EASE Suite: An introduction to a holistic and integrated chemical hazard and risk estimation platform

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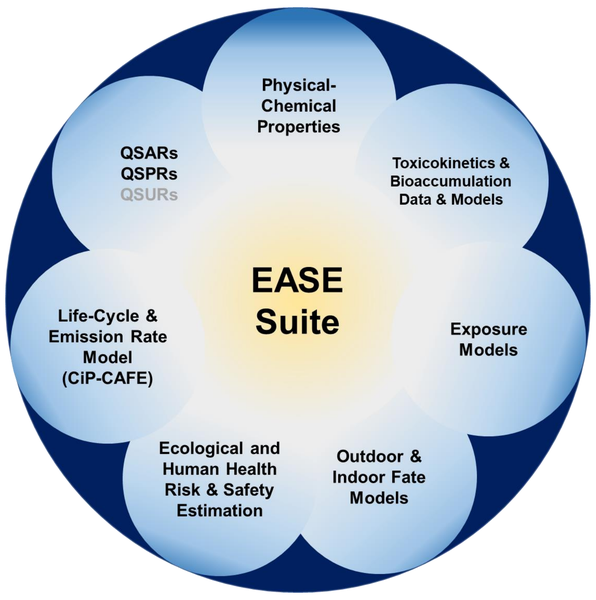


INTRODUCTION

- Under US law (TSCA / LCSA [1]) thousands of new and existing chemicals are subject to ecological and human health assessment; however, there are often extensive data gaps for PBT, exposure and risk assessment. Models and tools are required to address data gaps and integrate available data sources.
- There are challenges implementing state of the science information to inform decision-making because resources are limited and it can be difficult to access, operate and apply fit-for-purpose exposure models.
- Efficient and effective tools can address current challenges in various regulatory contexts and the rapid ability to apply risk-based prioritization methods can optimize resource use and prioritize uncertainty to systematically build confidence in decision-making.

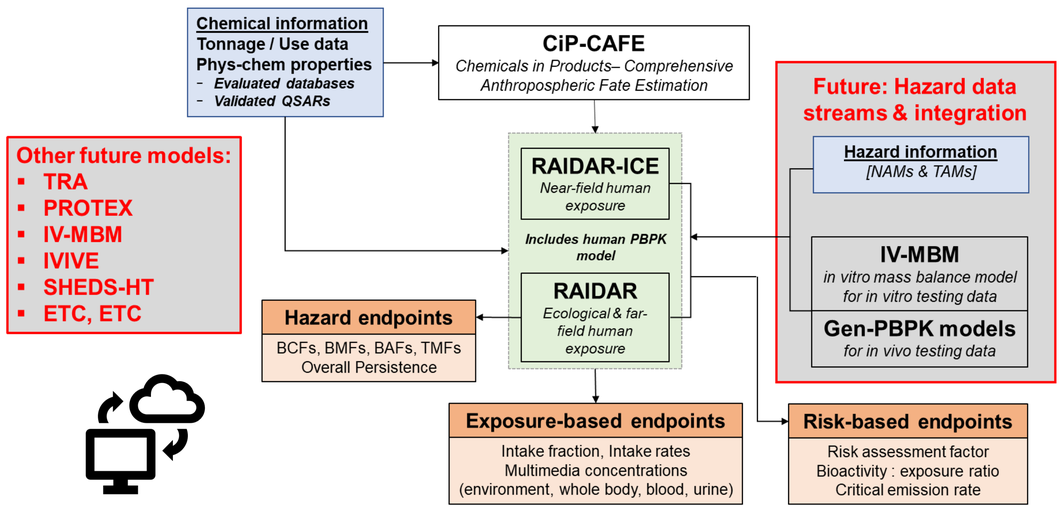
OBJECTIVE

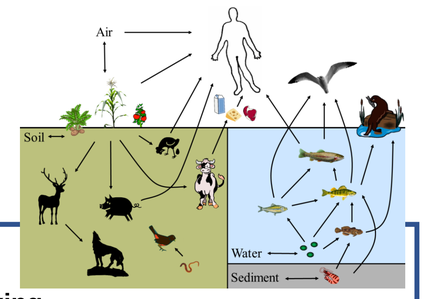
- Introduce concepts of the **Exposure And Safety Estimation (EASE) Suite** platform and demonstrate and evaluate its application in a case study for aggregate human exposure estimation.
- Outline how the prototype can evolve to include additional models and data sources.
- *Seek multi-stakeholder engagement and participation in the development and evolution of EASE Suite*.

Some Benefits of EASE Suite:

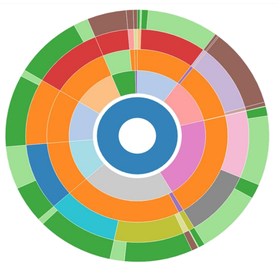
- Integrates curated databases, validated QSA(P)Rs, and environmental fate and exposure models
- "**AUTOPARAMETERIZES**" built-in fate, bioaccumulation and exposure models from SMILES notation while allowing user-preferred inputs of select parameters
- Quickly provides screening-level ecological and human assessment data with evaluated models
- **MODULAR**: can choose to use the entire flow (e.g., from production volume to exposure and safety estimation) or just a particular model (e.g. RAIDAR-ICE for indoor fate and human exposure)
- Works on multiple devices and can be implemented on a network server (e.g., www) or behind firewalls
- Can be expanded to include other models, tools and databases and to provide batch-mode operations
- Can be customized to best suit end-user preferences and assessment challenges

Current (and Planned) EASE Suite Framework





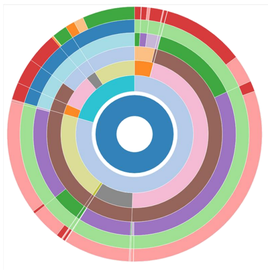
Physical-Chemical Properties



Current information included:
- >130,000 experimental and predicted physical-chemical property data for >25,000 organic chemicals
- Various QSA(P)Rs with **Applicability Domain** output *including* some EPI Suite predictions

Some possible next-steps:
- Expand to include more data and properties
- Include summary statistics (uncertainty) and thermodynamic consistency calculations
- Option to filter, select and export data of interest

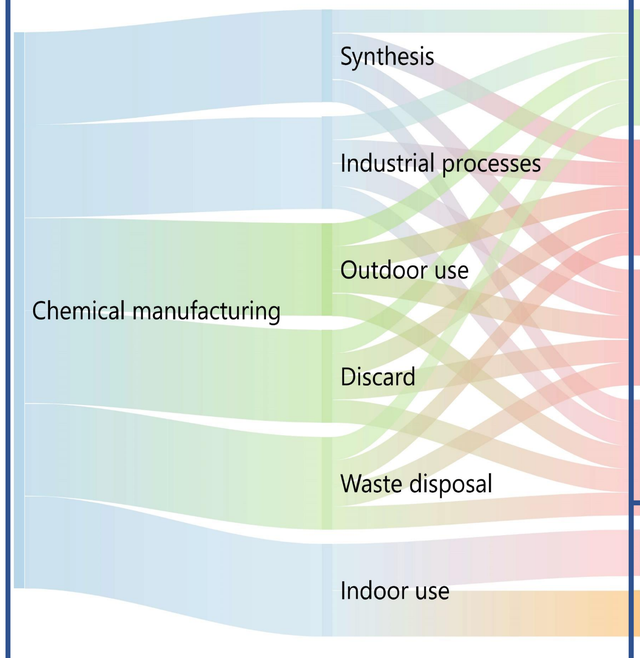
Toxicokinetics (TK) Data



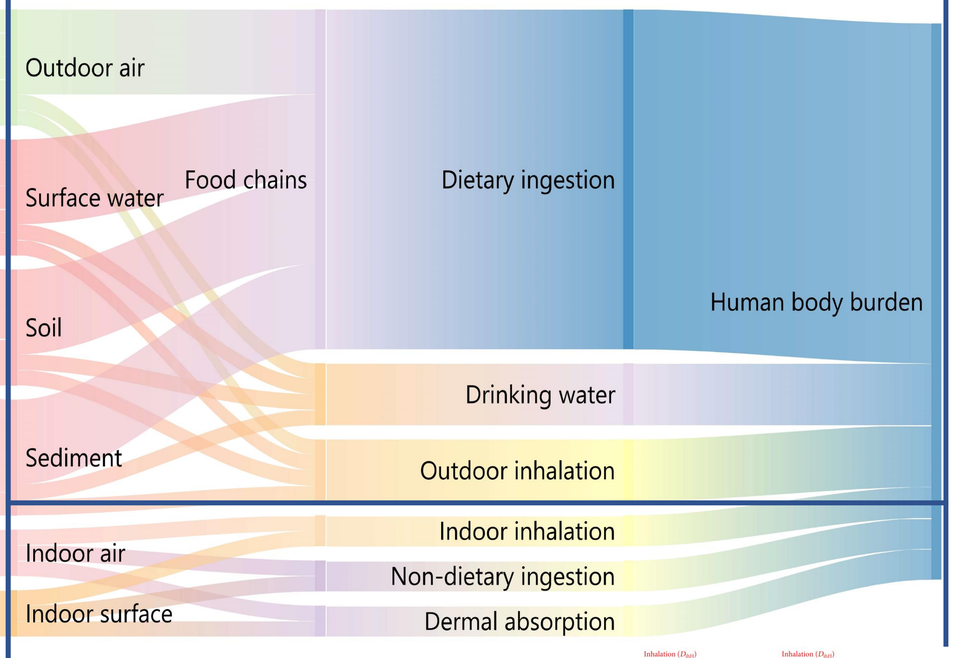
Current information included:
- >30,000 curated in vitro and in vivo TK and bioaccumulation data for > 10,000 chemicals in rodents, humans and fish
- QSARs for predicting biotransformation half-lives

Some possible next steps:
- Expand to include more data
- Develop and validate more TK-QSARs, e.g., CL_H & V_D
- Include summary statistics (uncertainty) for data
- Option to filter, select and export data of interest

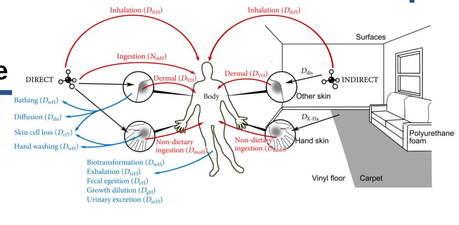
CiP-CAFE [2]:
Life-Cycle Emission Rate Estimates



RAIDAR [3]:
Risk Assessment IDentification And Ranking

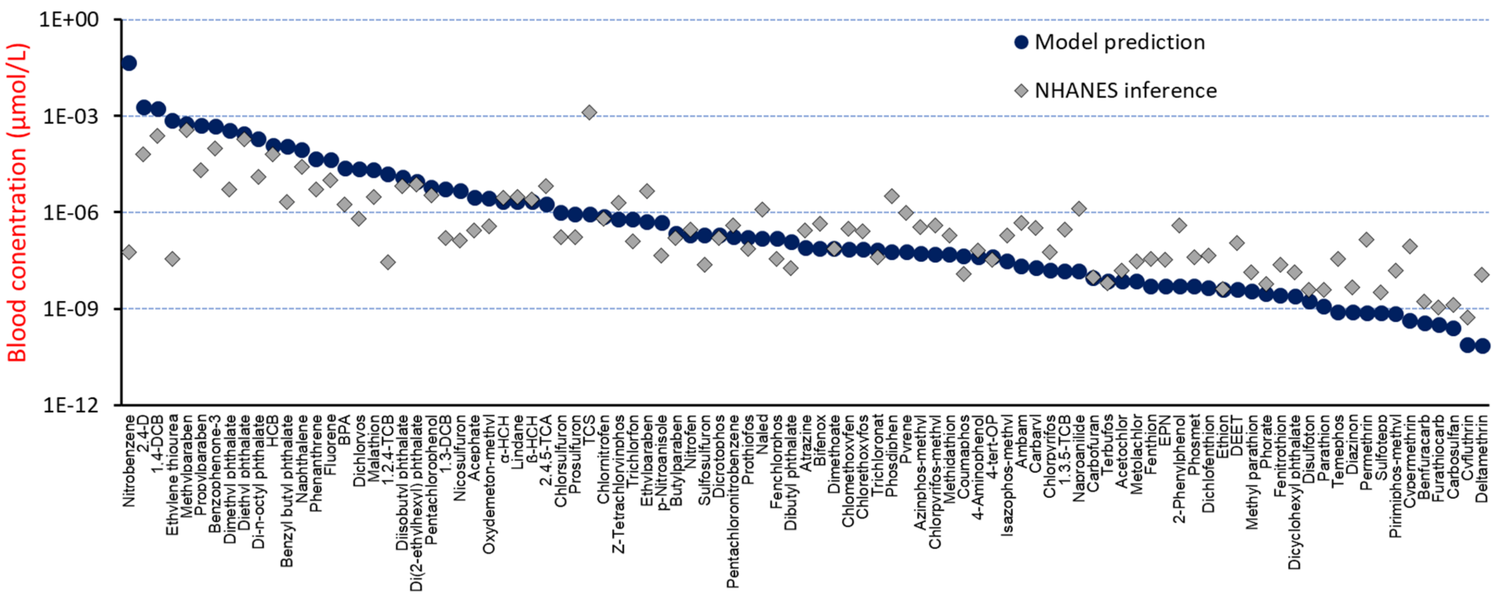


RAIDAR-ICE [4]:
RAIDAR – Indoor and Consumer Exposure



CASE STUDY APPLICATION: AGGREGATE HUMAN EXPOSURE ESTIMATION

- Apply **EASE Suite** to predict aggregate human exposure estimates (steady-state blood concentrations) using **only TWO input parameters** for each chemical: 1 – SMILES; 2 – Production Volume
- Obtain and enter SMILES and Production Volume estimates for 95 organic chemicals with different use categories (e.g., industrial, biocide, cosmetics and personal care).
- Simulate life-cycle chemical emissions (CiP-CAFÉ), environmental fate and far-field human exposure (RAIDAR) and indoor fate and a physiologically-based toxicokinetic model (RAIDAR-ICE), e.g., Atrazine (**right**).
- Evaluate EASE Suite predicted blood concentrations with inferred blood concentrations from the US NHANES population biomonitoring data [5] (**below**).
- Demonstrated proof of concept; seek to expand current capacity and continue applications and evaluations.



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