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Supplemental Material

Advancements in Life Cycle Human Exposure and Toxicity Characterization

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Table S1: Key points for advancing current exposure and toxicity characterization in life cycle impact assessment and similar comparative assessment frameworks

1. General assessment framework ▪ Can we use the framework illustrated in Figure 1 (main text) based on an earlier scientific consensus building effort (Hauschild et al. 2008; Rosenbaum et al. 2008) as a starting point for including the broad range of human health impacts from exposure to toxic chemical substances into life cycle impact assessment?
2. Fate and exposure assessment ▪ What changes or refinements are available for the proposed extended near-field and far-field framework (described further below), e.g., additional compartments, transfer processes, or exposure pathways to be considered? ▪ Which existing studies, methods, and models are best or more usefully suited as starting points for arriving at a consistent set of intake fractions and product intake fractions? ▪ What improvements are needed for the indoor fate and exposure model (e.g., gaseous dermal uptake, non-dietary dust ingestion, sorption to walls) compared to Rosenbaum et al. (2015)? ▪ What is the role of archetypes in the proposed framework (e.g., differentiating product application methods or exposed population groups: generic average estimate with large uncertainty vs. intermediate estimates with less uncertainty vs. final site- and time-specific estimates with least possible uncertainty)? ▪ How can we best consider occupational exposure over the entire supply chain and end-of-life management, and how can we best address occupational exposure in developing/emerging countries? ▪ How should we address variability (locations, populations, etc.) in exposure estimates as outlined in Zeise et al. (2013)? ▪ What is a meaningful resolution or tiered approach for addressing geographical archetypes and for addressing spatial modeling? ▪ How can long-term localized emissions (e.g., from landfills into groundwater) be addressed? ▪ What is the influence of food processing (e.g., washing, cooking, or baking, contact with packaging) on chemical residues in food and formation of secondary pollutants (e.g., polycyclic aromatic hydrocarbons)? ▪ How can we properly address transformation and degradation products and track their pathways among different compartments and eventually reaching humans, and what are the necessary and available data? ▪ What is the role of biomarkers for gaining further insight into and evaluating exposure estimates? In particular, how can biomarkers be used to gain insight on intake fractions and chemical transformation?
3. Dose-response assessment and effect severity ▪ What is a practical way for life cycle impact assessment to address the non-linearity of dose-response relationships and identify non-linear dose-response functions available for organic and inorganic substances that could be practical for a large number of substances? ▪ Which existing studies, methods, and models are best as starting points for determining which dose-response models we should apply in life cycle impact assessment? ▪ How can we best determine the working point on the dose-response curve, accounting for

the cumulative effect of all potential stressors (e.g., in a tiered approach following screening based on assuming linear dose-response across substances)?

- How can we best account for the interaction between the degree of concentration (in time, space, population—i.e., non-homogeneity) of exposure and the degree of non-linearity in dose-response?
- In what instances can a chemical 'mode of action' or "Adverse Outcome Pathway", which indicate how a substance elicits an effect, be used to determine the likely shape of the dose-response curve corresponding to the fraction of the population above any apparent threshold? Can it furthermore be used to estimate a point of departure, potentially in conjunction with incidence rates or assessed with biomarker data to evaluate approaches?
- What are the best suited existing and emerging chronic toxicity data to assess potential disease incidence in a consistent way for human populations?
- How can we best use existing acute toxicity data from e.g., the European REACH regulation (http://echa.europa.eu/information-on-chemicals) or ChemIDplus (http://chem.nlm.nih.gov) with acute-to-chronic extrapolations?
- What metric of disease incidence relative to population intake dose can be derived from available and emerging toxicity data and is consistent with the spatiotemporal resolution provided in life cycle assessment?
- What role can in-vitro to in-vivo human extrapolation have for our toxicity estimates, e.g., ToxCast (http://actor.epa.gov/dashboard)?
- How can we best link external and intake dose to internal dose for cases where toxic response data are based on internal exposure?
- Where and how can we best use epidemiological data to evaluate the disease incidence metric?
- What are the uncertainties for extrapolating effects from animals to humans and for using predictive toxicology?
- What are the prospects and processes for identifying and differentiating the relevant human health effect endpoints and dose-responses and severities for a large number of substances?
- What are appropriate human health damage metrics and why?
- How can disability weights be best identified or established to consistently account for severity of different (mortality and morbidity) health effects, and what are the uncertainties for using disability weights when aggregating health effect endpoints?

4. Emission-to-effect modeling for metals

- How can the essentiality and human deficiencies of selected substances (e.g., essential trace elements) and the vulnerability of humans to those substances be adequately considered?
- How should and could speciation of metals for human exposure be considered in line with work on speciation in the environment (e.g. Gandhi et al. 2010)?
- Is a groundwater compartment necessary (mainly for landfill emissions of metals and including drinking water treatment with filtration as loss process) and if yes, what are available approaches and data to be used as a starting point for consistent implementation into the existing modeling framework?
- How can dynamic aspects in human toxicity characterization related to the environmental fate of metals be considered?

5. Additional remarks

- What additional comments or recommendations could improve the (product) intake fractions, effect information, and severity factors?

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