USEtox—the UNEP-SETAC toxicity model: recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment

**Ralph K. Rosenbaum · Till M. Bachmann ·
Lois Swirsky Gold · Mark A. J. Huijbregts ·
Olivier Jolliet · Ronnie Juraske · Annette Koehler ·
Henrik F. Larsen · Matthew MacLeod ·
Manuele Margni · Thomas E. McKone · Jérôme Payet ·
Marta Schuhmacher · Dik van de Meent ·
Michael Z. Hauschild**

Abstract

Background, aim and scope In 2005, a comprehensive comparison of life cycle impact assessment toxicity characterisation models was initiated by the United Nations Environment Program (UNEP)–Society for Environmental Toxicology and Chemistry (SETAC) Life Cycle Initiative, directly involving the model developers of CalTOX, IMPACT 2002, USES-LCA, BETR, EDIP, WATSON and EcoSense. In this paper, we describe this model comparison process and its results—in particular the scientific consensus model developed by the model developers. The main objectives of this effort were (1) to identify specific sources of differences between the models' results and structure, (2) to detect the indispensable model components and (3) to build a scientific consensus model from them, representing recommended practice.

R. K. Rosenbaum (✉) · M. Margni
Department of Chemical Engineering, CIRAIG,
École Polytechnique de Montréal,
2900 Édouard-Montpetit, Stn. Centre-ville, P.O. Box 6079,
Montréal, QC, Canada H3C 3A7
e-mail: ralph.rosenbaum@polymtl.ca

T. M. Bachmann
European Institute for Energy Research (EIFER),
University of Karlsruhe,
Emmy-Noether-Strasse 11,
76131 Karlsruhe, Germany

L. S. Gold
University of California Berkeley,
and Children's Hospital Oakland Research Institute (CHORI),
Oakland, CA, USA

M. A. J. Huijbregts · D. van de Meent
Department of Environmental Science,
Radboud University Nijmegen,
P.O. Box 9010, 6500 GL Nijmegen, The Netherlands

O. Jolliet
Center for Risk Science and Communication,
University of Michigan,
Ann Arbor, MI, USA

R. Juraske · M. Schuhmacher
Chemical Engineering School,
Rovira i Virgili University,
43007 Tarragona, Spain

R. Juraske · A. Koehler
Institute of Environmental Engineering,
Ecological Systems Design, ETH Zurich,
Wolfgang-Pauli-Strasse 15,
8093 Zurich, Switzerland

H. F. Larsen · M. Z. Hauschild
DTU Management Engineering,
Technical University of Denmark,
Produktionstorvet, Building 424,
2800 Lyngby, Denmark

Materials and methods A chemical test set of 45 organics covering a wide range of property combinations was selected for this purpose. All models used this set. In three workshops, the model comparison participants identified key fate, exposure and effect issues via comparison of the final characterisation factors and selected intermediate outputs for fate, human exposure and toxic effects for the test set applied to all models.

Results Through this process, we were able to reduce inter-model variation from an initial range of up to 13 orders of magnitude down to no more than two orders of magnitude for any substance. This led to the development of USEtox, a scientific consensus model that contains only the most influential model elements. These were, for example, process formulations accounting for intermittent rain, defining a closed or open system environment or nesting an urban box in a continental box.

Discussion The precision of the new characterisation factors (CFs) is within a factor of 100–1,000 for human health and 10–100 for freshwater ecotoxicity of all other models compared to 12 orders of magnitude variation between the CFs of each model, respectively. The achieved reduction of inter-model variability by up to 11 orders of magnitude is a significant improvement.

Conclusions USEtox provides a parsimonious and transparent tool for human health and ecosystem CF estimates. Based on a referenced database, it has now been used to calculate CFs for several thousand substances and forms the basis of the recommendations from UNEP-SETAC's Life Cycle Initiative regarding characterisation of toxic impacts in life cycle assessment.

Recommendations and perspectives We provide both recommended and interim (not recommended and to be used with caution) characterisation factors for human health and freshwater ecotoxicity impacts. After a process of consensus building among stakeholders on a broad scale as well as several improvements regarding a wider and easier applica-

M. MacLeod
Institute for Chemical and Bioengineering, ETH Zurich,
Wolfgang-Pauli-Strasse 10,
8093 Zurich, Switzerland

T. E. McKone
Lawrence Berkeley National Laboratory,
University of California Berkeley,
Berkeley 94720 CA, USA

J. Payet
Institute of Environmental Science and Technology,
École Polytechnique Fédérale de Lausanne,
1015 Lausanne, Switzerland

D. van de Meent
National Institute of Public Health and the Environment (RIVM),
3720 Bilthoven, The Netherlands

bility of the model, USEtox will become available to practitioners for the calculation of further CFs.

Keywords Characterisation factors · Characterisation modelling · Comparative impact assessment · Comparison · Consensus model · Freshwater ecotoxicity · Harmonisation · Human exposure · Human toxicity · LCIA · Life cycle impact assessment · Toxic impact

1 Background, aim and scope

In 2002, the United Nations Environment Program (UNEP) and the Society for Environmental Toxicology and Chemistry (SETAC) launched an International Life Cycle Partnership, known as the Life Cycle Initiative, to enable users around the world to put life cycle thinking into effective practice. The Life Cycle Impact Assessment (LCIA) programme within this initiative aims to (1) establish recommended methodologies and guidelines for the different impact categories, and ultimately consistent sets of [characterisation] factors, and (2) make results and recommendations widely available for users through the creation of an information system that is accessible worldwide (see Jolliet et al. 2003a). In this context, identification and quantification of impacts on human health and ecosystems due to emissions of toxic substances are of central importance in the development of sustainable products and technologies. Toxicity indicators for human health effects and ecosystem quality are necessary both for comparative risk assessment and for LCAs applied to chemicals and emission scenarios. Yet, in practice, these toxicity factors are not typically addressed in LCIA for many reasons, one of which is that different methods often fail to arrive at the same toxicity characterisation score for a substance (Pant et al. 2004). The Task Force on ecotoxicity and human toxicity impacts, established under the LCIA programme, aimed at making recommendations for characterisation factors (CF) for toxicity using a methodology simple enough to be used on a worldwide basis for a large number of substances but incorporating broad scientific consensus. To reach this goal, a comprehensive comparison of existing human and ecotoxicity characterisation models was carried out to establish recommended practice in chemical characterisation for LCIA by means of constructing a scientific consensus model.

Several methodologies have been published that account for fate, exposure and effects of substances and provide cardinal impact measures. Among these methods are IMPACT 2002 (Jolliet et al. 2003b; Pennington et al. 2005), USES-LCA (Huijbregts et al. 2000), Eco-Indicator 99 (Goedkoop et al. 1998) and CalTOX (Hertwich et al. 2001; McKone et al. 2001; McKone 2001). These methods adopt environmental multimedia, multi-pathway models to account for the

environmental fate and exposure processes. Characterisation methods like EDIP (Hauschild and Wenzel 1998) account for fate and exposure relying on key properties of the chemical.

Model comparisons on the level of chemical fate—without considering exposure—have been published by Cowan et al. (1994), Maddalena et al. (1995), Kawamoto et al. (2001), Wania and MacKay (2000), Bennett et al. (2001), Wania and Dugani (2003), Stroebe et al. (2004) and Scheringer et al. (2004). An OECD expert panel compared nine multimedia models by applying a set of 3,175 hypothetical chemicals (Fenner et al. 2005). In this effort, the most influential model elements were identified and incorporated into a consensus model, called 'The Tool' (Wegmann et al. 2008), which calculates long range transport potentials (LRTP) and overall persistence for chemical hazard assessment. Depending on chemical partitioning properties, the OECD study identified the following model elements as influential for the LRTP calculation: setup and parameterisation of regional, continental and global scales in a nested structure; transport in air, river water and seawater; full spatial coupling between media; geo-referenced surface area ratios, degradation of the aerosol-bound fraction; setup of the environmental conditions; and zonal averaging of environmental parameters.

Some comparisons have also been conducted taking into account the (human) exposure and/or toxic effects part of impact models. Huijbregts et al. (2005a) compared inhalation and ingestion intake fractions (iF) calculated by CalTOX and USES-LCA for 365 compounds. Several model characteristics were found to be important sources of differences, e.g. presence and treatment of a seawater compartment, layering of the soil compartment, consideration of rain events and drinking water treatment. A few studies have dealt with the comparison of characterisation factors in the context of LCIA, among them Dreyer et al. (2003) and Pant et al. (2004) who concluded that for toxic impacts on human health and ecosystems, more detailed analyses are needed to identify causes for the large differences found between the methods. In the OMNIITOX project, a detailed model comparison was conducted with CalTOX, IMPACT 2002 and USES-LCA, and a systematic approach was developed to compare models and identify sources of differences between the models on the level of environmental mechanisms (Margni 2003; Rosenbaum 2006).

These studies were used as the starting point for the UNEP–SETAC model comparison. Although other studies have been published dealing with the comparison of multimedia fate models, few attempts have been made to compare models capable of estimating fate and exposure. Even less effort has been made to compare models on the

level of toxic effects and final characterisation factors. Finding a scientific consensus among method developers and subsequently a broad consensus among all stakeholders results in a recommended method and sound user guidance that will greatly enhance the practical implementation of toxicity impacts in LCA. This research aimed to address these issues by:

- Comparison of seven toxicity characterisation models applying a chemical test set comprising 45 organic substances to identify the most influential model choices.
- Development of a scientific consensus model—named USEtox in recognition of the UNEP–SETAC Life Cycle Initiative under which it was developed;
- Providing recommended LCIA characterisation factors for more than 1,000 chemicals for both human toxicity and aquatic freshwater ecotoxicity;
- Providing recommendation for future model development.

This paper begins with a description of the principles that guided the model development, the main features of USEtox and of the other models used for the comparison exercise and the chemical database used to calculate characterisation factors. It then summarises the results from the UNEP–SETAC model comparison study regarding recommended characterisation factors and the development of a scientific consensus model, called USEtox, for chemical impact characterisation related to human toxicity and freshwater ecotoxicity. This paper is part of a series of publications presenting the process of scientific consensus building (Hauschild et al. 2008) as well as the comparison results and the USEtox model in detail regarding (1) chemical fate and ecotoxicity, (2) human exposure and (3) human health effects respectively (the latter three papers are currently being prepared).

2 Materials and methods

2.1 Principles and process for USEtox development

Expert workshops The model development had as a foundation the recommendations of a series of expert workshops (Jolliet et al. 2006; Ligthart et al. 2004; McKone et al. 2006). Their recommendations were used to construct a model that represented the consensus of experts about what a meaningful toxic impact characterisation model for human toxicity and freshwater ecotoxicity needed to take into account in the context of comparative assessment.

Model comparison A quantitative comparison was conducted on seven existing LCIA models to identify the most influential parameters and reasons for differences between models. The models included in the comparison were

selected in an open process in which developers of models characterising environmental fate, human exposure, human toxicity and ecotoxicity were invited to participate. This invitation was accepted by the developers of CalTOX (McKone et al. 2001), USA; IMPACT 2002 (Pennington et al. 2005), Switzerland; USES-LCA (Huijbregts et al. 2005c), Netherlands; BETR (MacLeod et al. 2001), Canada and USA; EDIP (Wenzel et al. 1998), Denmark; WATSON (Bachmann 2006), Germany and EcoSense (EC 1999, 2005), Germany. Not all models included in the comparison were capable of describing the entire emission-to-characterisation factor relationship, but all models were compared for midpoints that they could calculate. A succinct qualitative comparison of the models can be found in the Electronic supplementary material.

This comparison was carried out using a chemical test set composed of 45 organic substances (Margni 2003; Margni et al. 2002) covering a wide range of property combinations according to the following criteria: environmental partitioning, exposure pathways, overall persistence, long range transport in air, the importance of feedback between environmental media according to Margni et al. (2004) and extreme hydrophobicity. The test set of non-dissociating and non-amphiphilic organic chemicals is provided in the Electronic supplementary material. For the substances in the chemical test set, each model developer calculated with his own model results representing fate, exposure, effects and overall impact characterisation factors. In a series of workshops (Bilthoven 5/2006, Paris 8/2006, and Montreal 11/2006), the results were discussed in order to identify the main reasons for differences. Between the workshops, a list of specific changes was implemented in each model with the goal of harmonising the models, removing unintended differences.

Development principles Finally, USEtox was developed following a set of principles including:

1. Parsimony—as simple as possible, as complex as necessary;
2. Mimetic—not differing more from the original models than these differ among themselves;
3. Evaluated—providing a repository of knowledge through evaluation against a broad set of existing models;
4. Transparent—being well-documented, including the reasoning for model choices.

The scientific consensus model USEtox (named in recognition of the UNEP–SETAC Life Cycle Initiative under which it was developed) is the main outcome of the comparison exercise, and its name also conveys the message that the toxicity categories should be included in LCA.

2.2 USEtox short description

USEtox calculates characterisation factors for human toxicity and freshwater ecotoxicity. As demonstrated in Fig. 1, assessing the toxicological effects of a chemical emitted into the environment implies a cause–effect chain that links emissions to impacts through three steps: environmental fate, exposure and effects.

Linking these, a systematic framework for toxic impacts modelling based on matrix algebra was developed within the OMNIITOX project (Rosenbaum et al. 2007) and peer-reviewed in a UNEP–SETAC workshop by an independent expert panel, who recommended the framework for further developments within the Life Cycle Initiative, where it was then adopted for USEtox (Jolliet et al. 2006). The links of the cause–effect chain are modelled using matrices popu-

Fig. 1 Framework for comparative toxicity assessment
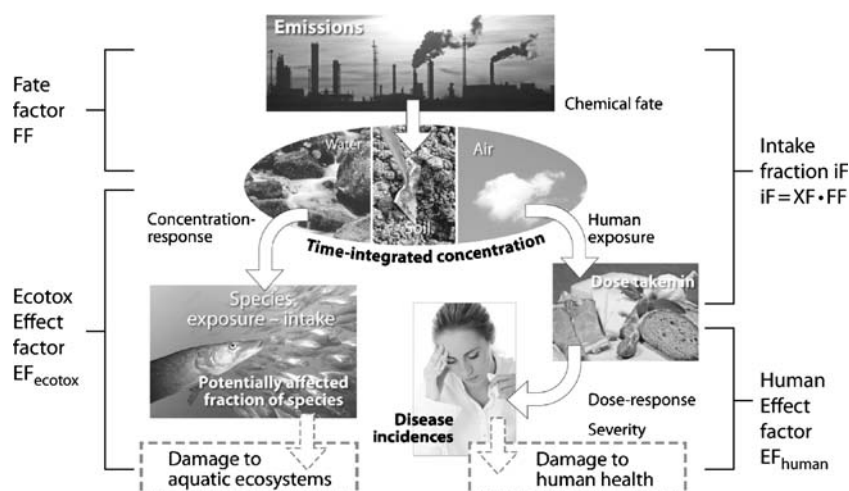
lated with the corresponding factors for the successive steps of fate $\left(\overline{FF}\right)$ in day, exposure $\left(\overline{XF}\right)$ in day^{-1} (only human toxicity) and effects $\left(\overline{EF}\right)$ in cases/kg$_{intake}$ for human toxicity or PAF m^3/kg for ecotoxicity. This results in a set of scale-specific characterisation factors $\left(\overline{CF}\right)$ in cases/kg$_{emitted}$, as shown in Eq. 1.

$$\overline{CF} = \overline{EF} \times \overline{XF} \times \overline{FF} = \overline{EF} \times \overline{iF} \qquad (1)$$

As depicted in Fig. 2, USEtox spans two spatial scales. The continental scale consists of six environmental compartments: urban air, rural air, agricultural soil, industrial soil, freshwater and coastal marine water. The global scale has the same structure as the continental scale, but without the urban air, and accounts for impacts outside the continental scale. The main compartmental characteristics are listed in Table 1. The landscape parameters used can be found in the Electronic supplementary material. The fate model calculates the mass increase (kg) in a given medium due to an emission flow (kg/day). The unit of the fate factor is in days. It is equivalent to the time-integrated concentration × volume over the infinite of a pulse emission (Heijungs et al. 1992; Mackay and Seth 1999). Inter-media transport and removal processes at the two spatial scales required to calculate the fate factor matrix $\overline{FF}$ will be further explained in the respective chemical-fate paper currently in preparation. The emission scenarios are continental emission to urban air, rural air, freshwater and agricultural soil.

The human exposure model quantifies the increase in amount of a compound transferred into the human population based on the concentration increase in the different media. The human exposure factors in the exposure matrix $\overline{XF}$ at the two geographical scales include exposure through inhalation of (rural and urban) air and ingestion of drinking water (untreated surface freshwater), leaf crops (exposed produce), root crops (unexposed produce), meat, milk and fish from freshwater and marine aquatic compartments for the total human population. Human exposure factors have the dimension per day. The exposure parameters used are listed in the Electronic supplementary material. The fate and the exposure matrices combine into the intake fraction matrix $\left(\overline{iF}\right)$ that describes the fraction of the emission that is taken in by the overall exposed population. Further details will be discussed in the respective exposure paper currently in preparation. The ecological exposure factor equals the dissolved fraction of a chemical (dimensionless) and accounts for the bioavailability of a chemical by converting the fate factors in terms of total concentration to dissolved concentration.

Human effect factors in USEtox relate the quantity taken in by the population via ingestion and inhalation to the probability of adverse effects (or potential risk) of the chemical in humans. It is based on toxicity data for cancer and non-cancer effects derived from laboratory studies. Under the assumption of a linear dose–response function for each disease endpoint and intake route, the human effect factor is calculated as $0.5/ED_{50}$, where the ED_{50} is the lifetime daily dose resulting in a probability of effect of 0.5. We allow for up to four separate human effect factors: cancer from ingestion exposure, non-cancer effects from ingestion exposure, cancer from inhalation exposure and non-cancer effects from inhalation exposure. Human effect factors have the dimension disease cases per kilogram intake. Differences in metabolic activation of chemicals between animal tested and humans are not considered. For further insights into the human health effects step, we refer to the related paper currently in preparation. For freshwater

Fig. 2 Compartment setup of the consensus model
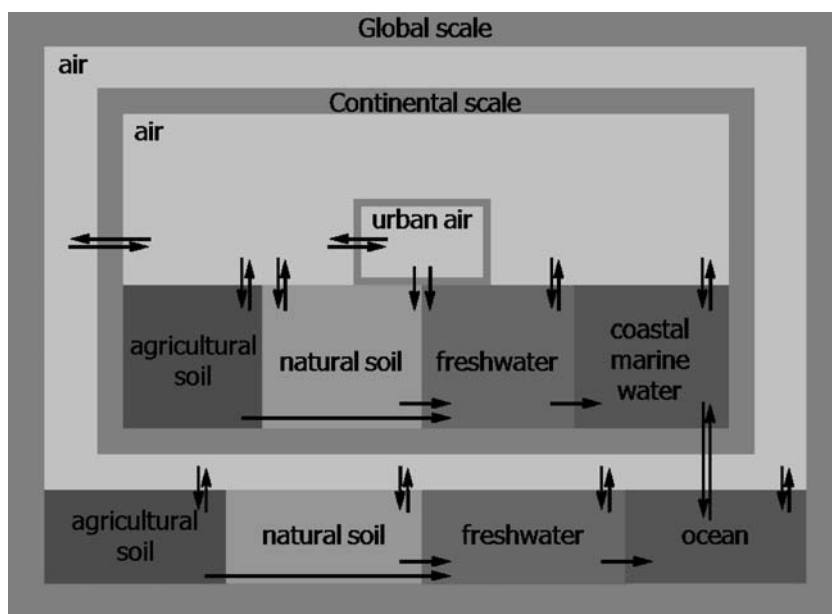
Table 1 Key model elements identified in the comparison and implemented in the consensus model

Topic	Description	How it has been dealt with in USEtox
Fate: Inclusion of an urban air compartment	Nesting an urban air box in the continental air box allowing to account for higher inhalation impacts in areas with higher population density.	Chemicals coming from the urban air compartment are transferred to rural air via advection, to rural soil via deposition and to rural surface water via run-off from the surface considered as 100% paved, or removed via degradation.
Fate: Inclusion of a global zone	Allows for assessment of global-scale impacts for substances that are subject to long-range transport.	Nested model structure includes the global scale.
Fate: Accounting for intermittent rain events	Many steady-state fate models overestimate transfer of chemicals from the atmosphere to the surface by rain because they assume constant rain conditions.	An algorithm approximating the effect of intermittent rain events (Jolliet and Hauschild 2005) has been implemented in the consensus model.
Fate: Distinguishing soil types	Human exposure via agricultural produce is related to agriculturally used soil only, which represents just a fraction of the total soil surface.	Using two soil types, agricultural and natural soil, accounts for the fraction of agricultural soil relative to the total soil surface and also allows for specific (e.g. pesticide) emissions occurring on agricultural soil only.
Fate: Soil compartment setup	Soil usually is a complex medium consisting of several multi-layered sub-compartments with distinct fate properties.	In order to keep it reasonably simple and transparent, the soil compartment is a homogeneous single-layer compartment with a depth of 10 cm.
Fate: Marine compartments	Persistent pollutants (particularly metals) get unrealistically high characterisation factors due to long residence time in the deep sea.	Deep sea modelled as a sink, exposure and impacts only modeled in coastal waters.
Fate: Sediments	The consideration of sediment compartments in fresh and marine water and related processes, e.g. resuspension and burial, lead to significant differences between models for individual substances.	Sediment has been omitted as compartment.
Human exposure: Plant uptake model	Significant differences in vegetation uptake algorithms were identified in the multimedia fate/exposure models under consideration.	The consensus model uses a simplified one-compartment approach suitable to account for chemical exposure limiting the root concentration factor (RCF) for high K_{ow} ($>10^5$) compounds to 200 and distinguishing leaf surfaces from overall above-ground plant tissues when calculating the plant–air partition coefficient.
Human exposure: Biotransfer into meat and milk	Current biotransfer models for meat and milk are very uncertain and provide unrealistic results for highly hydrophobic chemicals.	Due to the lack of updated methods we followed the recommendation of the European Commission Technical Guidance Document, truncating the Travis and Arms (1988) model at log $K_{ow} > 6.5$ and <3 to a constant value (EC 2003). Biotransfer for meat are corrected for human meat consumption (beef, pork, poultry, goat/sheep) and their respective individual farm animal intake and fat content.
Human toxicity effects	According to recommendations from external experts (Jolliet et al. 2006; McKone et al. 2006), effect indicators for human toxicity based on best estimate of effect concentrations (ED_{50} or ED_{10}, possibly extrapolated from NOAEL), rather than reference dose that embeds safety factors.	According to recommendations human effect factors are calculated as $0.5/ED_{50}$. Route to route extrapolation has been studied in further details. Factors for chemicals with uncertain extrapolations are marked as interim. Regarding the uncertainty related to severity and the lack of evidence for significant differences when combining dose-response slope and severity of disability, equal severity has been assumed so far for cancer and non-cancer.
Aquatic ecotoxicity effects	For the LCA comparative purpose, the characterisation factor should be chosen at the HC_{50} level (geometric mean of effect concentrations, EC_{50}) not for the most	Aquatic ecotoxicological effect factors are then calculated as $EF_{ecotox} = 0.5/HC_{50}$. This is especially important when comparing data poor substances with extensively

Table 1 (continued)

Topic	Description	How it has been dealt with in USEtox
	sensitive species (Jolliet et al. 2006; Ligthart et al. 2004).	tested substances such as metals. Factors for data poor chemicals are marked as interim.
Overall characterisation factors	Present model is mostly designed and valid for non polar, non ionic organic chemicals.	Factors for metals, amphiphilic and dissociating substances are marked as interim factors.

ecosystems, the effect factor is calculated using the same linear assumption used for the human effect factor, i.e. linearity in concentration–response which results in a slope of $0.5/HC_{50}$. The HC_{50}, based on species-specific EC_{50} data, is defined as the hazardous concentration at which 50% of the species are exposed above their EC_{50}. The EC_{50} is the effective concentration at which 50% of a population displays an effect (e.g. mortality). Aquatic ecotoxicological effect factors have the dimension cubic metre per kilogram.

After multiplication of the scale-specific fate factors, exposure factors and effect factors (see Eq. 1), the final characterisation factor for human toxicity and aquatic ecotoxicity is calculated by summation of the characterisation factors from the continental- and the global-scale assessments. For human toxicity, carcinogenic and non-carcinogenic effects are also summed (assuming weighting factor equals 1), resulting in a single characterisation factor per emission compartment. The characterisation factor for human toxicity (human toxicity potential) is expressed in comparative toxic units (CTU_h), providing the estimated increase in morbidity in the total human population per unit mass of a chemical emitted (cases per kilogram), assuming equal weighting between cancer and non-cancer due to a lack of more precise insights into this issue. The characterisation factor for aquatic ecotoxicity (ecotoxicity potential) is expressed in comparative toxic units (CTU_e) and provides an estimate of the potentially affected fraction of species (PAF) integrated over time and volume per unit mass of a chemical emitted (PAF m^3 day kg^{-1}).

These general principles resulted in the key elements displayed in Table 1, which summarises the key requirements for running the consensus model and indicates how these have been addressed. It provides an overview of both expert recommendations that were used as a basis to build the model and model choices that have been particularly influential. The right column lists how these recommendations have been implemented in USEtox whilst maintaining transparency and parsimony.

2.3 Chemical database

A database of chemical properties was set up with data aiming to (a) have a consistent set of data (b) of a certain minimum quality (c) for as many chemicals as possible for which characterisation factors can be computed. This includes three types of datasets: (1) physico-chemical properties, (2) toxicological effect data on laboratory animals as a surrogate to humans and (3) ecotoxicological effect data for freshwater organisms. A complete list of the minimum dataset needed to run the model can be found in the Electronic supplementary material. Recognising that the primary objective of this task is not to generate and/or estimate chemical properties and toxicity data, we focused our effort on identifying and collecting existing reviewed databases for which scientific judgement was already made in selecting and recommending values from a large range of values collected from the literature. For each of the three types of datasets, we (1) identified the existing databases, (2) defined a selection scheme and criteria for data gathering and (3) compiled the database for all the chemicals for which effect data are available.

Human effect data Building on the workshop recommendations for comparative assessment of McKone et al. (2006), the effect factor takes as a point of departure the effect dose 50% (ED_{50}) from the carcinogenic potency database (CPDB) by Gold et al. (2008, 2005). For cancer, the harmonic mean of all positive ED_{50} is retained for the most sensitive species of animal cancer tests between mice and rats after application of an allometric factor proportional to bodyweight to the power of 0.25 (Vermeire et al. 2001). The use of a harmonic mean rather than an arithmetic or geometric mean is consistent with the use of the inverse of the ED_{50} in the model. Furthermore, the harmonic mean is similar to the most potent site and has the advantage of using results from all positive experiments (Gold et al. 1989). Compared to previous data used in LCA, chemicals with all negative carcinogenic effect data were also included as true zero carcinogenic effect factors and distinguished from missing data. In the case of effects other than cancer, for most of the substances, insufficient data were available to recalculate an ED_{50} with dose–response models. For chemicals with no evidence of carcinogenicity, the ED_{50} has been estimated from no-observed effect level (NOEL) by a NOEL-to-ED_{50} conversion factor. NOELs were derived from the IRIS database and from the World Health Organisation. If relevant, conversion factors to

extrapolate from short-term to long-term exposure were applied as well (see Huijbregts et al. 2005b for further details). For both carcinogenic and non-carcinogenic effects, a route-to-route extrapolation has been carried out, assuming equal ED_{50} between inhalation and ingestion route and flagging the factor as interim when large differences may occur (see Section 2.4).

Ecotoxicological effect data Two databases with ecotoxicity effect data on average EC_{50} values (i.e. HC_{50}s) were available, covering, respectively, 3,498 (Van Zelm et al. 2007) and 1,408 chemicals (Payet 2004), the first one being based on EC_{50} values from the RIVM e-toxBase (www.e-toxbase.com) and the second one on data mainly from ECOTOX (2001) and IUCLID (2000). Even though there is no consensus on which averaging principles HC_{50} should be estimated (on basis of trophic levels or single species), we pragmatically suggest to use these available HC_{50} data all based on geometric means of single species tests data (Larsen and Hauschild 2007). Further, we prioritise chronic values as long as they represent measured EC_{50} values and are not extrapolated from NOEC values (Jolliet et al. 2006; Larsen and Hauschild 2007). Second priority is given to well-documented acute data, applying a best estimate extrapolation factor as an acute-to-chronic ratio (ACR), e.g. 1.9 for organic substances and 2.2 for pesticides—except for carbamate and organotin where no ACR were available from Payet (2004). The HC_{50} value, which is applied as effect factor, is then pragmatically based on averages of single species test data.

Physical–chemical data The EPI Suite™ chemical database (USEPA 2007) has been selected as the default database. Freely available from the EPA website, it covers all the physical–chemical parameters included in the other databases (Howard 2006, personal communication): PHYSPROP (Howard and Meylan 1997), SOLV-DB (NCMS 2008), Handbook of Environmental Degradation Rates (Howard et al. 1991) and Environmental Fate Data Base (SRC 2008). Additional specific compilations for bioconcentration factors for fish (Meylan et al. 1999), biotransfer factors for milk and meat (Rosenbaum 2006) and degradation half-lives (Mackay et al. 2006; Sinkkonen and Paasivirta 2000) were identified. As a general rule, whenever available, experimental data were favoured over estimated data. For selected chemical properties, we adopted the following priority list for data selection:

- Bioconcentration factors for fish:

  Select among the 600+ measured data from the Meylan et al. (1999) compilation
  EPISuite data based referring to the bilinear model of Meylan et al. (1999), including correction factors

Bilinear model of Meylan et al. (1999) without correction factors

- Biotransfer factors for milk and meat:

  Experimental data collected by Rosenbaum (2006), 75 entries for BTF_{milk} and 40 for BTF_{meat}
  Estimation based on a modified version of the Travis & Arms model, according to the TGD (EC 2003)

- Half-lives:

  Data from Sinkkonen and Paasivirta (2000) for dioxins and PCBs
  Mackay Handbook (Mackay et al. 2006)
  EPI Suite™ using factors from (Aronson et al. 2006) to convert the degradation probability in half-lives and multiplication factors of 1:4:9 to extrapolate degradation half-lives for water, soil and sediment compartments respectively (Phil Howard, personal communication).

2.4 Distinction between recommended and interim characterisation factors

In USEtox, a distinction was made between interim and recommended characterisation factors reflecting the level of reliability of the calculations in a qualitative way. First, characterisation factors for 'metals', 'dissociating substances' and 'amphiphilics' (e.g. detergents) were all classified as interim due to the relatively high uncertainty of addressing fate and human exposure for all chemicals within these substance groups. Dissociative substances were identified using a systematic procedure, based on pK_a[1], whilst amphiphilics have been classified using a list of marketed detergents received from Procter & Gamble (Pant 2008, personal communication). This preliminary flagging of chemicals with interim characterisation factors has been carried out at our best available knowledge. However, we stress the fact that it is always the responsibility of the user to verify if a given chemical is inorganic,

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[1] The following procedure has been applied: (1) selecting those (665) chemicals from the list of 5,019 substances that had a pK_a value listed, (2) scoring substances that can donate a proton 'a' and those that can accept a proton as 'b', (3) calculating the fraction of the substance that is expected to be present in its original, neutral form at pH 7 and (4) flagging acids with $pK_a <6$ and bases with $pK_a >8$ 'F' [note that these are the substances with F(neutral) <10%]. Chemicals that are listed as salts need special attention. If the K_{ow} listed for these chemicals pertain to the salt form, the K_{ow} may be used to estimate K_p. If it pertains to the conjugated acid or base, it needs to be corrected: Neglecting the possible contribution of the ionic form to hydrophobicity, we can use the product F(neutral) $\times K_{ow}$ as a basis for estimating K_{aw}, K_p and BCF.

dissociating or amphiphilic/surfactant and whether its CF has to be considered as interim. A report back to the authors will be greatly appreciated in such a case.

For the remaining set of chemicals, consensus has been reached that recommended aquatic ecotoxicological characterisation factors must be based on effect data of at least three different species covering at least three different trophic levels (or taxa) in order to ensure a minimum variability of biological responses.

For human health effects, recommended characterisation factors were based on chronic or subchronic effect data, whilst characterisation factors based on sub-acute data were classified as interim. Furthermore, if route-to-route extrapolation was applied to obtain ingestion or inhalation human health effect factors, a subdivision was made between recommended and interim characterisation factors. Human health characterisation factors based on route-to-route extrapolation from animal data were considered interim if 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 were also considered interim if the expected fraction absorbed via inhalation was a factor of 1,000 higher compared to the fraction absorbed via ingestion. This factor of 1,000 indicates that exposure by inhalation may be far more toxic than by ingestion for a few chemicals. In these cases, the interim characterisation factor would underestimate the potential impact by inhalation.

We determined 789 recommended characterisation factors for potential carcinogenic human health effects and 344 for non-carcinogenic human health effects. Interim characterisation factors were determined for 217 carcinogenic chemicals and 71 non-carcinogenic chemicals. Four hundred seventeen of the carcinogenic characterisation factors corresponded to chemicals with negative effect data, i.e. with a characterisation factor close to 1E−50 (to differentiate from non-available factors set to 0). This results in a number of recommended CFs for total human health effects of 991 (all CFs used must be classified as recommended) plus 260 interim CFs (at least one CF was classified as interim). For aquatic ecotoxicity, the substance coverage for recommended factors is 1,299 chemicals. The 1,247 substances with less than three species tested are included as interim factors. A full list of recommended and interim characterisation factors for both human health and freshwater ecotoxicity impacts for emissions to urban air, rural air, freshwater and agricultural soil are available in the Electronic supplementary material in Excel format. They are accompanied by a selection of relevant intermediary parameters such as central fate factors, intake fractions for inhalation and ingestion, effect factors for human health cancer and non-cancer as well as freshwater ecotoxicity. Interim CFs might be used in LCA studies, but with great caution and under awareness of their

large inherent uncertainty. In the case that an LCA result is dominated by impact scores based on interim CFs, we advise to proceed with great caution to their interpretation underlining that these factors are neither recommended nor endorsed. If improved data become available or the model is updated in the future, interim factors could eventually be recalculated and become recommended factors if consequently they fulfil the criteria. Such a process is foreseen for the maintenance of both model and database.

# 3 Results

3.1 Model comparison results

Figures 3 and 5 show the results of the harmonisation. By showing the comparison graph for the last comparison round (Montreal workshop in November 2006) in combination with Figs. 4 and 6, we demonstrate the evolution of harmonisation of the models during the process. In the figures, USEtox is used as reference model, and the plots thus demonstrate that the characterisation factors produced with USEtox fall within the ranges of the factors produced by the other characterisation models in the comparison. This is in accordance with the second development principle mentioned earlier, that it shall be mimetic, not differing more from the original models than these differ among themselves.

3.1.1 Human health impacts

Figure 3 compares human health characterisation factors calculated by several models for continental emissions to rural air as a representative example; all other emission scenarios can be found in Electronic supplementary material. The harmonisation of most influential model elements reduced variability to four orders of magnitude.

For any substance in the plots, the range given by the results of the old characterisation methods can be taken as measure of the model uncertainty accompanying the characterisation factor produced by USEtox or by any of the other models. In order to quantify the precision of USEtox against the other models, we employ the residual error (RE), also known as the standard error of the log of the estimate or the standard deviation of the log of residuals. The RE and its use in such context is discussed by McKone (1993). The RE was calculated for both situations presented above, i.e. the USEtox CFs vs. the CFs of all other models before and after their harmonisation. The results are shown in Fig. 4 in terms of RE. The RE is related to the squared geometric standard deviation: $GSD^2 = 10^{RE^2}$, which represents the geometric factor that captures the two standard deviations prediction interval, i.e. the 95%

Fig. 3 Comparison of characterisation factors for organics calculated by the consensus model against the other models for human health impacts due to a continental emission to rural air. The plot shows the model comparison after harmonisation (Montreal workshop)
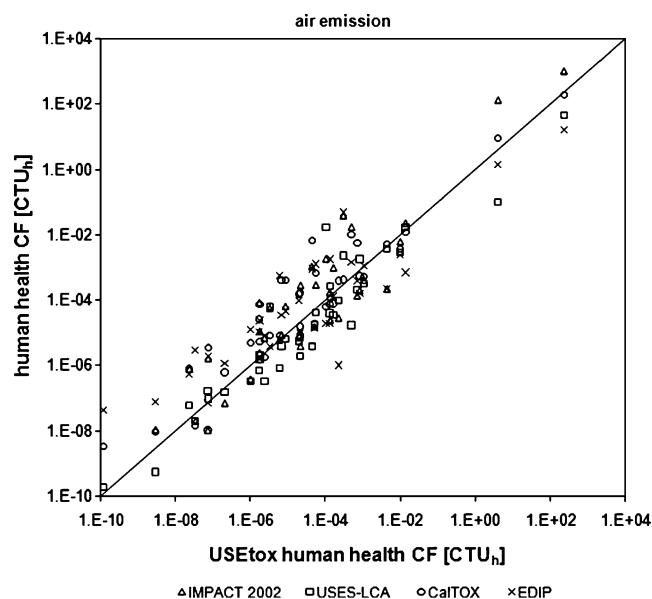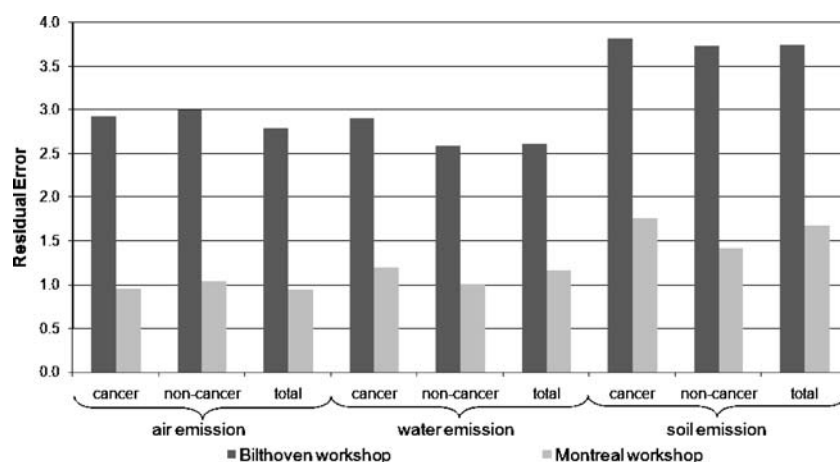
confidence interval (mean value divided, respectively, multiplied by the GSD^2).

Via harmonization, the RE was reduced by a factor of two to three, which represents a narrowing of the variation among models within the 95% confidence interval by three to more than four orders of magnitude, now spanning four to six orders of magnitude instead of ten to 14 orders of magnitude.

3.1.2 Freshwater ecosystem impacts

Figure 5 shows the model comparison of freshwater ecotoxicity characterisation factors after continental emissions to freshwater (all other emission scenarios are shown in Electronic supplementary material). The adapted models showed a variation of three orders of magnitude with USEtox.

As shown in Fig. 6, the harmonisation of the models reduced the RE of the aquatic ecotoxicity characterisation factors by a factor of two to three, narrowing down the variation among models within the 95% confidence interval to only two to four orders of magnitude instead of six to ten orders of magnitude, which represents a reduction of variation/model uncertainty by two to three orders of magnitude.

4 Discussion

4.1 Scientific consensus model

Initial differences among models for toxicity characterisation factors were considerably reduced by harmonisation, as their

Fig. 4 Residual error of the human health characterisation factors from USEtox vs. all other models (IMPACT 2002, CalTOX, USES-LCA, EDIP) before (*dark grey*) and after (*light grey*) harmonisation
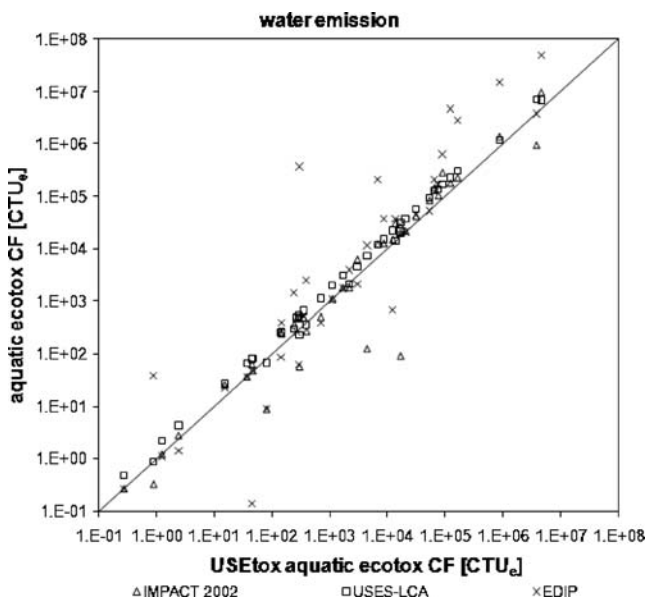
Fig. 5 Comparison of characterisation factors for organics calculated by the consensus model against the other models for aquatic ecosystem impacts due to an emission to water. The plot shows the model comparison after harmonisation (Montreal workshop)
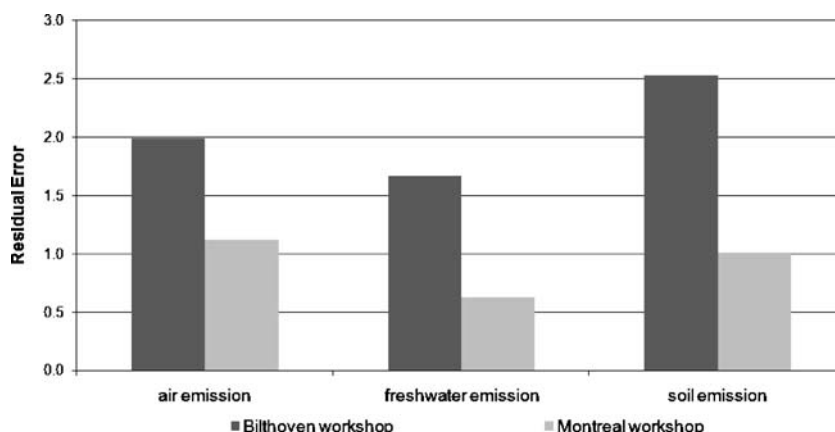
sources were identified. The results from the USEtox model fall within the range of those of the other models, emulating their results with a minimum of complexity. Applying USEtox to a well-referenced database, recommended characterisation factors are now available for:

- Human toxicity: 991 organic substances (+260 interim CFs);
- Freshwater ecotoxicity: 1,299 organic substances (+1,247 interim CFs).

As main findings of the workshops (further discussed in the papers currently under preparation), some of the model choices that were found to be particularly influential are:

- Setup of the soil compartment, e.g. inclusion of sub-compartments, distinction between soil usage types…;

- Process formulations, e.g. sedimentation, intermittent rain,…;
- Defining a closed or open system environment (i.e. open system: inclusion of a global spatial scale that accounts for impacts outside the continental scale which would be incorrectly attributed to the continental scale if the system was closed);
- For human toxicity:
  - Nesting an urban box in a continental box (allowing to account for higher inhalation impacts in areas with higher population density);
  - Calculating biotransfer and bioconcentration factors in food products;
  - Harmonic means of TD_{50}s and ED_{50}s were taken as a starting point, using animal–human extrapolation factors of 4.1 for rats and 7.3 for mice, based on allometric factors.

- For ecotoxicity:
  - Disregarding impacts in the ocean which is modelled as a sink. The current version is only modelling impacts in the freshwater compartment.
  - Applying HC_{50} based on EC_{50} values as effect indicator representing the average sensitivity of the species for comparative purposes rather than focusing on the most sensitive species as is frequently done in risk assessment.

4.2 Uncertainty and precision

Based on comparisons among the different models, we estimate that the precision of the new CFs is within a factor of 100–1,000 for human health and 10–100 for freshwater ecotoxicity. Such a precision of two to three orders of magnitude is significantly lower than the roughly 12 orders of magnitude variation between the CFs of the different chemicals that we obtain from each individual model. The

Fig. 6 Residual error of the freshwater ecotoxicity characterisation factors from USEtox vs. all other models (IMPACT 2002, USES-LCA, EDIP) before (*dark grey*) and after (*light grey*) harmonisation

uncertainty range in model results is due to variation between the models and does not include parameter uncertainties attached to the input data used to calculate the CFs, as input data were kept the same. As a first estimate of the underlying model uncertainty (i.e. without parameter uncertainty) inherent in the recommended CFs, Table 2 provides their GSD^2 under the assumption that they are log-normally distributed. These estimates are based on the residual error discussed in Section 3.1.1.

Apart from differences in model structure, important sources of uncertainty of the USEtox results are, among others, the uncertainty and variability related to input parameters and the lack of accurate mechanistic QSARs to estimate substance properties like carryover rates to meat and milk, limited data on bioconcentration factors for fish, lacking data on chemical degradation rates and large uncertainties related to both human health and ecotoxic effect data. The latter comprise issues such as the use of chronic and acute data, route-to-route extrapolations (i.e. from oral administration in rodent tests to inhalation by humans) and the application of a linear dose–response curve for both the human health and the aquatic ecotoxicity effect factors calculation. Furthermore, we chose to set the human effect factor to zero if no toxicology information is available. The assumption of homogenous compartments, even for such complex media as soil or water, represents a further uncertainty, as in the USEtox model, any chemical entering these compartments is immediately diluted perfectly within the volume. The vegetation model used in the exposure model does not include any degradation process because data are not available. This will overestimate exposures of humans via agricultural produce and meat/milk, further increasing the uncertainty of biotransfer processes modelling in USEtox.

Both 'recommended' and 'interim' characterisation factors are provided. The main difference between recommended and interim characterisation factors is related either to the applicability of USEtox to the respective substances or the availability and quality of the necessary input data. Currently, USEtox is applicable to generic, non-dissociating and non-amphiphilic organic substances. Notably, it does not account for speciation and other important specific processes for metals, metal compounds, and certain types of organic chemicals. As the needed improvements in the modelling practice for these groups of compounds are still under elaboration, we decided to provide interim factors for the time being. Furthermore, for a number of chemicals, the minimum data quality could not be met, e.g. for estimation of the aquatic ecotoxicity effect factor in situations where data for less than three species were available. This led to the decision to not actually recommend factors for such substances whilst research is currently ongoing but to at least provide interim characterisation factors that might be used if needed, but which are not endorsed by the UNEP–SETAC initiative. The uncertainty of these factors is very large, but given the overall range of chemical variation, they might be used with caution.

As already mentioned, missing data and knowledge impose limitations to the use and interpretation of the model and its results. We also note that certain human exposure routes, such as indoor air and dermal exposure are currently not included. Limiting factors in terms of data availability are notably data on human toxicity, ecotoxicity, biotransfer and degradation. For these important inputs, we had to rely on QSAR methods with all their intrinsic uncertainties. For other endpoints such as marine or terrestrial ecosystems, almost no experimental data are currently available. Further research should be undertaken to improve the respective data basis and bridge this data gap.

5 Conclusions

USEtox provides a parsimonious and transparent tool for human health and ecosystem CF estimates. It has been carefully constructed as well as evaluated via comparison with other models and falls within the range of their results whilst being less complex. It may thus serve as an interface between the more sophisticated state-of-the-art expert models (such as those compared in this study and which frequently change due to latest scientific developments being included) and the need of practitioners for transparency, broad stakeholder acceptance and stability of factors and methods applied in LCA. Based on a referenced database, USEtox has been used to calculate CFs for several thousand substances and forms the basis of the recommendations from UNEP–SETAC's Life Cycle Initiative regarding characterisation of toxic impacts in life cycle assessment. USEtox therefore provides the largest substance coverage presently available in term of numbers of chemicals covered. Furthermore, model uncertainty has partly been quantified. USEtox thus represents a significantly improved basis for a wider application of human health and ecotoxicity characterisation factors in LCA

Table 2 Model uncertainty estimates for the recommended characterisation factors

Characterisation factor	GSD^2
Human health, emission to rural air	77
Human health, emission to freshwater	215
Human health, emission to agricultural soil	2,189
Freshwater ecotoxicity, emission to rural air	176
Freshwater ecotoxicity, emission to freshwater	18
Freshwater ecotoxicity, emission to agricultural soil	103

which will be further discussed via recommendations in the following section.

6 Recommendations and perspectives

6.1 Guidance for the use of toxicity factors

In LCA, a toxicity impact score IS_t is calculated as $IS_t = \Sigma_i(CF_{ti} \times M_i)$ with M_i being the mass emitted per emission scenario i multiplied with the corresponding toxicity characterisation factor CF_{ti} summed over all emission scenarios i. For example, benzo[a]pyrene emissions of 0.1 kg to continental air and 0.2 kg to continental freshwater (per functional unit, respectively) would be characterised with a human toxicity impact score as follows: $IS_t = CF_{hum\text{-}tox\text{-}benzo[a]pyrene\text{-}to\text{-}cont\text{-}air} \times 0.1$ kg + $CF_{hum\text{-}tox\text{-}benzo[a]pyrene\text{-}to\text{-}cont\text{-}freshwater} \times 0.2$ kg$=3.01E{-}6 CTU_h \times 0.1$ kg$+1.26E{-}5 CTU_h \times 0.2$ kg$=2.82E{-}6$ CTU_h/kg. This human toxicity impact score can then be summed with that of other substances from the inventory. The toxicity factors, i.e. characterisation factors, presented here must be used in a way that reflects the large variation of ten 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 ten 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 ten 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 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.

6.2 Future perspectives

A full quality check of effect data from the two freshwater ecotoxicity data sets is recommended for the second phase of the UNEP–SETAC Life Cycle Initiative, including a check for the occurrence of NOEC extrapolation and for the representation of taxa and trophic levels. Furthermore, research on how to include chronic data and how to estimate average toxicity (based on data for individual single species or averaged on trophic levels) is also needed and strongly recommended for the second phase of the UNEP–SETAC Life Cycle Initiative.

For the upcoming second phase of the UNEP–SETAC Life Cycle Initiative, the following future activities are foreseen:

- Increase of substance coverage and quality assurance of substance data;
- User-friendly programming of the model, which currently only exists as a research model in Excel;
- Including parameter uncertainty in the uncertainty estimates on the USEtox CFs;
- Development of USEtox to accommodate the metals;
- Development of USEtox to accommodate indoor emissions in homes and workplaces;
- Recommendations regarding differentiation between midpoint and endpoint characterisation;
- Full documentation of USEtox;
- Research on how to include chronic data and how to estimate average toxicity (single species or trophic levels);
- Inclusion of terrestrial and marine ecotoxicity as endpoints in USEtox;
- Reliability check of freshwater ecotoxicity CFs based on one or two effect data only (including a check for the occurrence of NOEC extrapolation and on the representation of taxa and trophic levels);
- Industry workshops on comparative assessment of chemicals and training courses in USEtox;
- Consensus building among stakeholders.

comparison and scientific consensus model development. The authors are grateful for the participation of Miriam Diamond, Louise Deschênes, Bill Adams, Andrea Russel, Jeroen Guinée, Pierre-Yves Robidoux, Stefanie Hellweg, Evangelia Demou, Stig Irving Olsen, Cécile Bulle, Sau Soon Chen, Manuel Olivera, Julian Marshall, Bert-Droste Franke, Peter Fantke, Oleg Travnikov, Dick de Zwart, Peter Chapman, Kees van Gestel and Thomas H. Slone.

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