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Coupled near-field and far-field exposure assessment framework for chemicals in consumer products

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ABSTRACT

Humans can be exposed to chemicals in consumer products through product use and environmental emissions over the product life cycle. Exposure pathways are often complex, where chemicals can transfer directly from products to humans during use or exchange between various indoor and outdoor compartments until sub-fractions reach humans. To consistently evaluate exposure pathways along product life cycles, a flexible mass balance-based assessment framework is presented structuring multimedia chemical transfers in a matrix of direct inter-compartmental transfer fractions. By matrix inversion, we quantify cumulative multimedia transfer fractions and exposure pathway-specific product intake fractions defined as chemical mass taken in by humans per unit mass of chemical in a product. Combining product intake fractions with chemical mass in the product yields intake estimates for use in life cycle impact assessment and chemical alternatives assessment, or daily intake doses for use in risk-based assessment and high-throughput screening. Two illustrative examples of chemicals used in personal care products and flooring materials demonstrate how this matrix-based framework offers a consistent and efficient way to rapidly compare exposure pathways for adult and child users and for the general population. This framework constitutes a user-friendly approach to develop, compare and interpret multiple human exposure scenarios in a coupled system of near-field ('user' environment), far-field and human intake compartments, and helps understand the contribution of individual pathways to overall human exposure in various product application contexts to inform decisions in different science-policy fields for which exposure quantification is relevant.

1. Introduction

Chemicals in products have the potential to expose consumers through product use and the general population through emissions to the environment (Bergfeld et al., 2005; Fantke and Jolliet, 2016; Geueke et al., 2014; Molander et al., 2012; Nazaroff and Weschler, 2004). Quantitatively evaluating near-field consumer and far-field population exposures to product-related chemicals is relevant for various science-policy fields including life cycle impact assessment, LCIA (Ernstoff et al., 2016), chemical alternatives assessment, CAA (Lavoie et al., 2010), risk-based assessments and high-throughput screening, HTS (Dionisio et al., 2015; ECHA, 2012; Shin et al., 2015). LCIA aims at considering exposures along all product life cycle stages and accounts for exposures mediated through environmental emissions based on interconnected compartments, but currently mostly fails to consider exposures to chemicals from product use (Jolliet et al., 2015). In risk-oriented assessments, multiple exposure pathways can be addressed, but typically in a disconnected way based on different modeling systems and levels of detail (van Leeuwen and Vermeire, 2007). For example, recent HTS approaches include multi-pathway consumer exposure, but pathways like inhalation and dermal permeation are either decoupled using two different probabilistic modeling strategies without a unifying mass balance equation (Isaacs et al., 2014), or consumer use scenarios are not combined with post-use environmental emissions (Delmaar et al., 2013). In CAA, exposure to product-related chemical emissions is currently mostly not considered or restricted to qualitative evaluations of consumer exposure (Jacobs et al., 2016).

Comprehensively accounting for the all relevant transfers and exposure pathways, which build on different underlying models, is therefore an unresolved problem across science-policy fields. Exposure pathways can involve multiple indoor and outdoor transfers before resulting in human consumer or population exposure. Near-field consumer exposure thereby refers to chemical intakes by humans using a considered product or in the vicinity of product use, and far-field population exposure refers to aggregated intakes by humans (product users and non-users) via environmental emissions. Pathways within the vicinity of product use, such as inhalation of chemicals released from products

indoors, skin permeation of chemicals in dermally applied products, and ingestion of chemicals in food and beverages often dominate exposure (Fantke et al., 2011; Wambaugh et al., 2013). Nevertheless, exposure following chemical emissions to the environment can in certain cases be of comparable magnitude depending on the product-chemical combination (Ampleman et al., 2015; Jones-Otazo et al., 2005). Considering and comparing multiple exposure pathways is therefore critical to capture overall exposure to chemicals in consumer products and to identify dominating exposure pathways. The diverse nature of exposures to chemicals from products in the vicinity of consumers, however, poses a challenge for consistently integrating models for multiple near-field pathways in a compatible way with models for far-field pathways mediated through environmental emissions.

To rigorously address this problem, a framework is needed that fully and consistently integrates different models for consumer and population exposures. To accommodate future developments and the needs of specific assessments it is important that such a framework allows for flexibility, while at the same time maintaining mass balance and physicochemical principles across inter-compartment transfers and exposure pathways capturing chemical fate indoors and outdoors. Flexibility is important with respect to data input and model selection to align with specific assessment goals, e.g. worst-case or average product use scenarios. Finally, to allow for consistent comparison across exposure pathways, chemicals, and products, such a framework should be based on comparative exposure metrics like the recently proposed product intake fraction (Jolliet et al., 2015), defined as chemical mass taken in by humans – via all relevant exposure pathways during and after product use – per unit mass of chemical in the product.

In response to these needs, we propose a novel multimedia modeling framework that couples pathways accounting for human exposures to chemicals in consumer products. First, the overall framework is defined, structuring exposure pathways as interactions between chemicals, products, environmental compartments, and humans, in order to follow the pathway from the mass of chemical used in a product to ultimate human intake. Second, after quantifying the mass of chemical used, the mathematical framework is presented to calculate exposure pathway-specific product intake fractions (PiFs) and intakes based on a multi-compartmental transfer fractions matrix approach. Finally, the applicability of our framework is illustrated in two examples of chemicals in cosmetics and flooring materials. This framework sets up a flexible structure to consistently quantify and compare any consumer product human exposure to its chemical constituents via all relevant product use-related exposure pathways.

2. Methods

2.1. Product intake fraction framework

Building on a consistent set of terms defined in Table 1, we present a comprehensive Product Intake Fraction Framework for coupled consumer and population exposures to chemicals in consumer products (referred to as *PiF Framework*) following three main steps (Fig. 1). The near-field environment is represented by a set of *near-field compartments* in the vicinity of product users. In the PiF Framework, we first quantify the chemical mass that enters a defined *compartment of entry* (Fig. 1a; Table 1). Second, the framework captures the fate and transport processes resulting in transfers of chemicals between any near-field and far-field compartment, until finally reaching humans. The combination of various multimedia transfers expressed as *direct transfer fractions* yields *cumulative transfer fractions* or, when received by human intake compartments, cumulative *product intake fractions* describing *exposure pathways* from the compartment of entry to humans via specific

Table 1
Definition of terms used in the PiF Framework for assessing human exposure to chemicals in consumer products.

| Term	Definition
Compartment terms	
Near-field compartment	Any **indoor or near-consumer** location or environment within the vicinity of the use of a considered product ('user' environment), to and from which chemical transfers occur and within which removal processes occur. Near-field compartments include indoor air, consumer products and objects themselves, and their surfaces (e.g. 'skin surface layer' for products applied on top of the skin surface, or 'article interior' for products like flooring materials).
Far-field compartment	Any location or environment that is **distant from the use of a considered product**, to and from which chemical transfers occur and within which removal processes occur. Far-field compartments include environmental media (e.g. 'ambient air', 'freshwater' like rivers and lakes, or 'soil'), biota (e.g. agricultural crops, wild animals and plants), or technological systems (e.g. waste water treatment plants and landfills).
Human intake compartment	Any physical location in the **interior of humans via which the chemical is first taken in**, representing a specific route of chemical intake into the human body. Human intake compartments include the 'respiratory tract' for inhalation, 'gastrointestinal (GI) tract' for ingestion, and skin 'epidermis' for dermal uptake.
Compartment of entry	Compartment into which or within which a **chemical is first applied or used** (e.g. 'article interior' for a chemical embedded in flooring material or 'skin surface layer' for chemicals in dermally applied cosmetics) and from which exposure to chemicals in consumer products originates following different pathways. The compartment of entry is specific to a product use scenario.
Transfer source compartment	Any compartment, from which a chemical mass transfer occurs.
Transfer receiving compartment	Any compartment, to which a chemical mass transfer occurs.
Inter-compartment transfer terms	
Direct transfer fraction	Chemical mass fraction in any compartment that is **passing a boundary to any adjacent or nested compartment** via advective, diffusive, or chemical processes, such as deposition, volatilization or dermal uptake. Direct transfer fractions can be derived from different types of models (e.g. ratios of rate constants). For each transfer source compartment, all direct transfer fractions plus the fractions lost (e.g. by degradation) that are incorporated in the underlying transfer fractions models plus the fraction left in the product always sum up to unity (100%). All models used to determine direct transfer fractions need to build on **mass balance principles** to ensure overall consistency.
Cumulative transfer fraction	Overall chemical mass fraction originating from a certain source compartment that **eventually reaches** any **receiving near-field, far-field or human intake compartment** as a combination of all involved multimedia transfers.
Human exposure terms	
Product intake fraction (PiF)	Chemical mass within a product that is eventually taken in by humans per unit of chemical mass in that product (Jolliet et al., 2015), determined here as the cumulative transfer fraction from a compartment of entry that **eventually reaches a certain human intake compartment** of the considered exposed users or population group.
Exposure pathway	The course a chemical takes from its source to the person(s) being contacted (US-EPA, 1992), determined here as a **sequence of inter-compartmental chemical transfers** originating from a product and ending with human intake. An example exposure pathway is a chemical originally encapsulated in a solid object defined as compartment of entry 'article interior', which is then emitted to 'indoor air' and subsequently inhaled by product users, or further transferred to 'ambient air' and inhaled by the general population.
Exposure route (or route of exposure)	A particular **means of intake** for a chemical into the human body (US-EPA, 1992), i.e. inhalation via breathing; ingestion via intentional dietary consumption or inadvertent non-dietary intake; dermal contact between skin and external surfaces, air or products; or injection (mainly in the medical domain, e.g. vaccination).
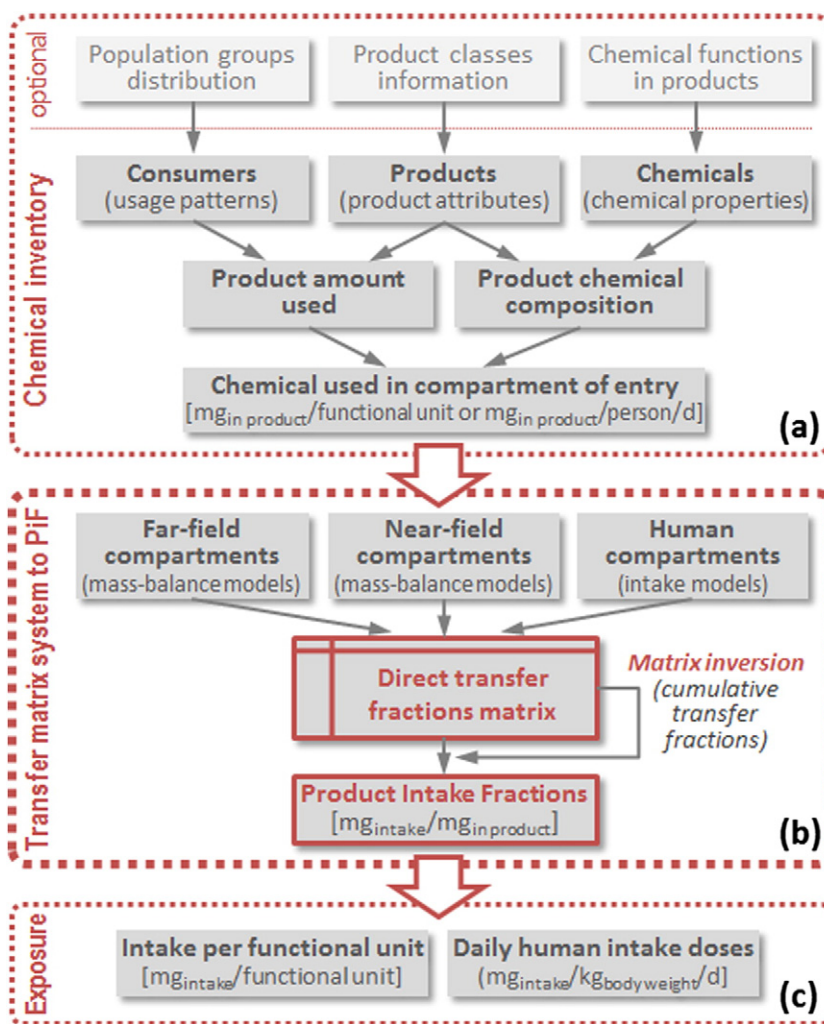
Fig. 1. PiF Framework flow chart of data and matrix calculation modules to quantify human exposure to chemicals in consumer products via all relevant multimedia transfer and exposure pathways.

exposure routes (Fig. 1b). Product intake fractions are thereby fully compatible with multimedia compartment models applied for exposure assessment using intake fractions as a metric relating human exposure to chemical mass emitted into far-field compartments or to indoor air. As final step of the framework, the initial chemical mass entering the compartment of entry is combined with the estimated product intake fractions to yield mass intake estimates either related to chemical or product function as emitter- or producer-focused metrics used in function-based assessments like LCIA and CAA (Hauschild, 2005; Jacobs et al., 2016), or to yield daily intake dose as receptor-focused metric used in risk-based assessments (van Leeuwen and Vermeire, 2007) (Fig. 1c). For each exposure route (e.g. dermal uptake for 'epidermis') per user or exposed population, this intake $I_{i,j}$ [mg$_{intake}$] of a chemical in a product is defined as

$$I_{i,j} = m_{0,j} \times PiF_{i,j} \tag{1}$$

where $m_{0,j}$ [mg$_{applied}$] is the product-specific mass of chemical initially applied or released to the jth compartment of entry, and $PiF_{i,j}$ [mg$_{intake}$/mg$_{in\ product}$] is the chemical mass fraction cumulatively transferred from the jth compartment of entry to the ith human receiving compartment of exposure, accounting for all multimedia transfers between near-field and far-field compartments.

2.2. Chemical mass allocated to a compartment of entry

Chemical inventory (i.e. mass of each chemical within a product) can be compiled from available databases (CPNP, 2013; Dionisio et al., 2015; Fitzpatrick, 2004; Goldsmith et al., 2014; Hall et al., 2007; Loretz et al., 2006; Loretz et al., 2008; Loretz et al., 2005), estimated, or specified according to the assessment goal, e.g. only for certain chemicals of concern. As input for the framework, the inventoried chemical mass is allocated to a compartment of entry according to the product and its use scenario. For example, chemicals in cosmetics can enter the near-field environment via the 'skin surface layer' compartment of entry, whereas chemicals in flooring enter the near-field environment from the 'article interior'. The unit describing the chemical mass allocated to a compartment of entry can be specified according to the assessment type, e.g. chemical mass per kilogram body-weight per day for risk-based assessments, or per chemical functional use or product functional unit for CAA and LCA, respectively. For example, if the product functional unit is defined as providing clean hair for a person over 1 year, the corresponding mass inventory that is allocated to the compartment of entry is determined as the amount of product required to fulfill the functional unit multiplied by the chemical fractions in the product (Koniecki et al., 2011). As inventory result, the mass of chemical in the compartment of entry constitutes the starting point for quantifying exposure.
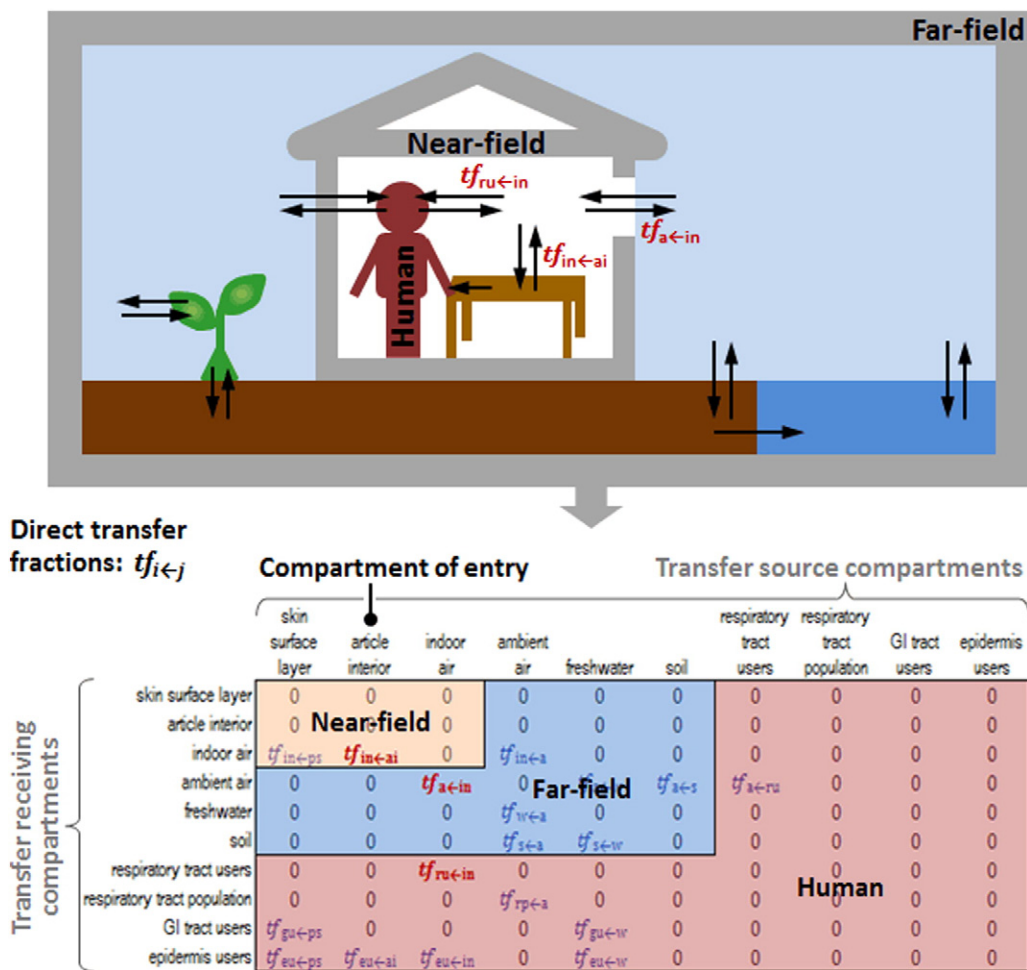
Fig. 2. Simplified scheme (top) and matrix representation (bottom) of coupled near-field, far-field and human intake compartments for exposure modeling of chemicals in consumer products. Inter-compartmental chemical transfers are represented by direct transfer fractions (arrows) and the corresponding matrix elements (chemical-specific $tf_{i \leftarrow j}$) from a *source* column compartment j to an adjacent or nested *receiving* row compartment i. Transfer fractions in bold indicate how arrows in the schematic graphic are captured in the matrix.

2.3. Direct and cumulative transfer fractions and product intake fractions

Starting from the compartment of entry, a series of consecutive transfers between various near-field and far-field compartments can occur until a chemical is finally taken in by humans (Fig. 2). In the PiF Framework, all transfers between and removals within compartments are considered on a consistent mass balance basis aiming to ultimately relate the chemical mass in a compartment of entry to human intake. The main innovative aspect of the PiF Framework is to structure chemical mass fractions transferred between compartments in a matrix of direct transfer fractions, to then calculate cumulative transfer fractions by matrix inversion, and to finally extract from the resulting cumulative matrix the PiFs corresponding to the considered product-specific compartment of entry.

2.3.1. Direct transfer fractions

Direct transfers between near-field, far-field, and human intake compartments are integrated in the square matrix $\mathbf{TF} \in \mathbb{R}^{n \times n}$ of direct transfer fractions $tf_{i \leftarrow j}, i,j \in \{1, \ldots, n\}$ of structure:

$$\mathbf{TF} = \begin{pmatrix} tf_{1 \leftarrow 1} & \cdots & tf_{1 \leftarrow n} \\ \vdots & \ddots & \vdots \\ tf_{n \leftarrow 1} & \cdots & tf_{n \leftarrow n} \end{pmatrix} \text{ with } tf_{i \leftarrow j} = \begin{cases} tf_{i \leftarrow j} & \text{for } i \neq j \\ 0 & \text{for } i = j \end{cases}$$ with col-

umn and row indices for j transfer *source* compartments (matrix columns in Fig. 2) and i transfer *receiving* compartments (matrix rows in Fig. 2), respectively. From the matrix columns, a scenario-specific compartment of entry is defined, from which any human exposure to chemicals in a product originates. Elements $tf_{i \leftarrow j} \neq 0$ of $\mathbf{TF}$ for $i \neq j$

represent chemical mass fractions directly transferred between two adjacent compartments. If no inter-compartment transfer is defined, then $tf_{i \leftarrow j} = 0$ for $i \neq j$, while $tf_{i \leftarrow j} = 0$ for all $i = j$. Each matrix element (direct transfer fraction), can be determined using models of the desired level of complexity, which must themselves satisfy mass balance principles to ensure an overall mass balance in the matrix framework. Losses within compartments due to e.g. degradation are considered in the underlying transfer fraction models and contribute to reduce transfers to other compartments. Transfers from the compartment of entry are determined by the product use scenario and the chemical properties. For example, estimating transfers to indoor air from a given compartment of entry will depend on the use circumstances (e.g. as a function of the thickness and duration of use of a product) and the chemical behavior (e.g. if volatile). In addition, transfer fractions of a chemical will depend on the compartment of entry characteristics. A transfer from the interior of a vinyl floor (compartment of entry 'article interior') to indoor air will differ from a transfer to indoor air of the same chemical within a cleaning product applied on top of the vinyl floor. However, transfers between non-compartment of entry compartments (e.g. from indoor air to outdoor air) for a given chemical are independent of the product being assessed but are mechanistically derived as a function of chemical- and compartment-specific properties. This distinction demonstrates the strength of the matrix approach that is flexible and easily adaptable to new product scenarios, where only the compartment of entry needs to be modified or added, while all other compartments and related direct transfer fractions remain the same and are estimated using the preferable or best available models. Transfers to humans also

depend on human time activity patterns (e.g. time spent indoors and outdoors) and characteristics of the exposed populations (e.g. how many persons live in a household or use a specific product), where time activity patterns can be integrated in the specific models underlying individual elements of the transfer fraction matrix.

2.3.2. Cumulative transfer fractions

Cumulative transfer fractions between compartments are calculated from the matrix of direct transfer fractions by matrix inversion. As starting point, the initial chemical mass of 100% in the jth transfer source compartment is defined by the jth column of the identity matrix $\mathbf{I} \in \mathbb{R}^{n \times n}$ with ones on the main diagonal and zeros elsewhere. Once all direct (first-level) transfer fractions are determined for all considered compartments, i.e. $\mathbf{TF}$ is populated, it becomes possible to calculate the second-level transfer fractions as $\mathbf{TF}^2$ referring to transfer fractions subsequent to direct transfer fractions. This process can be repeated infinitely for higher levels and summed up to yield overall cumulatively transferred fractions accounting for all multimedia transfers. This cumulative infinite sum is directly obtained by inverting the difference between $\mathbf{I}$ and $\mathbf{TF}$:

$$\mathbf{TF}^{\text{cum}} = \mathbf{I} + \mathbf{TF} + \mathbf{TF}^2 + \dots + \mathbf{TF}^n = (\mathbf{I} - \mathbf{TF})^{-1} \qquad (2)$$

where elements of $\mathbf{TF}^{\text{cum}}$ for each column represent cumulatively transferred chemical mass fractions from the column source compartment to the receiving row compartments (Margni et al., 2004).

2.3.3. Product intake fractions

Like other compartments, all human intake compartments occur as columns and rows in the matrices of Eq. (2). For the matrix column representing a scenario-specific compartment of entry, elements of $\mathbf{TF}^{\text{cum}}$ corresponding to cumulative fractions transferred to human 'respiratory tract', 'gastrointestinal tract', and 'epidermis' provide product intake fractions, PiF, via inhalation, ingestion, and dermal uptake, respectively (Fig. 3b). Each PiF is the sum of all direct (first-level) and indirect (up to n^{th}-level) transfers in Eq. (2) contributing to the exposure pathway from a compartment of entry to a specific human intake compartment. Different scenarios can finally be compared based on PiFs

(a) direct transfer fractions

transfer receiving compartments	near-field: skin surface layer	near-field: article interior	near-field: indoor air	far-field: wastewater treatment plant	far-field: ambient air	far-field: freshwater	far-field: soil
skin surface layer	0	0	0	0	0	0	0
article interior	0	0	0	0	0	0	0
indoor air	2.97E-01	3.64E-01	0	0	0	0	0
wastewater treatment plant	5.00E-01	0	0	0	0	0	0
ambient air	0	0	9.95E-01	0	0	5.12E-03	3.55E-02
freshwater	0	0	0	9.81E-01	1.07E-02	0	2.22E-01
soil	0	0	0	1.81E-02	1.61E-01	1.22E-03	0
respiratory tract users ≥5 yrs	0	0	4.76E-03	0	0	0	0
respiratory tract users <5 yrs	0	0	2.10E-04	0	0	0	0
respiratory tract population ≥5 yrs	0	0	0	0	1.03E-07	0	0
respiratory tract population <5 yrs	0	0	0	0	3.79E-09	0	0
GI tract population ≥5 yrs	0	0	0	0	0	8.27E-07	5.08E-05
GI tract population <5 yrs	0	0	0	0	0	1.39E-08	2.67E-06
epidermis users ≥5 yrs	2.03E-01	0	0	0	0	0	0
epidermis users <5 yrs	0	6.90E-06	0	0	0	0	0

(b) cumulative transfer fractions / product intake fractions

transfer receiving compartments	near-field: skin surface layer	near-field: article interior	near-field: indoor air	far-field: wastewater treatment plant	far-field: ambient air	far-field: freshwater	far-field: soil
skin surface layer	1	0	0	0	0	0	0
article interior	0	1	0	0	0	0	0
indoor air	2.97E-01	3.64E-01	1	0	0	0	0
wastewater treatment plant	5.00E-01	0	0	1	0	0	0
ambient air	3.00E-01	3.64E-01	1.00E+00	5.76E-03	1	5.19E-03	3.68E-02
freshwater	5.07E-01	1.69E-02	4.65E-02	9.86E-01	4.67E-02	1	2.24E-01
soil	5.79E-02	5.85E-02	1.61E-01	2.02E-02	1.62E-01	2.06E-03	1
respiratory tract users ≥5 yrs	1.41E-03	1.73E-03	4.76E-03	0	0	0	0
respiratory tract users <5 yrs	6.23E-05	7.63E-05	2.10E-04	0	0	0	0
respiratory tract population ≥5 yrs	3.09E-08	3.75E-08	1.03E-07	5.93E-10	1.04E-07	5.35E-10	3.79E-09
respiratory tract population <5 yrs	1.14E-09	1.38E-09	3.79E-09	2.18E-11	3.81E-09	1.97E-11	1.39E-10
GI tract population ≥5 yrs	3.36E-06	2.99E-06	8.22E-06	1.84E-06	8.26E-06	9.32E-07	5.13E-05
GI tract population <5 yrs	1.62E-07	1.56E-07	4.30E-07	6.77E-08	4.32E-07	1.94E-08	2.69E-06
epidermis users ≥5 yrs	2.03E-01	0	0	0	0	0	0
epidermis users <5 yrs	0	6.90E-06	0	0	0	0	0

↑ hand cream 4 min. scenario (skin surface layer column) ↑ wood flooring 50 days scenario (article interior column)

Fig. 3. Matrix of direct transfer fractions (a) and matrix of cumulative transfer fractions (b) for phenoxyethanol in hand cream used for 4 min (left-most column in both matrices) and in wood flooring used over 50 days (second left-most column in both matrices). Columns for human intake compartments are not shown as all related elements are zero.

across the various exposure pathways for different compartments of entry as all other matrix columns are scenario-independent.

2.4. Intake per functional unit and daily intake dose

Combining as shown in Eq. (1) the chemical mass in the compartment of entry with the corresponding PiFs (extracted as a column vector from the $\mathbf{TF}^{cum}$ matrix) is the basis for finally yielding intake per functional unit or chemical functional use, and daily intake doses per kg body-weight and day (Fig. 1c). One interest of the proposed framework is to offer the possibility to bridge the LCIA and CAA emitter and risk assessment receptor perspectives by differentiating receptors like adult and child product users exposed in the near-field environment during product use and the general population exposed via far-field emissions.

2.5. Illustration of PiF framework for chemicals in hand cream and flooring

We illustrate the PiF Framework by applying it to evaluate chemicals used in two products. We model phenoxyethanol (CAS 122-99-6), used as preservative and solvent in hand cream (cosmetic product) and as an adhesive in wood flooring (building material). For hand cream, we also evaluate exposure to methyl paraben (CAS 99-76-3), and compare to phenoxyethanol considering 4 min and 3 h of dermal contact as exposure durations. For wood flooring, we also evaluate exposure to dibutyl phthalate (CAS 84-74-2) and compare to phenoxyethanol considering product use durations of 50 days and 15 years. These chemical-product combinations were chosen to demonstrate the framework for two entirely different products that contain the same chemical, and for two chemicals in the same product with different properties and thus with distinct fate and exposure behaviors. We selected two example product use durations to further demonstrate the capability and flexibility of the framework to assess differences related to product use patterns.

2.5.1. Initial chemical mass

Chemical inventory mass in product, $m_{0,j}$ [mg], is obtained as $m_{0,j} = f_{c,p} \times M_{0,p}$ with defining compartment of entry $j =$ 'skin surface layer' for hand cream as product applied by adult users and $j =$ 'article interior' for wood flooring as product, and with $m_{0,j} = 0$ for all other compartments; $f_{c,p}$ [mg/mg] as chemical mass fraction in the product, and $M_{0,p}$ [mg] as initial product used (hand cream) or installed (flooring).

2.5.2. Direct transfer fractions

The matrix of direct transfer fractions is populated from two sets of underlying mass balance models. The first set of models describes transfer fractions from the compartment of entry for each product to other receiving compartments. For chemicals in hand cream scenarios the 'skin surface layer' is the compartment of entry and dynamic mass balance-based models are used to consistently determine volatilization to indoor air, absorption by the human epidermis, and fraction washed-off to the Waste Water Treatment Plant (WWTP). For chemicals in flooring scenarios the 'article interior' is the compartment of entry and a two exponentials model is used to estimate volatilization to indoor air, dermal contact of child users, and transfer to landfill after 15 years. The second set of models describes direct transfer fractions from all other transfer source compartments common to all chemical-product-exposure duration combinations. All models customized to calculate scenario-specific and scenario-independent transfer fractions along with physicochemical substance properties, product characteristics, and transfer fractions are summarized in the Supplementary information (SI, Section S-1).

3. Results

The PiF Framework allows for contrasting chemicals with their specific physicochemical properties, exposure pathways, affected population groups, and chemical-product-application combinations. The

following section presents the chemical mass applied, transfer fractions, PiFs and exposures for the two chosen products.

3.1. Exposure to phenoxyethanol in hand cream and flooring

3.1.1. Scenarios definition and mass of phenoxyethanol applied

For hand cream, we based the calculation on a user applying 400 mg product daily and a phenoxyethanol mass fraction (w/w) of 0.0086, leading to an application of 3.4 mg/person/d. For wood flooring, we used a weight of 12 kg flooring per m^2 and a phenoxyethanol mass fraction of 300 ppm, leading to a chemical mass of 3600 mg/m^2. Per household, an area of 113.6 m^2 was used by an average of 2.6 persons. Both scenarios are further detailed in SI (Table S1).

3.1.2. Matrix of direct transfer fractions

Fig. 3a shows the matrix of direct transfer fractions resulting from combining various underlying transfer fraction models. Direct transfer fractions from all source compartments (matrix columns) – except the compartment of entry – to receiving compartments (matrix rows) are derived only once and remain the same across chemical-product use scenarios (i.e. hand cream and flooring) for the same chemical. This allows convenient comparison between the two phenoxyethanol scenarios in Fig. 3a in a single matrix, where only transfer fractions associated with the compartment of entry are scenario-specific and need to be estimated separately. 'Skin surface layer' (left-most matrix column) and 'article interior' (second left-most column) were defined as compartments of entry for hand cream and flooring scenarios, respectively. Zeros in this matrix indicate that no transfer fraction was estimated, which also includes the two top-most rows for the compartment of entry as no interaction is assumed between the considered scenarios.

The left-most column of Fig. 3a reflects direct transfer fractions for phenoxyethanol applied via hand cream, which after a short exposure duration of for example 4 min leads to fractions of 30% emitted to indoor air, 20% absorbed into skin epidermis (SI, Table S1), and leaving 50% washed off and further transferred to WWTP. Considering a longer exposure duration, before the hand cream is washed off, of for example 3 h, would lead to fractions of 41% directly absorbed into skin epidermis, almost 59% emitted to indoor air, and only 0.003% transferred to WWTP (SI, Fig. S1). This underlines the importance of considering the exposure duration before wash-off in the underlying transfer fraction models. Subsequent columns in Fig. 3a describe 'indoor air', 'WWTP', and the different outdoor compartments, and contain the direct transfer fractions from these compartments that ultimately further influence exposure. As an example, we find that of the fraction of 30% emitted to indoor air, 0.48% are further transferred to users via inhalation, while >99% are further transferred to ambient air, where the general population is marginally exposed via inhalation.

For phenoxyethanol used in wood flooring ('article interior') over 50 days, the second left-most column of Fig. 3a shows that a fraction of 36% is emitted to indoor air, while only 0.0007% are transferred directly to epidermis of children crawling on the floor (SI, Table S1), considering the average number of persons ≥5 years of age and children <5 years of age per household (US-EPA, 2011). This leaves a fraction of 63.7% remaining in flooring material. All transfer fractions for a given column compartment plus the removal, e.g. via degradation, plus the chemical mass fraction left in the compartment after a certain exposure duration sum up to unity. Looking at phenoxyethanol in flooring over 15 years, >99% are emitted to indoor air, while <0.002% are transferred to epidermis (SI, Fig. S1). Additional or other pathways may be important for specific product application scenarios like hand-to-mouth dust ingestion (Weschler et al., 2008), mouthing of children toys (Bouma and Schakel, 2002), or exposure to chemicals migrating into food (Poças and Hogg, 2007). To address such transfers and pathways, the present framework allows to flexibly including the corresponding transfer fractions from the relevant models, e.g. in case of hand-to-mouth dust ingestion a dust compartment could be added

along with models for estimating air-to-dust, dust-to-hand, and hand-to-mouth transfers.

Overall, this first matrix facilitates a consistent comparison of direct transfer fractions across scenarios, where for each column compartment, the total of all transfers plus losses within this compartment and the fraction of chemical remaining in that compartment at the considered exposure duration add up to 100%.

3.1.3. Matrix of cumulative transfer fractions

Cumulative transfer fractions for both scenarios of phenoxyethanol in hand cream and wood flooring are shown in the second matrix in Fig. 3b and are directly obtained from inverting the matrix that is the result of subtracting the matrix of direct transfer fractions from the identity matrix in Eq. (2). In this resulting matrix of cumulative transfer fractions, each column provides the cumulative transfers from a transfer source compartment to all relevant receiving compartments. Values of ones on the main diagonal of Fig. 3b (matrix elements where source and receiving compartment are the same) indicate an initial 100% mass in each column source compartment that can be transferred or otherwise removed.

The left-most column in Fig. 3b illustrates for phenoxyethanol applied via hand cream that an overall amount of 51% is ultimately transferred to freshwater following (a) the fraction of 50% directly washed off to WWTP and subsequent transfer to freshwater, and (b) emission to indoor air and subsequent transfer to outdoor air via ventilation and further to freshwater via deposition. This cumulative transfer fraction to freshwater also includes a small fraction of phenoxyethanol in freshwater that is volatilized into ambient air and irrigated on soil, from which respectively a minor fraction is transferred back to freshwater. The sum of cumulative transfer fractions per column source compartment usually exceeds 100%, since the same chemical mass can be transferred through several compartments before being eliminated from the modeled system. Looking at the wood flooring scenario, the second column of Fig. 3b shows that the 36% of phenoxyethanol directly emitted to indoor air after 50 days (Fig. 3a) are leading to cumulative transfer fractions of 5.9% to soil and 1.7% to freshwater via ventilation from indoor to ambient air and subsequent deposition.

3.1.4. Product intake fractions

The total exposure is captured by the bottom eight rows of the matrix of cumulative transfer fractions in Fig. 3b, as these provide human receptor-specific product intake fractions, thereby enabling direct comparison of PiFs for different considered populations and exposure pathways for each scenario. For phenoxyethanol in hand cream (left-most column), dermal uptake into epidermis of users constitutes the main exposure pathway from direct dermal contact with a PiF of 0.2 mg intake per mg of phenoxyethanol in hand cream (i.e. 20%, Fig. 3a, row 'epidermis users ≥5 years'). The second highest exposure for users is via inhalation with a PiF of 0.14% (mediated by 30% emission to indoor air and a related 0.5% indoor inhalation intake fraction from 'indoor air' to 'respiratory tract'), while environmentally-mediated ingestion exposure is marginal. In contrast, for children living in a household with product users but not applying hand cream themselves, inhalation exposure dominates with a PiF of 0.006%, i.e. 6×10^{-5} mg inhaled per mg in hand cream. PiF values increase for all persons in the household by about a factor of two across exposure pathways when assuming longer exposure duration of 3 h hand cream leave-on time with the highest PiF of 41% for users from direct dermal contact. Post-use emissions decrease as observed by lesser transfers to the WWTP from the compartment of entry.

The matrix also helps analyze the scenario of phenoxyethanol in wood flooring used over 50 days (second left-most column in Fig. 3b). The highest exposure for all household persons is via inhalation. Extending the product use duration and assessed exposure from 50 days to 15 years only increases PiF for phenoxyethanol in flooring by about a factor of two (SI, Table S1). The PiF Framework helps to quantitatively evaluate and easily visually compare the importance of different near-

field and far-field compartment transfers and population-specific exposure pathways.

3.1.5. Human exposure

Multiplying the considered mass of phenoxyethanol applied via one application of hand cream in 1 day by the respective PiF yields intake, i.e. 0.005 mg intake over 4 min and 0.01 mg intake over 3 h. For flooring, the framework estimates for 1 m^2 wood flooring installed an inhalation intake of 6.5 mg over 50 days, which only increases up to 18 mg over 15 years. When comparing exposure to the same chemical in two functionally distinct products, the contribution to daily intake doses can be a more meaningful metric than the total mass taken in (which is more applicable to compare functionally equivalent products). Fig. 4e–f compares daily intake doses for phenoxyethanol and shows that children living in a household with flooring containing phenoxyethanol have the highest exposure via inhalation (0.28 mg/kg/d after 50 days). The average daily dose over 15 years is strongly reduced by a factor of 40, due to greater intake during the initial days of product use when
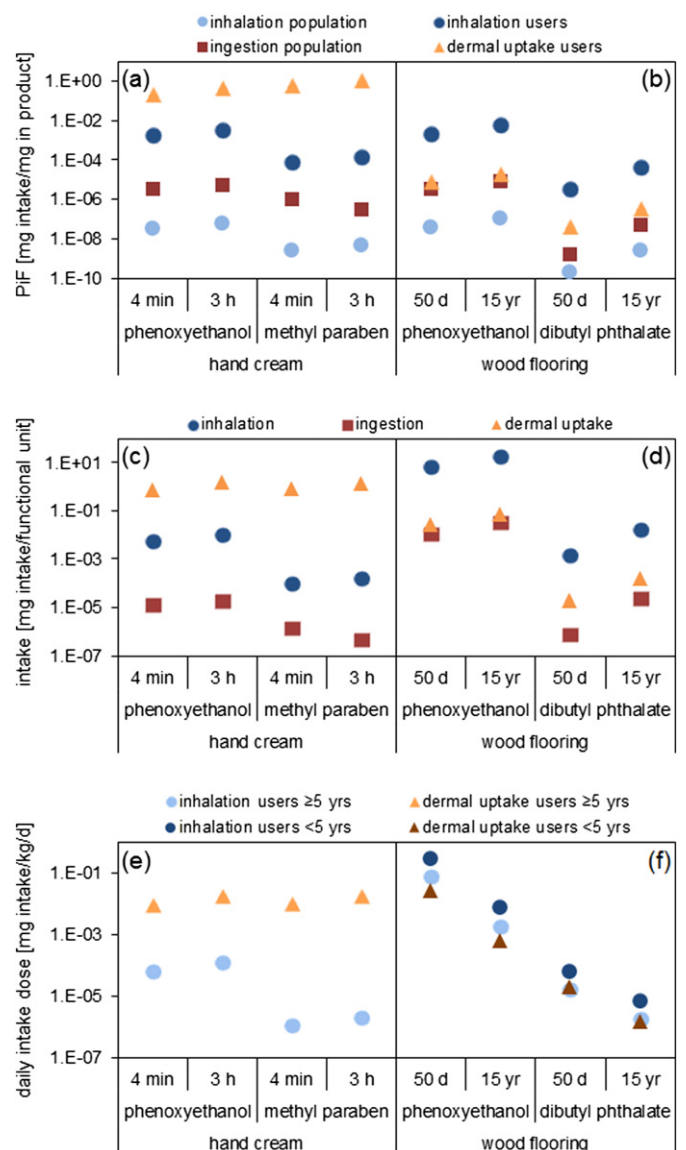

Fig. 4. Exposure route-specific product intake fractions, PiF (a–b), cumulative intake of users and the general population per functional unit of 1 hand cream application per day (c) and 1 m^2 wood flooring (d), and exposure route-specific daily intake dose for product users for phenoxyethanol and methyl paraben in hand cream used over 4 min and 3 h (e) and for phenoxyethanol and dibutyl phthalate used in wood flooring over 50 days and 15 years (assuming children crawling on the floor) (f).

chemical transfer is highest. Note that for such long exposure durations, the receptor properties (e.g. body weight) would need to be adjusted for population groups like children. The daily dose from a hand cream user is approximately a factor of 10 lower than exposure to phenoxyethanol through flooring during the first 50 days after installation. These results demonstrate that the PiF Framework can be used to easily contrast different product use scenarios and how they contribute to daily exposure for different age groups.

3.2. Exposure to different chemicals in hand cream and flooring

3.2.1. Chemical substitution in hand cream

Using the PiF Framework to evaluate chemicals that may be potential alternatives to each other in the same product application, we selected phenoxyethanol and methyl paraben used as preservatives in hand cream after 4 min and 3 h of dermal contact. Product intake fractions are given in Fig. 4a, and scenario-specific direct and cumulative transfer fractions are provided in the SI (Figs. S6–S9). For hand cream, the framework shows that dermal exposure dominates across scenarios as could be expected. Bringing transfer fraction models for near-field and far-field compartments consistently together, the PiF Framework also allows population exposure estimates from the cumulative transfer fraction of ~50% from hand cream via WWTP to freshwater (as discussed above) leading to potential population exposure via drinking water, and a cumulative transfer fraction of 30% via indoor to outdoor air leading to potential population exposure via inhalation. Compared with consumer exposure, chemical fractions originally in the product inhaled and ingested by the general population are orders of magnitude lower. Multiplying PiFs by the respective quantities applied per day (3.4 mg/d for phenoxyethanol, and 1.4 mg/d for methyl paraben), we obtain comparable intakes after 3 h of ~1.4 mg/d for both phenoxyethanol and methyl paraben (Fig. 4c). This means that for both CAA and LCIA, the respective impacts of these two substances in hand cream will directly reflect their relative difference in toxicity potentials and illustrates how the PiF Framework helps to quantitatively compare different chemicals in the same product use scenarios.

3.2.2. Chemicals with different functions in flooring

To contrast chemicals that can occur together in a certain product application but with different functions, we compare phenoxyethanol and dibutyl phthalate in wood flooring for 1 m² flooring applied over 15 years. The volatile organic chemical (VOC) phenoxyethanol leads to overall inhalation PiFs of a factor of ~150 higher than exposure to the semi-volatile organic chemical (SVOC) dibutyl phthalate in the same flooring (Fig. 4b). For dibutyl phthalate, 99% are still in the flooring when sent to landfill (SI, Fig. S4), whereas for phenoxyethanol almost 100% have been emitted to indoor air after 15 years (SI, Fig. S2) with a negligible release to landfill. The matrix-based PiF Framework enables to quickly and easily assess the ultimate impacts of how physicochemical properties of different chemicals mediate exposure over the considered exposure duration in the underlying transfer fraction models. Population exposure via ingestion following transfer to landfill and then transfer to freshwater could, however, potentially reach magnitudes close to inhalation and dermal exposure of users for more persistent and bioaccumulative chemicals. At the level of intake, the difference between chemicals is further amplified when multiplying the PiFs by a factor of 7.5 higher mass of phenoxyethanol (3600 mg/m²) versus dibutyl phthalate (480 mg/m²) based on their respective concentrations in flooring. Cumulative intake of phenoxyethanol is dominated by inhalation for users in the near-field (i.e. all persons in the household with flooring) with a cumulative daily intake dose of 0.3 mg/kg/d by children after 50 days (Fig. 4d, f). This exposure is orders of magnitude higher than for dibutyl phthalate after 50 days. For both chemicals, average daily exposure is higher during the first 50 days of use compared to average daily exposures over 15 years (see Fig. 4f) as the emission rate declines over time. Fig. 4 highlights the strength of

our framework to assess how chemicals with different physicochemical properties and specific product applications influence exposure patterns of different population groups across pathways.

4. Discussion

4.1. Application in different science-policy fields

The PiF Framework was designed to consistently and transparently account for human exposure to chemicals in products via different pathway ensuring mass balance across pathways. Exposure originates from a product's compartment of entry and multiple transfers between near-field, far-field and human intake compartments are accounted for and combined in the transfer fraction matrices. The PiF Framework enables to integrate in a linear system transfer fractions that account for non-linear or dynamic phenomena as captured by the underlying models. Additional intermedia transfers or human receptor populations can be included by easily extending and flexibly populating the framework, whenever additional models become relevant or available, or when existing models are updated e.g. for addressing hand-to-mouth exposure, or to better account for concentration gradients indoors. When updates are made to a product use scenario, only the respective elements of the matrix of direct transfer fractions need to be adapted without having to change other inter-compartment transfer fractions, as the matrix is populated with direct transfer fractions between adjacent or nested compartments only. This also holds true when using the matrix to evaluate various products, where only the compartment of entry-related transfer fractions for the product must be specified, while all other matrix elements remain valid. The matrix approach is thus internally consistent, builds on comparative and compatible metrics, and is flexible in its application to the multitude of diverse chemicals, products, intermedia transfers, exposure pathways, and population groups. Existing exposure assessment frameworks cover a variety of goals, e.g. focusing on exposure to consumer products (Dudzina et al., 2015; Isaacs et al., 2014; Safford et al., 2015), or exposure through the environment (Ciffroy et al., 2016; Sarigiannis et al., 2014), or both, however, in a decoupled way (Delmaar et al., 2013). Thereby, exposure to chemicals in a product via the environment is not easily comparable. The present approach offers a unique solution, namely that consumer product exposure and exposure via environmental media (resulting from emissions via consumer product production, use, and disposal) are finally combined in a single comparative framework that can flexibly and consistently be updated for various chemical-product combinations and with various underlying models of different complexity. While the present framework itself does not evaluate stochastic distributions, it can easily be populated with stochastic or dynamic results of underlying models to capture relevant variabilities. The flexibility of the PiF Framework is therefore not only mathematically convenient but can be adapted in different science-policy fields and assessment approaches.

4.1.1. Life cycle impact assessment (LCIA)

The PiF Framework is specifically applicable in an LCIA context, where other exposure models (Chevillotte et al., 2014; Comiskey et al., 2015; Delmaar et al., 2015; Dudzina et al., 2015; Egeghy et al., 2011; Isaacs et al., 2014; Safford et al., 2015) would be more difficult to adapt to the specific assumptions. One main reason for this is the product-centric focus of the framework, where the mass allocated to the compartment of entry for a product can easily be scaled to the functional use of a product. Current LCIA multi-compartment models start from first-order transfer rate constants (Rosenbaum et al., 2008), but are currently restricted to transfers resulting from emissions, and not product releases, and thus estimate exposure as emission-based intake fractions. Using PiF as exposure metric, which is compatible with intake fractions, allows for easily extending existing multimedia models to also include exposures originating from consumer products. PiFs can be further

linked to toxicity effect factors as available in LCIA methods to yield characterization factors normalized per chemical mass in product instead of chemical mass emitted. This way, the PiF Framework can be fully embedded in the life cycle assessment approach estimating exposure and subsequent potential human health impacts based on the functional unit of an assessment.

4.1.2. Chemical alternatives assessment (CAA)

Optimized for a flexible and rapid screening of chemicals in products, the PiF Framework is well-suited to inform CAA aiming to minimize human exposure to hazardous substances. Current CAA frameworks usually lack quantitative exposure estimates (Jacobs et al., 2016), and fail to integrate consumer with population exposures although acknowledged as being important (NRC, 2014). Providing an easily interpretable quantitative framework can improve the consistency of CAA approaches for alternative substances used in the same product, especially when their physicochemical properties or initial concentrations result in different exposure magnitudes. When combined with chemical toxicity information, the PiF Framework provides the exposure estimates needed to help inform decisions aiming to protect humans from exposure to hazardous chemicals. With this, the PiF Framework helps move away from assuming equal exposure and just looking at hazard, which will in several cases yield misleading conclusions.

4.1.3. Risk-based assessment and high-throughput screening

Consumer exposure and exposure from environmental emissions are both part of risk assessment and PiF brings both aspects together in a single comparative metric as shown for exposure to methyl paraben during the combined use of personal care products, where exposure estimates compared well to empirical biomarkers (Csiszar et al., 2016). The PiF Framework provides the platform to assess various product-chemical combinations and to consistently account and compare across transfers, exposure pathways, and exposed populations, and can also be used to estimate aggregate exposure to one chemical in multiple products. To use the PiF Framework within risk-based contexts, selecting an appropriate exposure time frame is crucial to ensure that daily exposure estimates are not under-estimated. Using flooring as an example, daily exposure was demonstrated to be higher during the first 50 days than over 15 years due to emission rates declining over time (Fig. 4f). Furthermore, when applying PiF in risk-based screening assessments, resulting intakes should be differentiated between individuals (in contrast to LCIA, in which exposure is usually summed up over all exposed individuals), such that daily intake doses can be directly compared to bioactive or toxic doses to arrive at risk metrics. Exposure and bioactivity have been compared in risk-based screening for example with respect to bioactive doses, e.g. oral equivalency dose calculated from in vitro bioactivity assays (Wetmore et al., 2015; Wetmore et al., 2012), to derive a bioactivity quotient (Shin et al., 2015), or to estimate cancer or non-cancer risks by comparing estimated intakes to dose-response levels. HTS assessments often screen many chemicals in a multitude of products. With its flexible matrix structure and instantaneous calculation through matrix inversion, the PiF Framework is well-suited as a HTS approach for multiple chemical-product combinations and maintains mass balance principles across all near- and far-field transfers and pathways, which has not yet been demonstrated in existing HTS models (Isaacs et al., 2014; Shin et al., 2015). Where possible, the PiF-based exposure estimates and the individual transfer fraction models can be evaluated against monitoring or empirical data.

5. Limitations

A main limitation of the PiF Framework and other exposure assessment tools is the availability and accuracy of underlying data (e.g. chemical concentrations in products), and the accuracy of the models used to populate the matrix of direct transfer fractions. These models indicated

that the most sensitive parameters affecting exposure will be specific to each chemical-product combination. For example, for cosmetics applied to human skin, exposure duration can be the most sensitive parameter on short time scales for chemicals with high estimated skin permeation coefficients (due to high Kow and low molar mass), where in contrast, for chemicals with low estimated skin permeation coefficients (due to low Kow and high molar mass) the thickness of the applied cosmetic product is a sensitive parameter due to diffusion-limited transport (Ernstoff et al., 2016). In contrast, for chemicals in flooring materials, diffusivity and material-air partition coefficient together with the chemical concentration in the flooring material are the main drivers of the amount volatilized to air and subsequently inhaled by humans (Huang and Jolliet, 2016). These findings stress the importance of obtaining accurate physicochemical properties used in model estimations. Several limitations of the mathematical basis of the PiF Framework have also to be underlined and have different implications depending on the goal of an assessment. First, user input is required to populate the matrix and the framework itself does not mathematically account for continuous dynamics or changes in transfer rates through time. If multiple exposure durations are to be assessed, the direct transfer fractions from the compartment of entry (e.g. for transfer from 'skin surface layer' into 'epidermis' and to 'WWTP' for cosmetics) must be recalculated by the various underlying transfer fractions models to re-populate the matrix. Second, the proposed framework is primarily product- or emitter-oriented, instead of person- or receptor-oriented as first-order transfer fractions are generally product-specific. Thus, our matrix system can currently evaluate only one (type of) product in a particular application at a time. This product-oriented perspective is well-suited to quantify product-related exposure in LCIA, inform CAA to compare alternative scenarios for chemicals in specific product applications, and support the comparison of multiple chemicals in HTS contexts. However, to inform risk assessment, where the goal is to estimate exposure to chemicals of concern through all sources of exposure (e.g. all products, and emissions to the environment from industrial sources), the matrix system would need to be run and results stored for all relevant product-application scenarios and for the relevant exposed receptor populations. When considering various chemical-product combinations, related transfer fractions could be stored in a multi-dimensional array, which can be programmed to solve multiple matrix-based solutions. Results could subsequently be aggregated or compared to exposure to one or various chemicals occurring in multiple products. Although we have illustrated the framework for compartments of entry for consumer products based on PiF, the same approach and matrix system can be used for industrial sources with compartments of entry being in the far-field environment.

6. Conclusions and future research needs

Cumulative multimedia transfers and product intake fractions for different population groups and exposure pathways are efficiently summarized in a single matrix, which constitutes a user-friendly approach to develop, evaluate and interpret multiple chemical-product-application scenarios for human exposure. This framework is an important step toward consistently coupling exposure pathways to chemicals in consumer products in the near- and far-field environments in a quantitative way to inform various science-policy fields. To fully integrate near-field exposure in life cycle assessment studies, however, a full operationalization in existing platforms is required to disseminate the PiF Framework to practitioners. Furthermore, life cycle inventory databases will have to be extended to also provide information on chemical mass applied via the various consumer products in addition to providing information at the level of emissions into the (far-field) environment. More generally and especially relevant for CAA, whenever such data are not available (which might be the case for a large share of existing chemical-product combinations), estimation approaches will

be necessary to derive chemical fractions in consumer products for specific in-product functions. Transfer fraction models also need to be supplemented by methods estimating relevant physicochemical properties particularly for new or not yet marketed chemicals that are considered as potential alternatives to widely used harmful substances, but for which various measured properties are often missing (Fantke et al., 2015). Finally, the development of transfer fraction models for all relevant multimedia and cross-environment transfer and exposure pathways will be required, which also covers pathways for which no useful models could be identified yet. This might also require defining and introducing new compartments of entry, for which we consider the modular PiF Framework a suitable and flexible starting point.

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Appendix A. Supplementary data

Background material for the illustrative product use scenarios can be found online at http://dx.doi.org/10.1016/j.envint.2016.06.010.

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