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Life-Cycle Assessment

AQUATIC ECOTOXICOLOGICAL INDICATORS IN LIFE-CYCLE ASSESSMENT

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Abstract—This paper compares available options for the aquatic ecotoxicological effect factor component in life-cycle assessment (LCA). The effect factor is expressed here as the change in risk per unit change in cumulative exposure, Δeffect/Δexposure. The comparison is restricted to approaches linked, implicitly as well as explicitly, to species-sensitivity distributions (SSDs). This draws on recent insights for chemical mixtures and identifies the implications of different model choices. In spite of the many options, assumptions, and areas for further research, it is concluded that a single effect factor basis represents the best available practice for use in LCA at this time, $\Delta PAF_{ms}/\Delta C = 0.5/HC50$, where ΔPAF_{ms} is the change in the (potentially affected) fraction (PAF) of species that experiences an increase in exposure above a specified effect level, accounting for the presence of complex background mixtures (ms), ΔC is the change in cumulative exposure concentration of the chemical of interest, and HC50 is the median, chronic hazardous concentration for regional, multiple-species systems. The resultant aquatic effect factors are risk-based and can be estimated readily for many chemicals using available methods, without the need to describe the entire SSDs and without the need for additional data. For example, the octanol–water partitioning coefficient provides a sufficient estimation basis for about 50% of existing chemicals that have a narcosis mode of action. This also is relevant in LCA for chemicals that are at low concentrations in the environment, concentrations below the biological thresholds at which more specific modes of action would be of relevance.

Keywords—Life-cycle impact assessment Risk assessment Ecotoxicological indicators Potentially affected fraction Mixture toxicity

INTRODUCTION

Life-cycle assessment (LCA) is a methodology for evaluating the consumption of resources and the potential impacts of emissions associated with all the stages in a product's life cycle, from raw material acquisition, manufacturing, use, reuse, and recycling to final disposal. Having established the boundaries of a product's life cycle and the aims of the assessment (goal and scope definition), the related resource consumptions and emissions are identified and tabulated (inventory analysis). For chemicals, these inventory data usually represent the mass of emissions occurring at multiple sites, at different points in time, and over differing durations, to provide the product of interest (a good or a service).

In the life-cycle impact assessment (LCIA) phase, the emissions inventory data are multiplied by characterization factors to provide indicators in the context of various impact categories (such as global warming, stratospheric ozone depletion, tropospheric ozone creation, eutrophication/nutrification, acidification, toxicological impacts to humans, and toxicological impacts to ecosystems). Udo de Haes et al. [1] presented an overview of the different impact categories, the associated characterization factor and indicator options, as well as ways in which comparisons can be realized across the various impact category indicators.

For chemical emissions, and unlike many other chemical assessment approaches, characterization factors express the relative importance of a unit mass (e.g., 1 kg) of a chemical released into the environment. Available characterization factors [1–9] account for a chemical's fate in the environment and species exposure, as well as for differences in exposure-response (see Eqn. 1).

characterization factor:

$$\frac{\text{effect}}{\text{emission}} = \frac{\text{fate}}{\text{emission}} \cdot \frac{\text{exposure}}{\text{fate}} \cdot \underbrace{\frac{\text{effect}}{\text{exposure}}}_{\text{effect factor}} \qquad (1)$$

In the context of aquatic ecotoxicological effects, the effect factor often is expressed in terms of concentration-response. This is appropriate if the second term (exposure/fate, the exposure factor) in Equation 1 is taken into account in the effect factor, for example using field or mesocosm study data. More commonly, however, the pure phase concentration in water is related directly to the species response (exposure factor = 1). We note this unresolved issue and refer to exposure-response throughout the remainder of this paper.

In spite of recent advances, interpreting the relevance of available toxicological characterization factors in terms of damage to ecosystems remains problematic [10–13]. This is due largely to adopting regulatory assessment approaches and data for use in comparative assessments, such as LCA, without making appropriate modifications. For example, effect factors used for calculating ecotoxicological characterization factors still are commonly based on chronic regulatory thresholds, like the predicted-no-effect concentration (PNEC) [3,5,8]. The resultant characterization factors contribute to weighting inventory data in the context of political, or policy-based, hazard measures. The final indicators are interpretable in terms of regulatory hazard equivalents, often being presented relative to a reference chemical in the form of, for example, 2,4D (regulatory hazard) equivalents—the ratio of the policy-based

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hazard of a unit emission (kg/hour) of one chemical relative to that of the reference chemical 2,4D [7].

Regulatory hazard equivalents do not relate necessarily to consistent levels of protection in terms of risks or potential impacts [10,13,14]. Measures such as PNECs were not developed for use in relative comparison applications such as LCA. Use of regulatory data and approaches in LCA can result in hidden bias in favor of certain chemical emissions, against others. As a partial consequence, the International Organisation for Standardisation's document ISO 14042 currently states that ''LCIA results do not predict impacts on category endpoints, exceeding of thresholds, safety margins, or risks.''

Based on Heijungs [15] and Jolliet [16], and later illustrated in Mackay and Seth [17], the change in cumulative exposure (integrated over time and space) associated with a unit mass (kg) of a chemical released into the environment can be estimated using available models and data. Multiplying the cumulative exposure of a species per kg of emission by an appropriate ecotoxicological effect factor provides characterization factors for use in comparative applications, such as LCA, that can then be interpreted in terms of cumulative risk and potential damages or impacts [9,18]. Given the differences in objectives, this differs from current regulatory risk assessment approaches for individual chemicals in which concentrations at specific points in time and space are compared to policy-based thresholds to ensure compliance with agreed levels of protection.

Adopting this recent framework proposal of estimating cumulative effects in LCA, this paper focuses on the influence of the main options at this time for the aquatic ecotoxicological effect factor.

Huijbregts et al. [5] for LCA proposed an approach based on the hazardous concentration affecting 5% of species (HC5) for aquatic ecotoxicological effects, reflecting the underlying basis of some regulatory measures such as predicted-no-effect-concentrations (PNEC) [19–22]. Payet and Jolliet [23] presented the assessment based on median impact (AMI) method based on the hazardous concentration affecting 50% of species (HC50). The EcoIndicator 99 [6] approach for aquatic ecotoxicological effects is based on the HC50 and on the concept of the marginal change in the potentially affected fraction (PAF) of species in the presence of chemical mixtures (PAF_{ms}, ms denotes multiple substances) [24]. Huijbregts et al. [25] proposed an approach based on marginal changes in PAF_{ms} but that accounts for response, as well as concentration, addition in chemical mixtures.

Establishing the underlying relationships, environmental relevance, and quantitative differences among these effect factor options is crucial for identifying the current state-of-the-art and recommending best available practice for use in LCA. To achieve this, the paper consists of the following four sections: A brief overview of the underlying principles and the options in relation to SSDs for aquatic (water column) ecosystems (the main focus of this paper); a description and analysis of the differences between the effect factor options in terms of gradients related to the SSD curves (Δeffect/Δexposure); exploration of the likely influences of additional stressors, in this case the presence of mixtures of other chemicals, on the resultant appropriateness of the different gradient options for the effect factors; and a discussion of which effect factor (gradient) basis is likely to be most appropriate in current practice, given their underlying environmental relevance and assumptions.

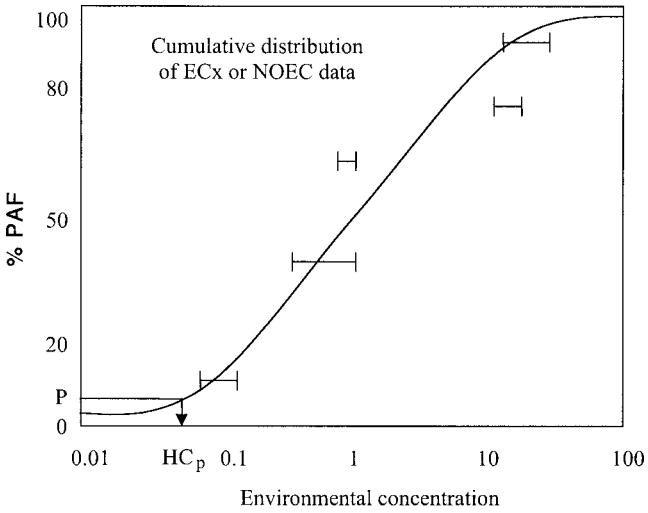

Fig. 1. Species-sensitivity distribution, adapted from Kelepper et al. [24]. Estimation of the hazardous concentration (HC) of a chemical that results in a potentially affected fraction (PAF) of P% of all species in an ecosystem from a statistical distribution of individual species no-observed-effect concentration (NOEC) or effect concentration (ECx) data.

Parameter uncertainty, the uncertainty attributable to input data as commonly determined using, say, Monte-Carlo analysis, is not addressed in this paper. Exceptions are made where it is relevant in establishing the underlying differences between the effect factor options. Similarly, the practical differences between the many methodological options for estimating values such as the HC5 or the HC50 are beyond the scope of this paper.

SSDs: Issues and LCA

The underlying concepts of SSDs are well established [19,20]. The SSDs are adopted, both explicitly as well as implicitly, as the fundamental basis of many ecotoxicological effect factors in LCA [26]. Such distributions provide a description of the relationship between the exposure concentration in a medium and the potentially affected fraction of species (PAF) [19,20] (see Fig. 1). Traas et al. [27] stated that the PAF can be interpreted in terms of risk, representing the potential fraction of species that are affected above a defined effect (or no-effect) level.

Underlying test data. In the context of long-term (chronic) exposure and common practice, the PAF often reflects the fraction of species that are at risk of being affected due to exposure to a given chemical above their no-observable-effect concentration (NOEC) for mortality, growth, and reproduction. The NOEC values usually are derived from experimental data for single species. The NOECs indicate concentrations below which effects cannot be distinguished statistically from the control in an experiment—essentially a no-detect level.

Test endpoints other than the NOEC also can be adopted. Benchmark measures like chronic median effective concentrations (EC50s) can provide a more consistent risk basis than NOECs for use in relative comparison applications such as LCA [20,23,28–31]. Another possible option, for example, is the EC5, as adopted in Dutch Environmental Quality Standards [32].

Although such a move to benchmarks, as well as the provision of associated confidence intervals, would represent an improvement in all types of assessments, this issue does not

influence the selection from among the options for effect factors in LCA. All the underlying data options for SSDs could be adopted in any of the current proposals. This issue therefore is not explored further in this paper.

Acute versus chronic data. As laboratory test data availability is limited and predominantly associated with acute exposures, extrapolation techniques often are adopted to help estimate the data of relevance in the chronic exposure context that is of interest in most LCAs [26]. Although such extrapolation techniques remain essential elements of LCA and of other assessments, the associated parameter uncertainties essentially will be identical in the various available effect factor proposals. These extrapolation techniques and the associated uncertainties, therefore, also are not explored further in this paper, although caution is advocated when adopting extrapolation procedures from regulatory methodologies to first establish their appropriateness for use in relative comparison applications such as LCA.

Environmental relevance. Although they are well-established, the fundamental concepts of SSDs and PAFs are not beyond criticism [19,20,26,33,34]. Forbes and Forbes [33], for example, stated that SSDs do not reflect the extent to which potentially affected species are exposed beyond a NOEC (or an ECx benchmark if used), nor do they necessarily reflect the associated consequences. Forbes and Calow [34] noted that many SSDs do not reflect accurately taxonomic and trophic structure, although they also noted that the relative importance of such issues requires further study.

How different exposure levels affect the population of ecosystems, their structure (abundance, trophic composition, species richness, species composition, individual species condition, biodiversity), and their function (nutrient flow, energy flow, decomposition) remains unclear. Current SSD measures are, however, at least representative for species assemblages, having limitations in less likely cases where functional changes are manifested before structural ones. Again, these issues are applicable equally for all the presented options addressed in this paper and therefore cannot be used as a basis for distinction.

Practicality. Other criticisms relate to how well common statistical models reflect the actual shapes of SSDs and how easy it is to fully describe the SSD for large numbers of chemicals [19,26,33,35]. However, entire SSDs are not represented in any LCA method [1], nor are they represented explicitly in regulatory approaches [22]. Specific summary statistics from the distributions, values such as the median (HC50), the 5th percentile (HC5), or similar, provide the basis of LCA effect factors. It is not necessary to know the entire distribution. Nevertheless, as explored in the following sections, some LCA methods rely on the assumption of a statistical model for the distribution, including at very low exposure concentrations where uncertainties can be very high and for which such assumptions may not be defendable.

Extent of contamination. In addition to the SSD-related issues, some LCA methods also account for the area [6] or the volume [9] affected per unit emission. This helps account for the fact that contaminating a large quantity of water, such as a lake, to a given level of risk is not the same as contaminating a smaller one to the same risk level. These further considerations and their influence are not explored here, as they can be taken into account equally with all the effect factor options considered.

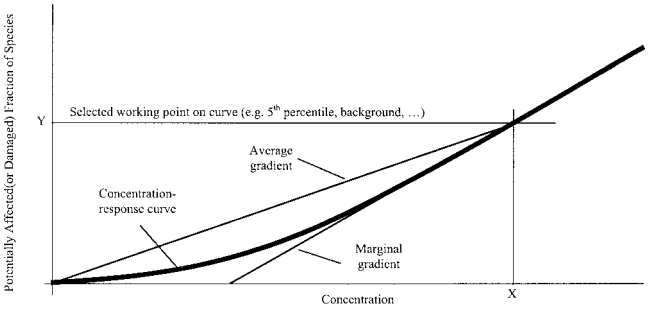

Fig. 2. Marginal versus average (or linear) gradients (Δeffect/Δexposure) for a chemical.

Gradients, working points, and benchmarks

Most toxicological effect factors in recent LCA methodologies [3,5,6,8,23] can be interpreted in terms of gradients related to SSD curves. The gradient expresses the change in effect per unit change in exposure (Δeffect/Δexposure in Eqn. 1).

Effect factors are estimated using at least one of the following three methods. Method 1 is division by a so-called benchmark concentration, a concentration that corresponds on an SSD curve to a specific PAF of species in the ecosystem such as the HC5 (see Fig. 1). Method 2 is multiplication by a linear gradient, the gradient between a chosen working point and the origin of the curve (see Fig. 2). This gradient is termed the average gradient in LCA texts [36] and sometimes is referred to as a slope factor in other application contexts. Method 3 is multiplication by a tangential gradient at a chosen working point on the curve (see Fig. 2). This is termed the marginal gradient [36].

In a relative context there is no practical difference between directly using the benchmark concentration (method 1) and using the average gradient (method 2). Methods 1 and 2 differ only by a constant. Method 1 provides a relative measure, but still implicitly assumes the linear concentration-response relationship that is explicit in method 2. Method 1, therefore, is not addressed further.

Average gradient

An average gradient (see Fig. 2) provides a measure of a contaminant's contribution to existing risks, for example. The marginal gradient provides a measure of the change, or perturbation, in risks associated with a small change in exposure concentration. There will be no difference between using the marginal versus the average gradient (methods 2 and 3) if the SSD essentially is linear from the origin to the selected working point (linear exposure-response). Therefore it is necessary to establish the relevance of assuming linearity.

Low concentrations. At low exposure levels, below the typical experimental observation range, the shape of an SSD is highly uncertain. Estimation of the gradient similarly will be highly uncertain and assuming linearity as a default may be justifiable pragmatically at this time.

Figures 3, 4a, and 4b [37] illustrate the potential differences of the dose-response curves and corresponding gradients at low concentrations using common parametric models. The most straightforward approach, perhaps reflecting the current state of our knowledge at such low concentrations, is to assume a linear gradient between the origin and a benchmark concentration (HCx). This is analogous to the example of common

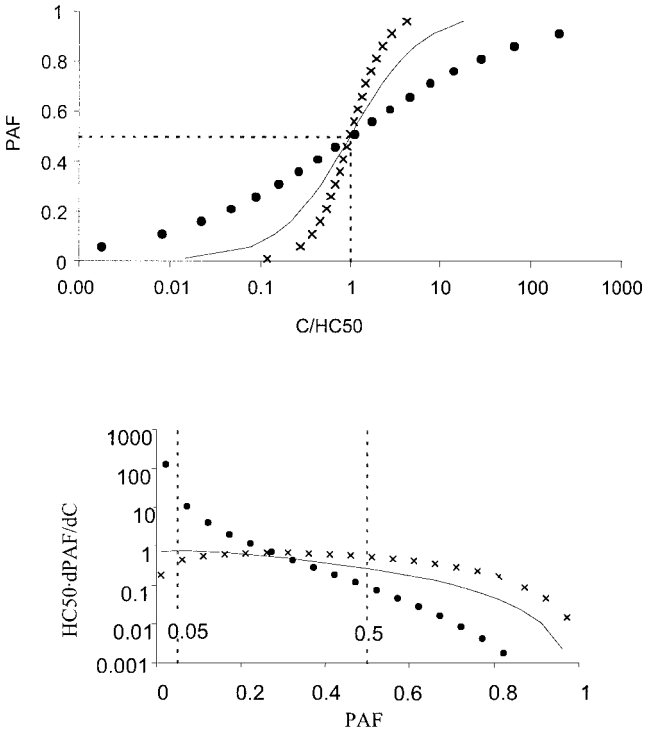

Fig. 3. Generic plots of concentration (C) versus potentially affected fraction (PAF) of species (top), species sensitivity distribution, and the corresponding normalized marginal gradients (HC50 × dPAF/dC; bottom) for a maximum likely range of β-values using a log-logistic model. The β-values are presented for different toxicological modes-of-action based on the likely range reported by de Zwart [37]. To avoid the need to plot a separate set of curves for each chemical with a different β-value, the concentration was normalized on the *x*-axis by the median hazardous concentration (HC50). This is explained in further detail in the marginal gradient section. −, β = 0.4; ×, β = 0.2; ●, β = 1.

use of linear low dose–response slope factors in human health assessments in LCA [1].

Thresholds. At low concentrations, exposure also may be below biological (or mechanistic) thresholds and the risk of the associated effect is zero. Assuming a linear exposure-response relationship would be somewhat misleading. However, such biological thresholds usually are not known. It is important to note that such biological thresholds may be neither equivalent to available regulatory or policy-based thresholds (e.g., PNECs) for multiple species systems, nor to statistical NOECs for individual species.

From a mathematical perspective, if a biological threshold concentration were much lower than the chosen working point, say the fifth percentile (HC5), then the value of the effect factor would not change appreciably. For example, assuming linearity,

$$\frac{\Delta\text{effect}}{\Delta\text{exposure}} = \frac{0.05}{\text{HC5} - \text{threshold}} \approx \frac{0.05}{\text{HC5}} \tag{2}$$

The question would remain, however, as to whether exposure occurs above or below biological thresholds at different locations and times of interest in each LCA study. The presence of other stressors and chemicals with an additive effect mechanism also would need to be taken into account in order to conclude that an exposure situation indeed is below the threshold, as addressed later in this paper. Obviously, even in the limited number of cases where biological thresholds are known, answering such a question generally is not feasible from a practical perspective. This threshold issue therefore is not taken into account in current practice, even when considering low exposure concentration scenarios. The exception is in deciding which effect endpoints are likely to be of relevance under typical exposure conditions.

Calculation. Some current methods calculate a linear (low) exposure-response gradient from a benchmark concentration such as the fifth percentile (HC5) [3,5,8]. The effect factor is then 0.05/HC5, as in Equation 2. Payet and Jolliet's method [23], for example, proposes use of the median (HC50) as the benchmark or point of departure for low-exposure response. The effect factor is then 0.5/HC50.

Payet and Jolliet [23] noted that the uncertainty of the median is less than that of the fifth percentile estimate and that the median can be calculated without having to assume the shape of the SSD (either explicitly using data or implicitly using extrapolation methods). The implications of these choices for the benchmark are explored later in this paper, as they partially depend on the nature of background mixtures.

Marginal gradient

The marginal gradient provides a measure of the change in risk that is associated with a (marginal) change in exposure concentration [6]. This is estimated at a working point (HCx) and is relevant for small changes in concentration (see Fig. 2). The working point may be chemical-dependent and may vary depending on location.

Many LCA approaches [19,20] assume a log-logistic SSD (Eqn. 3) to help estimate marginal gradients, including at low-exposure concentrations. Assessing the validity of such a model assumption in an LCA is not usually feasible.

$$\text{PAF} = \frac{1}{1 + \exp\left(-\left(\dfrac{\log \text{C} - \log \text{HC50}}{\beta}\right)\right)} \tag{3}$$

In Equation 3, β is a measure of the spread of the curve. This can be expressed in terms of the standard deviation σ of the log(ECx) values, $\beta = (\sqrt{3}/\pi)\cdot\sigma(\log \text{ECx})$. The position of the curve relative to the *x*-axis is specified by the median concentration of the ECx (or NOEC) data set, the HC50. This commonly is estimated in LCA using the geometric mean of available test data when sufficient data are available [6,23].

Huijbregts et al. [25] estimated the marginal gradient at different working points on the log-logistic curve by calculating the change in PAF for a small change in concentration. Differentiating Equation 3, the normalized tangential gradient at a given PAF is,

$$\frac{\Delta\text{PAF}}{\Delta\left(\dfrac{\text{C}}{\text{HC50}}\right)} \approx \frac{\log(e)\cdot\left(\dfrac{1}{\text{PAF}} - 1\right)\cdot 10^{\{\hat{a}\ \ln[(1/\text{PAF})-1]\}}}{\beta\cdot\left(\dfrac{1}{\text{PAF}}\right)^2} \tag{4}$$

The concentration is normalized in Equation 4 relative to the median (HC50), hence, also normalizing the gradient. The advantage of this is that the normalized gradient is not a function of the HC50. The normalized marginal gradient then can be expressed and investigated independently of the HC50 for a range of PAFs and β-values [6]. Only the shape of the curve varies for different chemicals, irrespective of the location of the curve on the *x*-axis. This has useful implications.

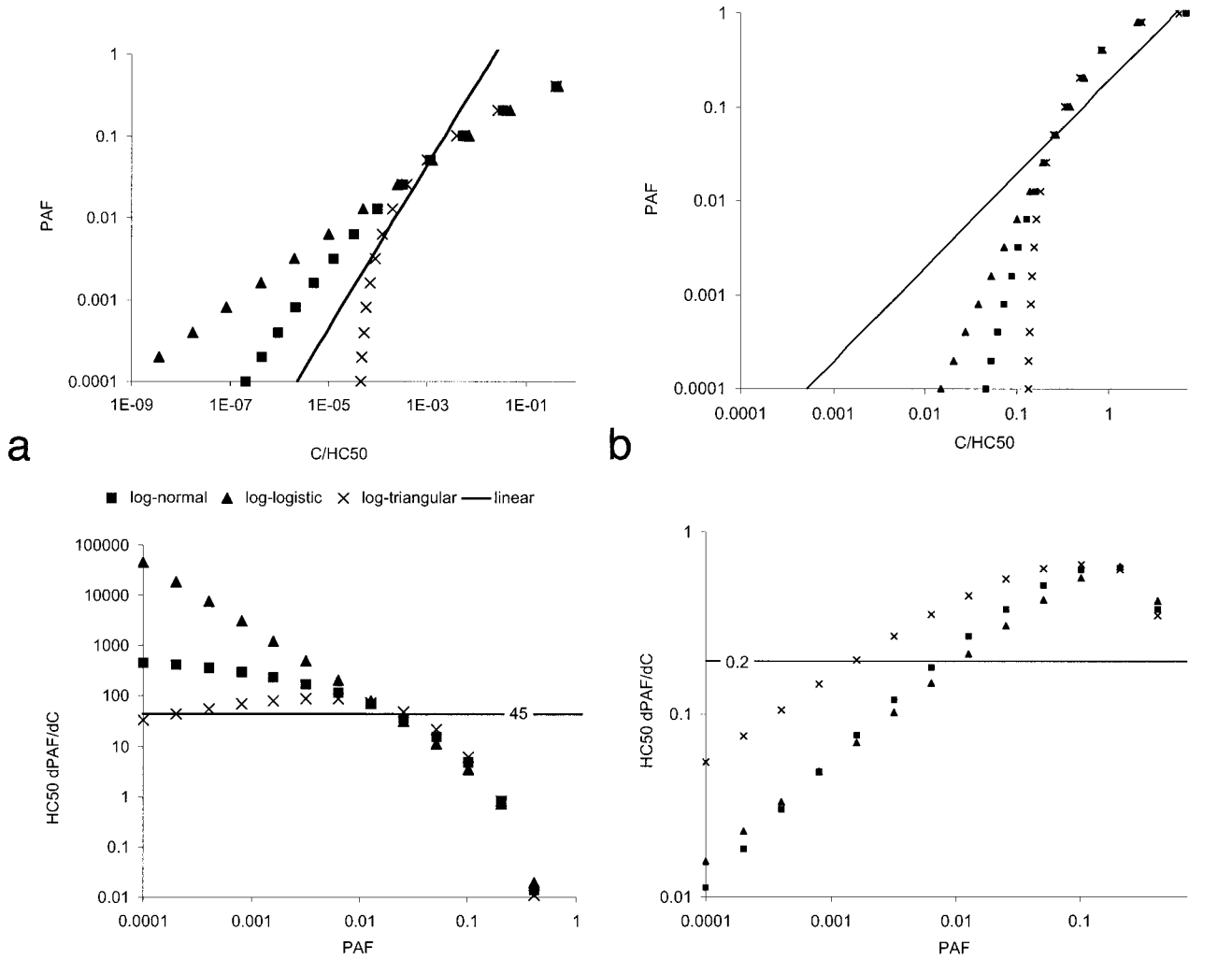

Fig. 4. (**a**) Comparison of normalized concentration (C divided by the median hazardous concentration [HC50], top) and corresponding normalized marginal gradients (HC50 × dPAF/dC, bottom) versus potentially affected fraction (PAF) of species for four distribution models for $\beta = 1$ ($\equiv$ standard deviation$_{log} = 1.8$). The linear (or average) gradient is given by 0.05/HC50. (**b**) Comparison of distributions (top) and gradients (bottom) for four distribution assumptions for $\beta = 0.2$ ($\equiv$ standard deviation$_{log} = 0.36$).

Gradient variation. The normalized marginal gradient is not a strong function of β in some background situations, as illustrated in Figure 3. Exploiting this observation and adopting a fixed value, the EcoIndicator 99 approach [6] promoted the estimation of marginal gradients using only a chemical's HC50. A full description of the SSD shape is not necessary and model-related uncertainty will be minor. However, this is providing that such background situations, high working points on the SSDs, and the model selected are appropriate.

Distribution model. The normalized tangential gradient in Figure 3 is plotted assuming a log-logistic distribution. The gradient can differ significantly, however, when selecting other distribution models. Figure 4 illustrates these differences in a comparison of gradients for common unimodel parametric distributions.

If β is high, for example, for chemicals that have specific modes of toxic action, and if the working point is low, then the gradient is strongly dependent on the choice of distribution model. This is illustrated in Figure 4a. This also was outlined in the previous section (see *Average gradient* section) and is a basis for justifying a linear gradient in practice if such low exposure situations are applicable.

At a high working point, particularly for chemicals with a low β, the different marginal gradients usually correspond within a factor of approximately ten (Fig. 4b). The choice of model may be of low importance for estimating a marginal gradient in LCA. The need exists therefore to establish the appropriate working point on an SSD. This first requires consideration of influences from other stressors, including the influence of background chemical mixtures on the appropriateness of a working point.

Implications of chemical mixtures on the working point

This section focuses on the influence of background mixtures on the working point selection, hence on the applicability of the different gradient options for use as effect factors in LCA.

Mixtures are now partially taken into account in a number of propositions for LCA [6,25]. The same principles can be adopted when considering the influence of other, nonchemical

stressors. In this context, it should be noted that chemical mixtures might not play the largest role compared to such other stressors in determining the most appropriate working point(s) in regional scale assessments. This is an issue that warrants further research.

To be relevant, particularly at typically low-exposure concentrations, an effect factor should not be established for a chemical in complete isolation. Substances that are discharged at concentrations considered individually harmless can act together in receiving waters, producing sublethal as well as lethal consequences [38]. Deneer et al. [39], for example, demonstrated for *Daphnia magna* that chemicals significantly contributed to the toxicity of a mixture consisting of 50 chemicals at a fraction of 0.0025 of their acute toxic effect concentration. Enserink et al. [40] and Faust et al. [30], among a growing list of others, provided similar inputs to the related debates.

Chemical interaction. If two chemicals interact (toxicokinetically and/or toxicodynamically), then these interactions are described as antagonistic or synergistic (reducing or increasing expected additive effects, respectively). However, commonly it is assumed that such interactions are rare or small enough at low chemical exposure levels to be insignificant [41]. Such chemical interactions are not addressed further in this paper or in current LCA practice.

Addition. In the case of additive effects and for a single species, mixtures are assessed using the concepts of concentration and response addition (also termed independent action) [30,41–47].

Concentration addition: If chemicals have similar toxicological mechanisms (or modes-of-action), then the effects of the mixture are estimated by adding the concentrations of the chemicals scaled by their median toxicity (e.g., EC50) (implicitly assuming that the chemicals act as dilutions or clones of one another).

Response addition: If chemicals have completely independent toxicological mechanisms, then the effects will be independently additive. The responses are first determined for each chemical (or subgroup of concentration-additive chemicals) and then the individual responses can be summed (see also Appendix 1).

In the case of entirely concentration-additive effects, the working point on an SSD would correspond to the overall background PAF in a given location. The marginal and average gradients in an LCA would be a function of the overall background PAF in the region of consideration, as assumed in the EcoIndicator 99 approach [6].

In cases of response addition, the effect is entirely independent of that of other chemicals. The working point, hence the gradient, will depend only on the background concentration of the particular chemical of interest (or the related subgroup of concentration-additive chemicals). Knowledge of the overall background PAF will then be irrelevant to establishing the appropriate working point.

Extending mixture theory to multiple species

The theories of concentration and response addition can be extended to multiple species systems, combining them with the concepts of SSDs [19,45,47]. This extension provides some insight into the likely influence of mixtures on the working point for estimating effect factors in LCA.

The following scenarios are based on an extension of mixture theory for single species by Hamers et al. [45].

Scenario 1. If chemicals exhibit similar toxicological mechanisms (or modes-of-action) for all species, then the change in PAF associated with the addition of another chemical can be described using a single SSD curve, analogous to the concentration-addition theory for single species described above. This would imply that the working point would correspond to the overall background PAF (denoted PAF_{ms} in this multiple substance context), Equation 5a in Table 1.

Scenario 2. If chemicals affect completely independent groups of species, then the independent changes in PAF will be additive, analogous to response-addition for single species. The working point is independent of the overall background PAF, Equation 5b in Table 1.

These scenarios are illustrated in Figure 5 and reflect two extreme hypothetical cases. Given that the β-value of most chemicals likely is to be between the extremes plotted and given the related uncertainties, the assumption of linear addition appears again to be a reasonable pragmatic approximation. This is explored further in the following section.

Appendix 2 presents additional detail related to the underlying concepts of PAFs in the context of mixtures, as well as demonstration studies in the context of LCA. Based on a third scenario it is argued that estimating the change in absolute PAF_{ms} is unlikely to be practically feasible in LCA (even if it were a desirable objective). The fraction of species experiencing an increase in exposure above a specified effect level can be estimated, however, using the same response and concentration addition theories outlined above (scenarios 1 and 2). Therefore we proceed in this paper with the notion of species experiencing additional increases in exposure above a specified effect level, rather than changes in overall or absolute PAF.

Choosing the relevant working point(s)

The effect factor options, or gradients, are a function of the working point selected on an SSD. The relevant working point depends on the influence of the background mixtures present in regions of interest, as well as on other nonchemical stressors. In this section we explore some of the evidence to suggest an appropriate working point, considering Equations 5a and 5b in Table 1 and, quantitatively, what, if any, are the implications of the differences in the context of LCA.

Low working points

If the background PAF_{ms} is less than 0.05 for a chemical, or for a mixture of concentration-additive chemicals, then the gradient prediction will be a strong function of the distribution model chosen (Fig. 4). In the typical absence of insights at such low PAF_{ms} levels to justify any particular model, or to warrant additional complexity, it is preferable from a practical perspective to perform comparisons in terms of a default linear gradient (a straight line between the origin and the specified working point, or benchmark, on the SSD). Chemicals and emissions would be compared in LCA studies by assuming an effect factor such as 0.05/HC5 or 0.5/HC50. These effect factors would be given by Equations 6a and 6b, as well as 7a and 7b, in Table 1. Model uncertainty will be high, but the assumption of a default linear low exposure-response relationship already is standard practice in the context of, for example, many human health assessments.

HC50 versus HC5. The linear gradient could be based on the median (0.5/HC50) or on the fifth percentile (0.05/HC5). Adopting the HC50 basis may help minimize uncertainty and avoid any assumption of a specific parametric distribution [23].

Table 1. Summary of gradient measures based on log-logistic distribution assumptions (similar equations are derived for other parametric distributions). C = concentration; HCx = hazardous concentration affecting x% of species; PAF = potentially affected fraction of species; ms = mixture; β = a measure of the spread of the species sensitivity distribution curve; K_{ow} = octanol–water partitioning coefficient; and subscripts a and b denote two chemicals (the equations readily can be extended to n chemicals)

Equation	Key assumptions	Concentration addition (Scenario 1)	Response addition (Scenario 2)
5a, 5b	By definition	$\Delta PAF_{ms} = \left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)\frac{\Delta PAF}{\Delta\left(\frac{C}{HC50}\right)}$	$\Delta PAF_{ms} = \left[\frac{C_a}{HC50a}\frac{\Delta PAF}{\Delta\left(\frac{C_a}{HC50a}\right)} + \frac{C_b}{HC50b}\frac{\Delta PAF}{\Delta\left(\frac{C_b}{HC50b}\right)}\right]$
6a, 6b	Linear gradient below HC5 (Normalized gradient = 0.05/HC5)	$\Delta PAF_{ms} = \left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)\cdot\frac{0.05}{HC5/HC50}$ Assuming a log-logistic distribution above PAF = 0.05, and setting PAF = 0.05 when C = HC5 in Equation 3, $\frac{HC50}{HC5} = 10^{2.94\beta}$ Substituting this into the above equation, $\Delta PAF_{ms} \approx \frac{10^{3\beta}}{20}\cdot\left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)$ For $0.2 < \beta > 1$, $\Delta PAF_{ms} = 0.2\cdot\left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)$ to $\Delta PAF_{ms} = 43\cdot\left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)$	Following a derivation analogous to that for concentration addition, $\Delta PAF_{ms} \approx 0.05\cdot\left(\frac{C_a\cdot 10^{3\beta_a}}{HC50a} + \frac{C_b\cdot 10^{3\beta_b}}{HC50b}\right)$
7a, 7b	Linear gradient below HC5 (Normalized gradient = 0.5/HC50)	$\Delta PAF_{ms} = 0.5\cdot\left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)$	$\Delta PAF_{ms} = 0.5\cdot\left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)$
8	Narcosis concentration–addition, as outlined in Appendix 3 β = 0.4, based on [48] and [37]	Substituting β = 0.4 in Equation 4, Equation 5 gives, $\Delta PAF_{ms} = 0.74\cdot\left(\frac{C_a}{HC50a} + \frac{C_b}{HC50b}\right)$ For non-polar narcosis [48], $\log HC50 = -0.85 \times \log K_{ow} - 1.6$	

The normalized marginal gradient is $10^{2.94\cdot\beta}/20$, assuming a linear gradient from the HC5, as in Equations 6a and 6b. Assuming a linear gradient from the HC50, the normalized marginal gradient simplifies to 0.5 (see Eqns. 7a and 7b). Equations 7a and 7b are not a function of beta, do not depend on the choice between marginal or average assessments, and do not require a distinction between response or concentration addition.

Based on an extreme maximum range of SSD gradients, β = 0.2 to 1 for all modes-of-action [37]. The factor $10^{2.94\cdot\beta}$ in Equations 6a and 6b could vary between 4 and 870. This variation represents the maximum difference that may be expected between assuming linear gradients for concentration and response addition scenarios (Equations 6a and 6b, respectively). This also represents the maximum difference between adopting Equations 6a and 6b versus 7a and 7b in Table 1, hence between the effect factor of 0.5/HC50 versus 0.05/HC5.

Although assuming a linear gradient from the HC50 (Eqns. 7a and 7b) is more practical, this analysis suggests potential introduction of up to a factor of 100 difference compared to using Equations 6a and 6b. However, based on de Zwart [37], β = 1 is a rare extreme that may not even exist. In most cases β will be less than 0.7. The uncertainty of assuming a linear gradient from the HC50 (Eqns. 7a and 7b) therefore will be less than a factor of ten in LCA for nearly all chemicals.

The ultimate overall uncertainty will still, nevertheless, depend on the accuracy of the median (HC50) estimate (such parameter uncertainty not being addressed in this paper), whether the working point is in reality below about PAF_{ms} = 0.05 for a particular chemical, the reliability of the implicit or explicit parametric model if HC5 is adopted as the gradient basis, and the robustness of assuming a linear low concentration gradient. Therefore, it is unlikely that adopting Equations 7a and 7b compared to 6a and 6b will be a significant source of additional uncertainty in LCA.

Endpoint relevance. Equation 7a further simplifies to Equation 8 in situations where narcosis is applicable, as outlined in Appendix 3 [48]. Over 50% of major contaminants [49] may have a narcotic mode of action, as well as many other chemicals when existing in complex mixtures (at low concentrations that are below mechanistic thresholds for the more specific modes of action that are often of concern at regulated levels of exposure, but not necessarily in an LCA context). The potential error in the effect factor associated with incor-

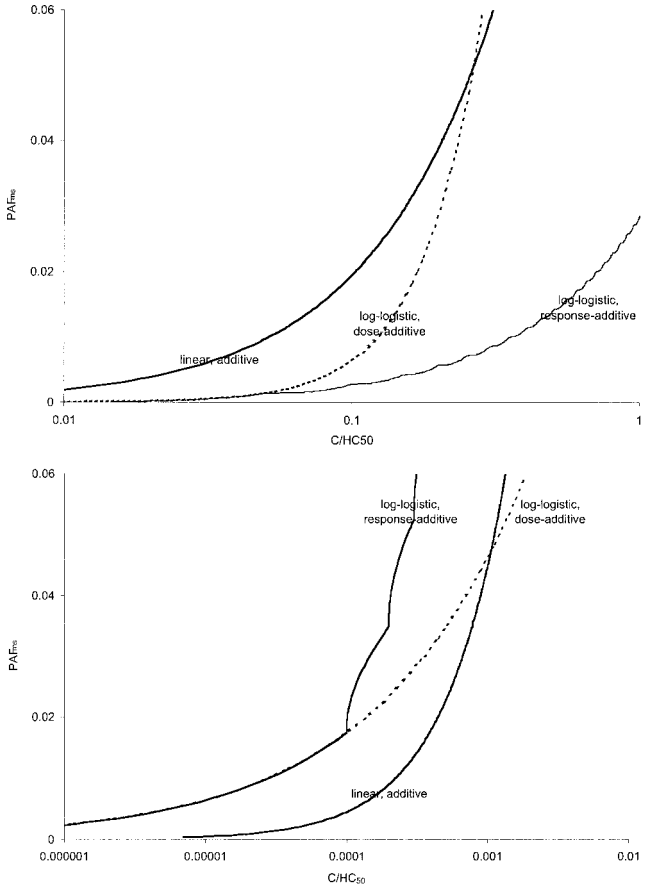

Fig. 5. Theoretical comparison of concentration-addition and response-addition potentially affected fraction of species (PAF) estimates for a mixture (ms) of chemicals assuming linear and log-logistic exposure-response curves. The top plot reflects the exposure-response given consecutive increases of each chemical up to an illustrative maximum concentration of $C_i/HC50_i = 0.05$ per chemical. For all the chemicals, $\beta = 0.2$. In the bottom plot: $\beta = 1$ and $C_i/HC50_i \leq 0.0001$ per chemical. Results using log-triangular and log-normal distribution models are similar. HC50 = median hazardous concentration.

rectly assuming the mode of action in an LCA context can be, however, four orders of magnitude (see Appendix 4).

Supporting evidence. Given achievements in respect to legislative compliance, it might be considered that the number of species experiencing an increase in stress due to an individual chemical, in general, will be less than 5% (less than the HC5) [25,27,49–51]. However, the evidence is not always clear in some of these references for some known problematic chemicals.

High working points

Above PAF $\approx$ 0.05 (and below $\approx$ 0.95), the uncertainty associated with the marginal gradient is a relatively weak function of the distribution model selected, as illustrated in Figures 3 and 4. These insights, however, may only be true for the unimodel parametric models considered here and commonly adopted to describe SSDs.

Klepper and van de Meent [24] and Traas et al. [27] suggested that the overall background PAF_{ms} often can be above a 5% level (between 10 to 50%). As stated in earlier sections, this overall background PAF_{ms} is only of relevance when estimating the marginal change in effect if all the chemicals/stressors can be treated according to the rules of concentration addition. Nevertheless, as indicated in the previous subsection, the PAFs of even some individual contaminants can exceed the fifth percentile within certain regions, particularly for some metals [24,27,51].

Equations 5a and 5b in Table 1 provide general relationships for the change in PAF associated with a small change in exposure concentration, assuming the extremes of concentration or response addition, respectively. The potential extent of variation in the normalized marginal gradient term (e.g., Eqn. 4 for log-logistic distributions) is identical in both of these equations. Based on the maximum plausible range of gradients, $\beta = 0.2$ to 1 for all modes of action [37], accounting for the Dutch background PAF_{mix} range of 10 to 50% [24] and using Equation 4, the normalized gradient can vary between at least 0.1 to 6 PAF (see Fig. 3). Hence, given the likely higher significance of other uncertainties, adopting an effect factor in LCA such as $\Delta PAF_{ms} = 0.5 \times \Sigma\Delta C/HC50$, usually will be reasonable in most studies.

These findings for high background PAFs and concentration addition are similar to those of the effect factors when a linear gradient is assumed (Eqns. 7a and b and 8), as outlined in the previous section. This also corresponds to the EcoIndicator 99 effect factor [6] and the evolving Payet and Jolliet [23] approaches, noting that further differences can exist in the underlying data adopted and the methods used to estimate the HC50 (usually geometric mean).

CONCLUSION

The PAF of species calculated from SSDs provides a practical basis for ecotoxicological impact indicators in LCA. These indicators are interpreted in terms of the fraction of species experiencing an increase in exposure above a defined effect (or no-observed-effect) level, usually the chronic EC50 or NOEC. Use of such indicators is more consistent and environmentally relevant in LCA than adopting approaches based on regulatory thresholds, such as PNECs. The final indicators can be interpreted in terms of cumulative risk, rather than regulatory hazard equivalents, while no additional test data are required. In some cases the uncertainties will be high.

Whether accounting for the choice between an average or a marginal indicator in LCA, or between concentration or response addition in the presence of background chemical mixtures (ms), a single effect factor currently is recommended for all situations for aquatic species in the water column: $\Delta PAF_{ms}/\Delta C$, the change in the PAF of species that experience an increase in exposure above a specified effect level. As a species can be simultaneously stressed above this effect level, the results are not necessarily related to changes in absolute or overall PAF_{ms}. Furthermore, exactly how the affected species will influence the structure, including the biodiversity, as well as the function of ecosystems, remain research topics.

Weighing up the various arguments and assumptions from the scientific perspective presented in this paper, directly estimating the effect factor from the median effect level (HC50) is recommended as the best approach in LCA ($\Delta PAF_{ms}/\Delta C = 0.5/HC50$). Reflecting more familiar practices from regulatory assessment contexts, some existing LCIA methods have adapted approaches based on the fifth percentile (HC5, $\Delta PAF_{ms}/\Delta C = 0.05/HC5$). Given the uncertainties and the same data requirements in both options, it could be argued that the differences between using the HC5 basis and the HC50 basis will be statistically negligible in practice. Nevertheless, it should not be forgotten that the objectives of an LCA differ from

those of regulatory risk-screening assessments. Although the fifth percentile is used pragmatically in the latter context for setting levels of unacceptable risks attributable to individual chemicals, it is not necessarily the best basis for comparing emissions in applications such as LCA in terms of contributions to cumulative risks in the presence of multiple stressors and background chemical mixtures.

In practice, even if this study should facilitate the much-needed consensus on the choice of effect factor within the LCA community, differences are likely to remain in terms of the effect (or no-observed-effect) data adopted (e.g., EC50 vs NOEC) when estimating the HC50-based effect factor. A benchmark such as the EC50 is preferable. Such benchmarks reflect consistent levels of risk, are much less sensitive to the test experiment design, and facilitate estimation of associated uncertainty. On the other hand, selecting the most appropriate benchmark for use in comparative applications will require consideration of environmental relevance in the context of LCA, necessitating further research to scientifically support the basis chosen.

Additional to the debate of what is theoretically the most relevant effect factor, LCA requires the development of pragmatic approaches that can cover large numbers of chemicals. It should be noted that the recommended effect factor can be estimated readily, and with acceptable accuracy for decision support, from the octanol–water partitioning coefficient (K_{ow}) for chemicals that have a narcosis mode of action. This is applicable for possibly 50% of existing chemicals. Narcosis is equally relevant in the context of other chemicals that are present at low concentrations below the mechanistic thresholds at which they exhibit more specific modes of action. Building on such insights could facilitate rapid, as well as more relevant, assessments of large numbers of chemicals in the context of aquatic ecotoxicological effects in nonregulatory applications such as LCA. The potential error associated with incorrectly assuming the mode of action of relevance in an LCA can result in an error of up to four orders of magnitude. Therefore insights into the relevance of different modes of action in LCA remain needed.

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APPENDIX 1: RESPONSE ADDITION THEORY

Independent risks can be combined using the statistical law of independence, in which response additive effects cannot be considered in isolation—$PAF_{ms} = 1 - (1 - PAF_1) \cdot (1 - PAF_2)$, where PAF is the potentially affected fraction of species, ms is multiple substance, and subscripts 1 and 2 denote two chemicals. No correlation of responses is assumed, $r = 0$. However, for small risks, the statistical law of independence can be simplified (also corresponding to complete negative correlation, $r = -1$). The resultant difference between $PAF_{ms} = 1 - (1 - PAF_1) \cdot (1 - PAF_2)$ and $PAF_{ms} = PAF_1 + PAF_2$ will be of little practical consequence, in general.

Huijbregts et al. [25] assumed that the PAF_{ms} follows a probabilistic distribution between $PAF_{ms} = 0$ to 100%, following the statistical law of independence. The marginal gradient is estimated from

$$\frac{d\mathrm{PAF}_{ms}}{d(C/\mathrm{HC50})} = \frac{1 - \mathrm{PAF}_{ms}}{1 - \mathrm{PAF}_x} \cdot \frac{d\mathrm{PAF}_x}{d(C/\mathrm{HC50})} \qquad \text{(A1)}$$

where C is concentration, PAF_{ms} is the ambient overall PAF, PAF_x is the PAF associated with the chemical or group of chemicals (x) of interest, and HC50 is the hazardous concentration at which 50% of species are affected.

The statistical law of independence was not assumed, however, for Figure 5. The overall ambient PAF_{ms} is assumed to

be the sum of the PAF_x contributions. Quantification of the overall PAF_{ms} is not necessary. A limit of 100% PAF still exists, although mathematically this can be exceeded.

The marginal gradient of the approach of Huijbregts et al. [25] and the basis of Figure 5 differ by the first term in Equation A1, namely $(1 - PAF_{ms})/(1 - PAF_x)$. For typically small regional values of PAF_x, this simplifies to $1 - PAF_{ms}$. Based on $PAF_{ms} = 0.3$ in Huijbregts et al. [25], this systematic difference will be approximately 0.7 and essentially is negligible in life-cycle assessment.

APPENDIX 2: MULTIPLE-SPECIES SPECIES-SENSITIVITY DISTRIBUTIONS

Response versus concentration addition case study insights

In an illustrative comparison, Huijbregts et al. [25] suggested that response addition–based effect factors for use in a life-cycle assessment (LCA) could be at least two orders of magnitude higher than those using the EcoIndicator 99 [6] method, where only concentration addition was assumed implicitly. The study adopted a marginal gradient approach, but many of the response-additive estimates were in the low exposure-response portion of the curve where the assumption of a log-logistic distribution is highly uncertain. The likely model uncertainties, therefore, render such distinctions at low concentrations questionable, as was outlined in this paper and illustrated in Figure 4.

Different modes of action for different species

Chemicals can have concentration-additive effects for some groups of species, but response additive effects for others. A given chemical may not affect all species on a species-sensitivity distribution (SSD) via the same mode of action. Considering each species independently in terms of concentration or response addition prior to estimating SSDs for the mixtures is one potential solution; creating separate SSDs for groups of species affected by different modes of action is another. A need exists therefore to establish the importance of this issue and the practical implications of related modifications in the context of life-cycle assessment. However, as the results will be bounded between the concentration and response-addition marginal change estimates considered in this paper, this issue was not addressed explicitly and may prove unimportant.

Overlap of species affected in response addition: Influence on interpretation

A group of species affected by an independent mechanism of one chemical could be the same group affected by another chemical (PAF_{ms} = greater of PAF_1 or PAF_2 and $r = 1$, where PAF is the potentially affected fraction of species, ms is multiple substance, and subscripts 1 and 2 denote two chemicals). This differs from the assumptions made in the paper for concentration/response addition in multiple species systems. This complete positive correlation results in the definition of a third scenario that has important implications on the interpretation of effect indicator results in LCA, particularly in the context of validation.

Scenario 3. In the case of response addition, if a chemical affects species already affected by another chemical, then the combined effect will be equivalent to the higher PAF (not the sum, $PAF_1 + PAF_2$). Removal of the chemical that exerts a lower effect will have no influence on the overall PAF_{ms}.

It is unlikely that the order of species in one SSD curve will be identical to that in another. It is equally unlikely that the effects of adding a chemical to a mixture will be zero (Scenario 3). Hence, response and concentration addition (Scenarios 1 and 2 in the paper) provide extreme upper and lower bounds in terms of estimating the absolute PAF_{ms}.

In Scenario 3, the addition of a chemical that affects an already affected group of species will not result in a change in absolute PAF_{ms} (the affected species are already stressed above their no-observed-effect concentration [NOEC], for example). The added chemical, however, will result in an increase in the exposure above the NOEC of this group of species; hence, there is a potential for increase in the consequences (or damage).

A distinction, therefore, is needed between the change in the fraction of species experiencing an increase in stress and the change in the absolute or overall fraction stressed. Different calculation procedures are warranted for each and neither may be relevant in LCA. To denote this distinction, the introduction of a new term is possible, such as PAF(I), the potentially affected fraction of species that experience an Increase in stress. However, preference is given to adopting existing terminology while clearly stating the adopted basis in different applications.

In LCA, at least, estimating the change in absolute PAF_{ms} is unlikely to be practically feasible (even if it were a desirable objective). The fraction of species experiencing an increase in stress can be estimated, however, using the already established response and concentration addition theories outlined in the paper (scenarios 1 and 2). Scenario 3 becomes irrelevant. For example, if 10% of species are affected above their NOEC, then, in an extreme case, adding a further chemical that has a response-additive behavior may cause no additional increase in the absolute PAF. The absolute PAF remains 10%. If the response-additive chemical affects 5% of the already affected species, then 5% of the species will experience a further increase in exposure above their NOEC.

The environmental relevance of the PAF-based measures in LCA, therefore, will be in terms of a change in species experiencing an increase in exposure above an effect measure such as the NOEC or median effective concentration. In some cases, this may correspond to a change in the absolute number of species exposed above an effect measure, but further research would be needed to establish whether this could be a common situation.

APPENDIX 3: MIXTURE NARCOSIS

The potential long-term effects of contaminants at low concentrations (relative to the concentrations at which specific modes of action are likely) in mixtures can be estimated using concentration-addition principles for multiple-species systems (scenario 1 in the paper, Eqn. 8 in Table 1).

Over 50% of major contaminants are nonspecifically acting (narcotic) chemicals, even at high concentrations [49]. Concentration addition commonly is considered applicable for chemicals with such a narcosis mode of action [47]. Chemicals present in membrane tissues at concentrations below thresholds for specific modes of action similarly can impart a narcotic mode of action [39,43,47,49,51–58]. For example, an organochlorine insecticide present at 1/100th of its median lethal concentration may not be sufficient to elicit a neurotoxic effect at concentration levels of interest in life-cycle assessment, but can contribute to a generalized narcotic mode of action in a mixture [51].

Narcosis effect levels, such as the median effect concen-

tration, can be predicted reliably for multiple species using quantitative structure–activity relationships. For example, Verhaar et al. [48] introduced a straightforward octanol–water partitioning coefficient (K_{ow}) correlation to estimate hazardous concentration affecting 5% of species (HC5) for chemicals with a nonpolar narcosis mode of action, calculating HC5s for 240 of 2,000 high-production volume chemicals. The HC5 data were extrapolated and confidence intervals estimated with quantitative structure–activity relationship data for 19 taxonomic groups (with species representing primary producers, primary consumers, and top predators; representing a variety of ecological functions, morphological structures, as well as routes of exposure).

APPENDIX 4: NARCOSIS VERSUS SPECIFIC-ACTING HC50 COMPARISON

Incorrectly assuming the relevant mode of action in LCA has the potential to introduce significant uncertainty. Figure 6 presents a comparison of the hazardous concentration affecting 50% of species (HC50) estimated using the narcosis quantitative structure–activity relationships of Verhaar et al. [48] versus the values for organic chemicals in Huijbregts et al. [25] based on measurements. Where a narcosis mode of action is expected, the estimations usually are within a factor of ten. An important exception is Carbendazim, which has a HC50 approximately 3,000 times lower than the narcosis estimate. Carbendazim actually is a fungicide, with a widely varying toxicity to invertebrates and fish, hence not a narcotic. This potential difference corresponds with estimates of Verhaar et al. [48,59], for example, who noted that the effect concentration can be four orders of magnitude below the estimate when assuming narcosis.

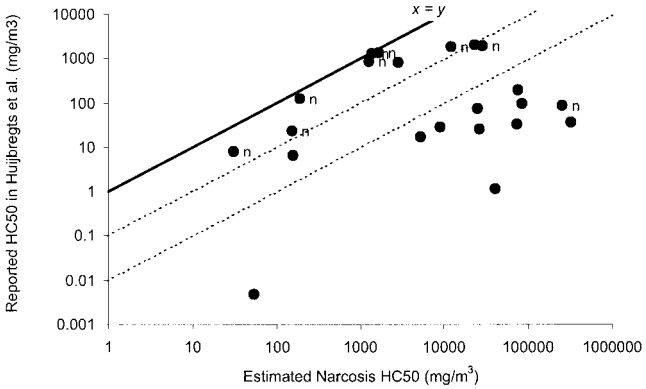

Fig. 6. Comparison of the median hazardous concentration (HC50) estimate using narcosis correlation of Verhaar et al. [48] against estimated HC50 values based on measured data [25]. (n denotes a narcosis mode of action, as suggested in Huijbregts et al. [25].)