USEtox® Update Form – Submission	
Issuing organization (name, address, country)	**National Institute for Public Health and the Environment (RIVM), Centre for Sustainability, Environment and Health, Bilthoven, The Netherlands**
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(1) Title (update title)

Ecotoxicity effect modelling based on HC20 derived from EC10-equivalents

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

Recent developments yielded novel modeling recommendations to derive ecotoxicity effect factors and novel ecotoxicity data sets. By combining both, updated USEtox ecotoxicity effect factors and related updated characterization factors can be derived, with immediate utility at, potentially, the global scale and national/international scales (e.g. European Environmental Footprint approaches).

(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. The need to update USEtox has been established based on wide discussions in the LCA community (Fantke et al. 2018, Saouter et al. 2017), leading to specific recommendations at the Pellston 2018 workshop (Owsianiak et al. 2019, Chapter 7), aligned with modeling/data choices made for the human toxicity effect factor derivation (Fantke et al. 2019, Chapter 4). The update is meaningful in practice, as:
   - It allows using the comprehensive base of chronic ecotoxicity data reported at lower effect levels than the currently applied 50% (EC50-values), strengthening the foundation of the derived effect factors.
   - The proposed ecosystem effect level (potentially affected fraction of species 20%) is more representative of actually occurring effect levels than the currently applied 50% (HC50) level, increasing the environmental relevance of the resulting effect factors.
   - The chemical ranking according to the new effect factors is anticipated to be more in accordance with current hazard ranking schemes based on e.g. PNEC values, reducing a source of criticism from companies claiming that LCIA priorities are currently partly in disagreement with other environmental prioritizations, e.g. under the European REACH regulation.
   - It provides global standards that can be widely supported by stakeholder acceptance (e.g., EC; UNEP) regarding modeling and data choices.
   - It covers a (far) wider array of compounds with chronic data, which is relevant as (new) products may contain any chemical compound.

b. The improvement seen from a practical point of view can be a global consensus data set (that is likely subsequently adopted by EC for formal Environmental Footprinting policies); in Europe, it would end a period of 'temporary' effect factors for the footprinting policies.

c. The improvement can be substantiated by expert efforts, which (i) reach consensus on the use of source data sets, (ii) analyze the selected (combined) data set using the Pellston recommendations, to yield (iii) updated USEtox ecotoxicity effect factors and an underlying report and tool. The final output is worth the effort, as all materials are ready to be shaped into USEtox effect factors; those likely directly serve policy purposes. Especially, in the EU-context, the EC and end-users can end the current 'temporary' situation.

(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. Two modifications are foreseen. In summary:
- Collating the global resources of potentially relevant input data sets.
- Curating and extrapolating the input data to arrive at a set of chronic EC10 equivalent effect data.
- Implementation of the Pellston recommendations for deriving a consistent set of ecotoxicity effect factors.

Each modification asks for making fundamental choices, followed by a standard-approach to derive the Effect Factors (which includes operational choices to solve technical problems, peer-review of results, etc.).

The *fundamental choices are key*. For the data sets, we can foresee the fundamental difference between the (current) JRC approach for the EC (which bases the EF's on the ECHA's ecotoxicity data + EFSA's OpenFoodTox data because those are obligatory entities in chemical safety assessment policies) and the (current) alternative approach to use the global set of curated scientific data (preferably neglecting 'dynamic' databases such as ECHA's). Fundamental choices for the modeling step have been made in the Pellston workshop.

The novel method diverges from the current situation by the aforementioned innovations (more data, and Pellston consensus-methods).

Work plan (methods, summary of steps)

Phase 1: Foundational choices

- Modeling: Take the Pellston report, and adopt as basis. Effect Factors will be HC20 of chronic EC10 equivalents.

- Data sets: start and run a process in which the fundamental choice is made on source data ('policy-agreed data', or 'open-science data' or 'combined'), and on final status of the Effect Factors (preferred: global use, and directly suitable for EC footprinting policy use).

Phase 2: Analyses

- Collate selected data sets
- Curate them (doubles, outliers, irrelevant test conditions, etc.)
- Derive per-compound $HC20_{EC10eq}$ (option: derive an EF-quality score, such that higher and lower-quality EF's can be known for the users).
- Peer-review outcomes and update USEtox to ecotoxicity EF's 2020
- Report, with full list of compound $HC20_{EC10eq}$ values
- Implement the EF's in software etc. depending on the previous steps

Calculation of effect factors:

Effect factors are obtained from the SSD slope between the hazard concentration for a 20% species response level, HC20:

$$EF = \frac{0.2}{\mathrm{HC20}_{\mathrm{EC10}^{\mathrm{eq}}}} \quad (1)$$

The $\mathrm{HC20}_{\mathrm{EC10}^{\mathrm{eq}}}$ is generally derived from arithmetic mean ($\mu_{\ln}$) and standard deviation ($\sigma_{\ln}$) of the log-normally distributed, available chronic $\mathrm{EC10}^{\mathrm{eq}}$ data points for all considered species, and the z-

value of this distribution corresponding to 20th percentile ($z_{0.2}$), which is a function of the number of available underlying toxicity data points, as:

$$\mathrm{HC20}_{\mathrm{EC10}^{\mathrm{eq}}} = \mathrm{e}^{(\mu_{\ln} + z_{0.2} \times \sigma_{\ln})} \tag{2}$$

with:

$$\mu_{\ln} = \ln \mu - \frac{\sigma_{\ln}^2}{2},\ \sigma_{\ln} = \sqrt{\ln\left(1 + \frac{\sigma^2}{\mu^2}\right)} \tag{3}$$

where μ and σ are respectively the arithmetic mean and standard deviation of the normal distribution of the underlying $\mathrm{EC10}^{\mathrm{eq}}$ data:

$$\mu = \frac{1}{n} \times \sum_{i=1}^{n}\left(\mathrm{EC10}_i^{\mathrm{eq}}\right),\ \sigma = \sqrt{\frac{1}{n} \times \sum_{i=1}^{n}\left(\mathrm{EC10}_i^{\mathrm{eq}} - \mu\right)^2} \tag{4}$$

Contextual

11. Align with relevant stakeholders, such as EC (JRC), GLAM
12. Align with requisites of funding, incl. JRC: provisional "willingness to collaborate handshake" made (between Serenella Sala and Leo Posthuma)
13. Steer the above process in order to improve utility of the outcomes (e.g., timeliness of new effect factors in relation to EC-policy update planning)

b. The update follows current recommendations for deriving ecotoxicity effect estimates based on a widely accepted species sensitivity distribution (SSD) approach. The update allows for a broader consideration of effect data and estimation methods, includes extrapolation between different effect metrics and acute/chronic exposures and provides exposure concentration estimates that are more environmentally relevant than previous estimates in USEtox. This will involve to define a hierarchy of input data (e.g. use in priority chronic EC10 data when available) and a comparison of available QSAR-based extrapolation and data gap filling approaches to arrive at chronic EC10 equivalents (e.g. Aurisano et al. 2019, Posthuma et al. 2019, Hou et al. 2020, Douziech et al. 2020). Further, Since uncertainty in the spread between species (i.e. σ) is very large if the SSD is based on limited ecotoxicity data (<10), it will be discussed if σ can be derived in a chemical-specific way and what to consider as reasonable amount of input data. Finally, the update allows for also considering data for marine and soil terrestrial ecotoxicity data, following the same underlying calculation of hazard concentrations (HC20) based on EC10-equivalents obtained from a wide range of available effect information.

(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:

- Owsianiak, M., Fantke, P., Posthuma, L., Saouter, E., Vijver, M., Backhaus, T., Schlekat, T., Hauschild, M., 2019. Ecotoxicity. 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. 138-172. http://lifecycleinitiative.org/training-resources/global-guidance-for-life-cycle-impact-assessment-indicators-volume-2/
- Posthuma, L., van Gils, J., Zijp, M.C., van de Meent, D., de Zwart, D., 2019. Species sensitivity distributions for use in environmental protection, assessment and management of aquatic

ecosystems for 12,386 chemicals. Environmental Toxicology and Chemistry 38, 905-917. http://doi.org/10.1002/etc.4373

Related/supporting publications:

- Aurisano, N., Albizzati, P.F., Hauschild, M., Fantke, P., 2019. Extrapolation factors for characterizing freshwater ecotoxicity effects. Environmental Toxicology and Chemistry 38, 2568-2582. http://doi.org/10.1002/etc.4564
- Douziech, M., Ragas, A.M.J., van Zelm, R., Oldenkamp, R., Jan Hendriks, A., King, H., Oktivaningrum, R., Huijbregts, M.A.J., 2020. Reliable and representative in silico predictions of freshwater ecotoxicological hazardous concentrations. Environment International 134, 105334. http://doi.org/10.1016/j.envint.2019.105334
- Fantke, P., Aurisano, N., Backhaus, T., Bulle, C., Chapman, P.M., Cooper, C.A., De Zwart, D., Dwyer, R., Ernstoff, A., Golsteijn, L., et al., 2018. Toward harmonizing ecotoxicity characterization in life cycle impact assessment. Environmental Toxicology and Chemistry 37, 2955-2971. http://doi.org/10.1002/etc.4261
- Hou, P., Jolliet, O., Zhu, J., Xu, M., 2020. Estimate ecotoxicity characterization factors for chemicals in life cycle assessment using machine learning models. Environment International 135, 105393. http://doi.org/10.1016/j.envint.2019.105393
- Saouter, E., Biganzoli, F., Pant, R., Sala, S., Versteeg, D., 2019. Using REACH for the EU environmental footprint: Building a usable ecotoxicity database, Part I. Integrated Environmental Assessment and Management 15, 783-795. http://doi.org/10.1002/ieam.4168
- Saouter, E., Wolff, D., Biganzoli, F., Versteeg, D., 2019. Comparing options for deriving chemical ecotoxicity hazard values for the European Union environmental footprint, Part II. Integrated Environmental Assessment and Management 15, 796-807. http://doi.org/10.1002/ieam.4169
- López i Losada, R., Owsianiak, M., Ögmundarson, Ó, Fantke, P. (2020). Metal residues in macroalgae feedstock and their implications for biorefinery microorganisms. Journal of Cleaner Production, *in review*.

b. A description of the update content is provided in the main publications under (a). The main followed methodological approach to derive HC20 is described in the last related/supporting publication listed under (a), while the overall SSD approach is described in the following publication:
   - Posthuma, L., Suter II, G.W., Traas, T.P., 2002. Species Sensitivity Distributions in Ecotoxicology. CRC Press, Boca Raton, FL, USA. http://doi.org/10.1201/9781420032314

c. A full documentation of the underlying data and approaches is found in above main and related/supporting publications including their supporting information documents. Note that the global SOLUTIONS database (collated, curated) can be uniformly used for chemical safety assessment (e.g., REACH), LCA and the retrospective approaches such as in the Water Framework Directive. We can highlight, that the database underlying effect factors is the updated, versatile-use basis to proceed further.

d. Data sources for the update are provided in above main and related/supporting publications, building on various European, US and other data sources.

e. The update content has been evaluated in the SOLUTIONS project, and the method has been tested widely against available ecotoxicological effect data.

(6) Applicability check

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

a. The update concerns all substances for which there are sufficient input data, and for which no specific problems arise. This includes organic substances and metals.

b. The update is fully considerable in practice as it follows the same logic as currently applied methods. The update builds on the SSD approach that has been widely applied in several projects and training courses. The proposed update serves LCA, risk assessment and water quality management, and the underlying SSD-principles and data curation methods are widely accepted. Since a robust estimation of HC20 requires more underlying effect data than a robust estimation of HC50, this will be facilitated by allowing for the use of more widely available chronic NOEC, LOEC and EC10 data, and by applying state-of-the-art QSAR approaches for extrapolating (e.g. between acute and chronic), data gap filling and estimating uncertainty.

c. We prepare for further updates, by (a) having a currently available, curated database as basis for that, and by (b) utilizing an R-script (allowing to re-run the curation and effect factor derivation analyses steps if additional data are added in the future). Different data sources might be explored in addition.

(7) Level of consistency with USEtox check
a. Parsimony: How is the update parsimonious?
b. Data selection hierarchy (for previously published CFs and databases) as published in the official USEtox papers in IJLCA

a. The proposed update is fully parsimonious in terms of following the exact same principles for effect data collection and modelling as currently applied in USEtox. However, the update will bring several scientific advances as compared to the current approach, mainly related to a much broader underlying effect data coverage, systematic data selection and curation principles, and a full statistical SSD-based approach for deriving hazard concentrations (HC20) at environmentally more relevant exposure concentration levels, without introducing additional complexity in the effect modelling.

b. The proposed update allows to make much broader use of the available chronic effect data, and will be clearly preferred over existing approaches that mainly rely on using acute effect data. Furthermore, the proposed update will be able to build on systematically curated dataset of ecotoxicity effect data collected from various data sources worldwide (Posthuma et al. 2019), which is clearly preferred over existing approaches. With this data selection hierarchy, we are fully aligned with recommendations in USEtox to start from best available data (Henderson et al. 2011). This update will affect previously published USEtox characterization factors and input data.

(8) Discussion of level of acceptance/consensus
a. Level of scientific acceptance/consensus in the community: Is update already used in published work?

a. This update builds on a careful balance between the currently applied approach in LCA (mainly using acute EC50 data) and the widely followed approach in risk assessment (mainly using both acute and chronic NOEC and ECx data). Both, the LCA approach and the risk assessment approach aim to address distinct questions, and are widely accepted and applied in their respective domains. It is widely accepted in LCA that the long-term perspective requires to reflect essentially chronic exposure. The update, hence, builds on several published studies connecting different effect metrics (NOEC, LOEC, ECx) and exposures (acute, chronic), e.g. Aurisano et al. 2019, Posthuma et al. 2019, Saouter et al. 2019. The modelling approach, i.e. deriving an EC10-equivalent metric as starting point for calculating a hazard concentration follows established statistical methods based on the widely accepted and published SSD concept (e.g. Posthuma et al. 2002).

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

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