USEtox® Update Form – Submission	
Issuing organization (name, address, country)	**University of Michigan, School of Public Health Environmental Health Sciences, Ann Arbor, MI, USA**
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(1) Title (update title)

Combined near-and far-field human exposure assessment framework

(2) Summary (1-2 sentences of main update content)

LCA studies of products do currently not consider consumer and population exposure to chemical constituents in consumer products during product use stage. Wambaugh et al. 2014 showed that chemicals found at the highest concentrations in serum and urine human biomonitoring data are associated with chemical usage in a near-field context in e.g. consumer products. Studies carried out on specific product-chemical combinations and indoor air exposures demonstrate that product-use-related exposure may substantially exceed environmentally mediated exposures and is therefore essential to consider when assessing exposure to chemicals in products. The proposed update builds on recommendations of the Valencia Pellston workshop 2018 (Fantke et al. 2019) to elaborate a combined near-and far-field matrix framework. This framework integrates USEtox 2.0 for the environmental and indoor part, and proposes additional exposure model components to cover chemicals in a series of household products. This includes personal care products, cleaning products, food contact materials, home-maintenance products, building products, toys and other articles.

(3) Reason(s) for updating USEtox (need, meaningfulness, added value)
- *a. Is the update meaningful to be considered in practice?*
- *b. What is the improvement from a practical point of view?*
- *c. Does the update entail an additional effort and is it worth it?*

a. This is very relevant since there is a high demand for a mass-balance-based approach to provide use-stage estimates of exposure to chemicals in consumer products. Other tools, such as the "point-based" BASF approach, need to be further improved and complemented by a full mass-balanced based approach.

b. It provides LCA and risk assessment practitioners with human (and ecosystem) exposure estimates (and related characterization factors if toxicity dose-response and effect factors and ecotoxicity factors are provided) for tens of thousands of product-chemical combinations. It further provides a model with a series of default products and chemical properties based on the newly-established US EPA Comptox database to consider new product-chemical combinations.

c. Underlying product-related exposure models are available for the above-mentioned products and QSARs for complementary input data, such as diffusion and material-air/water partition coefficients, have been published and are available. The main point is now to fully integrating these models and data into USEtox, which is a readily achievable effort.

(4) Method description
- *a. Explain main proposed USEtox modifications, how to achieve them and basics of scientific methods*
- *b. How does the proposed method deviate from existing/established methods?*

a. Fantke et al, 2016 developed a general a framework and a tool that combines consistently near-field and consumer exposure assessment with the USEtox far-field environmental exposures: The chemical mass per functional unit in the consumer product is multiplied by the product intake fraction (PiF) to yield the total exposure. The PiF represents the fraction of the chemical in products

that is taken in by exposed consumers and the general population that is exposed via chemical fractions lost as emissions to the environment during the product use stage (Jolliet et al., 2015), a metric that is fully compatible with the well-established intake fraction concept applied in USEtox.

To determine the PiF, we couple additional fate processes in consumer environments (near-field) with existing environmental compartments and processes (far-field) via a consistent and mass-balance-based set of direct transfer fractions (i.e. chemical mass fraction transferred between two adjacent or nested compartments, media or phases). The fraction directly transferred from the considered consumer product to other compartments and to humans are first entered as the left-most column of a direct transfer fractions matrix T, which shows the direct transfer fractions for the product specific compartment of entry. The other columns of this matrix T represent the fraction directly transferred from each environmental compartment to the other environmental or human compartments and are determined using USEtox rate constants. We then inverse the matrix (I-T) to yield the cumulative transfer matrix - $Tcum=(I-T)^{-1}$ to quantify the overall aggregated exposure to chemicals, where the bottom part of product-related first column directly yields the product intake fractions (Fantke et al., 2016).

Direct transfer fractions from the product to various near-field environmental, far-field environmental and human intake compartments are calculated using a series of complementary underlying mechanistic models. Depending on the product application and the compartment of entry in the near-field environment, a set of five main models is included into our framework for calculating direct transfer fractions. These are 'Direct emission', 'Article interior', 'Skin surface layer', 'Object surface', and 'Food contact material', complemented by a sorption model to account for reabsorption of chemicals on indoor surfaces (Fantke et al. 2019). **Table A1** (see Appendix below) summarizes the direct transfer fractions that are determined by each model and the respective exposure pathways. Each of these models is then parametrized, adapting model parameters such as thickness of applied chemical on skin, application surface, and the number of adults and children exposed to the considered product subcategory.

b. Compared to the existing version of USEtox, exposure compartments (such as gastrointestinal tract, respiratory tract, epidermis) are also considered in the fate mass-balance calculation and are fully coupled with the other environmental compartments already considered in USEtox.

(5) Documentation and transparency check
- *a. List of scientific publications: What is the main publication and what are related publications?*
- *b. Description of full update content*
- *c. Description of level of detail of documentation*
- *d. What are data sources behind parameterization? (provide original data sources of new/updated data/methods)*
- *e. How has the update content been evaluated?*

a. Main publications:
- Jolliet O, Ernstoff AS, Csiszar SA, Fantke P, 2015. Defining product intake fraction to quantify and compare exposure to consumer products. Environ. Sci. Technol. 49: 8924-8931 (http://doi.org/10.1021/acs.est.5b01083)
- Fantke P, Ernstoff AS, Huang L, Csiszar SA, Jolliet O, 2016. Coupled Near-Field and Far-Field Exposure Assessment Framework for Chemicals in Consumer Products. Environ. Int. 94: 508-518 (http://doi.org/10.1016/j.envint.2016.06.010)

Related/supporting publications:
- Huang L, Ernstoff ES, Csiszar SA, Fantke P, Jolliet O, 2017. A review of models for near-field exposure pathways of chemicals in consumer products. Sci. Total Environ. 574: 1182-1208 (http://dx.doi.org/10.1016/j.scitotenv.2016.06.118)

Personal Care and household Products

- Csiszar SA, Ernstoff AS, Fantke P, Meyer DE, Jolliet O, 2016. High-throughput exposure modeling to support prioritization of chemicals in personal care products. Chemosphere 163: 490-498 (http://dx.doi.org/10.1016/j.chemosphere.2016.07.065)
- Csiszar SA, Ernstoff AS, Jolliet O, 2017. Stochastic Modeling of Aggregate Exposure to Chemicals in Personal Care Products: Paraben Case Study. Journal of epidemiology and exposure science, 27, 152-159 (http://dx.doi.org/ 10.1038/jes.2015.85).
- Ernstoff AS, Fantke P, Csiszar SA, Henderson AD, Chung S, Jolliet O, 2016. Multi-pathway exposure modelling of chemicals in cosmetics with application to shampoo. Environ. Int. 92-93: 87-96 (http://doi.org/10.1016/j.envint.2016.03.014)

Building materials and articles

- Huang L, Anastas N, Egeghy P, Vallero D, Jolliet O, Bare J, 2018. Integrating exposure to chemicals in building materials during use stage. International Journal of LCA, on-line first (http://doi.org/10.1007/s11367-018-1551-8).
- Huang L, Jolliet O, 2016. A parsimonious model for the release of volatile organic compounds (VOCs) encapsulated in products. Atmos. Environ. 127: 223–235 (http://doi.org/10.1016/j.atmosenv.2015.12.001)
- Aurisano, N., Huang, L., Jolliet, O., Mila I Canals, L., Fantke, P. (2020). Chemicals of Concern in Plastic Toys. Environmental Science & Technology, *submitted*.

Food contact materials

- Ernstoff AS, Fantke P, Huang L, Jolliet O, 2017. High-throughput migration modelling for estimating exposure to chemicals in food packaging in screening and prioritization tools, Food and Chemical Toxicology, Volume 109 (1) 428-438 (http://doi.org/10.1016/j.fct.2017.09.024).

b. Description of full update content
Fantke, P., Aylward, L., Chiu, W., Gouin, T., Jolliet, O., Judson, R., Rhomberg, L., McKone, T.E., 2019. Human toxicity. in: Frischknecht, R., Jolliet, O. (Eds.). Global Guidance on Environmental Life Cycle Impact Assessment Indicators: Volume 2. UNEP/SETAC Life Cycle Initiative, Paris, France, pp. 80-103.

c. Description of the level of detail in the documentation
80 pages documentation complemented by multiple papers

d. What are data sources behind parameterization? (provide original data sources of new/updated data/methods
Data sources are described in the references listed under (f)

e. How has the update content been evaluated?
- Diffusion coefficients and material-air and material-water partition coefficients and skin permeations are key to determine fraction released from products to air, skin and other environmental compartments
- Packaging-food and solid material-water partition coefficients: Huang L, Jolliet O, 2019. A combined quantitative property-property relationship (QPPR) for estimating packaging-food and solid material-water partition coefficients of organic compounds. Science of the total environment. Science of The Total Environment 658, 493-500 (http://doi.org/10.1016/j.scitotenv.2018.12.062).
- Material- air partition coefficients: Huang L, Jolliet O, 2018. A quantitative structure- property relationship (QSPR) for estimating solid material- air partition coefficients of organic compounds, Indoor air, On-line first 1-10, (http://doi.org/10.1111/ina.12510).
- Diffusion coefficients: Huang L, Fantke, P, Ernstoff, A, Jolliet, O., 2017. A quantitative property-property relationship for the internal diffusion coefficients of organic compounds in solid materials. Indoor Air, 27(6), 1128-1140 (http://doi.org/10.1111/ina.12395).
- Skin permeation coefficient comparison: Ernstoff AS, Fantke P, Huang L, Jolliet O, 2017. High-

throughput migration modelling for estimating exposure to chemicals in food packaging in screening and prioritization tools, Food and Chemical Toxicology, Volume 109 (1) 428-438 (http://doi.org/10.1016/j.fct.2017.09.024).

- The underlying chemical properties (MW, Kow, Kaw, Koa, etc.) could either be extracted from EpiSuite/existing USEtox or from OPERA on the Comptox dashboard

(6) Applicability check

f. To which substances does the update apply? (all substances, inorganics, metals, etc.)
g. Feasibility and influence in application: Is the update possible to consider in practice?
h. What is foreseen in the future related to the update?

a. The update presently applies to organic substances.

b. The update has already been implemented in a matrix-based tool that is using USEtox as a framework, and tested in several research projects as well as in several training courses. It serves both LCA and risk assessment needs, looking at both intake fractions and individual and populations doses in mg/kg/d.

c. We foresee to integrate the near-field model component in the next USEtox version, and extending the product model coverage.

(7) Level of consistency with USEtox check

i. Parsimony: How is the update parsimonious?
j. Data selection hierarchy (for previously published CFs and databases) as published in the official USEtox papers in IJLCA

a. The transfer-fractions matrix is a parsimonious way to integrate dynamic models of chemical releases in a mass-balance based approach, coupled to the existing removal rates from USEtox. Underlying transfer fraction models (e.g. landfill or chemical release) can easily be replaced in the future as improved models will be published and approved.

b. Since the matrix approach uses the existing USEtox rate constants, it is compatible with and extends the existing USEtox version. Existing characterization factors will be updated based on new exposure results and extended to include additional exposure pathways and source compartments (near-field/product related).

(8) Discussion of level of acceptance/consensus

k. Level of scientific acceptance/consensus in the community: Is update already used in published work?

a. The approach was submitted to the UNEP/SETAC GLAM human toxicity task force, reviewed at the 2018 Pellston Valencia workshop and recommended for implementation. Several of the underlying models have been checked against measurements (releases from flooring by chambers – Huang and Jolliet 2016; comparison of paraben uptakes to NHANES US urine biomarkers – Csiszar et al., 2017; migration from food-contact materials – Ernstoff et al., 2017).

(9) Suggested reviewers (propose at least 2 independent reviewers)

- Dr. **Jon Arnot**, ARC Arnot Research and Consulting, 36 Sproat Ave. Toronto, Ontario Canada, M4M 1W4, Email: jon.arnot@utoronto.ca
- Dr. **Todd Gouin** (ensuring continuity with the Pellston workshop), TG Environmental Research, Sharnbrook, MK44 1PL, UK, Email: todd.gouin@environresearch.com
- Prof. **Miriam Diamond**, Department of Earth Sciences, University of Toronto, 22 Russell St. Toronto, Ontario, M5S 3B1, Canada, Email: miriam.diamond@utoronto.ca
- Dr. **Li Li**, School of Community Health Sciences, University of Nevada, Reno, Email: lili@unr.edu

Appendix

Table A1. Selected underlying near-field exposure models with main direct transfer fractions from compartment of entry, exposure pathways, model mechanisms, key parameters, and example products covered.

Model	Compartment of entry and main transfers and compartments considered	Direct exposure pathways	Model mechanism	Key parameters	Product example
Direct emission	Emissions to near-person, indoor, urban or continental air, to surface water, agricultural and natural soil, WWTP[1] and STP[2]	Inhalation and gaseous dermal uptake, ingestion pathways via drinking water, above ground produce, below ground produce, meat, milk and dairy products, and fish	Direct transfer fraction is simply the chemical mass emitted to a certain compartment divided by the original mass in product and is calculated as the ratio of transfer rate constant to total removal rate, using the USEtox rate constant K matrix (Rosenbaum et al, 2008, Henderson et al., 2011)	Half-lives and residence time in each environmental compartments. Bioaccumulation factors	All chemical emissions to environmental compartments
Article interior	Transfers from chemicals in article interior to near-person air or indoor air, to human epidermis via dermal contact, and to human GI tract via dust ingestion.	Dermal contact with article surface, dust ingestion in addition to inhalation and gaseous dermal uptake	Diffusion-limited (for e.g. VOCs) or partition-limited model (for e.g. SVOCs) for the transfer from article interior to indoor air. The diffusion-limited model accounts for the chemical's internal diffusion inside the article via Fick's 2nd Law, but does not need to account for the restricted long-term chemical's sorption on other indoor surfaces, yielding a two exponential model applicable to most VOCs (Huang and Jolliet 2016). The partition-limited model accounts for indoor sorption, but assumes the chemical is always evenly distributed inside the article since surface partitioning is limiting. The air is assumed in quasi steady state with the different surfaces. This yields a parsimonious two-compartment mass-balance model for article and indoor surfaces applicable to most SVOCs, solved into a two exponential explicit equation using eigenvalues and eigenvectors.	Diffusion coefficient inside the article D_m, solid material-air partition coefficient K_{ma}, material-water partition coefficient K_{mw}, which are predicted by Huang et al., 2017, Huang and Jolliet, 2018, Huang and Jolliet, 2019, respectively.	Chemicals encapsulated in article interior (e.g., building materials, furniture, toys, or arts and crafts)
Skin-	Transfer from	Direct dermal	The model uses a three-	Skin permeation	Personal care

Model	Compartment of entry and main transfers and compartments considered	Direct exposure pathways	Model mechanism	Key parameters	Product example
surface layer	skin surface layer to near-person air, to human epidermis, and to WWTP[1]	aqueous uptake in addition to inhalation and gaseous dermal uptake	compartment mass balance, whose compartments include skin, indoor air, and the product applied on the skin. The model assumes that volatilization and skin permeation are two competing loss processes for chemicals in the product applied on skin. (Ernstoff et al., 2016, Csiszar et al., 2017). The fraction remaining on the skin at the end of the exposure period is washed-off to Waste Water Treatment Plant	coefficient via aqueous solution K_{p_aq}, total gaseous-skin permeation coefficient $K_{p\_gas\_total}$, which are calculated by the methods used by ten Berge (2009) as applied by Csiszar et al. (2017).	products, hand dishwashing
Object surface	Transfer from object surface to near-person air, and indoor air, and to human epidermis	Dermal contact in addition to inhalation and gaseous dermal uptake	The model is a simplified version of the model from Earnest and Corsi (2013), which uses a four-compartment mass balance model, whose compartments include near-person surface, near-person air, far-person surface and far-person air. In this model, a transfer rate constant between near-person surface and the rest of the surface (far-person surface) is used to simulate the movement of the person when cleaning surfaces.	Air-water partition coefficient K_{aw}, which can be predicted or can preferably be estimated from the ratio of chemicals vapor pressure and water solubility when these parameters are available.	Surface cleaner detergents
Food contact material	Transfer from food packaging to food	Dermal contact, food ingestion	This screening-level model estimates the fraction of organic chemicals migrating from polymeric packaging materials into food matrices as a function of two main parameters, namely the diffusion coefficient within the packaging material and the packaging-food partition coefficient (Ernstoff et al., 2017)	Packaging-food partition coefficient K_{pf}.	Food packaging

[1]Wastewater treatment plant, [2]Solid waste treatment plant, [3]Semi-volatile organic compounds.