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Life cycle based alternatives assessment (LCAA) for chemical substitution†

Peter Fantke, *[a] Lei Huang, [b] Michael Overcash,[c,d] Evan Griffing[c] and Olivier Jolliet [b]

The world faces an increasing need to phase out harmful chemicals and design sustainable alternatives across various consumer products and industrial applications. Alternatives assessment is an emerging field with focus on identifying viable solutions to substitute harmful chemicals. However, current methods fail to consider trade-offs from human and ecosystem exposures, and from impacts associated with chemical supply chains and product life cycles. To close this gap, we propose a life cycle based alternatives assessment (LCAA) framework for consistently integrating quantitative exposure and life cycle impact performance in the substitution process. We start with a pre-screening based on function-related decision rules, followed by three progressive tiers from (1) rapid risk screening of various alternatives for the consumer use stage, to (2) an assessment of chemical supply chain impacts for selected alternatives with substantially different synthesis routes, and (3) an assessment of product life cycle impacts for alternatives with substantially different product life cycles. Each tier focuses on relevant impacts and uses streamlined assessment methods. While the initial risk screening will be sufficient for evaluating chemicals with similar supply chains, each additional tier helps further restricting the number of viable solutions, while avoiding unacceptable trade-offs. We test our LCAA framework in a proof-of-concept case study for identifying suitable alternatives to a harmful plasticizer in household flooring. Results show that the use stage dominates human health impacts across alternatives, supporting that a rapid risk screening is sufficient unless very different supply chains or a broader set of alternative materials or technologies are considered. Combined with currently used indicators for technical and economic performance, our LCAA framework is suitable for informing function-based substitution at the level of chemicals, materials and product applications to foster green and sustainable chemistry solutions.

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Introduction

Background

In a world of rapidly growing consumption of resources, diversity in consumer goods, and production quantities across economic sectors, we face an increasing pressure on essential biological, geochemical and hydrological systems that are relevant to sustain our current and future societies.[1,2] To meet national and international sustainable development goals (SDGs), reducing the use of harmful chemicals in consumer products and production processes along with managing chemical pollution is pivotal.[3–5]

The emerging and solutions-oriented field of Chemical Alternatives Assessment is well-suited to inform product design as well as to phase out and substitute hazardous chemicals by identifying and evaluating viable alternatives in various product applications. However, current frameworks suffer from inconsistencies in data and models applied, from relying on qualitative or semi-quantitative indicators, and from the lack of effectively and efficiently addressing exposure and life cycle impacts.[4,6–10] More specifically, quantifying exposure to chemicals in consumer products, and evaluating life cycle impacts associated with for example climate change, human and ecosystem toxicity, and water resources use, are commonly considered too complex and time-consuming.[11,12]

History shows that ignoring the quantification of the various exposures and life cycle impacts may leave important trade-offs and problem-shifting unaddressed and can thus lead to *regrettable substitutions*.[4,13] An example for problem-shifting is the substitution of antiknock agents in gasoline to

[a]*Quantitative Sustainability Assessment, Department of Technology, Management and Economics, Technical University of Denmark, Produktionstorvet 424, 2800 Kgs. Lyngby, Denmark. E-mail: pefan@dtu.dk; Fax: +45 45933435; Tel: +45 45254452*
[b]*Environmental Health Sciences, University of Michigan, 1415 Washington Heights, Ann Arbor, MI 48109-2029, USA*
[c]*Environmental Clarity, Inc., 2505 Fauquier Lane, Reston, VA, 20191, USA*
[d]*Environmental Genome Initiative, 2908 Chipmunk Lane, Raleigh, NC, 27607, USA*
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increase fuel compression ratios, where tetraethyl lead showing high neurotoxicity potential was replaced by methyl *tert*-butyl ether contaminating groundwater due to high water solubility—in this case, the problem is shifted from human toxicity to groundwater pollution.[14] Another popular problem-shifting example is the substitution of pesticide active ingredients in agricultural seed coating formulations to control insects like flea beetles damaging oilseed and other crops, where the organochlorine insecticide γ-hexachlorocyclohexane being toxic and potentially carcinogenic to humans was replaced by the neonicotinoid imidacloprid that has been linked to colony losses of pollinating insects.[15]

These and other examples highlight the urgent need to complement currently considered aspects by a more quantitative yet rapid substitution approach that includes relevant exposures and life cycle impacts.[13] How can such a quantification of exposure and life cycle impacts be consistently and efficiently included in the current substitution process? We seek to answer this question, and propose a roadmap for effectively integrating the quantitative assessment of exposure and life cycle impacts in Chemical Alternatives Assessment based on the following specific objectives: (a) to identify the key elements required for addressing multiple exposures and life cycle impacts, (b) to propose a tiered Life Cycle based Alternatives Assessment (LCAA) approach for quantitative screening of alternatives, and (c) to test the proposed approach in a proof-of-concept case study of plasticizers in vinyl flooring.

Chemical and product life cycles

The scope of an assessment is defined by the environmental and health implications of a chemical of interest and potential alternative(s) in a given product application. This requires taking a life cycle perspective of the chemical in its specific application context.[16] Both chemical of interest and the related product come with their own life cycles. Fig. 1 illustrates how these life cycles are interconnected, with multiple chemicals (and their distinct supply chains) being incorporated into the same product to fulfill different functions, such as plasticizers, pigments, fillers and stabilizers.

Chemical life cycles span the entire supply chain for harvesting resources, synthesizing, and processing a chemical, and related waste handling. Product life cycles do not only cover the considered and other chemicals included in the same product with their respective supply chains, but also include resources used and emissions related to energy converted during, for example, product manufacturing, product use, and product end-of-life handling (*e.g.* recycling). While life cycles are widely assessed at the level of product systems (*e.g.* in product Life Cycle Assessment[17]), chemical and product life cycles are not commonly considered in Chemical Alternatives Assessment. However, in many cases, it will be relevant to address the life cycle of the chemical of interest (and its alternatives) as well as the life cycle of the related product application, where amount of chemical in the product and the choice of alternatives are driven by the chemical function.[18]

Key requirements for addressing exposure and life cycle impacts

From analyzing current substitution practice and limitations summarized in recent reviews,[6,9,13,19] and state-of-the-art guidance documents,[20,21] we identify how the current substitution process can be structured and propose a framework to systematically address quantitative exposure and life cycle impacts. There are commonly three components assessed to identify, compare and select alternatives, namely chemical hazard, technical feasibility, and economic viability.[11,12] To consider potential trade-offs that might occur between costs or technical performance and exposure or risks for humans and ecosystems at the different life cycle stages of the given chemical-product combination, these components need to be complemented by assessing relevant exposures and life cycle impacts.[22] However, human exposure and a wider realm of impacts on humans and the environment in a life cycle perspective are usually not considered in substitution practice.[6,7,18] When addressed, indirect or qualitative exposure metrics are applied, such as dispersive potential or volume in commerce.[6,9] Such metrics are not well suited to analyzing trade-offs across chemicals with different properties, across exposure pathways of different populations (industry workers, product consumers or users, the general public) or across chemical and product life cycle stages (resources extraction, manufacturing, use, end-of-life treatment).[6,13,19] Hence, exposure should be systematically quantified in Chemical Alternatives Assessment, especially exposure in near-field environments, which refers to consumer exposure during product use and occupational exposure along chemical supply chains.[7,23–25] Occupational and consumer exposure estimates should be aligned with assessing far-field (*i.e.* environmentally-mediated) exposures considered in life cycle based assessments.[23,24] Exposure finally will have to be further aligned with considering additional impacts, such as climate change and water use, to uncover relevant trade-offs along supply chains of alternatives.

When extending chemical substitution by exposure and life cycle impacts, it should be considered that practitioners do not usually have the resources to conduct detailed quantitative assessments.[6,18] Thus, time- and resource-efficient approaches are needed, building on high-throughput methods to integrate enhanced exposure, hazard and life cycle data, and taking advantage of increasingly available big datasets for chemicals in consumer products.[6,7,10,18] Such approaches need to start from the chemical in-product function,[18] build on consistent mass balances,[23,25] include realistic product composition and use information,[26] consider competing fate and exposure processes and pathways,[27] use efficient data curation and extrapolation methods[28,29] as well as data analysis and visualization techniques.[30,31]

Finally, a single assessment level, where impacts are aggregated and where an overall score is calculated (as *e.g.* done in Life Cycle Assessment), is not appropriate. This is because

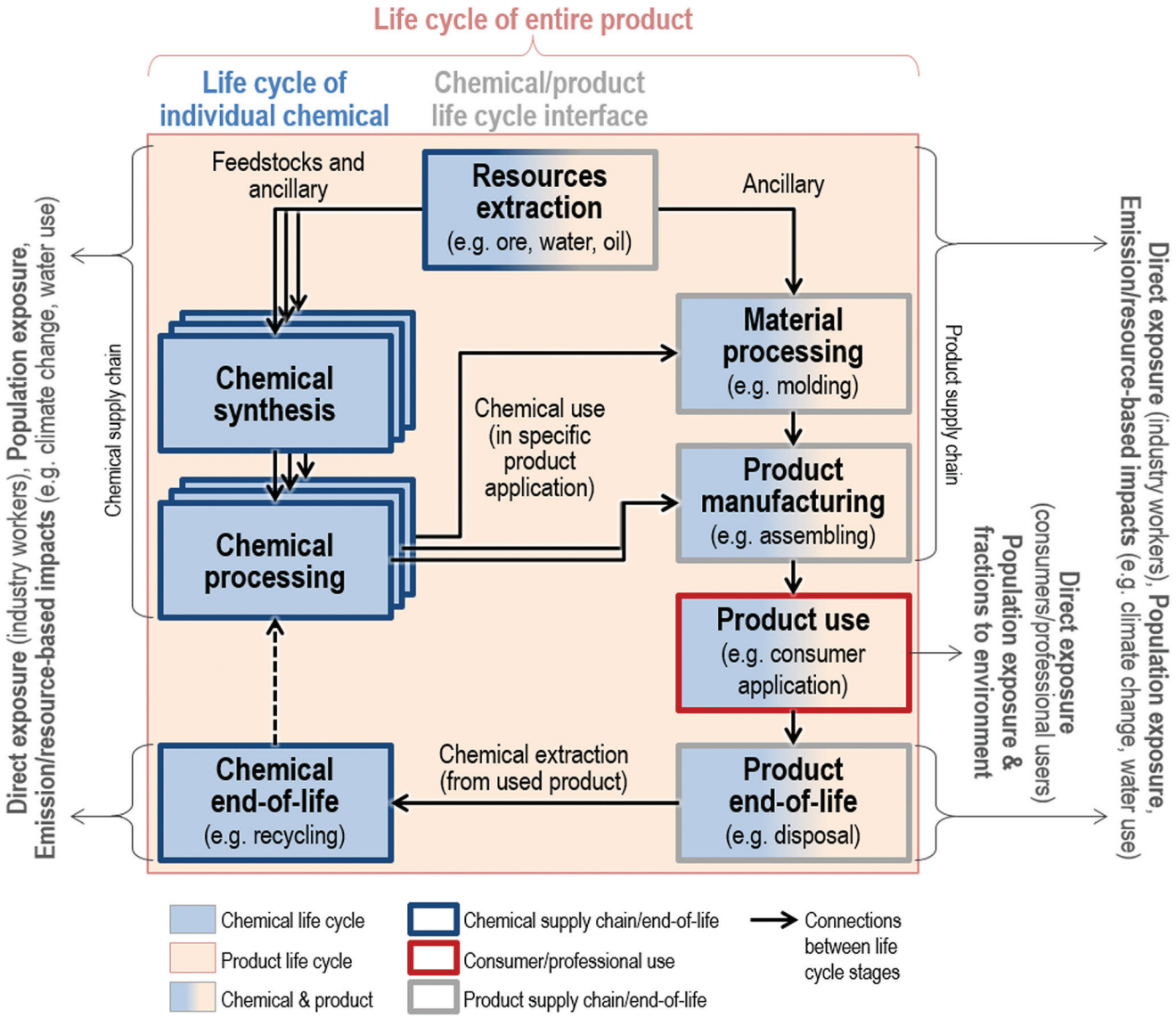

Fig. 1 Conceptual relationship between the life cycle of individual chemicals used in a specific product application and the related life cycle of the entire product as well as environmental impacts associated with different life cycle stages.

certain trade-offs are not acceptable when substituting harmful chemicals, such as optimizing energy-intensive processes at the expense of introducing a carcinogen. Hence, a tiered approach is required where first toxicity-related aspects during the product use stage are considered in a rapid screening assessment, before extending the scope to other life cycle stages and impacts where necessary.

Assessment framework

We propose a *Life Cycle based Alternatives Assessment* (LCAA) framework that consists of four different assessment steps (Fig. 2). We first identify relevant impact categories in cases where this is not known *a priori*, pre-screening the considered product to identify which chemical to target for substitution. Three tiers are then proposed with increasing coverage. Tier 1 focuses on toxicity impacts during the consumer use stage. It is a mandatory rapid risk screening step to screen out unacceptable candidates among a large set of possible alternatives. Tier 2 addresses the wider chemical supply chain as optional step to compare chemicals with substantial differences in their supply chains. Finally, Tier 3 covers the entire product life cycle as optional step to identify unacceptable trade-offs across substantially different life cycles of selected alternatives, with focus on the most important impact categories and those that are not correlated with chemical toxicity to cover a different, relevant dimension. Among possible impact categories, we propose to include climate change impacts (carbon footprint) and fine particulate matter ($PM_{2.5}$) impacts. Climate change is

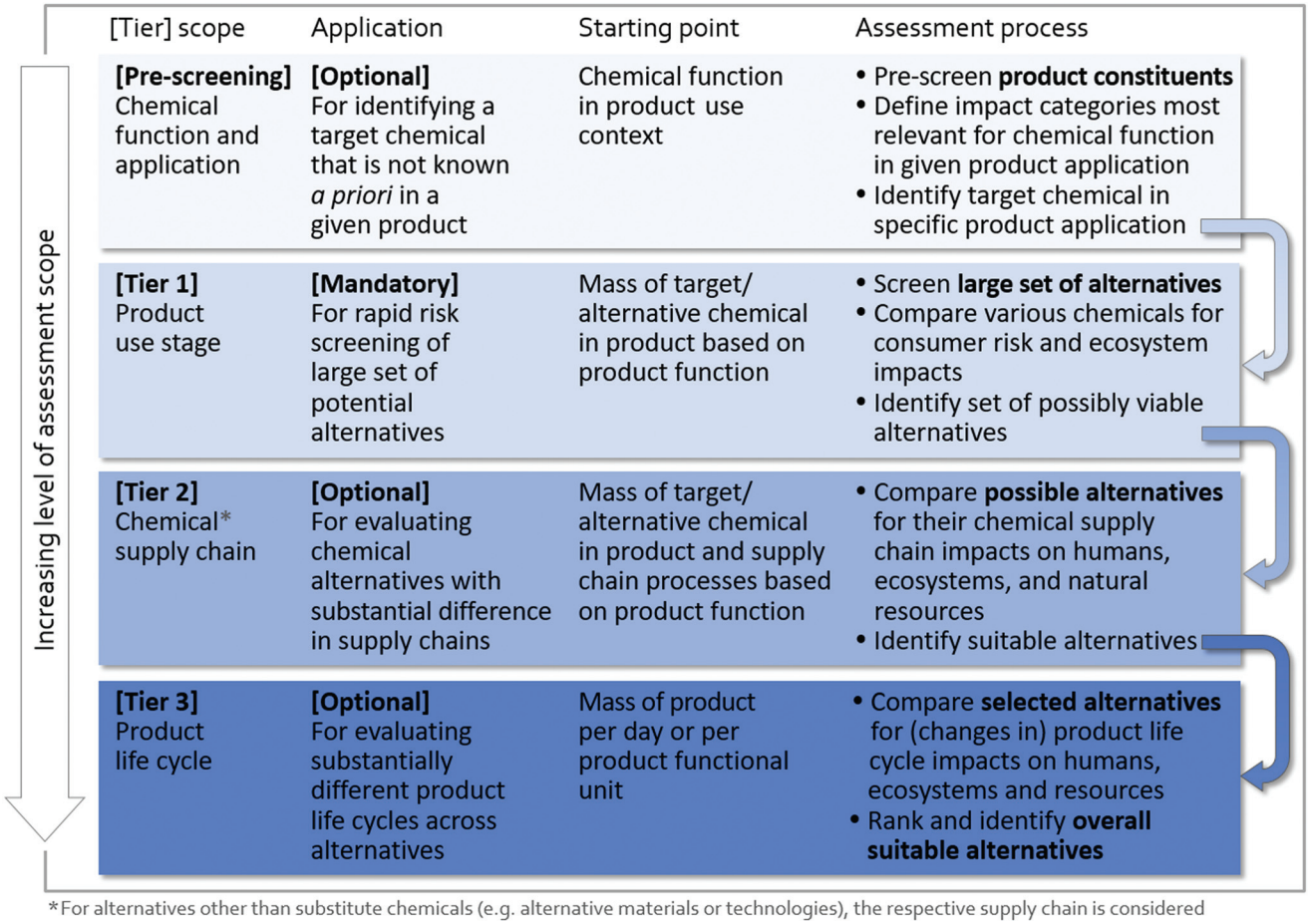

Fig. 2 Overview of the tiered Life Cycle based Alternatives Assessment (LCAA) framework to identify suitable alternatives for substituting hazardous chemicals in products and processes.

always included in product Life Cycle Assessments, and is a data-rich indicator that is strongly correlated with many other impacts but not with chemical toxicity, which makes it very complementary.[32] Exposure to $PM_{2.5}$ is the most important contributor to human disease burden according to the Global Burden of Disease study series[33] that is representative for outdoor emissions, whereas major exposures during consumer use are associated with indoor releases. Hence, these two impact categories complement our central focus areas, namely toxicity on humans and ecosystems.

To finally compare and rank suitable alternatives at any given assessment tier as input for substitution decisions, impact profiles of target chemical and alternatives can be presented at the level of detail required for the decision, from disaggregated detailed results for each chemical and life cycle stage, to single scores per focus area, such as human health, climate change and ecosystem quality.

Optional pre-screening and framing: identifying target chemicals

Starting from the chemical function in a given product application, we define relevant impact categories, instead of considering all possible impacts. We identify whether the chemical function requires bioactive chemicals (*e.g.* biocides, for which toxicity and ecotoxicity impacts are relevant) or a high product weight contribution (*e.g.* plasticizers, for which energy-related impacts are important). This is in line with suggestions to focus in the higher assessment Tiers 2 and 3 on respective major contributors to the variation in chemical supply chain and product life cycle impacts.[34]

These pre-screening considerations frame the overall scope of the subsequent assessment steps, where each of three tiers in Fig. 2 comes with a specific scope, set of elements, including assessment focus (*e.g.* human toxicity), metrics and methods used for impact characterization, and interpretation for the given decision context. An overview of the specific assessment elements for each tier is provided in Tables 1–3. The elements constitute an aligned set of quantitative and life cycle-based data, models, indicators, pathways and receptors that we propose to use in order to improve and extend the current scope and approach for addressing human and environmental impacts in Chemical Alternatives Assessment, using big data and tools already able to assess thousands of chemical-product combinations. To facilitate an efficient

Table 1 Focus areas and detailed elements of a Life Cycle based Alternatives Assessment (LCAA) for the Tier 1 assessment of direct impacts of target chemical and possible alternatives on user health and ecosystems

Scope level	Focus areas	Assessment elements[b]	Inventory analysis Chemical in product	Impact assessment: Fate and exposure	Impact assessment: Exposure-response	Impact assessment: Impact quantification	Interpretation and decision making
[Tier 1] Product-related chemical use[a]	Human toxicity related to consumer use stage	*Focus*	Determine chemical content in product	Determine relevant fate and exposure pathways and receptor populations	Determine relevant human health endpoints	Characterize cancer risk probability for carcinogenic effects and hazard quotients for non-carcinogenic effects	If needed, identify target chemical in given product application.
		Metric	Mass of chemical in product application	Product-based chemical intake fraction relating mass in product to user household intake using product type-specific models[23,24]	Cancer slope factor for carcinogenic effects; reference dose describing dose at which no appreciable health risks occur for non-carcinogenic effects	Disease incidence risk	Discuss, if target chemical is relevant for human toxicity, and screen large number of alternatives and identify suitable sub-set
		Method	$m_P = M_P \times wf_P$ wf_P is driven by chemical function, whereas m_P is selected to provide the same amount of product function across alternatives	$PiF_{u,x} = \frac{\sum_{e \in x} I_{u,e}^{\text{consumer}}}{m_P}$	Cancer: $CSF_x = \frac{0.5 \times f_a \times f_t}{\text{TD50}_{a,x}}$	Cancer: $R_{u,x} = D_{u,x} \times CSF_x$	*Criteria* Cancer: Is $R_{u,x}^{\text{alternative}} > R_{u,x}^{\text{target}}$? If yes, is $R_{u,x}^{\text{alternative}} < 10^{-6}$? If yes, still OK.
				$D_{u,x} = \frac{m_P \times PiF_{u,x}}{N_u \times BW_u}$	Non-cancer: $RfD_x = \frac{POD_x}{\prod_i UF_i}$	Non-cancer: $HQ_{u,x} = \frac{D_{u,x}}{RfD_x}$	Non-cancer: Is $HQ_{u,x}^{\text{alternative}} < 1$? If yes, OK.
	Ecotoxicity related to consumer use stage	*Focus*	Determine chemical content in product	Determine relevant fate pathways and receptor ecosystems	Determine relevant ecosystem endpoints and ecological species	Characterize ecotoxicity impacts	Discuss, if target chemical is relevant for ecotoxicity, and screen large number of alternatives and identify suitable sub-set
		Metric	Mass of chemical in product application	Cumulative increase in bioavailable chemical environmental concentration	Effect factor relating chemical hazard concentration to affected fraction of ecological species[37]	Impact score for exposed ecosystems	*Criteria*
		Method	$m_P = M_P \times wf_P$	$FF_{P \to r} = \frac{TF_{P \to r}^{\text{cum}}}{k_r^{\text{loss}}} \times XF_r$	$EF_r = \frac{0.2}{\text{HC20}_r^{\text{EC10}}}$	$ETS = m_P \times \sum_r FF_{P \to r} \times EF_r$	Is $ETS^{\text{alternative}} < ETS^{\text{target}}$? If yes, OK.

[a] Includes consumer use (*e.g.* use of detergents in private households) or professional use (*e.g.* use of detergents by facility cleaning company). [b] m_P: mass of target or alternative chemical (for pre-screening: mass of product constituents) in product application P [$mg_{\text{in product}}$ per d]; M_P: mass of product application P [mg_{product} per d]; wf_P: chemical weight fraction in product application P [$mg_{\text{in product}}$ per mg_{product}]; $PiF_{u,x}$: product intake fraction for user group u (*e.g.* children) *via* exposure route x (*e.g.* ingestion) [mg_{intake} per d per $mg_{\text{in product}}$ per d];[24] $I_{u,e}^{\text{consumer}}$: intake of chemical by user group u *via* exposure pathway e (*e.g.* drinking water ingestion) that belongs to exposure route x [mg_{intake} per d]; CSF_x: cancer slope factor [1/(mg_{intake} per kg_{BW} per d)], which can be obtained from $TD50_x$ when based on animal test data (default) or from f_{q^*}/q_x^* with $f_{q^*} = 0.8$ as $1/q^*$ to ED50 conversion factor [−][43] and q_x^* as carcinogenic low-dose slope factor [kg_{BW} d per mg_{intake}] when epidemiological data are available; $TD50_x$: daily dose inducing an effect in 50% of exposed individuals *via* exposure route x [mg_{intake} per kg_{BW} per d]; f_a: interspecies extrapolation factor [−] (ref. 44 (Table 8)); f_t: extrapolation factor from given test exposure duration to chronic exposure [−] with $f_t = 5$ for (sub-)acute tests and $f_t = 2$ for sub-chronic tests;[43] RfD_x: reference dose for exposure route x [mg_{intake} per kg_{BW} per d]; POD_x: point of departure (*e.g.* no-observable adverse effect level, NOAEL) for exposure route x [mg_{intake} per kg_{BW} per d]; UF: intra- and interspecies uncertainty factors [−];[45] R_x: cancer risk probability for exposure route x [−]; N_u: number of persons belonging to user group u [capita]; BW_u: body weight of a person belonging to user group u [kg_{BW} per capita]; HQ_x: hazard quotient for exposure route x [−]; $FF_{P \to r}$: environmental fate factor from product application P to environmental receptor compartment of ecosystem exposure r (*e.g.* freshwater) [$mg_{\text{bioavailable}}$ per $mg_{\text{in product}}$ per d]; $TF_{P \to r}^{\text{cum}}$: cumulative chemical transfer fraction from product application P to environmental receptor compartment r [$mg_{\text{transferred}}$ per d per $mg_{\text{in product}}$ per d]; k_r^{loss}: overall removal rate from environmental receptor compartment r [d^{-1}]; XF_r: fraction of chemical mass in environmental receptor compartment r that is bioavailable [$mg_{\text{bioavailable}}$ per $mg_{\text{transferred}}$]; EF_r: ecological effect factor for ecosystems in environmental receptor compartment r [PDF m^3 per $mg_{\text{bioavailable}}$] with PDF representing the potentially disappeared fraction of ecological species; $HC20_r^{EC10}$: chemical hazard concentration at which 20% of the exposed ecological species show a response above their specific EC10 (effect concentration at which 10% of individuals of an ecological species show a response over background) in environmental receptor compartment r [$mg_{\text{bioavailable}}$ per $m^3_{\text{compartment}}$];[37] ETS: use stage related ecotoxicological impact score [PDF m^3 d].

Table 2 Focus areas and detailed elements of a Life Cycle based Alternatives Assessment (LCAA) for the Tier 2 assessment of chemical supply chain impacts

		Assessment elements[b]					
			Inventory analysis	Impact assessment			
Scope level	Focus areas		Chemical supply chain processes	Chemical supply chain emissions	Characterization of fate, exposure, and effects	Impact quantification	Interpretation and decision making
[Tier 2] Chemical[a] supply chain and product-related chemical use	Human, ecosystem and resources impacts from chemical emissions and resources use along chemical supply chain	*Focus*	Derive process tree of chemical synthesis integration stages[39]	Model supply chain processes and derive emissions based on mass and energy balance (see Fig. 5)	Select comparative impact factors from state-of-the-art life cycle impact assessment methods[46,47]	Characterize chemical supply chain impacts and compare these for human toxicity and ecotoxicity with consumer use impacts	Discuss if chemical supply chain impacts dominate compared to consumer use impacts; check if target chemical is of concern for workers in the supply chain
		Metric	Mass of reactants needed to produce target chemical in product application	Emission factors from EGIP[39,40] if available, else from life cycle inventory databases (*e.g.* ecoinvent[48]) to determine detailed inventory data	Characterization factors for climate change impacts, fine particulate matter exposure, energy use, human toxicity, ecotoxicity, other impact categories if relevant according to environmental product declarations	Impact scores for chemical supply chain related emissions and resources used, and human toxicity and ecotoxicity impact scores related to consumer use	Supply chain impacts: Compare target chemical with alternatives, evaluating the contribution of both chemical supply chain and use stage
		Method	m_i^{anc}	General public, ecosystems: $E_{i,j}^{\mathrm{sc}} = m_i^{\mathrm{anc}} \times em_{i,j}$ Workers:[41] $t_s = ut_{s,u} \times c_u$	General public, ecosystems:[49] $CF_j = FF_j \times \sum_{x,e} XF_{j,x} \times EF_{j,x,e}$ Workers:[41] $CF_{j,s} = C_{j,s} \times BR_{s,\mathrm{tot}} \times \sum_e EF_{j,e}$ Climate change:[46] $CF_j = GWP_{100,j}$	Chemical supply chain: $IS^{\mathrm{sc}} = \sum_{i,j} E_{i,j}^{\mathrm{sc}} \times CF_j$ Workers: $IS^{\mathrm{work}} = \sum_{j,s} t_s \times CF_{j,s}$ Consumer use: $HTS^{\mathrm{use}} = m_P \times \sum_{u,x,e} PiF_{u,x} \times EF_{x,e}$ $ETS^{\mathrm{use}} = m_P \times \sum_j FF_{P\to r} \times EF_r$	Worker exposure: If worker exposure relevant for target chemical or alternatives, explore additional data and methods (*e.g.* from occupational hygiene) to include in human toxicity

[a] For alternatives other than substitute chemicals (*e.g.* alternative materials or technologies), the respective supply chain is considered. [b] Chemical supply chain impacts are linked to the product functional unit (FU), which could either be 'one day of service offered by the considered product' (*e.g.* installed flooring in a household), or 'a single overall product application' (*e.g.* flooring area installed in a household over a given time period); m_i^{anc}: mass of ancillary chemical reactant i that is required in the process supply chain of a target chemical produced for a functional unit [$\mathrm{mg}_{\text{ancillary chemical}}$ per FU]; $E_{i,j}^{\mathrm{sc}}$: inventory flow j (substance emission or resource use to a specific environmental compartment) for the supply chain of ancillary chemical i used per functional unit [$\mathrm{mg}_{\text{emitted}}$ per FU]; $em_{i,j}$: emission factor for inventory flow j per unit mass of the ancillary chemical i [$\mathrm{mg}_{\text{emitted}}$ per $\mathrm{mg}_{\text{ancillary chemical}}$]; t_s blue-collar worker hours per functional unit worked in sector s [h per FU]; $ut_{s,u}$ blue-collar hours worked in sector s per unit costs spent in manufacturing sector u related to the functional unit [h per $]; c_u costs in manufacturing sector u per functional unit [$ per FU]; CF_j: impact characterization factor for inventory flow j for any impact category (*e.g.* climate change) [impact per $\mathrm{mg}_{\text{emitted}}$]; FF_j: environmental fate factor for inventory flow j [$\mathrm{mg}_{\text{in compartment}}$ per $\mathrm{mg}_{\text{emitted}}$ per d]; $XF_{j,x}$: exposure factor for a receptor (*e.g.* humans) relating inventory flow j to exposure route x in a given exposure compartment (*e.g.* ingestion) [$\mathrm{mg}_{\text{exposure}}$ per d per $\mathrm{mg}_{\text{in compartment}}$]; $EF_{j,x,e}$: effect factor for effect e for any impact category [impact per $\mathrm{mg}_{\text{exposure}}$]; $CF_{j,s}$ impact characterization factor for exposure to inventory flow j per blue-collar worker hour spent in sector s [impact per h]; $C_{j,s}$ air concentration of chemical j in worker environments of sector s [kg m^{-3}]; $BR_{s,\mathrm{tot}}$ breathing rate of all exposed workers in sector s [$\mathrm{m}^3\ \mathrm{h}^{-1}$]; $EF_{j,e}$ effect factor for effect e (*e.g.* cancer) of chemical j on workers per kg intake [impact per kg]; IS^{sc} process supply chain impact score [impact per FU]; $GWP_{100,j}$ global warming potential for inventory flow j based on IPCC 2013 with climate feedback [$\mathrm{mg}_{\mathrm{CO_2\text{-}equivalents}}$ per $\mathrm{mg}_{\text{emitted}}$];[50] IS^{work} worker impact score [impact per FU]; terms used to describe consumer use (incl. disposal) human toxicity scores HTS^{use} [health impacts per FU] and ecotoxicity scores ETS^{use} [ecosystem impacts per FU] are detailed in Table 1.

Table 3 Focus areas and detailed elements of a Life Cycle based Alternatives Assessment (LCAA) for the Tier 3 assessment of impacts along the full product life cycle

		Assessment elements[c]					
			Inventory analysis	Impact assessment			
Scope level	Focus areas		Life cycle process system	Life cycle emissions	Characterization of fate, exposure and effects	Impact quantification	Interpretation and decision making
[Tier 3] Product life cycle[a]	Selected human, ecosystem and resources impacts[b] from chemical emissions and resources use along full product life cycle	*Focus*	Identify main chemicals and energy use during product manufacturing and use stage from product life cycle	Model life cycle emissions using life cycle inventory data to determine streamlined inventory data, separated by product life cycle stage	Select comparative impact factors from state-of-the-art life cycle impact assessment methods[46,47]	Characterize product life cycle impacts and compare them with chemical supply chain impacts for relevant impact categories	Discuss the contribution of consumer use and chemical supply chain impacts of target chemical and alternatives on overall product life cycle impacts
		Metric	Mass of constituent in the given product per functional unit	Emission mass calculated from life cycle inventory databases (*e.g.* EGIP,[39,40] ecoinvent[48])	Characterization factors for all relevant impact categories	Impact scores for product life cycle related emissions and resources used	Identification of key factors influencing product life cycle impacts and quantification of the reduction in impacts provided by alternatives
		Method	m_i^{cons}	General public, ecosystems: $E_{i,j}^{lc} = m_i^{cons} \times em_{i,j}$ Workers:[41] $t_s = ut_{s,u} \times c_u$	General public, ecosystems:[49] $CF_j = FF_j \times \sum_{x,e} XF_{j,x} \times EF_{j,x,e}$ Workers:[41] $CF_{j,s} = C_{j,s} \times BR_{s,tot} \times \sum_e EF_{j,e}$ Climate change:[46] $CF_j = GWP_{100,j} \times EF_{j,e}$	Product life cycle: $IS^{lc} = \sum_{i,j} E_{i,j}^{lc} \times CF_j$ Workers: $IS^{work} = \sum_{j,s} t_s \times CF_{j,s}$	

[a] Focus on those life cycle stages that differ between the product containing the harmful chemical *versus* the same product containing an alternative. [b] Focus on those impact categories that are relevant for the given chemical: if bioactive (*e.g.* biocidal) or colorant, consider human toxicity and ecotoxicity; if large mass contribution to formulation/material (*e.g.* filler or plasticizer), consider climate change impacts, energy use and exposure to fine particulate matter. [c] $E_{i,j}^{lc}$: life cycle emission for inventory flow j (substance emission or resource use to a specific environmental compartment) across constituent i (*e.g.* PVC) per product functional unit (FU) [$mg_{emitted}$ per FU]; $em_{i,j}$: emission factor for inventory flow j per unit mass of product constituent i [$mg_{emitted}$ pef $mg_{constituent}$]; m_i^{cons}: amount of product constituent i required per product functional unit [$mg_{constituent}$ per FU]; $EF_{j,e}$ effect factor inventory flow j for climate change impacts [impacts per $kg_{CO_2\text{-equivalent}}$]; terms used to describe blue-collar worker hours t_s [h per FU], characterization factors CF [impact per $mg_{emitted}$] for emissions and [impact per h] for worker exposure, and product life cycle impact scores IS^{lc} [impacts per FU] are detailed in Table 2.

process across assessment tiers with different scopes, we propose to combine complementary indicators from both risk assessment and life cycle impact assessment, in line with earlier recommendations.[35]

Tier 1: Direct human risk and ecotoxicity of target chemicals and alternatives

In Tier 1, which is always mandatory, we first need to understand the reasons, why a certain chemical is of concern and for identifying potential alternatives. We then propose to follow a best-in-class approach for identifying most suitable options among a large set of possible alternatives. Focus in this rapid screening step is on human health risks and ecotoxicity of target chemicals and alternatives related to the chemical in a given product use context. Alternatives are only considered suitable when performing substantially better than the target chemical regarding these impacts. For all other considerations and performance criteria, where the identified or given target chemical is not "of concern", performance results of alternatives might well be in the same order of magnitude as long as these are not substantially worse. Any possible alternative that introduces unacceptable trade-offs will be screened out, such as carcinogens.

Table 1 presents the quantitative methods proposed to assess exposure and related risk in Tier 1. We multiply the chemical amount in the given product by the product intake fraction (PiF) to yield consumer exposure doses *via* all relevant exposure pathways.[8,23,24] Heat maps displaying exposure doses as a function of the product category-specific factors driving variability in exposure, can be used to identify a suitable space

of alternatives.[30] For an efficient yet quantitative approach, resulting intakes are combined with cancer slope factors and reference doses to respectively characterize cancer risk probability for carcinogenic effects and hazard quotients for non-carcinogenic effects. For ecotoxicity, the chemical in product is multiplied by a cumulative transfer fraction to the relevant ecosystem environment, in order to determine fractions of potentially disappeared ecological species and related ecotoxicity impact scores for the product use stage (Table 1).[36,37]

Tier 2: Optional assessment of chemical supply chain impacts

Once product use related impacts have been screened for target chemical and possible alternatives, we broaden the assessment scope in Tier 2 to their respective supply chains, to compare chemicals with substantial differences in their supply chains. We propose to characterize cumulative long-term impacts related to supply chain emissions affecting workers, the general population and ecosystems (Table 2), and compare results against use stage scores from Tier 1. Further, we propose to assess relevant chemical supply chain impacts from exposure to $PM_{2.5}$ used as benchmark for toxicity-related impacts, impacts on climate change correlated with energy use and various impact categories other than chemical toxicity, and impacts identified to be relevant in the related environmental product declarations (EPD). This allows screening out unsuitable alternatives based on capturing relevant trade-offs between, for example, reduced consumer risk and more complex chemical synthesis and related greenhouse gas emissions from increased energy demand.

While generic or regional inventory data exist for various product life cycles,[38] specific and high-resolution chemical supply chain data are rather rare. Here, the Environmental Genome of Industrial Processes (EGIP)[39] constitutes a sound starting point to link chemical supply chain impacts to inventory data. EGIP builds on the publicly available literature to identify for target chemicals and alternatives the industrial routes, reactants, process equipment, process conditions (temperatures, pressures), and ancillary chemicals like solvents and catalysts. An industrially relevant route is chosen and the reactants for the assessed chemical become the next target, until arriving at elements or materials acquired directly from natural resources (*e.g.* ores, water, air, or crude oil). EGIP datasets determine the mass of reactants needed to produce each chemical at the necessary purity, and provide related quantities of environmental emissions at every process step.[40] The assessment of supply chain worker exposure relies on measured workplace concentrations either from first hand data when available for the production of target chemical and alternatives, or from existing databases combined with life cycle input-output data to cover the entire supply chain.[41,42]

Tier 3: Optional assessment of product life cycle impacts

In the presence of substantially different life cycles of selected alternatives, we finally characterize and compare in Tier 3 for the target chemical and the remaining alternatives the impacts from emissions and resources used over the full product life cycle, with focus on those impact categories that are considered relevant for a given target chemical function (Table 3). The scope for environmental impacts is broadened towards considering a wider range of impacts on human health, ecosystem quality and natural resources, relating these impacts to the given chemical function in the product use context. Considering that consumer and worker safety are important aspects to consider, consumer and occupational exposure can be evaluated at the level of product life cycle as complementary to population-level exposure from environmental emissions, of which the latter is commonly included in Life Cycle Impact Assessment.[17] This enables to consider relevant impacts over the whole life cycle and quantify the contribution of the target chemical on overall product impacts with both life cycle and direct (consumer and occupational) impacts. The same type of indicators and characterization factors as in Tier 2 can be used, though for a wider range of relevant impact categories, in order to uncover relevant trade-offs across substantially different life cycles of alternatives, for example, related to differences in end-of-life handling.

Proof-of-concept case study

We applied our proposed LCAA framework and the assessment process shown in Fig. 2 in a proof-of-concept case study to screen quantitative exposures and life cycle impacts for a hazardous plasticizer (identified target chemical) and potential chemical alternatives in a household building material (product use context). We start with a focus on risk for consumers and ecotoxicity impacts directly related to chemicals in the given product use context, followed by considering additional impacts along the chemical supply chain and wider product life cycle. Assessment elements including metrics and approaches followed at each tier are detailed in Tables 1–3.

Product application

As building material, we selected a homogeneous, single layer vinyl flooring with details on chemical composition provided in the ESI (Table S1†). As functional unit (FU) defining the basis for screening and comparing target chemical with alternatives, we used 100 m^2 of flooring area per average household in OECD countries usable for 15 years. This allows us to compare flooring constituents as well as different alternatives to an identified target chemical on a functional basis.

Pre-screening of product use-related risks

There might be cases where the most relevant target constituent in a product is not known *a priori*. In such cases, we first screen as optional step all flooring constituents for exposure and hazard associated with the flooring use. During the use stage, flooring chemicals can expose consumers *via* various routes, including inhalation, ingestion (of *e.g.* dust) and dermal uptake. This also includes flooring installation-related impacts as the use stage starts at first day of the flooring

installed in the household. Flooring mass per 100 m^2 household is 450 kg. For screening exposure to use stage emissions, we consider residents of the household where the flooring is installed, and the general population and ecosystems exposed to chemical mass emitted to the outdoor environment. Disposal stage-related emissions are associated with residues in the landfilled flooring after 15 years of household use. Exposure estimates[23] are multiplied by the initial substance mass in flooring to yield exposure doses, and further combined with cancer slope factors and reference doses[51] respectively yielding cancer risks and hazard quotients (Table 1). Cumulative transfers from flooring to freshwater are combined with initial mass in flooring and ecotoxicity effect information to yield ecotoxicity impact scores. Additional details about pre-screening inventory analysis and impact assessment are provided in ESI (Section S1†).

Results of the optional pre-screening are presented in Fig. 3, with additional details given in ESI (Section S6†). Results indicate that DEHP is the main contributor to consumer risk for cancer (cancer risk probability of 2×10^{-3} for children and 3×10^{-4} for adults) and non-cancer effects (unitless hazard quotient of 19 for children and 3 for adults), closely followed by vinyl chloride for cancer. Population impacts from chemical mass reaching the environment as emission during product use are consistently several orders of magnitude lower than consumer-related (*i.e.* household users) impacts. For ecotoxicity impacts on freshwater ecosystems, DEHP is again the dominating contributor among vinyl flooring constituents, with an impact score that is at least two orders of magnitude higher than that of other constituents. Ecotoxicity impacts for DEHP are dominated by the waste disposal stage; thus, it is important to already account in the pre-screening step for emissions and related ecotoxicity impacts during product disposal. Risks or ecotoxicity impacts could not be quantified for some constituents due to missing effect information (indicated with "no data" in Fig. 3). Based on this analysis, we selected as suspected target chemical di(2-ethylhexyl) phthalate (DEHP), used as plasticizer in vinyl flooring[52] and widely acknowledged as a chemical of concern.[53] Physicochemical properties of DEHP are given in ESI (Table S2†).

Tier 1: Selection and screening of possible alternatives based on use stage impacts

Possible, functionally equivalent alternatives to DEHP in vinyl flooring include three phthalate-based plasticizers, namely di(isoheptyl)phthalate (DIHP), butyl benzyl phthalate (BBP), dibutyl phthalate (DBP), and six other plasticizers, namely di(ethylhexyl) adipate (DEHA), hexanadedioic acid, di-C7-9-branched and linear alkyl esters (97A), dibutyl sebacate (DBS), butane ester 2,2,4-trimethyl 1,3-pentanediol diisobutyrate (TXIB), *o*-acetyl tributyl citrate (ATBC), and di(2-ethylhexyl) phosphate (DEHPA). Physiochemical properties of these substances and their substitution factors relating material hardness properties of alternatives to those of DEHP are given in ESI (Table S3†). We screened the identified possible alternatives against DEHP for emissions, and related exposure and

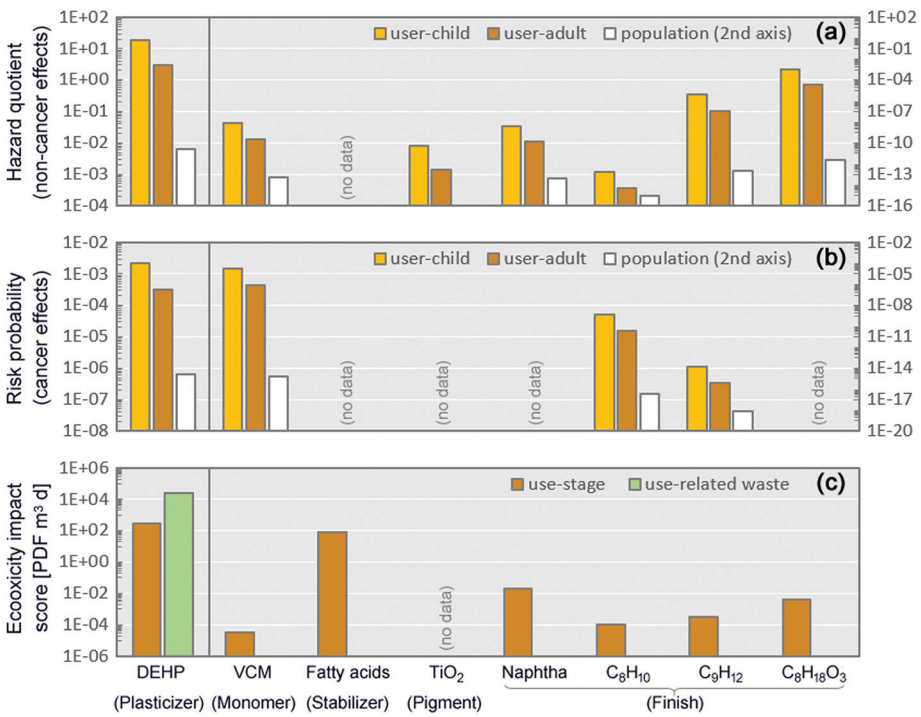

Fig. 3 Pre-screening product use related (a) non-cancer hazard quotients, (b) cancer risk probability, and (c) freshwater ecotoxicity impact scores for chemical constituents in 100 m^2 vinyl flooring, with population risks shown on the 2nd *y*-axis. Filler (calcium carbonate) and resin polymer (PVC) are excluded as they are assumed not to emit from the flooring material. VCM: vinyl chloride monomer, TiO_2: titanium dioxide, C_8H_{10}: ethylbenzene, C_9H_{12}: 1,2,4-trimethylbenzene, $C_8H_{18}O_3$: diethylene glycol diethyl ether.

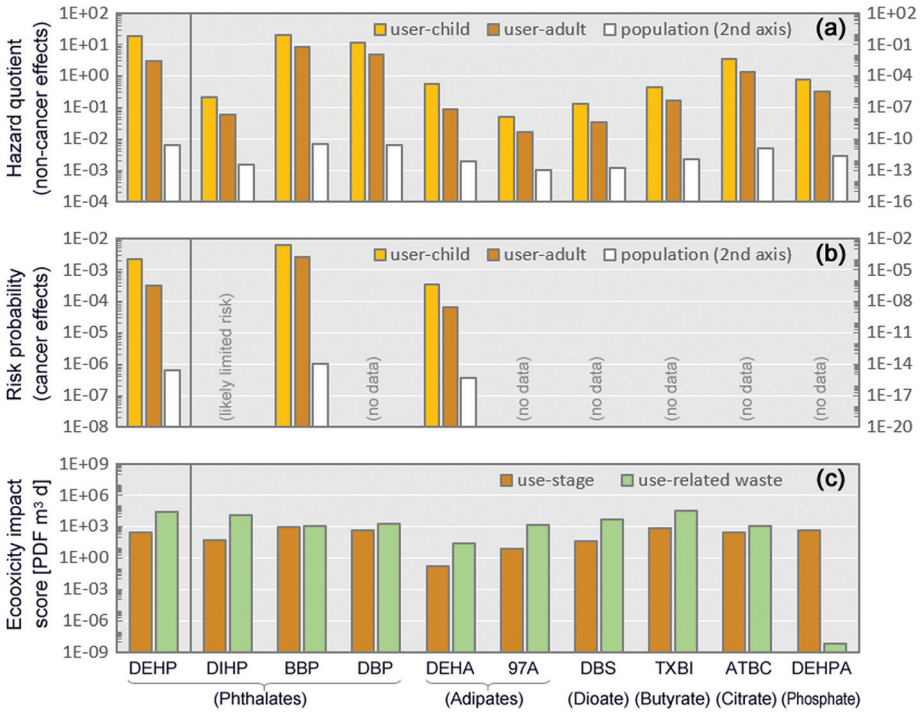

Fig. 4 Tier 1 product use related (a) non-cancer hazard quotients, (b) cancer risk probability, and (c) freshwater ecotoxicity impact scores for different plasticizer alternatives in 100 m^2 vinyl flooring, with population risks shown on the 2nd y-axis.

hazard associated with the use stage of the flooring product following the approach described in the pre-screening. Additional details are provided in ESI (Section S1†).

Screened health risks and ecosystem impacts associated with possible plasticizer alternatives during product use are presented in Fig. 4, with additional details given in ESI (Section S7†). Hazard quotients of all alternatives are lower than that of DEHP, except for BBP, DBP and ATBC. Among phthalates, DIHP has hazard quotients that are at least a factor 50 lower than for other phthalates. Among non-phthalate plasticizers, 97A and DBS show lowest hazard quotients. For evaluating cancer risk, we used the most extensive carcinogenic potency databased worldwide,[54] considering all tested substances for carcinogenic effects and containing both positive and negative chronic tests, which is much broader than the lists of declared carcinogenic substances. Yet, cancer risk could only be evaluated for DEHP, BBP and DEHA, with DEHA showing a cancer risk of 3×10^{-4}, which is one order of magnitude lower than that of DEHP, whereas BBP cancer risks are higher than those of DEHP. We indicated missing information on cancer potency as "no data" in Fig. 4b. For considering a given chemical with missing cancer data as potential alternative, it is recommended to conduct a systematic review to identify if any information on carcinogenicity is available, to first assess the likelihood that the chemical is carcinogenic.[55] Reviewing cancer information for DIHP yielded a state-of-the-science report from Environment Canada, stating that its cancer potency is evaluated as likely limited at environmentally relevant doses,[56] which we indicated in Fig. 4b. Population impacts are again consistently much lower than consumer-related impacts, confirming the focus of Tier 1 on the product users and co-residents. Population impacts, however, might be substantial for very persistent and bioaccumulating chemicals, such as per- and polyfluoroalkyl substances (PFASs).[57] Ecotoxicity impacts are lowest for DEHA, being at least a factor 20 lower than for other alternatives, DIHP being just slightly lower than DEHP. Ecotoxicity impacts on freshwater ecosystems are dominated by the waste disposal stage of the landfilled flooring product after 15 years of use for all plasticizers except DEHPA. This again highlights the importance of considering product disposal-related emissions and ecotoxicity impacts in Tier 1. When aggregating results into single scores for cancer risk, non-cancer risk and ecosystem impacts (ESI, Fig. S1†), we find that only DIHP and DEHA perform better than DEHP across all three aspects. Based on these screening results, we identify DIHP (phthalate) and DEHA (non-phthalate) as suitable alternatives to DEHP in this illustrative example. To demonstrate the feasibility of our approach beyond this mandatory rapid risk screening step, we investigate the suitability of these two alternatives in Tier 2, with focus on their chemical supply chains.

Tier 2: Comparison of supply chain impacts for selected alternatives

In an optional step, we evaluated the chemical supply chain impacts of target chemical and selected alternatives. Emissions of chemicals used in the supply chain of the target chemical and its two selected alternatives were derived from

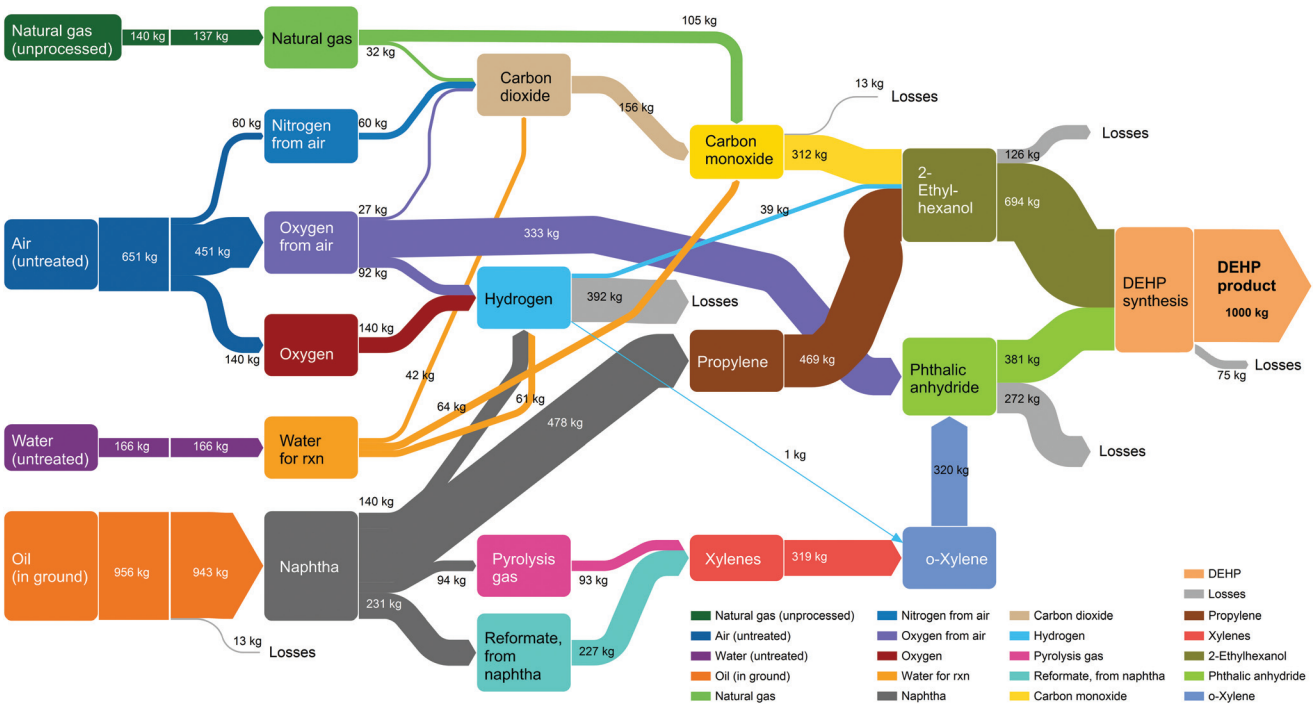

Fig. 5 Chemical supply chain inventory for di(2-ethylhexyl) phthalate (DEHP) with reactant mass flows from left to right side required for producing 1000 kg of DEHP target chemical mass and related emissions into the environment, with nodes representing the different chemical synthesis integration stages. Losses <10 kg are not shown.

the Environmental Genome of Industrial Processes (EGIP),[39] which is further detailed in ESI (Section S8†). The flows represented in an EGIP dataset are illustrated in Fig. 5 for DEHP as example chemical, with additional details given for DEHP and the two selected alternatives in ESI (Fig. S2 to Fig. S4†). These results illustrate that even for a relatively simple molecule, several synthesis steps are needed, requiring various natural resources and ancillary chemicals, each of which comes with chemical and other losses to the environment.

Chemical supply chain emissions were characterized in terms of damages on human health, ecosystem quality, and climate change by combining chemical-specific emissions with respective characterization factors expressed as potential impacts per unit emission (Table 2). For climate change, we used IPCC global warming potentials (GWP),[50] expressed in kg CO_2-equivalents per kg chemical emitted, summed over all chemicals. For toxicity-related impacts, we used the scientific consensus model USEtox,[49] which is widely used in comparative assessments.[58,59] For ecotoxicity, species loss is expressed as potentially disappeared fraction (PDF) of ecosystem species exposed over a given time and freshwater volume per unit mass emitted.[60,61] For human toxicity and exposure to fine particulate matter, lifetime loss is expressed as disability-adjusted life years (DALY),[62,63] consistently combining for the latter information for population exposure[64] and exposure-response slopes.[65] Toxicity-related impacts on workers for the plasticizer supply chain were evaluated using an input-output matrix-based approach.[42] Additional details are provided in ESI (Section S1†).

Chemical supply chain impacts expressed as toxicity and air pollution (*i.e.* $PM_{2.5}$) related damages on human health, climate change impacts and ecotoxicity-related damages associated with the three selected plasticizers are presented in the plasticizer-related left-side part of Fig. 6 (where chemical supply chain impacts are shown as integral part of the wider flooring life cycle impacts). Human toxicity-related health impacts are dominated by the use stage for all three plasticizers, followed by impacts related to $PM_{2.5}$ exposure and supply chain impacts on workers that are 2–4 orders of magnitude lower than use stage impacts (Fig. 6b, with further details in ESI, Fig. S5†). When aggregated into single scores, human health impacts for DIHP and DEHA are respectively more than a factor 50 and 30 lower than for DEHP (ESI, Fig. S6†). Ecotoxicity impacts are dominated by the waste disposal stage for DEHP and DIHP, and by supply chain impacts (including related waste) for DEHA. When aggregated, DEHA shows overall lowest ecotoxicity impacts; however, the difference across the three plasticizers is less than a factor of five. Climate change impacts show a similar picture with lowest impacts for DIHP, but with marginal differences across all three alternatives. In summary, DIHP and DEHA are still suitable alternatives to DEHP when including impacts along their chemical supply chains. To finally capture any potential impact trade-offs along the entire flooring life cycle, we again

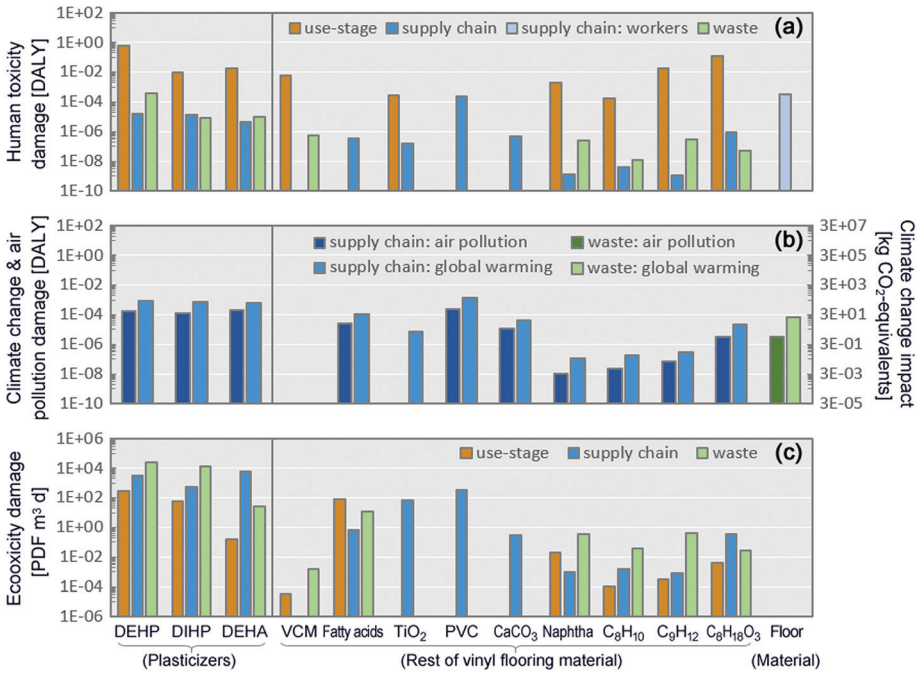

Fig. 6 Tier 3 product life cycle impacts for (a) human toxicity damages on human health, (b) climate change and air pollution (exposure to fine particulate matter) damages on human health, and (c) ecotoxicity damages on ecosystem quality for three alternative plasticizers in 100 m^2 vinyl flooring, and for all other relevant vinyl flooring constituents. Tier 3 covers the entire flooring life cycle including chemical supply chain and waste-related impacts. Climate change damages on human health are also shown as CO_2-equivalents. VCM: vinyl chloride monomer, TiO_2: titanium dioxide, PVC: polyvinyl chloride, $CaCO_3$: calcium carbonate, C_8H_{10}: ethylbenzene, C_9H_{12}: 1,2,4-trimethylbenzene, $C_8H_{18}O_3$: diethylene glycol diethyl ether.

broaden the assessment scope in Tier 3 to include the entire vinyl flooring life cycle for these three plasticizers.

Tier 3: Assessment of product life cycle impacts

Assessing life cycle emissions and impacts for the selected alternatives is mainly needed for considering distinct types of alternatives (*e.g.* chemicals *vs.* materials *vs.* technologies). However, to demonstrate the feasibility of our approach to address full product life cycle impacts, we also cover this most comprehensive tier in our case study. We included in this step the life cycle impacts of the remaining vinyl flooring constituents for comparison.

Emission inventory information over the entire life cycle of the vinyl flooring are derived from EGIP,[39] ecoinvent,[48] and the MOCLA model.[66] The full inventory data are given in ESI (Section S10†). Life cycle impacts on climate change, human health and ecosystem quality were calculated following the same approach as for chemical supply chain impacts (Table 3). To evaluate the contribution of climate change impacts on human health as compared to toxicity and $PM_{2.5}$-related impacts, climate change impacts were also translated into DALY per kg emitted.[46] Additional details are provided in ESI (Section S1†).

Flooring life cycle impacts are presented for human toxicity, climate change, air pollution, and ecotoxicity in Fig. 6, keeping life cycle stages separate to best contrast the contribution of each stage. Toxicity-related life cycle impacts on human health are consistently dominated by the use stage for most vinyl flooring constituents including the three alternative plasticizers, followed by plasticizer waste impacts and flooring supply chain impacts on workers, of which 16% is related to plasticizer supply chain impacts on workers. In case of DEHP, the plasticizer dominates human toxicity-related impacts, contributing up to 81% to overall human toxicity impacts from the flooring life cycle. DEHP alternatives contribute between 7% (DIHP) and 11% (DEHA) to flooring life cycle impacts on humans, which are in these scenarios dominated by finish components. PVC resin dominates climate change and air pollution related impacts on humans, together with plasticizers, with negligible differences across the three plasticizer alternatives. Highest ecotoxicity impacts are dominated by the three equally damaging plasticizers. However, while waste-related impacts on ecosystems dominate for DEHP and DIHP, related impacts for DEHA are dominated by its more complex supply chain. For vinyl flooring, climate change and air pollution impacts on humans only contribute between <1% (DEHP) and 8% (DIHP) to overall human health damages. In line with ecotoxicity impact results, this renders toxicity the main impact type when evaluating alternative plasticizers, which is especially problematic since plasticizers also have high product weight fractions. For all considered impacts, plasticizers are among the dominating flooring components along its

life cycle, indicating a substantial potential to improve the entire product's environmental performance when identifying suitable alternatives to DEHP as plasticizer.

When there are relevant trade-offs between target chemical and alternatives, considering the entire life cycle is crucial to understand which of these trade-offs matter, and to put such trade-offs into perspective of overall product performance. When differences in the life cycle are rather restricted as in our present example, this step could be omitted or is primarily used to understand how much the improvement matters for the overall product performance.

Across case study tiers, we have presented results at a high level of detail, allowing for best-possible interpretation of individual impact contributors. However, to facilitate a more user-friendly support of substitution decisions, impact results at any tier might also be aggregated into single scores per focus area. Fig. 7 illustrates this by summarizing Tier 3 life cycle impact results into a simple comparison of the three plasticizer alternatives among each other and with the rest of the vinyl flooring. In this aggregated figure, product use stage related damages on human health account for >98% across plasticizers and cumulatively for all other flooring ingredients. For climate change impacts, the supply chain dominates at the level of plasticizers and product, with >95% contribution. For ecotoxicity impacts, we see a more differentiated picture, with waste-related impacts dominating with 90–96% for the two phthalate plasticizers, while supply chain impacts dominate for DEHA (>99%) and cumulatively for all other flooring ingredients (82%).

When comparing Fig. 7 with aggregated single scores for Tier 1 and 2 (see ESI, Fig. S1 and S6†), there is a clear overall tendency across tiers that DIHP and DEHA perform slightly better than DEHP. Considering the uncertainties in our impact results (1–3 orders of magnitude for toxicity and ecotoxicity impacts), differences of less than two orders of magnitude across alternatives do not seem high. This indicates that more fundamentally different plasticizers are needed, and challenges the use of any existing plasticizer alternative to fulfill the related function in vinyl flooring without substantial impacts.

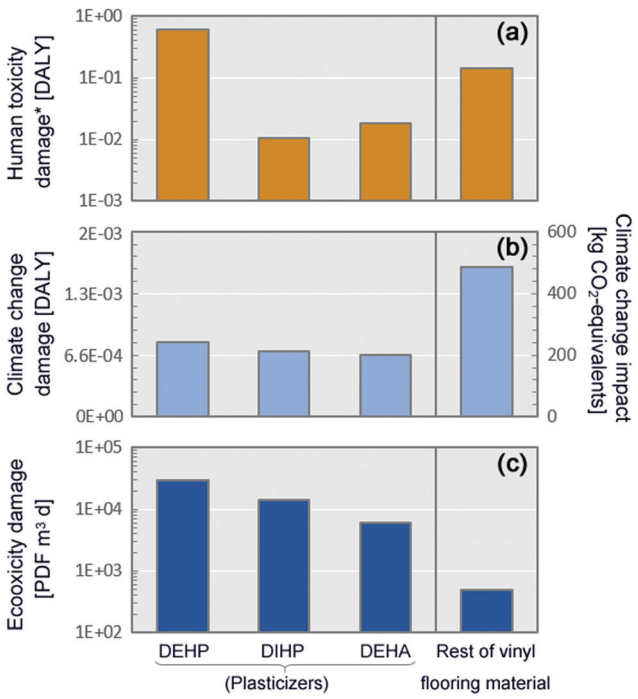

Fig. 7 Aggregated life cycle impacts for (a) human toxicity damages (*including air pollution) on human health, (b) climate change damages on human health, and (c) ecotoxicity damages on ecosystem quality for three alternative plasticizers in 100 m^2 vinyl flooring, and for the rest of the vinyl flooring material.

Discussion

Applicability and limitations of our approach

Quantitative screening tools are becoming available to cover thousands of chemical-product combinations, integrating at each assessment level exposure to target and alternative chemicals in products with the wider set of chemical supply chain and product life cycle impacts. The presented approach enables the practitioner to (a) identify a target chemical if this is not known *a priori*, (b) rapidly screen a large set of alternatives, (b) efficiently account for worker and population exposure associated with chemicals, (c) identify other types of life cycle impacts such as climate change impacts based on chemical function and product use context, and (d) consistently broaden the assessment scope where needed, to uncover relevant trade-offs.

Our case study demonstrates the feasibility of our approach and suggests that (a) vinyl flooring plasticizer is a main issue for both human and ecotoxicological impacts, highlighting the importance of a consistent screening of both aspects, (b) alternatives to DEHP enable a reduction of human health impacts by a factor 30 to 50, which is a minimum difference required considering the related uncertainty, (c) plasticizers due to their general high mass contribution to flooring have also important climate change impacts with alternatives only offering minimal improvement or rather similar scores, and (d) further research is needed to identify chemicals from different families to offer further improvements.

For a function-based substitution, starting from the chemical function is key for determining the chemical amount used for a given functional unit. The functional unit thereby provides a consistent comparison basis, and mainly depends on the product application context rather than on the chemical function. For both product-oriented and receptor- or risk-oriented approaches, it is advantageous to scale the functional unit to the amount that corresponds to the actual amount that a person is exposed to (daily dose), such as using 100 m^2 of a typical household in our case study.

Our approach also has several limitations. The nature of a screening assessment requires several assumptions. We used for various inputs (*e.g.* chemical flooring composition, house-

hold settings, population heterogeneity and use patterns) generic or default values, which should be adapted whenever case-specific information is available. For child exposure, we have on the one hand chosen a high-end hypothesis assuming there is always 1 child in the household, while on the other hand we did not use children adjustment factors to correct childhood exposure for lifetime cancer risk.[67]

Several chemicals lack cancer potency data. Such missing data should be comprehensively discussed in any substitution study according to current guidelines.[68] More generally, we propose the following approach for addressing missing data: first conduct a systematic review to identify potential information, as was carried out for DIHP showing that its cancer potency is likely limited at environmentally relevant doses. This is especially important for carcinogenic effects, were a judgement on the likelihood that the chemical is carcinogenic is first required before applying any extrapolation approaches.[55] Second, imputation and extrapolation techniques can be applied or further developed. For non-cancer effects, both a regression approach providing a point estimate and a non-parametric analysis providing distributions are proposed,[69] whereas other imputation techniques are applicable when distributions are well-defined. We applied results from such regression techniques to estimate diffusion and material-air partition coefficients used as input for our exposure model (see ESI, Section S4†). Recent advances in machine learning, such as random forest algorithms or neural networks, offer improved performance compared to pure regression, and were used in our study to estimate ecotoxicity effects[70] and non-cancer human effects.[51] Additional estimation approaches are urgently needed that account for both positive and negative carcinogenicity indications.

While such approaches allow to evaluate a wider range of alternatives and aspects, they introduce additional uncertainty. For example, when applying QSAR for ecotoxicity for DEHP, we would yield significantly higher effects than with currently available effect data. Using generic chemical supply chain and product life cycle worker impacts across plasticizers is another limitation, where we recommend to use product and chemical-specific supply chain information in cases where worker impacts dominate overall impact profiles. Further, among our considered target chemical and screened alternatives, only DEHP and DBP are included in the list of 235 organic substances contributing to worker impacts,[41] whereas no measured workplace concentrations for the other alternatives are currently available, leading to potential bias.

Despite its limitations, our framework is nonetheless useful to indicate relevant differences in performance profiles across alternatives. Finally, our framework requires a solid understanding of the substitution context to define relevant life cycle impacts, gather chemical supply chain information and apply different quantitative methods in a rapid-screening context.

Future research needs and way forward

To derive the chemical mass used for an equal functional performance across alternatives, substitution factors are required, but often not available. Such substitution factors need to related to a proper function for comparing alternatives for a given product application.

On the exposure assessment side, our framework already contains several product categories (*e.g.* building materials,[71] toys,[72] food contact materials,[73,74] cosmetics,[25] personal care products,[30,75] cleaning and home maintenance products, and pesticide active ingredients[76]), but various product categories still need to be introduced (*e.g.* electronics, textiles). Furthermore, our models needs to be parameterized for additional exposure scenarios to capture relevant consumer and occupational settings (*e.g.* to better capture worker exposure during flooring installation) and processes (*e.g.* modeling abrasion and subsequent transfer to dust removed by vacuum cleaning, where relevant).

Human toxicity and ecotoxicity estimates for the various chemicals relevant for Chemical Alternatives Assessment are often lacking, especially for inorganic substances,[77] and need to be complemented with high-throughput estimates. This requires additional efforts, building on stochastic tools, which also provide information on model applicability domain and uncertainty.[59,78]

Finally, in support of reducing the use of harmful chemicals in consumer products and production processes, it is essential to promote further efforts for including metrics to measure progress against targets for a sustainable development and a circular economy.[16,79]

Conclusions

We proposed a tiered, quantitative LCAA framework for assessing human (consumer, worker, general population) and ecological exposures, and a wider realm of life cycle impacts for application in Alternatives Assessment and chemical substitution. With our framework, we address an important limitation of current substitution approaches, and identify relevant trade-offs across exposure settings and life cycle stages. We demonstrate that it is crucial and possible to include chemical supply chain and life cycle impacts into the assessment scope to pinpoint potential impact hotspots in a given substitution context, which can help to avoid introducing unacceptable trade-offs. However, further research is needed to cover emission inventories and toxicity-related impacts for the wide range of presently used chemical-product combinations. The proposed approach for assessing exposure, risks and life cycle impacts should be incorporated into existing substitution frameworks, to combine our indicators with indicators for technical and economic feasibility, and identify related trade-offs in a decision analysis context as proposed in state-of-the-art Alternatives Assessment guidelines.[21] It is important that these trade-offs are also analyzed at the product level. With that, our LCAA framework is suitable for informing function-based substitution at the level of chemical, material and product application, and is also applicable to identify chemicals that should be prioritized for substitution.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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