Accessible Innovative Methods for the Safety & Sustainability of Chemicals & Materials (CHIASMA)

Focus on WP6 – Method Integration & Application

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Project Overview

The CHIASMA Project is fully aligned with the EU strategies for the development of the **Safe and Sustainable by Design (SSbD)** framework to ensure safety and sustainability of enabling and emerging technologies – including those based on chemicals and materials, as addressed in the EU's Chemical Strategy for Sustainability (2020), in the European Green Deal (2021) and in the Advanced Materials 2030 Initiative (AMI2030).

CHIASMA will focus on developing **New Approach Methodologies (NAMs)** and **improved Life Cycle Impact Assessment (LCIA)** approaches and strategies, to ultimately integrate these into the CHIASMA Framework for a combined assessment of **Safe & Sustainable by Design (SSbD)** to support REACH (Regulation for Registration, Evaluation, Authorisation and Restriction of Chemicals), CLP (Regulation for Classification, Labelling and Packaging of chemicals) & others.

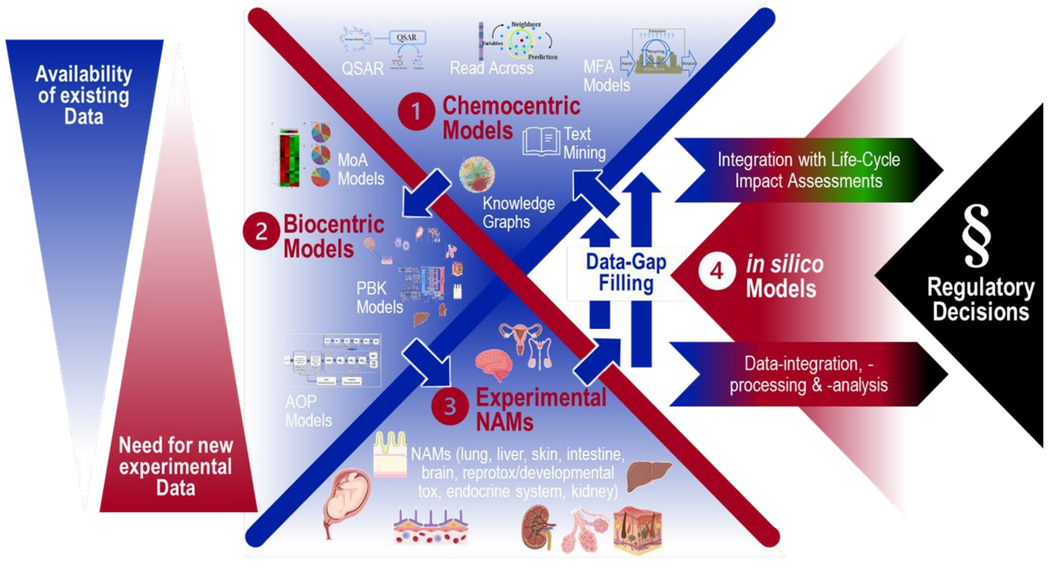


Figure 1: Illustration of the CHIASMA R&I approach to testing and assessment of materials using an iterative approach based on the integration of (1) chemocentric, (2) biocentric and (3) new experimental models into a conceptual framework for data-integration and -processing.

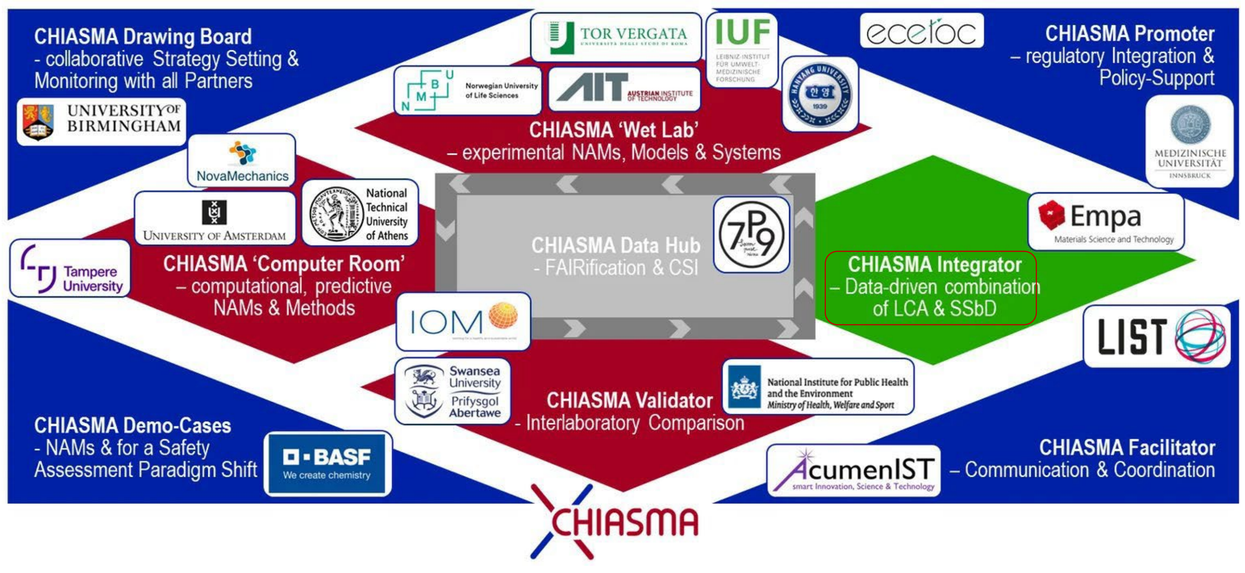


Figure 2: Annotated overview of the CHIASMA Project's workflow and the main Partner Roles.

WP 6 – Method Integration & Application

Objectives

1. To **evolve available concepts & theories** for Next Generation Risk Assessment (NGRA) **towards Next Generation Safety Assessment (NGSA)**.
2. To **enhance USEtox method** by expanding it with data from the NGSA, allowing a **better use of in vitro/in silico information**.
3. To **operationalize the EU SSbD framework by linking NGSA, LCA/MFA & LCIA**, using outcomes from the other WPs → CHIASMA-framework.

Stepwise Procedure

1 Evolution of traditional safety assessment to next generation safety assessment (NGSA)

Safety Assessment	Data	Variable	Extrapolation from model to assessment target	Variability of assessment target	Reference value	Classification
Traditional	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 protective for x% of population [with y% probability]	effect type: irritation, corrosion, CMR effect potency: acute toxic, sensitizing, STOT SE & RE
	algae+daphnid+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 environmental concentration protective for x% of species	effect potency: acute, chronic, PBM
Safety Assessment	**Data**	**Variable**	**Extrapolation from model to assessment target**	**Variability of assessment target**	**Reference value**	**Classification**
Next Generation	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 protective for x% of population [with y% probability]	effect potency: revised STOT SE & RE [+% prob. for category]
	algae+daphnid+fish cell data, in silico data	EC50 or BMC10 [+BMDL/BMDU]	time extrapolation?	Interspecies correlation estimates & species sensitivity distributions	usually environmental safe concentration rarely environmental concentration protective for x% of species	effect potency: acute, chronic, PBM [+% prob for category]

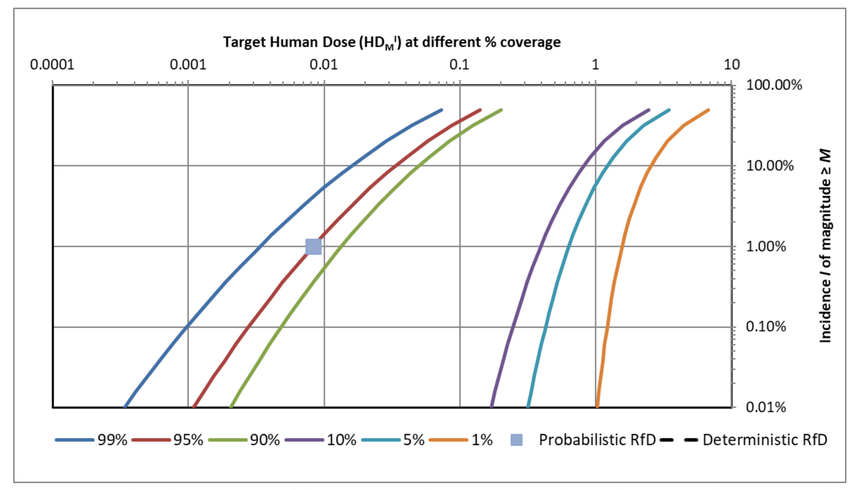
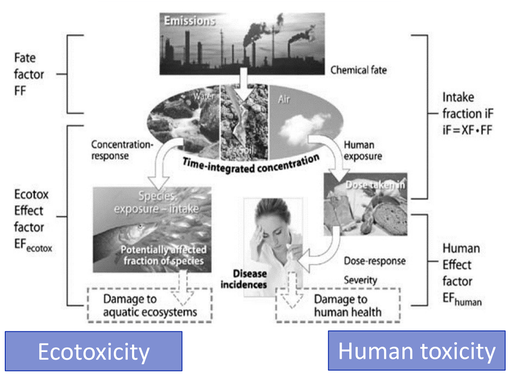


Figure 3. In vitro/In Silico derived points of departure may be integrated with available data on human variability and uncertainty (WHO 2017) to provide human references doses (HD) for protection targets in terms of specified probabilities for specified human population incidences.

2 Enhancement of USEtox method

Make use of *in vitro* & *in silico* data for EF within USEtox and combination of NGSA results with the approach from *Romeo et al., 2022 [1]*:

CF = FF *EX* EF



USEtox *– the UNEP-SETAC toxicity model (Rosenbaum et al. 2008)*

The five step calculation

1. Collection of in vivo / in vitro data, human and animal
2. Application of dosimetry models
3. Calculation of Benchmark Doses (BMD)
4. In vitro to in vivo extrapolation
5. Calculation of human toxicity EF

[1] Romeo, D., et al. (2022). *Environmental Science and Technology*, *56*(12), 8552–8560.

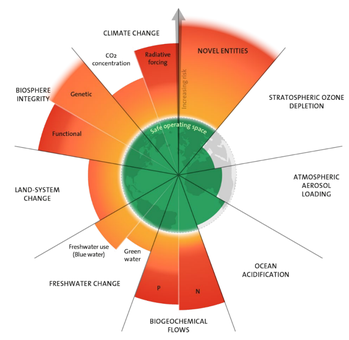
3 Absolute Sustainability Assessment

Safety dimension

Step 1: Hazard assessment of chemical/materials

Step 2: Human health, safety, and environmental aspects: Production and processing phase

Step 3: Human health, safety, and environmental aspects: Final application phase



https://www.stockholmresilience.org/research/planetary-boundaries.html

Step 4: Environmental sustainability assessment

Step 5: Social and economic sustainability assessment

Environmental dimension

Social and economic dimension

SSbD Assessment result

Stepwise approach for SSbD framework safety and sustainability assessment. (Caldeira et al. 2022)

4 Operationalization of the EU SSbD framework

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