Empa
Materials Science and Technology

In Vitro & In Silico-Derived Effect Factors for USEtox: A framework for Non-Animal Toxicity Characterization in LCA

CHIASMA

SETAC Europe 35th Annual Meeting

12 May 2025 – Marc Majó

SETAC

CHIASMA Project

Accessible innovative methods for the safety & sustainability assessment of chemicals & materials

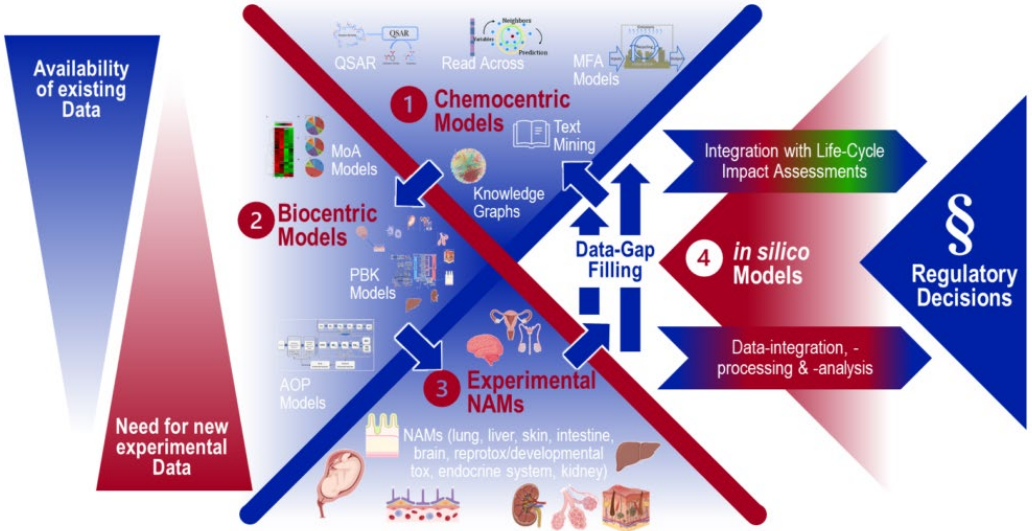
- Demostration of a comprehensive set of **New Approach Methodologies** (NAMs) and integration in a **user friendly, reliable and robust framework** to perform **human and environmental safety evaluation** in a regulatory context.

CHIASMA R&I approach for testing based on the integration of:

(1) Chemocentric

(2) Biocentric

(3) New experimental models

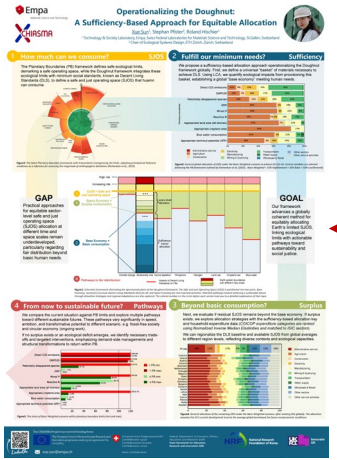


CHIASMA Project: WP6 Methods integration & Application

- To **evolve** available concepts & theories for Next Generation Risk Assessment (NGRA) beyond current OECD Guidance **towards a Next Generation Safety Assessment (NGSA)**.
- To **enhance the current USEtox method** for the assessment of human toxicity & ecotoxicity by expanding it with data from the NGSA, allowing a better use of *in vitro/in silico* information.
- **Enhancement of an absolute sustainability assessment**: Translating planetary boundaries into Material-Level in LCA
- To **operationalize the EU's SSbD framework** by linking NGSA, LCA/MFA, & LCIA across the EU's SSbD approach, using outcomes from WP1, WP2 and 3, in the form of the CHIASMA-framework.
- To **suggest possible evolutions for the regulatory frameworks** as such to fully realise the potential of the new integrated NGSA & SSbD methodology.

Poster presentation
Session: 5.01.P – Pushing the Limits: Incorporating Absolute Limits in Life Cycle Assessment
Poster ID: 5.01.P-Mo408

Title: Operationalizing the Doughnut: A Sufficiency-Based Approach for Equitable Allocation



Evolution towards next generation of Risk Assessment and integration with LCA

Evolution of

Traditional Safety Assessment

Next Generation Safety Assessment

safety assessment		data	Variable	extrapolation from model to assessment target	variability of assessment target	reference value	classification
traditional	human	rodent data (rarely dog or else)	usually NOAEL rarely BMD [+ BMDL/U]	interspecies extrapolation usually default factor 10 rarely data-based [+LCL/UCL], e.g. WHO 2017	human variability usually default factor 10 rarely data-based [+LCL/UCL], e.g. WHO 2017	usually human safe dose rarely human dose HD protective for x% of population [with y% probability]	effect type: irrit./corr., CMR effect potency: acute toxic, sensitizing, STOT SE & RE
	env	algae + daphnids + fish data	usually EC50 or EC10 or NOAEC rarely BMC [+ BMCL/U]	usually time extrapolation (factor 1 to 1000)	rarely: Interspecies Correlation Estimates & Species Sensitivity Distributions	usually environmental safe concentration rarely env. conc. protective for x% of species [with y% prob.]	effect potency: acute, chronic, PBM
Next Generation	human	human in vitro data, In silico data	bmc [+ bmdl/bmdu]	QIVIVE extrapolation [+ uncertainty from input data & model parameter]	human variability [+ uncertainty], e.g. from PBK and/or historical WHO data	human dose HD protective for x% of population [with y% probability]	effect potency: revised STOT SE & RE [+% prob. for category]
	env	algae + daphnids + fish cell data, In silico data	EC50 or bmc10 [+bmdl/bmdu]	time extrapolation?	Interspecies Correlation Estimates & Species Sensitivity Distributions	environmental concentration protective for x% of species [with y% probability]	effect potency: acute, chronic, PBM [+% prob. for category]

Integration with SSbD and LCA

NGSA

probably safe hazard & safe dose

for toxic bioactivity

in humans

in environment

SSbD

probably safe hazard &

safe MoE = safe dose / exposure

for production, use, waste, recycling

for human

for environment

LCA

probably acceptable impact on

environmental health

biodiversity

climate

society

socio-economy

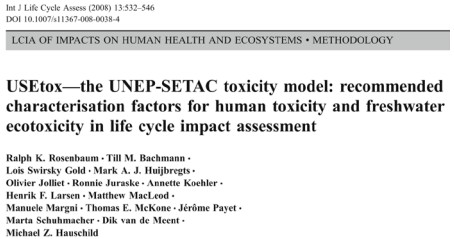
Adaption to USEtox

- Mathematical framework:
  - Fate modelling (FF) → Distribution of chemicals on environmental compartments
  - Exposure assessment (XF) → Via inhalation, drinking water and food
  - Effect assessment (EF) → Toxicity response based on animal data

$$CF = FF \cdot XF \cdot EF$$

Foundations for USEtox

R.K. Rosenbaum, et al. Int J Life Cycle Assess (2008)


Int J Life Cycle Assess (2008) 13:532–546
DOI 10.1007/s11367-008-0038-4

LCIA OF IMPACTS ON HUMAN HEALTH AND ECOSYSTEMS • METHODODOLOGY

USEtox—the UNEP-SETAC toxicity model: recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment

Ralph K. Rosenbaum · Till M. Bachmann · Lois Swirsky Gold · Mark A. J. Huijbregts · Olivier Jolliet · Ronnie Juraske · Annette Koehler · Henrik F. Larsen · Matthew MacLeod · Manuele Margni · Thomas E. McKone · Jérôme Payet · Marta Schuhmacher · Dik van de Meent · Michael Z. Hauschild

Refining: Exposure modeling, extrapolation methods, and expanding chemical applicability

R.K. Rosenbaum, et al. Int J Life Cycle Assess (2011)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LCIA OF IMPACTS ON HUMAN HEALTH AND ECOSYSTEMS (USEtox)

USEtox human exposure and toxicity factors for comparative assessment of toxic emissions in life cycle analysis: sensitivity to key chemical properties

Ralph K. Rosenbaum · Mark A. J. Huijbregts · Andrew D. Henderson · Manuele Margni · Thomas E. McKone · Dik van de Meent · Michael Z. Hauschild · Shanna Shaked · Ding Sheng Li · Lois S. Gold · Olivier Jolliet

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- Mathematical framework:

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Incorporation of *in vitro* & *in silico* data

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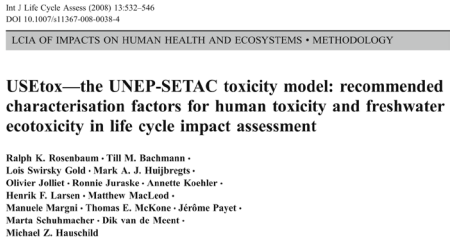
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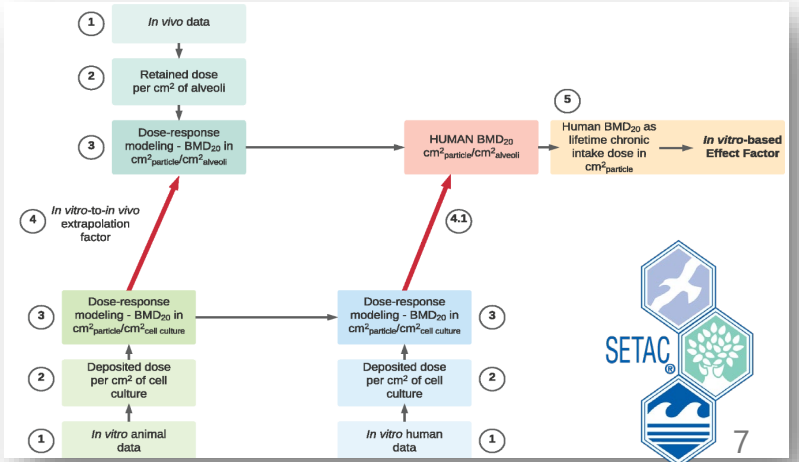
Adaption to USEtox: Effect assessment

- **Key steps,** D. Romeo, et al., *Environmental Science & Technology* **2022**:

1. Data collection in vitro and in vivo (animal and human).
2. Simulation of particle deposition and retention (in vitro and in vivo)
3. Benchmark Dose (BMD_{20}) calculations from dose-response curve fit.
4. In vitro-to-in vivo extrapolation (Ratio animal : in vitro animal BMD_{20})
5. Development of human EFs using human BMD_{20} from in vitro human BMD_{20}.



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PBK/QIVIVE

Reverse-engineer what in vivo external dose (mg/kg/day) corresponds to the internal concentration (BMD_{20}) observed in vitro

Physiological data
Chemical-specific data (QSAR-predited)
In vitro effect data

↓

Human equivalent dose (PoD)

NAMs in vitro models

Uncertainty & Variability

PBK and WHO information

Adaption to USEtox: Fate modelling & effect assessment

- Mathematical framework:

➢ Fate modelling → Distribution of chemicals on environmental compartments

Quantitative Structure-Activity Relationship (QSAR)

➢ Estimation of bioconcentration factors, degradation, solubility, volatility

Fill the gaps for novel chemicals/materials lacking experimental data

➢ Exposure assessment → Via inhalation, drinking water and food

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Incorporation of *in vitro* & *in silico* data

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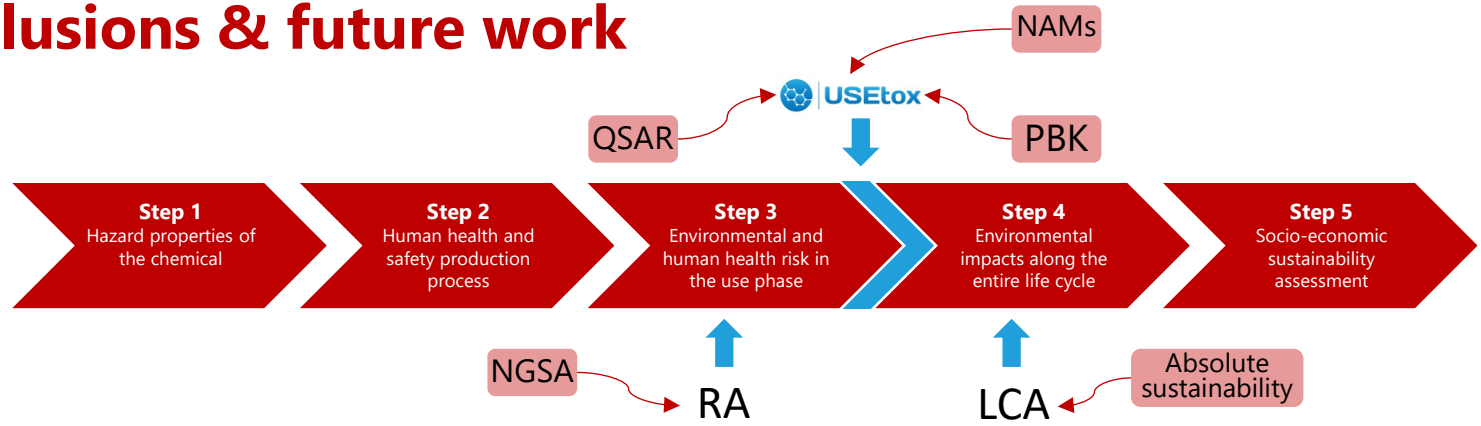
Incorporation of *in vitro* & *in silico* data

USEtox aligned with SSbD framework

Linking point between risk and sustainability

Conclusions & future work



Future work

- BMC modelling with in vitro data
- Adjusting and testing PBK modelling: compounds and effect
  - Gather data for parametrization and evaluation
  - Characterize uncertainties
  - Model framework development (PBK + QIVIVE + uncertainty)

- Progressing to the CHIASMA-SSbD operationalization with results from other WP

Empa – The Place where Innovation Starts

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CHIASMA

The CHIASMA Project has received funding from:

The European Union's Horizon Europe Research and Innovation programme under grant agreement No. 101137613.

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Federal Department of Economic Affairs, Education and Research EAER
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National Research Foundation of Korea

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