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Risk and Regulatory Hazard-Based Toxicological Effect Indicators in Life-Cycle Assessment (LCA)

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ABSTRACT

In life-cycle assessment (LCA), it is desirable to compare quantities of chemicals released into the environment in terms of the risk and consequences of toxicological effects. Many current methods rely directly on adaptations of regulatory-orientated approaches. The resultant hazard-based indicators reflect differences in maximum likely individual exposure in the region for an emission and differences in regulatory limits. Such regulatory hazard-based indicators, however, may not provide a consistent basis for relative comparison across chemicals in terms of toxicological risk, as they were not designed for this application purpose. It is therefore essential to consider other methods in LCA to provide comparative estimates, taking into account the full extent of toxicological risks and differences in consequences. This article provides a step-by-step description of the methodological similarities and differences between such risk and hazard based indicators for LCA. An example for benzo[a]pyrene demonstrates a risk-based methodology, highlighting relationships with regulatory approaches and problems that remain in current practice.

Key Words: life cycle assessment, LCA, risk assessment, toxicity, chemicals, impact indicators.

INTRODUCTION

Life cycle assessments (LCA) should provide indicators of toxicological effects based on the relative risk and associated consequences of chemicals that are released into the environment (Hogan *et al.* 1996; Assies 1997; Udo de Haes *et al.* 2002; Pennington *et al.* 2004). The scope and methodology of an LCA differs, however, from that of many approaches adopted for toxicological assessments in a regulatory

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context (Owens 1997; Potting 2000; Olsen *et al.* 2001; Wegener Sleeswijk 2001; Cowell *et al.* 2002).

Regulatory assessments of chemical emissions usually have the goal of evaluating whether there will be an unacceptable risk of a toxicological effect to an individual, subpopulation, or group of species. Focus is generally on ensuring limits set through policy are not surpassed by exposures at any location or point in time. For example, the maximum likely exposure in the region of an emission may be compared to a tolerable threshold. If this exposure is less than the agreed threshold then no further action is likely to be necessary from a regulatory perspective.

Life-cycle assessments provide insights for products that are complementary to those of many regulatory-, site-, or process-oriented risk assessments. A product's life cycle can include the extraction of raw materials, energy acquisition, production, manufacturing, use, reuse, recycling, and ultimate disposal. All these stages in a product's life cycle result in the generation of wastes, emissions, and the consumption of resources. These environmental exchanges contribute to impacts, such as climate change, stratospheric ozone depletion, photooxidant formation (smog), eutrophication, acidification, toxicological stress on human health and ecosystems, the depletion of resources, and noise, among others (Udo de Haes *et al.* 2002; Pennington *et al.* 2004). Whether or not current regulatory limits will be exceeded at specific locations or points in time by these exchanges is not the focus of an LCA.

An LCA practitioner tabulates an inventory of the emissions into the environment and the resources consumed at every stage in a life cycle, from the initial extraction of resources to ultimate disposal (ISO 1998; Rebitzer *et al.* 2004). For emissions, these are reported in terms of the mass of each chemical released at each stage of a life cycle to provide a specific amount of a product. In a subsequent step and the focus of this article, the mass of each chemical is multiplied by a "characterization factor" to provide impact indicators (ISO 2000; Udo de Haes *et al.* 2002; Pennington *et al.* 2004). These factors are available to LCA practitioners in databases. The impact indicators are then cross-compared and can be combined to give overall indicators.

$$\text{Impact Indicator} = \text{Released Mass} \times \text{Characterization Factor} \quad (1)$$

From Equation (1), a characterization factor linearly expresses the contribution to an impact category of a quantity of a chemical (*e.g.*, 1 kg) released into the environment. The factor will be chemical specific. It can also be a function of when and where an emission occurs. As an example of a characterization factor, the relative contributions of different gases to climate change are commonly compared in LCA in terms of carbon dioxide equivalents using Global Warming Potentials (GWPs). A GWP_{500} of 100 implies that a 1 kg release of a chemical contributes the same to climate change as 100 kg of carbon dioxide during, in this case, a 500-year time period. Similar characterization factors are required in LCA for other impact categories, including for toxicological impacts.

Characterization factors for toxicological impacts are necessarily based on models that account for a chemical's fate in the environment, species exposure, and differences in toxicological response, as outlined in Equation (2) (Guinée *et al.* 1996; Jolliet *et al.* 1996; Goedkoop and Spriensma 1999; Huijbregts *et al.* 2000; Hertwich

et al. 2001; Udo de Haes *et al.* 2002).

$$\frac{\text{Impact}}{\text{Emission}} = \underbrace{\frac{\text{Mass Distribution}}{\text{Emission}}}_{\text{Fate Factor}} \cdot \underbrace{\frac{\text{Intake}}{\text{Mass Distribution}}}_{\text{Exposure Factor}} \cdot \underbrace{\frac{\text{Incidence}}{\text{Intake}}}_{\text{Exposure-response Factor}} \cdot \underbrace{\frac{\text{Consequence}}{\text{Incidence}}}_{\text{Consequence Factor}} \qquad (2)$$

Characterization Factor

Many LCA approaches rely directly on adaptations of methodologies that were developed to support regulatory assessments (Hogan *et al.* 1996; Assies 1997; Olsen *et al.* 2001; Udo de Haes *et al.* 2002; Pennington *et al.* 2004), such as the European Technical Guidance Documents (TGD), associated support models, and related data for chemicals (European Commission 1996). These approaches can then provide Characterization factors such as:

$$\text{Characterization factor} = \frac{[\text{PEC/PNEC}]_x}{[\text{PEC/PNEC}]_{\text{ref}}} \qquad (3)$$

where PEC is a predicted exposure concentration for a given emission rate (kg/day) of a chemical, PNEC is a regulatory threshold called a predicted no effect concentration, subscript x denotes the chemical of interest, and subscript ref denotes a reference chemical.

When using approaches such as the PEC/PNEC ratios in Equation (3), inventory data are linearly weighted in terms of regulatory-based hazards. The indicator results are interpretable in terms of regulatory-based hazard equivalents. For example, a Characterization factor of 10 signifies that a chemical would have a regulatory hazard ratio (*e.g.*, PEC/PNEC) 10 times higher than that of the reference chemical for a given emission quantity. This is a convenient indicator basis as the regulatory methodologies are often well developed and consensus approaches exist. However, this does not necessarily imply that the risk or potential consequences of a toxicological effect will be 10 times higher (Heijungs *et al.* 1992; Perriman 1995; White *et al.* 1995; Klöpffer 1996; Owens 1999).

In applications like LCA it is desirable to account for the full extent of risk and differences in consequences, as far as practical and on a consistent basis. Characterization factors should reflect cumulative risk, the risk integrated over time and space that is associated with the release of a quantity of chemical into the environment. The desire to consider cumulative risk in LCA is a fundamental difference from many regulatory approaches, which focus more on peak exposures compared to acceptable thresholds. Nevertheless, this basis is consistent with the principles already adopted for the assessment of substances such as radionuclides, for other impact categories in LCA such as climate change, as well as in approaches necessary to support cost-benefit analyses.

This article provides a step-by-step description of the methodological differences for assessing toxicological effects using risk-based characterization factors in LCA

versus typical approaches that support regulatory assessments. An example for benzo[a]pyrene demonstrates the risk-based LCA methodology and highlights some of the uncertainties that are likely to remain in practice.

Contributions of emissions to acute and local scale effects are not addressed, including those associated with indoor exposures, direct exposure to products during their use phase, and to exposures in the work place. The focus here is on the contribution of emissions to the risk of toxicological effects and consequences at the pan-regional scale, typical of current LCA practice.

OVERALL FRAMEWORK

A mass of chemical released into the environment, M [kg] will distribute in time (t) and in space (x, y, z). Ecosystems and human populations will be exposed to a fraction of this mass, F, at an exposure rate E [hour^{-1}]. This exposure contributes to the risk of undesirable toxicological effects. The risk and potential consequences of effects are quantified by two terms: the exposure-response, β [*e.g.*, the likely number of incidences per kg of chemical taken in by the population] and the potential consequences or damage, D [*e.g.*, the number of years of life lost per incidence for human health]. Equation (4) expresses this mathematically.

$$\text{Impact}\,(x, y, z, t) = M(x, y, z, t) \cdot F(x, y, z, t) \cdot E(x, y, z, t) \cdot \beta(x, y, z, t) \cdot D(x, y, z, t) \qquad (4)$$

As in other applications, including most regulatory assessments, simplifying assumptions in this general framework will remain a necessity in common practice in LCA. Common assumptions in the overall framework include:

- fate (F), exposure rates (E), exposure-response (β), and consequences (D), are not functions of time,
- exposure-response (β) and consequences (D) are not a function of space.

These are helpful simplifications that also reflect the limited availability of temporally and spatially dependent data. In reality, these parameters can vary depending on location (*e.g.*, habitat characteristics, local stressors, mixtures, background concentrations) and time (*e.g.*, seasonal life stage sensitivity). The implications of many of these assumptions in comparative applications such as LCA, as well as in regulatory contexts, are only beginning to be quantified. They are generally not discussed further in this article.

The underlying steps necessary for calculating characterization factors based on this framework are outlined in Equation (2) and Figure 1. The following sections highlight key methodological differences with common regulatory approaches.

HUMAN DAMAGE FACTORS (HDFS)

Human Damage Factors (HDFs) (see Figure 1) are characterization factors for toxicological effects on human health. HDFs are considered in this article to be estimates of the risk and the consequences of toxicological effects that are attributable to the emission of a mass of chemical into the environment, integrated over time and space.

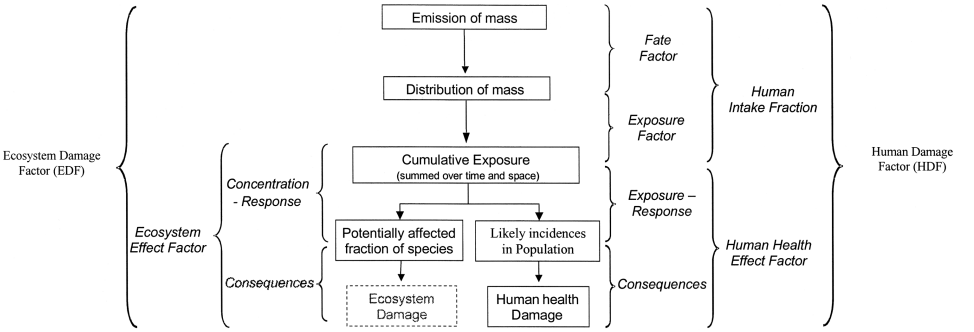

Figure 1. Framework and underlying methodological steps for calculating risk-based characterization factors for toxicological effects in LCA.

From Figure 1, HDFs consist of two key parameters:

- the intake fraction, that is the fraction of a release that will ultimately be taken in by the entire population accounting for the fate of a chemical and human exposure and
- the effect factor, the likely number of incidences and/or the consequences of a chronic toxicological effect per unit intake by the human population.

The following sections describe the underlying method for estimating HDFs. Key differences with approaches for supporting regulatory assessments are highlighted.

Chemical Fate

To estimate toxicological risk in any assessment, it is necessary to first consider how a chemical will distribute in the environment in time and space. In LCA, the mass of a chemical released into the environment is given in a life cycle inventory. Aquatic species, as an example, will be exposed to a fraction of this mass for a given duration. This depends on the fraction of the emission that transfers to water, the transfer fraction, and the chemical's residence time in the water (Margni *et al.* 2004). The fate factor, F [hour] in Equation (2) and Figure 1, is therefore the fraction of an emission that transfers to, for example, surface water multiplied by its residence time in the water.

Many regulatory assessment approaches include estimates of concentrations in a region for a continuous chemical emission using, *e.g.*, steady state mass balance models (Cowan *et al.* 1994; European Commission 1996). Fundamentally, these same fate models can also be used when estimating the fate factor in LCA. A convenient relationship exists between the fate factor and the concentration at steady-state for a continuous emission (Heijungs 1995; Jolliet 1995; Mackay and Seth 1999). This relationship is mathematically reflected in Equation (5) and illustrated in Figure 2.

$$F_{i,m} = \frac{\int_0^t M_{i,t}\,dt}{\int_0^t S_{m,t}\,dt} = \frac{\int_0^t M_{i,t}\,dt}{M_m} = \frac{M_{i,\text{steady-state}}}{S_m} \tag{5}$$

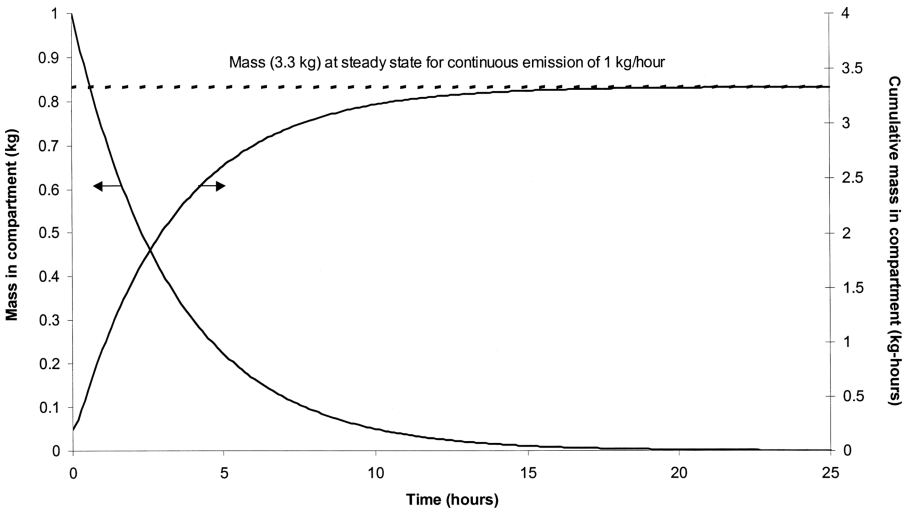

Figure 2. Illustration of relationship between the first order decay of 1 kg of a chemical in an environmental compartment (left axis) and the cumulative mass (mass × time) in that compartment (right axis). The cumulative mass in the compartment at infinite time is 3.3 kg-h. The fate factor (cumulative mass per kg emission) is therefore 3.3 h. At steady-state for a continuous emission of 1 kg/hour, the mass in the same compartment will be 3.3 kg (dotted line). The residence time of the chemical in this example is 3.3 h. As the emission was to the same compartment, the transfer fraction was 1. (decay equation: $dM/dt = -kM$, steady state mass balance: $S = kM$).

where M denotes the mass of a chemical [kg], i denotes the environmental compartment of interest, S is the flow rate of a continuous emission [kg day^{-1}], and m indicates the compartment of the emission.

Although the same fate models can theoretically be used in LCA, the needs can still differ in scope and parameterisation. In regulatory assessments, it is typical to estimate the concentration of a chemical in the region of an emission and to compare this with policy limits. At a regional scale, for example, a 200 × 200 km^2 multimedia model with compartments for air, water, soil, and so on, can be sufficient for this purpose (European Commission 1996). However, Figure 3 illustrates that more than 25% of the mass of many organic chemical emissions is likely to leave such a 200 × 200 km^2 region by advective transport in surface waters and in air.

To consider the full extent of the fate of an emission in LCA, a 200 × 200 km^2 region would not be suitable. LCAs must rely on mass balance models for larger regions (Cowan *et al.* 1994; Higashino *et al.* 1999; USEPA 1999; Wania *et al.* 2000; MacLeod *et al.* 2001; Woodfine *et al.* 2001; Pennington *et al.* 2005) for many chemicals to be able to account for the full extent of a chemical's distribution in the environment.

Human Exposure and the Intake Fraction

Regulatory assessments for toxicological human health effects are commonly based on estimates of a maximum individual exposure. Adopting a subsistence

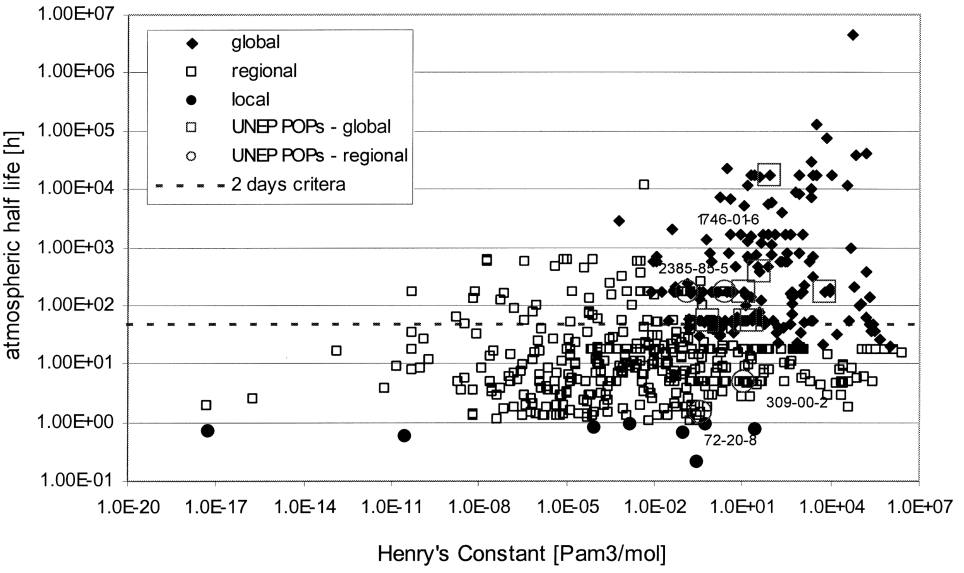

Figure 3. Example of non-dissociating organic chemicals classified using a Western Europe model (Pennington *et al.* 2005) in terms of advective losses. Chemicals with less than 25% advective loss from the vicinity of an emission (*e.g.*, approximately 200 × 200 km^2) are classified as "local." These tend to be removed rapidly from air by, *e.g.*, intermedia transport, reflected here by the Henry's Law partitioning coefficient, and by degradation. Chemicals with an advective loss greater than 25% from Western Europe (2500 × 2500 km^2) for a uniform atmospheric emission across the entire region were classified as "global." (POPs = Persistent Organic Pollutants, UNEP = United Nations Environment Programme).

exposure scenario, models estimate human intake from, for example, the level of contaminants in food grown in the region of an emission multiplied by a likely extreme individual consumption rate of that same local food. This provides an estimate of an individual's intake suitable for comparison against regulatory limits.

A subsistence scenario does not necessarily reflect the relative exposure from the perspective of the entire population. It can therefore be inappropriate if used in a comparative assessment context. The intake fraction provides an alternative basis for population-based risk assessment, see Figure 1.

The intake fraction (iF) is the fraction of a chemical released into the environment that will be taken in by the entire human population via food consumption, inhalation, and dermal exposure (Bennett *et al.* 2002). A high value such as iF = 0.001 reflects that humans will take in 1 part in 1000 of the mass of a chemical released. The ratio of the intake fractions for two chemicals will not necessarily equal the ratio of exposures estimated in a subsistence scenario in a regulatory context.

As for the fate of a chemical, the intake fraction can be estimated in practice using, for example, readily available steady-state models. Equation (6) expresses this

mathematically.

$$iF_m = \sum_{i,e} F_{i,m} \cdot E_{i,e} = \frac{\sum_{i,e} M_i \cdot E_{i,e}}{S_m} \quad (6)$$

where S is the emission rate [kg/day], $E_{i,e}$ is the intake coefficient, or exposure factor (see Figure 1), that describes the fraction of mass in an environmental compartment i that will be taken in by the human population per day [day^{-1}] via each exposure route (e), M_i is the mass of chemical in compartment i [kg], and m denotes the compartment of the emission.

Distinctions are retained between inhalation and ingestion intake fractions to facilitate the separate calculation of likely effects for each of these pathways. Dermal exposure is usually considered less important for effects at the regional exposure scale [36], thus is not commonly taken into account in many LCAs.

A so-called production-based scenario is necessary for estimating the intake fraction (Pennington *et al.* 2005). This relies on data for population density, agricultural production, and water supply. The intake fraction is estimated from the contaminant levels and the quantities of food and water that are destined for consumption. This differs from estimating intake for particular individuals, or population cohorts. In such cases the additional relationship of knowing where food is produced and where the food will be consumed becomes necessary.

Calculations for direct exposure to contaminants, such as from drinking water and through inhalation, will be methodologically similar in regulatory assessments and in LCA. For example, Equation (7) gives the exposure factor, E, for direct exposure to contaminants associated with drinking water extracted from an environmental compartment (i) that has a volume V_i.

$$E_{i,\,\text{direct(drinking water)}} = \frac{\text{population}_i \cdot \text{drinking rate } [m^3/\text{day}]}{V_i [m^3]} \quad (7)$$

This direct exposure factor is the fraction of water consumed per day by the population from a given water body. This is equivalent to the fraction of contaminant taken in per day by the population from that location, if neglecting additional terms for purification losses, and so on.

For indirect exposure, as in regulatory assessments, it is necessary to estimate how much contaminant will be in intermediate substrates, such as fruits, vegetables, livestock, and fish, relative to the levels in the environment. These contaminant estimates are then multiplied by the amount of each substrate that is produced for consumption from each location. This gives the exposure factor (E) for indirect exposure, the fraction of the contaminant mass in an environmental compartment (i) that will be taken in per day by the population via intermediate substrates such as beef (e), see Equation (8) (Pennington *et al.* 2005).

$$E_{i,\text{indirect}} = \frac{\sum_e BAF_{e,i} \cdot PR_{e,i}}{\rho_i \cdot V_i} \quad (8)$$

$PR_{e,i}$ [kg/day] is the rate of substrate produced (*e.g.*, beef) for human consumption that is associated with contaminants in environmental compartment i (*e.g.*, water, soil, or air). $BAF_{e,i}$ [kg_i/kg_e] is the bioaccumulation factor, the ratio on a mass

basis of the concentration in a substrate (*e.g.*, beef) relative in the environmental compartment (*e.g.*, water, soil, or air). The mass of the environmental compartment under consideration is the denominator in Equation (8), given by the compartment density, ρ_i [kg_i/m^3], multiplied by its volume, V_i [m^3].

If considered on a per capita basis, the exposure estimates for LCA using these methods are population averages. Considering only the exposure coefficient, differences with regulatory assessments will primarily be associated with food and water intake rates. Figure 4 presents the differences between individual food intake rates adopted in one subsistence approach for regulatory support versus those from a production-based LCA model on a per capita basis at the EU scale. These production-based estimates are similar to the average consumption values on a per capita basis. The values for regulatory support are generally similar to the maximum

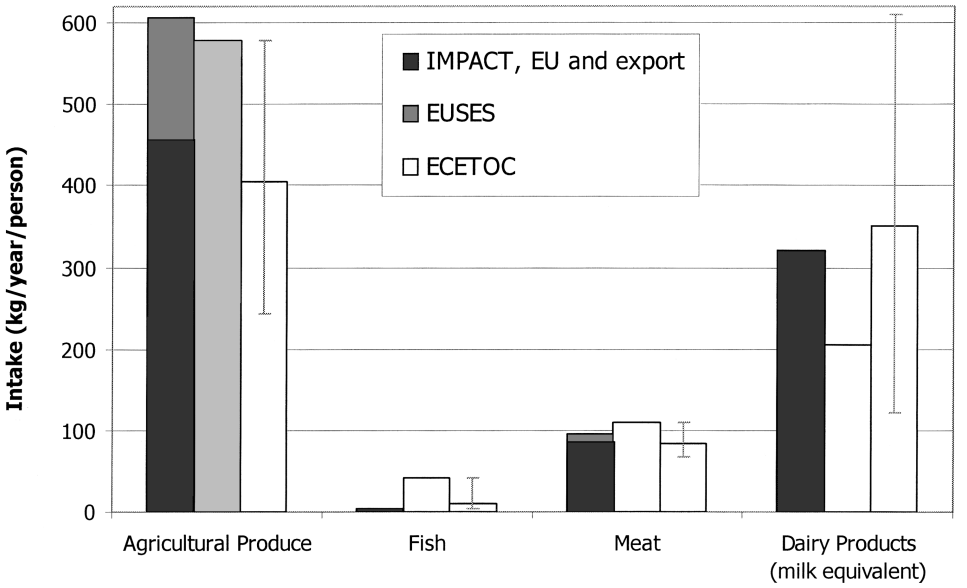

Figure 4. Comparison of annual ingestion rates associated with European food from a production-based LCA model called IMPACT (Pennington *et al.* 2005), from a subsistence-based approach that relies on maximum consumption rates per capita adopted for regulatory support in the model EUSES (European Commission 1996), and from European consumption survey results provided by ECETOC (1992 reference year) (European Commission 1996). The production-based approach accounts for the production of European food consumed within Europe (bottom of bar for IMPACT and comparable to basis of other data sets), as well as consumed outside of Europe (top of the bar in grey). Dairy product intakes reflect total milk production in the model IMPACT and the sum of dairy products expressed in milk equivalents assuming 11 kg milk per kg cheese and 22 kg milk per kg butter in the ECETOC survey. The sum of dairy products is not expressed in milk equivalents in EUSES, highlighting further methodological differences.

individual intake. Differences will be greater than presented in Figure 4 considering sub-continental scales. The intake estimates can vary depending on which substrate is most significant and where a chemical is released.

Human Health Effects

Having calculated the intake fraction, it is necessary to estimate the risk and consequences of toxicological effects that may be associated with such a population-based intake (see Figure 1).

Caution is necessary when adopting data and methods for LCA from other applications, as they were not always designed for use in a relative comparison context (Burke *et al.* 1996). Regulatory limits, or thresholds, can incorporate different levels of safety factors depending, for example, on data availability and the degree to which human health effects have been demonstrated. These limits can also be directly based on measurements such as No Observed Effect Levels (NOELs) from laboratory experiments. NOELs essentially reflect detection limits in the toxicological experiments. They do not necessarily reflect zero levels of risk and do not reflect consistent levels of dose-response that are suitable for use in relative risk comparisons (Gaylor 1992; Allen *et al.* 1994; Faustman *et al.* 1994).

The following sections outline the intake-response relationships developed for estimating risk-based Characterization factors in LCA.

Cancer effects

Crettaz *et al.* (2002) proposed a methodology for more consistently estimating human health effects in LCA. This method builds on the same benchmark dose-response concept proposed for, for example, U.S. regulatory assessments (Crump; USEPA 1996a, b).

Genotoxic carcinogens and mutagens are not considered generally to have threshold concentrations. Non-genotoxicological carcinogens do not damage DNA but become active in the proliferation of cancer through secondary mechanisms. Non-genotoxicological carcinogens have theoretical thresholds (van Leeuwen and Hermens 1996). The time at which exposure to carcinogenic substances occurs will also be important in estimating the risk and a number of chemicals will exhibit synergistic effects (Krewski *et al.* 1989). However, in the absence of a practical alternative to account for such issues, carcinogenic risks are usually assumed to all be additive with no threshold and independent of the time of exposure.

Equation (9) provides estimates of the likely contribution to cancer incidences that are associated with the intake of a mass of contaminant at the population level. This is based on the maximum likelihood estimate of the effect dose inducing a 10% risk over background, denoted as the ED_{10}.

$$\beta_{\text{human}} = \frac{0.1}{\text{ED}_{10}} \cdot \frac{1}{\text{BW} \cdot \text{LTh} \cdot \text{N}_{365}} \tag{9}$$

where: β_{human}: Intake-response relationship for substance on human health [likely incidences per mg intake], ED_{10}: Benchmark dose resulting in 10% risk of an incidence above background [mg/kg-day], BW: Average body weight [kg/person];

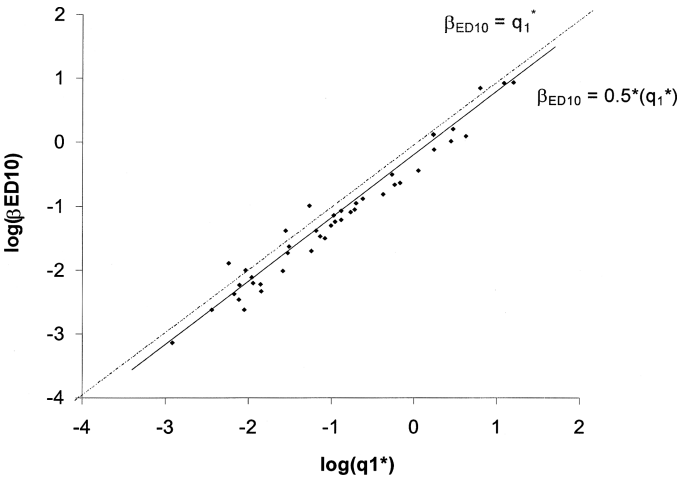

Figure 5. Comparison of the upper bound q_1^* as adopted by the U.S. Environmental Protection Agency (USEPA) for estimating the risk of cancer in a regulatory context and the slope factor β_{ED10} (0.1/ED10) for use in LCA for 44 chemicals ($r^2 = 0.95$, $n = 44$) (Crettaz *et al.* 2002; Pennington *et al.* 2002).

70 kg/person, LT_h: Lifetime of humans; 70 years, N_{365}: Number of days per year [days/year].

This intake-response relationship is based on the common default linear relationship from the slope of the straight line from the reference point, the ED_{10}, to the origin of the intake-response curve ($0.1/ED_{10}$ in Equation [9]) (Crettaz *et al.* 2002). Figure 5 highlights that these estimates can be consistent with those adopted in regulatory assessment contexts.

Noncancer effects

Although remaining necessary, estimation of the likely contribution to noncancer toxicological effects at the population level in LCA is particularly viewed with caution.

Hofstetter (1998) demonstrated how data based on, for example, epidemiological insights could be adopted for a limited number of chemicals for noncancer effects. In the absence of such alternative information and equivalent to the approach adopted for nongenotoxicological carcinogens, the benchmark ED_{10} and a linear intake-response relationship also provides a default basis to estimate contributions to non-cancer incidences (Pennington *et al.* 2002; Udo de Haes *et al.* 2002). As with cancer effects, no consensus exists for criteria to determine when such linear, or nonlinear, low-dose extrapolations are appropriate (Barton *et al.* 1998; Brand 1999). Experimental data are typically in the high dose domain and provide limited insights about the likely low dose-response relationships.

There is often an absence of biological data for thresholds and issues such as essentiality to assess whether the risk of noncancer effects will be zero, or not, at typical environmental exposure levels (Pennington *et al.* 2002). This is compounded by a limited practical ability to account for the influences on the dose-response of

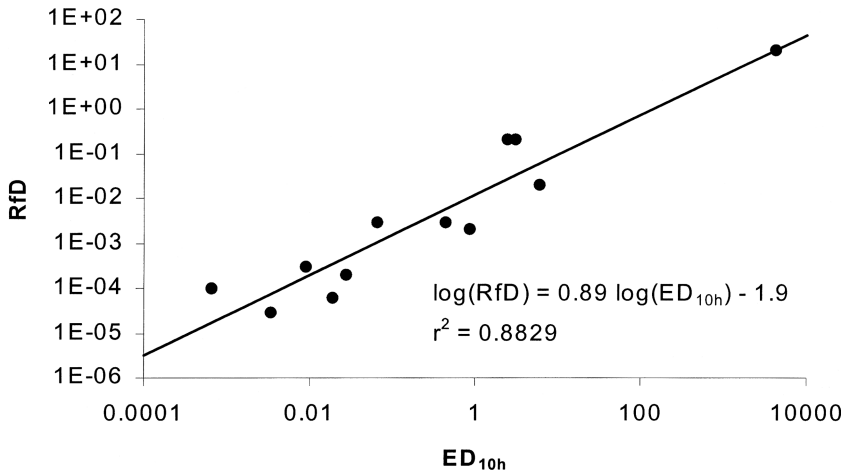

Figure 6. Comparison of ED_{10h} for 12 chemicals from bioassay data as recommended for use in LCA and Reference Dose policy thresholds (RfDs) as adopted by the U.S. Environmental Protection Agency for non-cancer effects (Pennington *et al.* 2002).

complex chemical mixtures found in the environment and often a lack of sufficient environmental background data to support alternative intake-response estimates. Biological thresholds should equally not be confused with the higher availability of limits for regulatory support, as these are generally based on measurements such as No Observed Effect Levels (NOELs) from laboratory experiments. As previously stated, NOELs do not necessarily correspond to levels of zero risk.

Figure 6 highlights the potential differences between adopting a benchmark approach for noncancer effects for indicators in LCA versus directly using limits developed for regulatory purposes. Differences can be introduced by both the inconsistencies in risk that are associated with the measured data used in regulatory assessments, as well as by variations in the safety factors underlying some of the regulatory data that are incorporated in the limits.

Potential consequences

Differences in the potential consequences of toxicological incidence (last step in Figure 1) are not quantified in regulatory applications, as risks are considered separately for each chemical. Ignoring differences in the consequences in LCA would implicitly assume that they are equal, for example, leukemia and mild asthma are equal. To avoid bias in relative comparisons such as LCA, knowledge of both the risk and the potential consequences should therefore be explicit.

Hofstetter (Hofstetter 1998) demonstrated that differences between the potential consequences of toxicological effects could be taken into account in LCA using common measures such as Disability Adjusted Life Years per incidence (DALY), external costs, and so on. Such metrics reflect a developing area of health science (Hofstetter 1998; Hofstetter and Hammitt 2002; Krewitt *et al.* 2002; Owens 2002; Pennington *et al.* 2002; Udo de Haes *et al.* 2002).

Equations (10) and (11) highlight the calculations of years of life lost per mg of intake using DALYs.

$$EF_{human} = \beta_{human} \cdot DALY_p \tag{10}$$

$$DALY_p = YLL_p + YLD_p \tag{11}$$

where: EF_{human}: Effect factor of substance on human [likely years lost/mg intake], β_{human}: Intake-response relationship [likely incidences per mg intake], $DALY_p$: Disability Adjusted Life Years per affected Person [year/incidence], YLLp: Years of Life Lost per affected Person [year/incidence], YLDp: Years of Life lived with a Disability per affected Person [year/incidence].

DALYs account for the differences in potential consequences of an incidence in terms of both mortality and morbidity (non-fatal effects) (Murray and Lopez 1996). Mortality is represented using statistics as the average Years of Life Lost (YLL_p) due to premature death as a result of an incidence. An equivalent number of years of life lost per incidence are proposed for morbidity cases using weighting factors. These weighting factors rely on social sciences and economics.

Considering 17 types of cancer and using only statistical data on a world scale from Murray and Lopez (Murray *et al.* 1996), the average $DALY_P$ value is ~13 years of life lost per incidence (Hofstetter 1998; Crettaz *et al.* 2002). All cancer effect DALYs are primarily associated with years of life lost through mortality, not morbidity. Prostate cancer has the lowest $DALY_P$ of ~4 year/incidence, whereas leukemia has the highest of ~28 year/incidence (Crettaz *et al.* 2002). Given this range, the uncertainty associated with not specifying the exact type of cancer in LCA and using a default value of ~13 years of life lost per incidence is likely irrelevant compared to other uncertainties (see later example for benzo[a]pyrene). This value does not include discounting to weight the importance of one year of life lost based on the age at which death occurs, discounting future damages compared to the present ones, or affects on others.

Quantifying the consequences of noncancer effects can be more controversial. For example, a panel of the International Life Science Institute (ILSI) subjectively sub-categorized toxicological effects in terms of their relative severity (Burke *et al.* 1996). Such categorization could be directly retained in LCA. Owens (Owens 2002) illustrated the feasibility and complexities of using this category-based approach for classifying hazard/risk-based factors according to different toxicological endpoints.

The ILSI category approach could also be modified to reflect different $DALY_P$ values, adopting, for example, the $DALY_P$ value of 13 year/incidence for the highest concern category given that cancer effects were allocated to this category. The two other lesser sub-categories could be scaled subjectively using arbitrary factors of 10 (Burke *et al.* 1996; Pennington *et al.* 2002). However, Hofstetter (1998) summarized values for chronic bronchitis in the range of 4×10^{-6} to 0.001 year/incidence. This 3 order of magnitude range also highlights the potential variation associated with morbidity cases from different social perspectives and the bias that can be introduced by the implicit assumption of equal severity if differences in toxicological consequence are not considered.

ECOTOXICOLOGICAL IMPACTS

Characterization factors for ecotoxicological effects, Ecotoxicological Damage Factors (EDFs), are analogous to Human Damage Factors (HDFs) (see Figure 1). EDFs are primarily estimated in current LCA practice for aquatic freshwater species, considering exposure to contaminants in surface waters at the pan-regional scale. This focus reflects the availability of toxicological data associated with typical regulatory assessments (Udo de Haes *et al.* 2002).

The fate of a chemical in the environment, hence ecosystem exposure, is calculated as described in a subsequent section. The fate factor, F, reflects the fraction of an emission that is transferred to water and the duration of the exposure (quantity × duration). Unless included in the exposure-response relationship, bioavailability and indirect exposure (biomagnification or secondary poisoning) are not taken into account in most LCA approaches (Udo de Haes *et al.* 2002; Pennington *et al.* 2004). Although acknowledging the potential importance of these issues, they are not considered further in this article.

Ecotoxicological exposure-response is commonly based in LCA, as in regulatory assessments, on the theories, and limitations, of species sensitivity distributions (SSDs) and the Potentially Affected Fraction (PAF) of species (Posthuma *et al.* 2002; Udo de Haes *et al.* 2002; Pennington *et al.* 2004). Equation (12) reflects a straightforward approach for use in LCA. This approach takes into account different theoretical options and proposals, including consideration of different observed background contaminant levels and mixture insights (Pennington *et al.* 2004). The resultant effect factors, β, are interpreted in terms of the likely fraction of species experiencing an increase in exposure above a defined effect level.

$$\beta_{\text{freshwater}} = \frac{\Delta \text{PAF}_{\text{ms}}}{\Delta \text{M}} \cdot \text{V} = \frac{0.5}{\text{HC}_{50}} [\text{PAF}_{\text{ms}} \text{m}^3 \text{kg}^{-1}] \tag{12}$$

$\beta_{\text{freshwater}}$	Change in the Potentially Affected Fraction of species that experience an increase in stress for a change in contaminant exposure above a predefined effect level [$\text{PAFm}^3\text{kg}^{-1}$]
PAF_{ms}	Potentially Affected Fraction of species when exposed in the presence of multiple substances [dimensionless]
C	Exposure concentration [kgm^{-3}]
M	Mass of contaminant [kg] in an environmental compartment
V	The volume of the environmental compartment [m^3]
HC_{50}	Median hazardous concentration affecting 50% of the species [kg/m^3]

Combining the fate factor and the exposure-response, the Characterization factor for freshwater ecotoxicity in LCA is thus expressed in PAF-m^3-years/kg. This reflects the change in PAF, the duration, and the volume of water affected for a quantity of mass released into the environment.

A separate factor is not included to account for differences in consequences for ecotoxicological effects, although the volume of water that will be affected is taken into consideration. Emissions are not equivalent if one results in a certain change in PAF in one small lake versus another that widely distributes to contaminate all the lakes in Europe but with the same change in PAF in each one.

Equation (12) is based on the median hazardous concentration affecting 50% of species, the HC_{50}. The benchmark, HC_5, is also sometimes adopted as a basis for setting regulatory limits such as PNECs (see Equation [3]). The HC_5 is the concentration that is likely to affect 5% of species. Using the HC_5, the effect factor in LCA could be $0.05/HC_5$ instead of $0.5/HC_{50}$. However, reasons for adopting the HC_{50} included that the uncertainty of the estimate is lower than on the HC_5 estimate particularly for small data sets of test results, and the HC_{50} is usually required anyway to estimate the HC_5 (Payet 2004; Pennington *et al.* 2004).

Theoretically, any test results could be adopted as the basis for estimating the HC_{50}. Payet (Payet 2004), for example, proposed the $EC_{50\text{-chronic}}$ as an underlying basis for LCA. The $EC_{50\text{-chronic}}$ is the concentration at which 50% of a specific species is likely to be affected due to chronic exposures. Again using such a test benchmark basis provides a more consistent basis than, for example, NOECs (No Observed Effect Concentrations) for use in LCA, uncertainties can be estimated, and links to actual consequences on ecosystems may be more readily established (Payet 2004).

Both acute and chronic toxicity test data, for a variety of test endpoints, can be adopted to estimate the $EC_{50\text{-chronic}}$, hence the HC_{50}. Estimates can be based on a single toxicological test result (de Zwart 2002), although the more test results the lower the uncertainty associated with sample size (de Zwart 2002; Pennington 2003; Payet 2004).

In Figure 7 are illustrated the potential differences in LCA between using Predicted No Effect Concentrations (PNECs), limits adopted in some regulatory applications (see also Equation [3]), and the HC_{50} benchmark approach (Payet 2004). The main discrepancy between the two methods in a relative comparison context will be associated with the 5 orders of magnitude variation about the 1:1 line. Differences in magnitude are due to conservatism in underlying extrapolation factors adopted for setting regulatory limits, that PNECs usually reflect the NOEC of the most sensitive species that was tested, and that NOECs will not necessarily reflect consistent levels of exposure-response.

ILLUSTRATION OF RISK-BASED LCA METHOD

The previous section highlighted underlying methodological differences between regulatory-hazard and risk-based characterization factors for LCA. This section illustrates the methodology and uncertainties of estimating the risk and potential consequences of toxicological effects for an emission of benzo[a]pyrene, B[a]P, in the context of LCA. The input data adopted here for this well-studied polycyclic aromatic hydrocarbon (PAH) are presented in Table 1. The following sections highlight the calculation steps and associated uncertainties.

Fate

Steady-state fate models, similar to those commonly used to estimate concentrations in some regulatory assessments, provide a convenient way to estimate fate factors in support of LCA (see Figure 1). It is necessary, however, to model the full distribution of chemicals such as B[a]P (see Figure 3). Modeling a 200×200 km^2 region may be suitable for estimating likely concentrations in the region of an emission

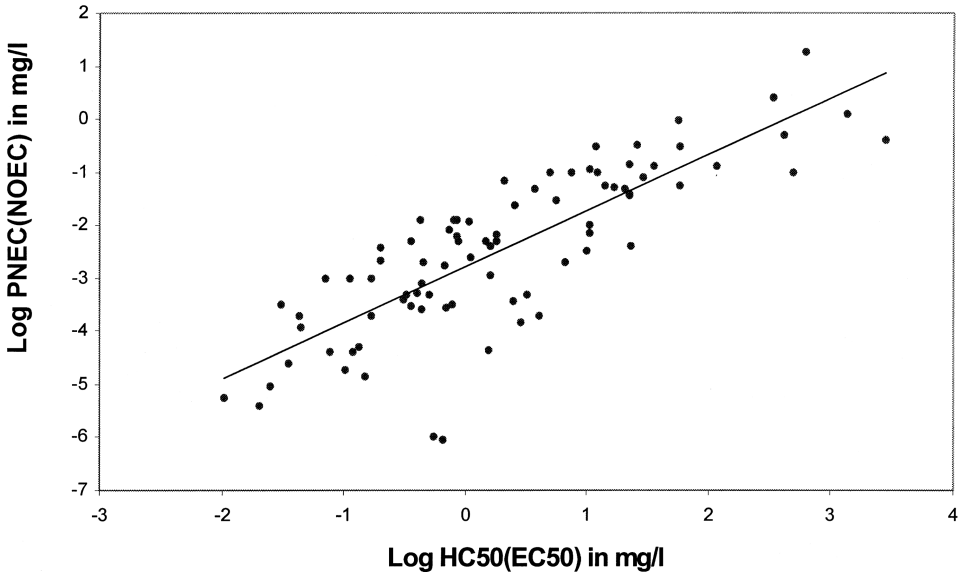

Figure 7. Predicted No Effect Concentration (PNEC) versus the median hazardous concentration affecting 50% of the species (HC_{50}) using chronic data for 83 chemicals (inorganic chemicals, non-organic pesticides and organic pesticides) (Payet 2004). The PNECs are based on the lowest NOEC with an extrapolation factor of 10. The HC_{50} data are based on the median EC_{50} data. The regression is Log ($PNEC_{NOEC}$) = Log ($HC50_{EC50}$) −2.8, with 95th percentile confidence limits on the slope of 0.9 and 1.2, on the intercept of −3 and −2.6.

for comparison against regulatory limits, but more than 70% of B[a]P air emissions would leave such a region.

A comparison of the concentration estimates from a steady-state model with monitoring data for emissions for Western Europe is presented in Figure 8. The ranges of the spatial model results and the monitoring data in Figure 8 also suggest that some concentrations, hence fate factor estimates in LCA, can vary by 4 orders of magnitude (see also ecotoxicological section below).

The average estimates are generally in reasonable agreement with the monitoring data. The largest discrepancies are for concentrations in soils and seawater. Seawater was modeled crudely (Pennington *et al.* 2005) and limited monitoring data were available. Monitored concentrations in soils are higher than the model estimates, but these monitoring data may not reflect typical values. Margni and colleagues (Margni *et al.* 2003; Pennington *et al.* 2005) presented more detailed insights for the evaluation of dioxins and furans, providing further discussion of the sources of such discrepancies.

Human Intake

The estimates of the intake fraction for B[a]P for use in LCA for each exposure pathway are presented in Figure 9 (see Figure 1). Summing these contributions, the

Table 1. Properties of Benzo[a]pyrene adopted in case study physical-chemical properties (Mackay *et al.* 1991–1997).

CAS	Molecular formula	Molecular mass (g/mole)	Henry's Law Constant (Pa m^3 mol^{-1})	Octanol-water partitioning coefficient (Log K_{ow})
50-32-8	$C_{20}H_{12}$	252	0.05	6

Estimated average degradation half-lives in days (Mackay *et al.* 1991–1997).

Air	Water	Soils	Sediments	Vegetation*
7	70	700	2300	7–700

* based on air to soil range.

Human health data, based on the oral TD_{50} (dose inducing tumors in 50% of test species) in Gold and Zeiger (1997) and on extrapolations to humans in Crettaz *et al.* (2002).

Oral Cancer ED_{10} (mg/kg-day)	$DALY_p$ (years of life lost per incidence)
0.04	13

Aquatic ecotoxicological data, based on median acute test data for 11 species (*Anabaena flosaquae*, *Chironomus thummi*, *Chlamydomonas reinhardtii*, *Daphnia magna*, *Daphnia pulex*, *Euglena gracilis*, *Nereis arenaceodentata*, *Poteriochromonas malhamensis*, *Raphidocelis subcapitata*, *Scenedesmus acutus*, *Xenopus laevis*) (Payet 2004).

Chronic geometric mean HC_{50} (mg/l)	Square geometric standard deviation on mean (estimated using Student *t*-test on log-values)
0.1	20

overall intake fraction is approximately 0.005. The human population is therefore estimated using these models to take in an average of 0.5% of the mass of B[a]P released into the environment. The intake fraction calculated directly using monitoring data and food production statistics is moderately lower, between 0.0003 to 0.004.

The model intake estimates in Figure 9 are above the plausible ranges from the monitoring data and food production statistics. This possible overestimation differs from the relationships for the underlying concentrations, suggesting uncertainties when predicting contaminant levels in food, especially in estimating biotransfer and bioaccumulation factors in livestock and in fish (Margni *et al.* 2003). These uncertainties equally exist in most regulatory orientated applications.

The spatially resolved and non-spatial model estimates of intake fraction in Figure 9 are generally comparable. For emissions from well distributed multiple sources, the intake is likely to approximate to the average of the estimates for point source emissions .(Pennington *et al.* 2005). This is also illustrated in Figure 8 for the environmental concentrations. Differences can be due to the assumptions and data adopted in non-spatial multimedia models, such as adopting a single average hydraulic residence time for all the water bodies in Western Europe (Pennington *et al.* 2005).

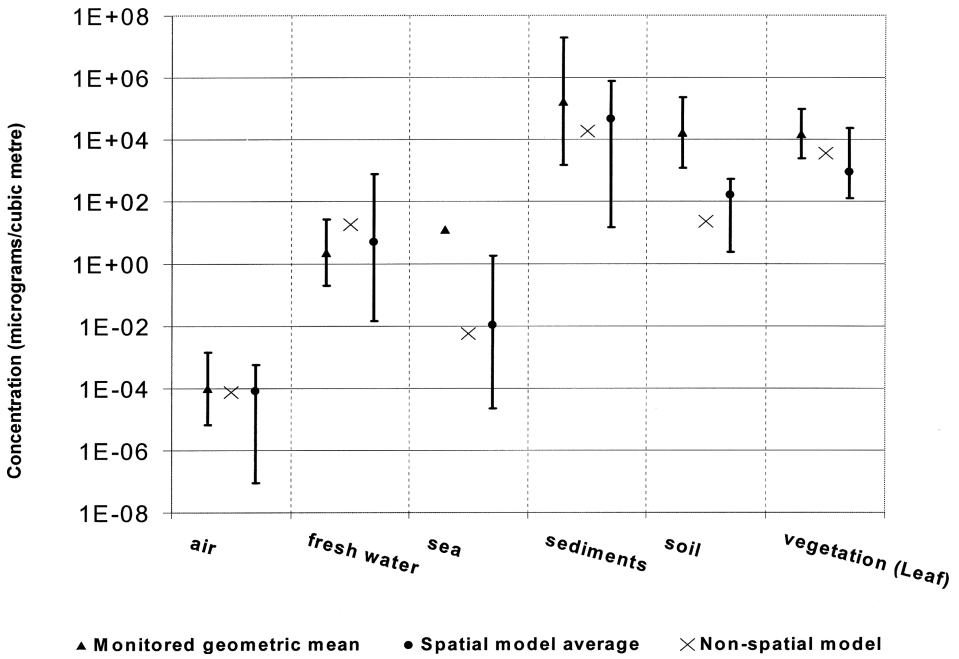

Figure 8. Comparison of estimated concentrations using spatially resolved and non-spatial versions of a multimedia model for Western Europe (Margni *et al.* 2003; Pennington *et al.* 2005) against monitoring data ranges based on the compilations by Manstseva *et al.* (2002). Western European emission estimates of B[a]P of ~300 ton per year were from the UNECE Cooperative Programme for Monitoring and Evaluation of the Long Range Transmission of Air Pollutants in Europe (EMEP) (Pacyna 1999; Mantseva *et al.* 2002). Average concentrations are total mass in each environmental medium divided by total volume. Monitored vegetation data are for grass, although the range was similar for other species.

It can also be necessary in some LCAs to estimate intake fractions for emissions that occur in specific regions. Figure 10 presents estimates of B[a]P intake fractions for atmospheric emissions in specific regions across Western Europe. Depending on the emission's location, the intake fraction of B[a]P can vary by approximately 2 orders of magnitude. This variation is lower than for the underlying concentrations, which varied in Figure 8 by up to 4 orders of magnitude depending on the emission location.

Based on Hofstetter (1998), there is 95% confidence that the average intake fraction estimates for chemicals such as B[a]P will be within a factor of 12 of the median estimate (median divided by and multiplied by 12). From Figure 9, this two orders of magnitude uncertainty range is arguably low. Accounting also for the spatial variations in Figure 10, an additional uncertainty factor of at least 10 would be necessary when assessing emissions in specific regions using the average intake fraction estimates. For an emission of B[a]P in a specific region, the uncertainty associated with using the average intake fraction estimate in the calculations for

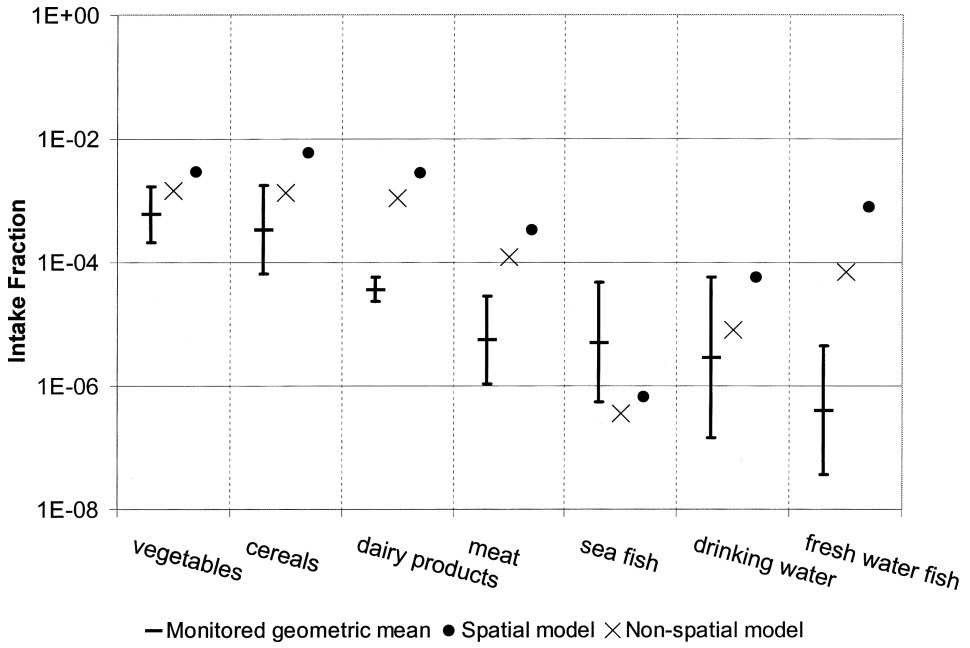

Figure 9. Comparison of intake fraction by food type for B[a]P emissions using Western European models (Pennington *et al.* 2005) and monitoring data (European Commission 2002). Monitoring data ranges reflect the maximum and the minimum estimates of intake fractions calculated from monitored substrate concentrations and food production statistics (EUROSTAT 2002). Emission quantities to air and water were based on data from EMEP (Pacyna 1999). Inhalation was negligible (see Figure 7 for comparisons for air concentrations).

LCA would then be moderately higher, a factor of 22(12 + 10) using the method outlined in Hofstetter (1998) and Rosenbaum *et al.* (2004).

Human Cancer Effects

B[a]P is a probable human carcinogen (USEPA 2003). Using toxicological test data (Gold *et al.* 1997) and the correlations for extrapolation of Crettaz *et al.* (2002), the benchmark ED_{10} = 0.04 mg/kg/day. Assuming a linear dose-response relationship and using Equation (9), an oral intake of 1 kg by the human population therefore has a maximum likelihood risk of contributing to ~1 cancer case.

The characterization factor, the Human Damage Factor (HDF), is the oral intake fraction of ~0.005 given in the previous section multiplied by the effect factor of 1 incidence per kg intake. This HDF for B[a]P is the median risk of a cancer incidence in the population, ~0.005 incidences per kg of B[a]P emitted.

According to Murray and Lopez (Murray *et al.* 1996), the total number of fatal cancer occurrences reported for the "established market economy" (population of 798 million) is estimated at 1,762,000 cases per year. From the characterization factor of ~0.005 incidences per kg, the 300 ton of B[a]P released per year in Western

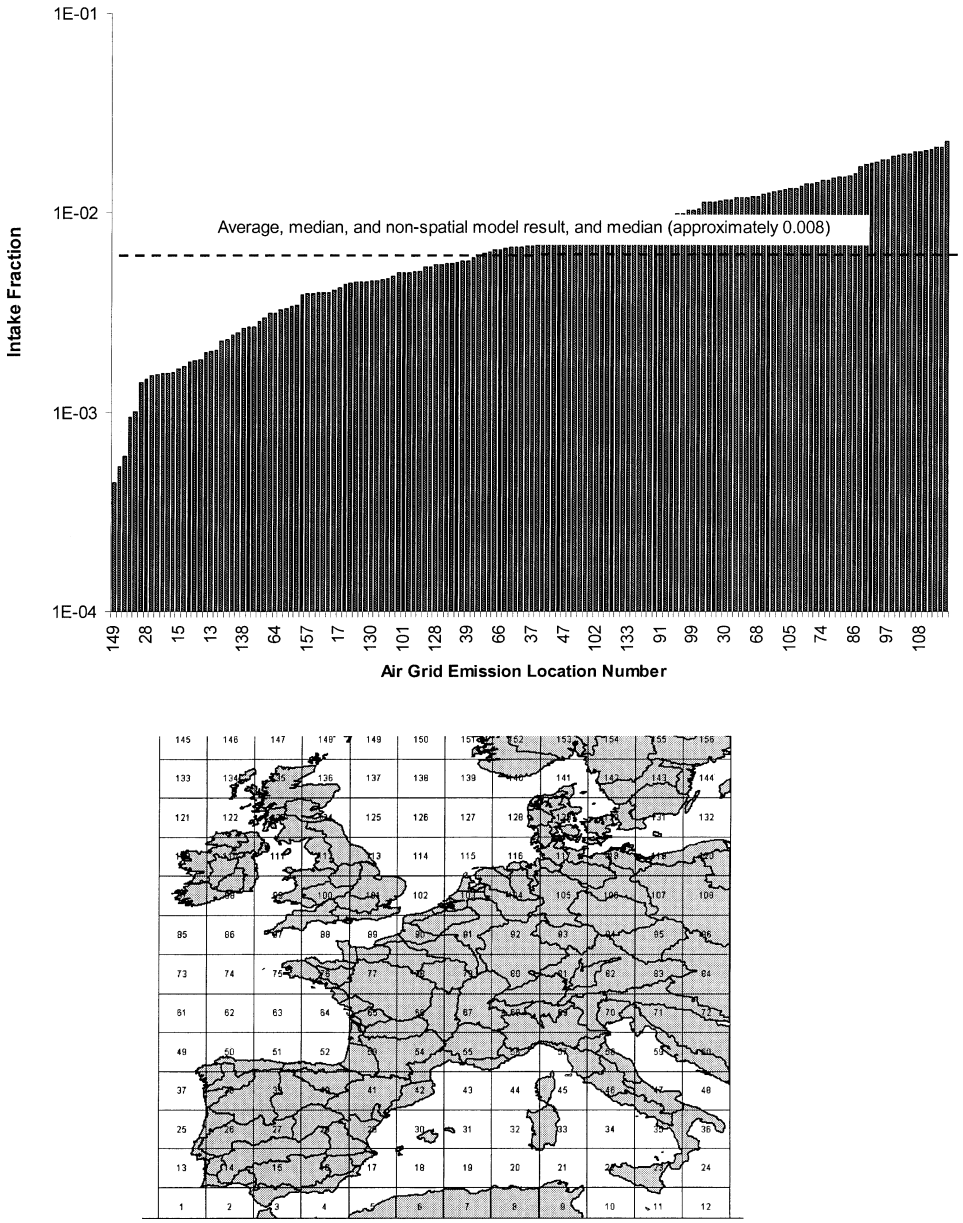

Figure 10. Comparison of human intake fraction as a function of the air grid cell of the emission, including the average and the estimate from a non-spatial clone of the multimedia model (Pennington *et al.* 2005). Atmospheric emissions in each 2 × 2.5 degree grid cells in Western Europe were modeled separately, as numbered.

Europe (Pacyna 1999) may contribute to 1,500 cancer cases per year worldwide (0.005 × 300,000). A typical regulatory threshold corresponds to say a risk of 430 cases per year in Europe (1 in a million cases multiplied by 430 million people).

Multiplying the risk of cancer occurrences by the years of life lost per incidence gives an estimate of the total number of years of life lost per kg released. On average a cancer incidence results globally in ~13 years of life lost per incidence (Hofstetter 1998; Crettaz *et al.* 2002). B[a]P therefore has a characterization factor (HDF) of 0.08 in terms of years of life lost per kg emitted (0.005 incidences per kg × 13 years of life lost per incidence).

The uncertainty estimates associated with the human intake fractions and effect factors are readily combined to estimate the overall uncertainty of a characterization factor (Rosenbaum *et al.* 2004). The overall uncertainty will approximate to the higher of that of the intake fraction and the effect factor.

The uncertainty of the effect factor is approximately a factor of 15, based on the estimation of the ED_{10} for humans from the original test data for rodents (Crettaz *et al.* 2002). The additional uncertainty attributable to the estimate of 13 years of life lost per cancer incidence is likely to be negligible. Other uncertainty could come from the low dose extrapolation (Crettaz *et al.* 2002) and, as B[a]P is only a probable human carcinogen (USEPA 2003), whether there will be concordance in cancer between humans and the observations using rodents (Goodman *et al.* 1991; Gold *et al.* 1999).

From the previous sections, the uncertainty of the intake fraction is a factor of 12 for a disperse emission of B[a]P, or 22 for an emission in a specific region when using the average. The overall uncertainty of the characterization factor is then 27(12 + 15) for a disperse emission and 37(22 + 15) for an emission in a specific region. Considering the median of 0.08 years of life lost per kg emission, the LCA characterization factor for human health therefore has 95th percentile confidence intervals of 0.002 (0.08/37) and 3 (0.08 × 37) DALY per kg for B[a]P emissions in specific locations.

Ecotoxicological Effects

From the chemical fate model (Pennington *et al.* 2005), the residence time of B[a]P in European freshwater is 2100 [h] or 0.24 [years]. A B[a]P emission to surface water will result in a freshwater species exposure of 0.24 years per kg emission. Analogously, for a continuous emission of 1 kg/year the average concentration would be 2×10^{-13} kg/m^3 (1 kg/year × 0.24 years divided by 2×10^{12} m^3 of European surface water).

The model also estimates the fraction of a B[a]P air emission that will transfer to water as ~0.01 (for emissions directly to water this transfer fraction is 1). Hence, an atmospheric emission of 1 kg will result in 100 times less exposure to aquatic species than a direct emission to water.

From the extrapolation of acute ecotoxicological test data for the 11 species listed in Table 1, an exposure 0.1 mg/l of B[a]P will affect 50% of the species in aquatic ecosystems above their chronic EC_{50} level (Payet 2004). Using this benchmark and Equation (12), the effect factor for B[a]P in terms of the potentially affected fraction of species (PAF) is 5 $PAF_{(chronic,EC50)}$ per mg/l exposure (0.5/0.1).

Combining the fate and effect factors yields an ecotoxicological characterization factor (EDF) of 1200 PAF-m^3-years per kg of B[a]P emitted to freshwater (0.24 kg-years × 5 PAF/(mg/L) × 1000 m^3/L). For atmospheric emissions, this will be 100 times lower (12 PAF-m^3-years/kg).

Acute to chronic extrapolation, the number of species tested, the types of species tested, the use of estimation techniques and models, as well as considerations such as the composition of background mixtures and the validity of the dose-response extrapolations of species sensitivity distributions all contribute to the uncertainty of ecotoxicological effect factor (Udo de Haes *et al.* 2002; Pennington *et al.* 2004).

Considering only the number of species tested, 11 for B[a]P, the uncertainty of the median estimate (HC_{50}) will be approximately a factor of 20 using standard *t*-test statistics (Table 1). Other methods suggest this uncertainty from sample size may be lower(Pennington 2003).

Based on Hofstetter (Hofstetter 1998), the uncertainty of the estimated concentration in freshwater is a factor of 6 or approximately 2 for an emission in a specific region (see earlier section). Thus, the overall uncertainty of the aquatic ecotoxicity characterization factor is 26(6 + 20) for a disperse emission and 42(22 + 20) for a location specific emission if using the average. The 95th percentile confidence interval for the Characterization factor of 1200 PAF-m^3-years per kg of B[a]P emitted to freshwater is about ±2 orders of magnitude.

DISCUSSION

A practical basis exists for the estimation of risk-based indicators for cancer effects for LCA using intake fractions and default linear exposure-response relationships calculated from benchmark toxicity data. These Human Damage Factors (HDFs) are in terms of either the likely number of cancer incidences or the number of years of life lost per kg of emission. The 95th percentile confidence interval can be ± two orders of magnitude, as was illustrated for benzo[a]pyrene. This could be higher if, for example, a linear exposure-response relationship is unlikely.

Estimating risk-based Human Damage Factors for noncancer health effects remains more controversial. The approaches and uncertainties are exactly the same as for cancer effects. However, estimates may only reflect an erosion of the margin of exposure—an impact on the capacity of the world to accommodate such emissions rather than an actual risk of an effect (Pennington *et al.* 2002). Quantifying consequences for noncancer morbidity effects can also involve methods such as weighting relative to years of life lost or monetization, which can differ according to social perceptions.

Justifiable approaches for estimating risk-based Ecotoxicological Damage Factors (EDFs) in LCA can be straightforward and practical. These take into account different theoretical options, including different observed background contaminant levels and mixture toxicity theories. Results typically reflect the potentially affected fraction of species, the duration of exposure, and the total volume of water affected (PAF-years-m^3) per mass of chemical released into the environment. Again uncertainty of ± two orders of magnitude may not be unusual, as demonstrated for benzo[a]pyrene. Not considering bioavailability, bioaccumulation, and nonlinear

variations in exposure-response due to phenomena such as essentiality may result in higher uncertainty in some cases.

CONCLUSIONS

Regulatory-based hazard equivalents provide a convenient and useful basis for indicators in life-cycle assessment (LCA). However, it is desirable to account for the full extent of toxicological risks and differences in consequences on a more consistent basis. This article demonstrated that the calculation of such risk-based indicators for toxicological effects for use in LCA is currently practical and feasible using available models and data. Nevertheless, as in other applications, uncertainties can be high and caution is particularly advocated for noncancer human health effects.

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