY life: Problems with ethics and validity of disability adjusted life years. Brit. Med. J. 319:1423-1425. doi:10.1136/bmj.319.7222.1423

Bennett DH, Margni MD, McKone TE, Jolliet O (2002a) Intake fraction for multimedia pollutants: A tool for life cycle analysis and comparative risk assessment. Risk Anal. 22:905-918. doi:10.1111/1539-6924.00260

Bennett DH, McKone TE, Evans JS, Nazaroff WW, Margni MD, Jolliet O, Smith KR (2002b) Defining intake fraction. Environ. Sci. Technol. 36:207A-211A. doi:10.1021/es0222770

Brandes LJ, den Hollander HA, van de Meent D (1996) SimpleBox 2.0: A nested multimedia fate model for evaluating the environmental fate of chemicals, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

Chaudhary A, Verones F, de Baan L, Hellweg S (2015) Quantifying land use impacts on biodiversity: Combining species-area models and vulnerability indicators. Environ. Sci. Technol. 49:9987-9995. doi:10.1021/acs.est.5b02507

Dong Y, Gandhi N, Hauschild MZ (2014) Development of comparative toxicity potentials of 14 cationic metals in freshwater. Chemosphere 112:26-33. doi:10.1016/j.chemosphere.2014.03.046

Dong Y, Rosenbaum RK, Hauschild MZ (2016) Assessment of metal toxicity in marine ecosystems: Comparative Toxicity Potentials for nine cationic metals in coastal seawater. Environ. Sci. Technol. 50:269-278. doi:10.1021/acs.est.5b01625

Dubus IG, Brown CD, Beulke S (2003) Sources of uncertainty in pesticide fate modelling. Sci. Total Environ. 317:53-72. doi:10.1016/S0048-9697(03)00362-0

Fantke P, Charles R, de Alencastro LF, Friedrich R, Jolliet O (2011a) Plant uptake of pesticides and human health: Dynamic modeling of residues in wheat and ingestion intake. Chemosphere 85:1639-1647. doi:10.1016/j.chemosphere.2011.08.030

Fantke P, Juraske R, Antón A, Friedrich R, Jolliet O (2011b) Dynamic multicrop model to characterize impacts of pesticides in food. Environ. Sci. Technol. 45:8842-8849. doi:10.1021/es201989d

Fantke P, Wieland P, Juraske R, Shaddick G, Itoiz ES, Friedrich R, Jolliet O (2012) Parameterization models for pesticide exposure via crop consumption. Environ. Sci. Technol. 46:12864-12872. doi:10.1021/es301509u

Fantke P, Wieland P, Wannaz C, Friedrich R, Jolliet O (2013) Dynamics of pesticide uptake into plants: From system functioning to parsimonious modeling. Environ. Modell. Softw. 40:316-324. doi:10.1016/j.envsoft.2012.09.016

Franco A, Trapp S (2008) Estimation of the soil-water partition coefficient normalized to organic carbon for ionizable organic chemicals. Environ. Toxicol. Chem. 27:1995-2004. doi:10.1897/07-583.1

Franco A, Trapp S (2010) A multimedia activity model for ionizable compounds: Validation study with 2,4-dichlorophenoxyacetic acid, aniline, and trimethoprim. Environ. Toxicol. Chem. 29:789-799. doi:10.1002/etc.115

Gandhi N, Diamond ML, Huijbregts MAJ, Guinée JB, Peijnenburg WJGM, van de Meent D (2011) Implications of considering metal bioavailability in estimates of freshwater ecotoxicity: examination of two case studies. Int. J. Life Cycle Assess. 16:774-787. doi:10.1007/s11367-011-0317-3

Golsteijn L, van Zelm R, Hendriks AJ, Huijbregts MAJ (2013) Statistical uncertainty in hazardous terrestrial concentrations estimated with aquatic ecotoxicity data. Chemosphere 93:366-372. doi:10.1016/j.chemosphere.2013.05.007

Golsteijn L, Iqbal MS, Cassani S, Hendriks HWM, Kovarich S, Papa E, Rorije E, Sahlin U, Huijbregts MAJ (2014) Assessing predictive uncertainty in comparative toxicity potentials of triazoles. Environ. Toxicol. Chem. 33:293-301. doi:10.1002/etc.2429

Hauschild MZ, Huijbregts MAJ, Jolliet O, Macleod M, Margni MD, van de Meent D, Rosenbaum RK, McKone TE (2008) Building a model based on scientific consensus for life cycle impact assessment of chemicals: The search for harmony and parsimony. Environ. Sci. Technol. 42:7032-7037. doi:10.1021/es703145t

Hellweg S, Demou E, Bruzzi R, Meijer A, Rosenbaum RK, Huijbregts MAJ, McKone TE (2009) Integrating human indoor air pollutant exposure within life cycle impact assessment. Environ. Sci. Technol. 43:1670-1679. doi:10.1021/es8018176

Henderson AD, Hauschild MZ, van de Meent D, Huijbregts MAJ, Larsen HF, Margni M, McKone TE, Payet J, Rosenbaum RK, Jolliet O (2011) USEtox fate and ecotoxicity factors for comparative assessment of toxic emissions in life cycle analysis: sensitivity to key chemical properties. Int. J. Life Cycle Assess. 16:701-709. doi:10.1007/s11367-011-0294-6

Huijbregts M, Hauschild M, Jolliet O, Margni M, McKone T, Rosenbaum RK, van de Meent D (2010) USEtoxTM User Manual Version 1.01, (http://www.usetox.org)

Huijbregts MAJ, Rombouts LJA, Ragas AMJ, van de Meent D (2005) Human-toxicological effect and damage factors of carcinogenic and noncarcinogenic chemicals for life cycle impact assessment. Integr. Environ. Assess. Manage. 1:181-244. doi:10.1897/2004-007R.1

Hutchinson TH, Scholz N, Guhl W (1998) Analysis of the ECETOC Aquatic Toxicity (EAT) database IV - Comparative toxicity of chemical substances to freshwater versus saltwater organisms. Chemosphere 36:143-153. doi:10.1016/S0045-6535(97)10026-1

IARC. 2019. List of classifications. International Agency for Research on cancer. https://monographs.iarc.fr/list-of-classifications-volumes/. Accessed dd 2 April 2019.

Kier G, Kreft H, Lee TM, Jetz W, Ibisch PL, Nowicki C, Mutke J, Barthlott W (2009) A global assessment of endemism and species richness across island and mainland regions. Proc. Nat. Acad. Sci. 106:9322-9327.

Kounina A, Margni M, Shaked S, Bulle C, Jolliet O (2014) Spatial analysis of toxic emissions in LCA: A sub-continental nested USEtox model with freshwater archetypes. Environ. Int. 69:67-89. doi:10.1016/j.envint.2014.04.004

Larsen HF, Hauschild M (2007) GM-troph: A low data demand ecotoxicity effect indicator for use in LCIA. Int. J. Life Cycle Assess. 12:79-91. doi:10.1065/lca2006.12.288

Margni MD, Pennington DW, Bennett DH, Jolliet O (2004) Cyclic exchanges and level of coupling between environmental media: Intermedia feedback in multimedia fate models. Environ. Sci. Technol. 38:5450-5457. doi:

Owsianiak M, Rosenbaum RK, Huijbregts MAJ, Hauschild MZ (2013) Addressing geographic variability in the comparative toxicity potential of copper and nickel in soils. Environ. Sci. Technol. 47:3241-3250. doi:10.1021/es3037324

Owsianiak M, Veltman K, Hauschild MZ, Hendriks AJ, Steinmann ZJN, Huijbregts MAJ (2014) Elucidating differences in metal absorption efficiencies between terrestrial soft-bodied and aquatic species. Chemosphere 112:487-495. doi:10.1016/j.chemosphere.2014.05.024

Owsianiak M, Holm PE, Fantke P, Christiansen KS, Borggaard OK, Hauschild MZ (2015) Assessing comparative terrestrial ecotoxicity of Cd, Co, Cu, Ni, Pb, and Zn: The influence of aging and emission source. Environ. Pollut. 206:400-410. doi:10.1016/j.envpol.2015.07.025

Payet J (2004) Assessing toxic impacts on aquatic ecosystems in life cycle assessment (LCA). Doctoral thesis Thesis, Ecóle Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, 232 pp

Posthuma L, de Zwart D (2006) Predicted effects of toxicant mixtures are confirmed by changes in fish species assemblages in Ohio, USA, rivers. Environ. Toxicol. Chem. 25:1094-1105. doi:10.1897/05-305R.1

Rosenbaum RK, Margni MD, Jolliet O (2007) A flexible matrix algebra framework for the multimedia multipathway modeling of emission to impacts. Environ. Int. 33:624-634. doi:10.1016/j.envint.2007.01.004

Rosenbaum RK, Bachmann TM, Gold LS, Huijbregts MAJ, Jolliet O, Juraske R, Koehler A, Larsen HF, MacLeod M, Margni MD, McKone TE, Payet J, Schuhmacher M, van de Meent D, Hauschild MZ (2008) USEtox - The UNEP-SETAC toxicity model: Recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment. Int. J. Life Cycle Assess. 13:532-546. doi:10.1007/s11367-008-0038-4

Rosenbaum RK, McKone TE, Jolliet O (2009) CKow: A dynamic model for chemical transfer to meat and milk. Environ. Sci. Technol. 43:8191-8198. doi:10.1021/es803644z

Rosenbaum RK, Huijbregts MAJ, Henderson AD, Margni M, McKone TE, van de Meent D, Hauschild MZ, Shaked S, Li DS, Gold LS, Jolliet O (2011) USEtox human exposure and toxicity factors for comparative assessment of toxic emissions in life cycle analysis: Sensitivity to key chemical properties. Int. J. Life Cycle Assess. 16:710-727. doi:10.1007/s11367-011-0316-4

Semple KT, Doick KJ, Jones KC, Burauel P, Craven A, Harms H (2004) Defining bioavailability and bioaccessibility of contaminated soil and sediment is complicated. Environ. Sci. Technol. 38:228A-231A. doi:10.1021/es040548w

Stroebe M, Scheringer M, Hungerbühler K (2004) Measures of overall persistence and the temporal remote state. Environ. Sci. Technol. 38:5665-5673. doi:10.1021/es035443s

van Zelm R, Stam G, Huijbregts MAJ, van de Meent D (2013) Making fate and exposure models for freshwater ecotoxicity in life cycle assessment suitable for organic acids and bases. Chemosphere 90:312-317. doi:10.1016/j.chemosphere.2012.07.014

Vermeire T, Pieters M, Rennen M, Bos P (2001) Probabilistic Assessment Factors for Human Health Risk Assessment. RIVM Rapport 601516005, TNO report V3489, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

Verones F, Huijbregts MAJ, Chaudhary A, de Baan L, Koellner T, Hellweg S (2015) Harmonizing the assessment of biodiversity effects from land and water use within LCA. Environ. Sci. Technol. 49:3584-3592. doi:10.1021/es504995r

Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V et al. (2012) Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 380:2163-2196. doi:10.1016/S0140-6736(12)61729-2

Wenger Y, Li D, Jolliet O (2012) Indoor intake fraction considering surface sorption of air organic compounds for life cycle assessment. Int. J. Life Cycle Assess. 17:919-931. doi:10.1007/s11367-012-0420-0

Wheeler JR, Leung KMY, Morritt D, Sorokin N, Rogers H, Toy R, Holt M, Whitehouse P, Crane M (2002) Freshwater to saltwater toxicity extrapolation using species sensitivity distributions. Environ. Toxicol. Chem. 21:2459-2467. doi:10.1002/etc.5620211127