Including Transformation Products into the Risk Assessment for Chemicals: The Case of Nonylphenol Ethoxylate Usage in Switzerland

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A method for applying the risk assessment approach using ratios of predicted environmental concentrations (PECs) and predicted no-effect concentrations (PNECs) to mixtures of parent compounds and their environmental transformation products is presented. Nonylphenol ethoxylates (NPnEOs) and a selection of their most relevant transformation products are investigated as a case study illustrating the method. The PEC values of NPnEO and its transformation products are calculated with a regional multimedia fate model including the transformation kinetics of the NPnEO degradation cascade. PNEC values are derived from a selection of toxicity data on NPnEO and its transformation products. The toxicity of the emerging mixture of NPnEO and its transformation products is then estimated under the assumption of concentration addition (similar mode of action). On this basis, PEC-to-PNEC ratios for the aquatic environment and the sediment are calculated for the individual components of the mixture and the mixture itself. For this purpose, average release rates of NPnEO and its transformation products from Swiss sewage treatment plants were used. While the PEC values of the individual components do not exceed the corresponding PNEC values, the risk quotient of the mixture in water is greater than 1. In sediment, the mixture does not exceed a risk quotient of 1. A combination of sensitivity and scenario analyses is employed to identify the upper and lower bounds of the results.

Introduction

Many chemicals are transformed to structurally related transformation products in the environment before they are mineralized. Each of these transformation products displays its own toxicity and persistence. Accordingly, the EU Technical Guidance Document on the risk assessment of notified new substances (TGD) states a need to include such transformation products into risk assessment for chemicals (ref 1, Part II, p 253). However, common practice of risk assessment does not cover the transformation products of industrial chemicals for several reasons: (i) the relevant transformation products have to be identified and characterized, (ii) the transformation kinetics has to be explored, (iii) the group of chemicals forms a complex mixture that is difficult to assess, and (iv) toxicity data for transformation products is often lacking. (For pesticides, the regulatory requirements in Europe are more stringent than for other industrial chemicals in that the identification, analysis, and risk assessment of all relevant metabolites is mandatory for their registration (2, 3).) All of these tasks pose methodological problems and increase the time and effort required for the assessment. Accordingly, there are only a limited number of studies dealing with the risk assessment of transformation products of industrial chemicals (e.g., refs 2 and 4–8).

One approach to include transformation products into the risk assessment of their parent compounds is to identify important transformation products, such as DDE formed out of DDT or nonylphenol stemming from nonylphenol ethoxylates, and to perform a risk assessment for these substances individually (2, 9). However, this approach does not account for a variety of other transformation products being present at the same time nor does it cover the toxicity of this mixture of different chemicals.

In an alternate approach, Fenner et al. (7) and Quartier and Müller-Herold (8) have included the transformation kinetics into the assessment. They have calculated the environmental exposure to parent compounds and transformation products as they are being formed in the degradation cascade. Here, as a next step, we include the effect assessment into this approach so that a risk assessment in terms of a risk quotient (quotient of predicted environmental concentrations (PEC) and predicted no-effect concentrations (PNEC)) can be accomplished. We investigate the still widely used nonylphenol ethoxylates (NPnEO) and their transformation products, including short-chain NPEs, nonylphenol carboxylic acids, and nonylphenol, as a case study (short: NPEs).

First, we calculate predicted environmental concentrations of the different chemicals with an open regional multimedia fate model that reflects the conditions in Switzerland and includes the transformation kinetics of NPnEO (10). Next, the toxicity of the emerging mixture of NPnEO and its transformation products is assessed under the assumption of a similar mode of action of the single compounds and, therefore, concentration addition (11, 12). The combination of fate modeling and mixture toxicity assessment leads to a risk quotient for the entire group of chemicals. Finally, to explore the reliability of the results, we carry out a sensitivity and scenario analysis and compare the results to those from two other risk assessments of nonylphenol and nonylphenol ethoxylates (9, 12).

The overall aim of the study is to demonstrate how the concomitant release and formation of transformation products can be included into the risk assessment of parent compounds and to argue in favor of such an inclusion into the practice of risk assessment.

Methods

Multimedia Model for Switzerland. To calculate predicted environmental concentrations (PECs), a regional steady-state (level III) model for Switzerland including the transformation kinetics of NPnEO (10). It describes the multimedia behavior and fate of NPnEO and of all of its transformation products, as well as the transformation reactions shown in Figure 2. Each transformation reaction is represented in the model calculations in terms of media-specific fractions of formation, \( f_i \), which indicate the relative amount of a precursor \( x \) that is transformed into a transformation product \( y \). The math-
TABLE 1. Model Dimensions and Transport Parameters for Switzerland (CH)

<table>
<thead>
<tr>
<th>Compartment Dimensions</th>
<th>value (m)</th>
<th>compartment volume CH</th>
<th>value (m³)</th>
<th>interfacial area CH</th>
<th>value (m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>soil (hₕ)</td>
<td>0.1</td>
<td>soil (vₕ)</td>
<td>3.96 × 10⁹</td>
<td>air/soil</td>
<td>3.96 × 10¹⁰</td>
</tr>
<tr>
<td>water (hₙ)</td>
<td>3</td>
<td>water (vₙ)</td>
<td>5.20 × 10⁹</td>
<td>air/water</td>
<td>1.73 × 10⁹</td>
</tr>
<tr>
<td>air (hₐ)</td>
<td>1000</td>
<td>air (vₐ)</td>
<td>4.13 × 10¹³</td>
<td>total (area)</td>
<td>4.13 × 10¹⁰</td>
</tr>
<tr>
<td>sediment (hₕed)</td>
<td>0.02</td>
<td>sediment (vₕed)</td>
<td>3.47 × 10⁷</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Environmental Properties Different from Values in Ref 13

<table>
<thead>
<tr>
<th>parameter</th>
<th>symbol</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>rain rate</td>
<td>Uᵢrain</td>
<td>4 × 10⁻³ m/d</td>
</tr>
<tr>
<td>wind velocity</td>
<td>Uᵢwind</td>
<td>4.32 × 10⁻⁸ m/d</td>
</tr>
<tr>
<td>water outflow</td>
<td>Uᵢwater</td>
<td>1.46 × 10⁻⁹ m/d</td>
</tr>
</tbody>
</table>

Switzerland. The media dimensions and all parameters deviating from the globally averaged properties in ref 13 are given in Table 1. In addition, a surface mixed sediment layer (SMSL) has been introduced as a fourth medium, and the model has been changed to represent an open system (i.e., it is assumed that the chemical can be removed from the system through advective transport in air and water and through burial into the permanent sediment). The quantification of the transfer processes in the SMSL model and of the removal processes is described in the Supporting Information (Section A).

Solving the model for steady-state conditions as described in the Supporting Information (Section A) results in a concentration vector $c^{st}$ (in mol/m³), which contains the steady-state concentrations for each chemical $x$ in each compartment $i$. These are used as predicted environmental concentrations (PECs) to calculate the risk quotients.

**Risk Quotient for a Mixture of Parent Compound and Transformation Products.** For a single compound $x$, the risk to the organisms living in a given environmental compartment is commonly expressed as risk quotient (RQ*), which compares the concentration $c^*$ of the compound $x$ in that compartment to some measure of its toxicity (e.g., ECₙₗ* for a chemical mixture acting independently on a given target organism. Because information about the interaction between components is often lacking and difficult to deduce from the chemical structures, no interaction is assumed in most cases as a first estimate (15, pp 107–111). Two basic concepts can be distinguished in this case. The first is independent action (IA; also, response addition), assuming that the mixture components act independently on different receptor systems. The second is concentration addition (CA), which means that the mixture components have the same mode of action and the same slope of their dose–effect curves so that, at each concentration level, one component can be substituted by an equi-effective amount of another component.

For calculating the risk of the mixture of parent compound and transformation products, we assume CA (for a discussion of this assumption and the mode of toxic action of NPEs, see the Supporting Information, Section B). CA has been shown experimentally (16) and numerically (17) to overestimate the mixture toxicity of independently acting chemicals by maximally a factor of 10. Therefore, CA might be considered.
an appropriate approach for a routine effect assessment of most types of chemical mixtures (16).

Given CA, the concentrations of all of the components of a mixture can be transformed into an equivalent concentration $c_{EQ}^x$ of a reference compound by summing up the concentration of each component multiplied by its relative potency $RP^x$. The relative potency $RP^x$ is defined as the ratio of the toxic potency of the reference compound ($EC_{ref}^x$) divided by that of the compound $x$ ($EC^x$). The total risk of the mixture can then be assessed by comparing the equivalent concentration $c_{EQ}^x$ with a given toxicity threshold of the reference compound (eq 1).

$$RQ_{mix} = \frac{\sum x c_{EQ}^x}{\sum x EC_{ref}^x} = \frac{\sum x RQ^x}{\sum x \frac{EC_{ref}^x}{EC^x}} = \sum x \frac{EC_{ref}^x}{EC^x} \frac{RQ^x}{x}$$

Equation 1 shows the usual expression for the mixture risk quotient (1, 12, 15, 18) indicating that, under the assumption of concentration addition, the risk for exposure to a mixture can be expressed as the sum of the single risk quotients $RQ^x$ of all of the toxicants of concern. Equation 1 implies that several subthreshold (i.e., ineffective) exposures could have a cumulative adverse effect.

In the methodology suggested here, the concentration of the single substances is not measured but predicted by means of the previously described multimedia model. Therefore, predicted environmental concentrations $PEC^x$ are used instead of measured concentrations $c^x$ to determine the risk quotients $RQ^x$. Also, not the measured effect concentrations $EC^x$ are used as toxicity thresholds but predicted no-effect concentrations $PNEC^x$, which are extrapolated from the $EC^x$ values by applying extrapolation factors $EF^x$ that account for inter- and intraspecies variability, acute to chronic extrapolation, and extrapolation from observed effects to predicted no-effect levels, thus $PNEC^x = EC^x / EF^x$. Accordingly, the definition for the mixture risk quotient $RQ_{mix}$, as used here is

$$RQ_{mix} = \sum x PNEC^x / \sum x \frac{PEC^x}{PNEC^x} = \sum x \frac{PEC^x}{PNEC^x}$$

According to the EU TGD (1), an EF of 1000 is applied if only acute toxicity data ($L(E)C_{50}$) are available for a substance. This EF can be lowered (100, 50, or 10) if long-term studies have been conducted. The value of the EF then depends on the number of trophic levels for which long-term endpoints were measured and on whether the species with the lowest NOEC (no-observed effect concentration) also shows the lowest acute toxicity (1).

**Case Study: Nonylphenol Ethoxylates**

**Usage of Nonylphenol Ethoxylates in Switzerland.** Nonylphenol ethoxylates (NPE) are high production volume chemicals that have been used for over 40 years as detergents, emulsifiers, and dispersing agents. NPE containing products are used in many sectors, including textile processing, pulp and paper processing, oil and gas recovery, steel manufacturing, and power generation (12). In Switzerland, NPE were banned from use in domestic cleaning agents in 1987. However, industrial NPE usage still exceeds 400 tons per year in Switzerland (19). The current use leads to a total NPE amount of 240 t treated yearly in Swiss sewage treatment plants, of which approximately 45% (i.e., 108 t/y) are still found in the secondary effluents (60%) and digested sewage (40%) (20). A detailed derivation of the yearly releases of the different NPE components in secondary effluents of Swiss sewage treatment plants is given in the Supporting Information (Section C). It results in the following estimated releases of the different NPE components: 18.7 t/y of long-chain NPnEO, 14.7 t/y of short-chain NP1/2EO (approximate ratio 3:1), 30.7 t/y of carboxylic acids NP1/2EC (approximate ratio 1:6), and 2.7 t/y of NP in secondary effluents, as well as 18.7 t/y of NP applied to the soil with the sewage sludge. These releases are used as model inputs.

**Fate of NPnEO and Its Transformation Products in the Natural Environment.** The partition coefficients and half-lives of the compounds, which are required as substance-specific input parameters for the exposure model, are listed in Table A3 in Section D of the Supporting Information. Half-lives were collected from a broad set of original publications and were adjusted to an average temperature of 283 K.

The relative importance of the degradation pathways of NPnEO (see Figure 2) depends on the environmental conditions (see Table 2). If there is enough oxygen present, as is the case in surface water and upper soil layers, the carboxylation of NPnEO to NP1EC and NP2EC is favored. Therefore, the fractions of formation $\theta_{1,w}$ and $\theta_{1,sed}$ are estimated to be 0.7 (see Table 2). In aerobic media, NP is expected to mineralize quickly. So, the fractions of formation of NP in aerobic compartments, $\theta_{1,air}, \theta_{2,air}, \theta_{3,air}, \theta_{4,air},$ and $\theta_{5,air}$, are set to 0 (note, however, that the mineralization of NP1EC and NP1EO, proceeds through NP).

In the sediment, where there are anaerobic spots, NP formed out of NP1EC or NP1EO may be more persistent. Because the exact fraction of persistent NP being formed is not known, the formation of persistent NP from NP1EC and NP1EO and direct mineralization of NP1EC and NP1EO are assumed to be equally important ($\theta_{3,air}$ is set to 0.5 and $\theta_{2,sed}$ to 0.25). Further, under anaerobic conditions, the formation of NP2EO from NPnEO becomes more important than under aerobic conditions; therefore, the fraction of formation $\theta_{4,air}$ is set to 0.5.

The importance of oxidation of NP2EO to NP2EC and of NP1EO to NP1EC is not known exactly, so the fractions of formation $\theta_{1,sed}$ are set to 0.5 for all media i (see Table 2).

In air, efficient degradation by attack of OH radicals is assumed. The pathways of this process are, therefore, not modeled explicitly.

**Toxicity of NPnEO and Its Transformation Products.** To derive a predicted no-effect concentration (PNEC) for each single substance, a broad set of toxicity data was evaluated, containing data from databases in refs 9, 12, 21, and 22. The EU study (9), Servos (21), and Staples et al. (22) distinguish between data points that are considered valid and well-

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**TABLE 2. Fractions of Formation in Soil, Water, and Sediment**

<table>
<thead>
<tr>
<th>reaction no. (r) in Figure 2</th>
<th>fractions of formation in soil (theta_{r,s})</th>
<th>fractions of formation in water (theta_{r,w})</th>
<th>fractions of formation in sediment (theta_{r,sed})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.7</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>6</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>7</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0.25</td>
</tr>
</tbody>
</table>

*In air, no transformation reactions according to the scheme in Figure 2 are expected. The fractions of formation were determined from transformation schemes taken from refs 34–38.*
documented and those that should be used with care. Here, only “valid” data were included.

It is known that, besides general acute and chronic toxicity, NPE also cause estrogenic responses in aquatic organisms that occur at concentrations similar to those at which chronic effects occur (23). However, the relative intensity of this effect for the different compounds is still an unresolved issue (see ref 23 vs ref 24). The risk through estrogenic behavior is, therefore, not yet addressed in this study.

For all substances, PNEC values in water were deduced from acute toxicity data by applying an EF of 1000 (see Table 3). Derived that way, the PNEC values in water reproduce the tendency of increasing toxicity with decreasing chain length reported by Servos (21), with NP being the most toxic compound. Accordingly, the relative potencies (RP) occurring in eq 1 reflect the relationships between the acute toxicity data.

PNEC values for the sediment were derived from the PNECs in water by using the equilibrium partitioning approach (25). The resulting values in μg/kg sediment are also listed in Table 3.

Only for two chemicals, NP and NPnEO, there are, according to the TGD (1), sufficient chronic data available for deriving the aquatic PNEC from these chronic data. Using these data for NP and NPnEO leads to different PNECs (given in Section E of the Supporting Information) and, as a consequence, also to different relative potencies of the components of the mixture. These relative potencies now reflect the relationships between the chronic NOECs of NP and NPnEO, on the one hand, and the acute data, combined with an implicitly assumed acute-to-chronic ratio, of the other four compounds, on the other hand.

We think that the first choice, that is, comparing the chemicals with respect to experimental data for the same endpoint (acute toxicity) and with a fixed EF, leads to more reliable relative potencies, which, in turn, are required for the mixture toxicity assessment. Therefore, we use the PNEC values based on EF = 1000 in our “standard scenario”. For comparison, we investigate the effect of the PNEC values derived from chronic NOECs for NP and NPnEO in the alternative scenario B1 (see following section on sensitivity and scenario analysis and Table 5; also see Section E in the Supporting Information).

A third approach for deducing PNECs is to analyze distributions of species sensitivities and to define the acceptable environmental concentration as the concentration at which 5% of the species is exposed above their toxicity threshold (26). In ref 12, a hazardous concentration for 5% of the species (HC5, 40 μg/L) is determined for NP from the log-probit transformed distribution of acute toxicity data. Extrapolation factors of 4 and 10 are applied that account for the acute-to-chronic ratio and for sublethal effects and species differences, resulting in a PNEC_{sub} of 1 μg/L. The PNECs of the other substances are deduced by using factors between 2 and 200, expressing the relative toxicities of the chemicals. (This approach assumes the same slope of the

### TABLE 3. Selected Toxicity Values of NPnEO and Its Transformation Products

<table>
<thead>
<tr>
<th>compound</th>
<th>LC50 g/L water</th>
<th>LC50 g/kg sediment</th>
<th>LC50 g/kg soil</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPnEO</td>
<td>96</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>NP2EC</td>
<td>900</td>
<td>990</td>
<td>2000</td>
</tr>
<tr>
<td>NP1EC</td>
<td>39</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>NP2EO</td>
<td>110</td>
<td>110</td>
<td>20.7</td>
</tr>
<tr>
<td>NP1EO</td>
<td>39</td>
<td>39</td>
<td>15</td>
</tr>
<tr>
<td>NPc</td>
<td>1000</td>
<td>1000</td>
<td>1000</td>
</tr>
</tbody>
</table>

*a lowest acute lethal concentrations (LC50) were taken from a database that was compiled from refs 9, 12, 21, and 22. b Values for NP9EO and NP15EO were used. c CAS Registry Number: 84852–15–3.

**FIGURE 3.** Mass fractions of NPE in the compartments soil, water, and sediment (on a molar basis). Fractions in air are below 0.1% for each compound (not shown).

**Results**

**Predicted Concentrations.** Figure 3 shows the mole fractions of NPnEO and its transformation products in the compartments soil, water, and sediment in the steady state. In air, no relevant amounts of any of the compounds were found. All compounds except NP partition mainly between water and sediment with the acids NP2EC and NP1EC found predominantly in water because of their higher water solubility. NP, being the only compound emitted to soil (adsorbed to sewage sludge), is mainly found in the soil compartment.

Water concentrations range from 0.012 μg/L for NP to 0.30 μg/L for NP2EC (see Table 4 for the concentrations of all compounds), while concentrations in sediment range from 0.15 μg/kg for NP1EC to 5.7 μg/kg for NP1EO.

To evaluate these results, the water concentrations obtained from the model are compared in Table 4 with measured concentrations for five locations in Swiss rivers (27). Only for the river Glatt measurements are given that include NP, the short-chain ethoxylates as well as the acids. Our calculated concentrations for these five compounds deviate from the measured concentrations in the Glatt by a factor of 1.2–5. For NP2EO and NP1EO, the calculated concentrations lie within the range of the measurements at all five locations, while the concentration calculated for NP lies below the detection limit of the measurements.

The tendency toward underprediction in the model results might be due to the fact that the calculations represent averages of all Swiss waters, while the measurements were conducted in rivers with characteristically high anthropogenic loads.

Sediment concentrations have not been extensively measured yet, so a comparison with the predicted concentrations is not possible here.

![Image](image_url)
Risk Assessment. Risk quotients were calculated for water and sediment. The risk quotients of the individual compounds, $RQ_x$, and the mixture risk quotient, $RQ_{mix}$, in water are listed in Table 5 (scenario “standard”). The most relevant result here is that none of the single compounds’ contributions to the overall risk stem from the three most toxic compounds, namely, NP, NP2EO, and NP1EO. This is still the case, although all their concentrations are lower than the concentrations of the other compounds (NPnEO and short-chain acids), which are less toxic than NP by a factor of about 50–100.

Risk quotients in sediment are generally lower. They vary between 0.021 for NP1EC and 0.071 for NP1EO. The sequence of compounds in order of decreasing risk in sediment is NP1EO, NP2EC, NP, NP2EO, NPnEO, and NP1EC. The mixture risk quotient lies below 1 with a value of 0.289.

In the following, investigations about uncertainty are conducted for water only because the mixture risk quotient in water lies above the critical limit.

Sensitivity and Scenario Analysis. The values of the risk quotients in water as given for the standard scenario in Table 5 depend strongly on the assumptions and input parameters that enter the calculation of the PEC and PNEC values. The uncertainty in the PEC values is largely due to uncertainty and variability in model input parameters such as the emission rates, the degradation rates, and the partition coefficients. It also depends on choices regarding the model geometry and the model algorithm such as the transformation scheme expressed by the fractions of formation $\theta_{X,Y}$. The uncertainty in the PNEC values stems from uncertainty about the completeness of the collected toxicity data and from the model chosen to extrapolate from effect concentrations to no-effect concentrations. In the following, we discuss the influence of the most important uncertainties on the risk quotients $RQ_x$ and $RQ_{mix}$.

First, the sensitivity of $RQ_{mix}$ to changes in 68 input parameters related to the six chemicals was investigated (emission rates, degradation rates, partition coefficients, PNEC values, fractions of formation). For that purpose, the normalized sensitivity of $RQ_{mix}$ to a one percent change in each input parameter was evaluated as described by Morgan and Henrion (28). All sensitivities exceeding 0.01 are shown in Figure 4. As expected, the $RQ_{mix}$ is most sensitive to the PNEC values and emission rates because it is directly proportional to these two types of parameters. The order of these sensitivities corresponds to the extent that each parameter contributes to $RQ_{mix}$.

The only relevant sensitivity other than to the PNEC values and emission rates is to the degradation rates and fractions of formation in water. As the degradation rates and fractions of formation contribute only indirectly to the PEC and $RQ$ values, they are less influential though. One surprising result is the quite high influence of the Henry’s law constant of NP. A possible reason for this is that its value of 11.0 (Pa·m$^3$)/mol is high enough that a slight change considerably influences the distribution of NP between water and air. This assumption is supported by the fact that NP has been measured in air occasionally (29).

To relate the model inherent sensitivities given in Figure 4 to the uncertainties found for the input parameters, we defined a number of different scenarios for each type of input parameter that the mixture risk quotient was found to be sensitive to (degradation rates, PNEC extrapolation model, Table 5. Calculated RQ$^4$ Values in Water of Single Components x and RQmix of the NPE Mixture$^a$

<table>
<thead>
<tr>
<th>uncertain parameter</th>
<th>scenario description</th>
<th>$RQ_{mix}$</th>
<th>$RQ_{mix}$</th>
<th>$RQ_{mix}$</th>
<th>$RQ_{mix}$</th>
<th>$RQ_{mix}$</th>
<th>$RQ_{mix}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>degradation rates</td>
<td>(A1) upper limit</td>
<td>0.229</td>
<td>0.304</td>
<td>0.094</td>
<td>0.323</td>
<td>0.645</td>
<td>0.568</td>
</tr>
<tr>
<td></td>
<td>degradation rates</td>
<td>0.051</td>
<td>0.145</td>
<td>0.069</td>
<td>0.067</td>
<td>0.462</td>
<td>0.475</td>
</tr>
<tr>
<td></td>
<td>(A2) lower limit</td>
<td>0.363</td>
<td>0.448</td>
<td>0.065</td>
<td>0.524</td>
<td>0.664</td>
<td>0.646</td>
</tr>
<tr>
<td>PNEC extrapolation models</td>
<td>(B1) PNEC$^a$ calculated strictly according to TGD</td>
<td>0.010</td>
<td>0.304</td>
<td>0.094</td>
<td>0.323</td>
<td>0.645</td>
<td>0.151</td>
</tr>
<tr>
<td></td>
<td>(B2) PNEC$^a$ taken from distributional assessment in (12)</td>
<td>$1.03 \times 10^{-3}$</td>
<td>$1.51 \times 10^{-3}$</td>
<td>$0.94 \times 10^{-3}$</td>
<td>0.018</td>
<td>0.035</td>
<td>0.012</td>
</tr>
<tr>
<td>fractions of formation</td>
<td>(C1) equal shares for parallel reactions$^b$</td>
<td>0.229</td>
<td>0.299</td>
<td>0.087</td>
<td>0.369</td>
<td>0.655</td>
<td>1.833</td>
</tr>
<tr>
<td></td>
<td>(C2) enhanced formation of NP2/1EC from NP2/1EO in aerobic compartments$^c$</td>
<td>0.229</td>
<td>0.317</td>
<td>0.107</td>
<td>0.323</td>
<td>0.591</td>
<td>0.567</td>
</tr>
<tr>
<td></td>
<td>(C3) no NP formation in the sedimentd</td>
<td>0.229</td>
<td>0.304</td>
<td>0.094</td>
<td>0.323</td>
<td>0.645</td>
<td>0.556</td>
</tr>
</tbody>
</table>

$^a$ Uncertain parameters such as degradation rates and fractions of formation as well as PNEC extrapolation models are varied in the different scenarios. The standard scenario relates to the input parameters as given in Tables 2 and 3 and in A3 in the Supporting Information. $^b$ $\theta_{x,y} = 1$; $\theta_{x,y} = 0.5$; $\theta_{x,y} = 0.5$; $\theta_{x,y} = 0.5$; $\theta_{x,y} = 0.33$; $\theta_{x,y} = 0.33$. $^c$ $\theta_{x,y} = \theta_{x,y} = 0.9$; $\theta_{x,y} = \theta_{x,y} = 0.9$. $^d$ $\theta_{x,y} = 0$; $\theta_{x,y} = 0$.
fractions of formation) and calculated the corresponding RQ values (PNEC-x(i) in graph). Only sensitivities exceeding 0.01 are shown.

One alternative PNEC extrapolation model is to derive each PNEC strictly according to data availability and TGD recommendations for extrapolation factors (scenario B1, as mentioned previously in the case study section). This led to higher PNEC values and, correspondingly, to lower risk quotients for NP and NPNEO and to a reduction of RQmix from 2.16 to 1.53.

A rather different picture is obtained (scenario B2) if the PNEC values are used that were obtained from the distributional assessment of toxicity values as it was conducted by Environment Canada and Health Canada (12). This is the only scenario where RQmix drops well below 1 to a value of 0.07 due to the fact that the PNEC values in scenario B2 lie by a factor of 20–200 higher than those of the standard scenario (see Discussion).

Scenario C1 for the case of the different transformation schemes assumes an (in this case, hypothetical) worst-case information situation where nothing is known about the importance of the different pathways. Therefore, equal fractions of formation were attributed to all parallel reactions (i.e., 100% transformation in the case of single pathways, 50% transformation in the case of two parallel pathways, and 33.3% transformation in the case of three parallel pathways). This assumption was made for the soil, water, and sediment compartments equally. This scenario C1 leads to a considerably higher RQmix of 3.47, which is mainly due to the scenario’s assumption that toxic NP is formed in all compartments. The other formation scenarios, C2 and C3, address two main uncertainties about the transformation scheme. Scenario C2 concerns the question to what extent the acids are formed through the oxidation of short-chain ethoxylates (reactions 5 and 7 in Figure 2) and to what extent they are formed directly from longer-chain ethoxylates (reactions 1 and 2 in Figure 2). Scenario C3 represents a situation in which the sediment environment is not sufficiently anaerobic for NP to be formed, so that NP1EO and NP1EC are directly mineralized (reactions 3a and 8a in Figure 2). Interestingly, in both scenarios, RQmix shows only small deviations from the standard scenario (±2%). Consequently, the importance of knowing the exact transformation scheme seems to be low as compared to other uncertainties.

Assuming that the different scenarios in Table 5 cover the most important uncertainties, we conclude that the uncertainty of RQmix is smallest due to uncertainties in the fractions of formation (variation of RQmix by ±2% in scenarios C2 and C3), usually within a factor of 2 for different sets of degradation rates, but on the order of at least 1 order of magnitude for different PNEC extrapolation models.

Discussion

We first discuss our results in the light of two other recent risk assessments for the same substance family. The first one is the EU risk assessment for nonylphenol (9) and the second one is a risk assessment for nonylphenol and its ethoxylates, conducted by Environment Canada and Health Canada (12).

In the EU risk assessment for nonylphenol, ethoxylates were only considered under the aspect that their biotransformation contributes to the biggest part of NP released into the environment but were not assessed themselves. The EU assessment investigates a variety of possible release scenarios of NPE from households and industry into water. Local and regional PECs for NP were calculated under standard worst-case assumptions (ref 1, Part IV), thus reflecting hot spot situations and overestimating average concentrations in European rivers and lakes. On the toxicity side, a PNEC of 0.33 μg/L was used, which lies between the value chosen in this study (0.021, μg/L) and the value of the Canadian study (1, μg/L). Given these assumptions, the EU risk assessment identifies environmental risks for nearly all applications of NPEs as well as for the production of NP and NP derivatives (RQ values for NP range from ~0.6 up to approximately 1400). Accordingly, a ban of NPE in all water-relevant use categories is suggested.

In our regional model for Switzerland, the risk quotient of nonylphenol alone is around 0.6. Obviously, if only NP was considered, no high risk would be deduced from our generic, regional risk assessment. However, in our analysis, we find that NP only accounts for 2.2% of the total mass in the water compartment and for only 26% of the total risk identified from NPNEO and its transformation products. Because all of these compounds exist together as mixture in the environment, our results indicate that assessing the risk of the overall mixture (RQmix) is required.

In the Canadian study (12), concentrations in receiving waters for all compounds considered in our analysis were measured. These measured concentrations were used to calculate the risk from each single compound as well as the overall risk of the group of compounds. Regarding the risk quotients of the single compounds, the relative magnitude of our RQ values corresponds to the relative frequency with which the single compounds exceed a risk quotient of 1 in the Canadian study. Both studies agree that NP1EO poses the highest/most frequent single risk, followed by the other two more toxic compounds NP2EO and NP, and that the acids NP2EC and NP1EC exhibit lower single risks.

The comparison of our study with the EU risk assessment and the Canadian study and the results of the scenario analysis indicate that there are two factors that dominate the judgment about the risk of a specific chemical. First, we showed that it depends heavily on whether and, if so, on how many transformation products are considered. For the special case of NPNEO, whose transformation products are more toxic than the parent compound itself, the transforma-
tion products account for 89% of the overall risk. For other compounds, the effect might be less pronounced but still relevant.

Second, the judgment about the existence of risk depends on the PNEC extrapolation model chosen. In this respect, EU TGD guidelines are more restrictive than North American ones, which often use the distributional approach. PNEC values deduced with the distributional approach are usually larger for two reasons: (i) the distributional assessment relies on the idea that protection of 95% of all species is sufficient, while the TGD approach aims at protecting all species by basing the PNEC on the effect level of the most sensitive species (here, HC₅ of 40 μg/L (distributional) vs lowest LC₅₀ of 20.7 μg/L (TGD)), and (ii) the distributional assessment uses lower extrapolation factors than the generic ones suggested in the TGD to account for the remaining uncertainties regarding acute-to-chronic ratio, sublethal effects, and species differences (here, 40 (distributional) vs 1000 (TGD)).

Another factor influencing the judgment about risk is the assumption of concentration addition. In cases where it is not applicable but is still used as an estimate of mixture toxicity, it will overestimate the toxicity by maximally a factor of 10. All in all, the mixture risk quotient in this study is subject to two conservative assumptions regarding PNEC extrapolation and evaluation of mixture toxicity and one nonconservative assumption in that possible estrogenic effects are excluded from the evaluation of the mixture toxicity at all.

Regarding the further applicability of the method presented here, the following assumptions need to be considered: (i) the use of averaged landscape parameters (no local conditions), the steady-state conditions, the selection of transformation products, and fractions of formation on the PEC side, and (ii) the assumption of concentration addition and the choice of extrapolation factors on the PNEC side.

With respect to these model limitations, the agreement between measured and modeled concentrations as well as the correspondence between the relative risks of the compounds in (12) and those found in our model calculations is considered sufficient. Therefore, we suggest that the method proposed here could be used with due consideration of the aforesaid assumptions, to assess the risk of other compounds with environmentally relevant transformation products (e.g., odorants such as nitro musk (30), surfactants used in shower gels and shampoos (31), halogenated alkanes (32), or PAHs (33)).

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Supporting Information Available

Additional information on the model mathematics, the NPE releases, the toxicity of NPE, and the substance-specific model input parameters. This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited


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