

Project 8: Applying Emerging Science to Inform Risk Screening and Assessment

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Risk Assessment Issues Being Addressed

- More rapid and informed evaluation of:
 - Potential health effects posed by hundreds to thousands of chemicals
 - Potential risks resulting from various exposure scenarios
- To facilitate:
 - Hazard determinations
 - Dose-response model selection
 - Application of AOP/MOA and biomarker data
 - Dosimetry to inform linkage of data streams
 - Cumulative risk characterizations
 - Susceptible population evaluation
- Applications to better understand and characterize national, community, or site-specific risks

Project Objectives

- Evaluate the utility of emerging data and computational methods
- Evaluate application of new rapid screening & prioritization methods to pilot national, community or site-specific assessments
- Update models and approaches to seamlessly link exposure, dose and response measures
- Provide knowledge on utility of new approaches and data types to build capacity and accelerate application in risk assessment
- Engage peer reviewers and stakeholders; address community concerns

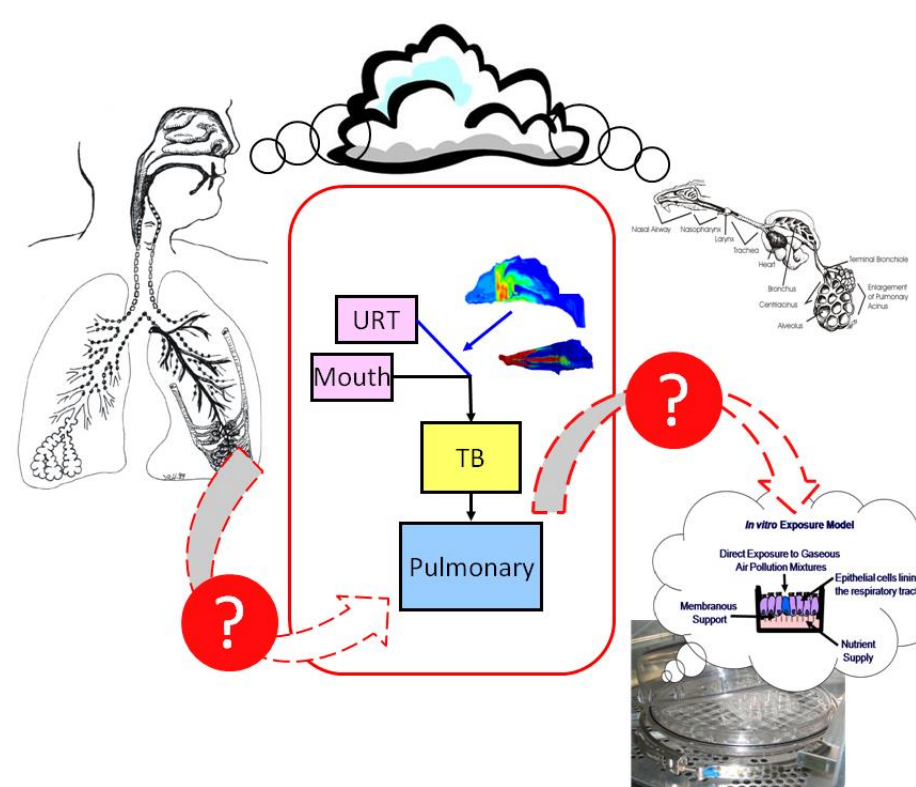
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Tasks

- Task 8.1: Disease-based integration of new data types.**
- Task 8.2: Characterization and application of high-throughput platform-based quantitative screening estimates**

Work in these two tasks will apply data mining and other computational techniques to characterize their utility for describing disease pathogenesis. The approaches will evaluate from either disease outcomes (Task 8.1) as the apical endpoint of an adverse outcome pathway (AOP) or start (Task 8.1) with a chemical's mode of action (MOA) and molecular initiating event (MIE) as denoted in the yellow arrows.

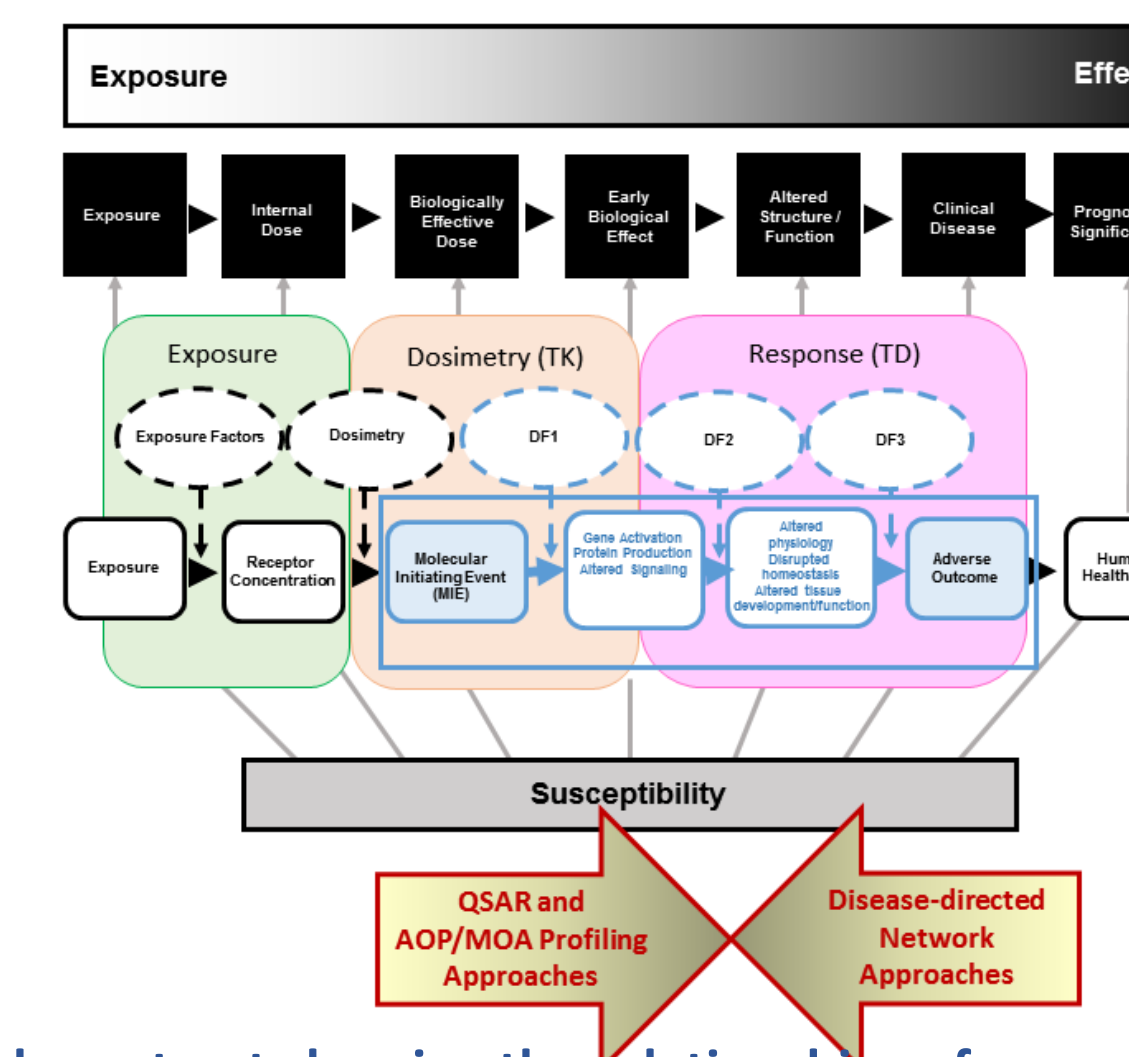
- Task 8.3: Dosimetry21: Advancing multi-scale dosimetry models to incorporate AOP/MOA and biomarker data**



Interspecies extrapolation and translation of experimental in vitro dose

- Task 8.4: Evaluation and application of new exposure data and methods**

- This task will evaluate and apply new forms of exposure data and methods to better quantify exposure to an environmental containment and characterize activity and behavior across a variety of life stages or risk for exposure.
- The resultant products will enable risk assessors in EPA Program and Regional Offices to take advantage of the increasingly available amount of exposure related information and state-of-the-science technologies to develop, in a timely manner, more precise and population pertinent exposure estimates.



Conceptual construct showing the relationships of computational approaches in Project 8 and schematics developed for biomarkers, AOP and MOA applied to risk assessment.

- Mechanistic dosimetry models have proven useful to predicting internal dose and aid interspecies extrapolation
- With the advent of *in vitro* AOP testing, creating context for the translation of experimental design and inferences for dose-response becomes critical.
- Various dose metrics are needed to accurately translate internal dose across the experimental designs underlying diverse data used in risk assessment, including: epidemiological (including biomonitoring), clinical, *in vitro* and *in vivo* toxicological studies, and *in silico*.
- Portal-of-entry (POE) models are especially important to the HHRA program – over 70% of the inhalation values on IRIS are based on or consider POE effects.
- POE models will complement efforts in the CSS program on rapid exposure and dosimetry.
- The goal of this task is to develop a Federal consortium to leverage resources and expertise, share model structures, and advance knowledge in support of multi-scale modeling. Suites of model structures for each route of exposure will be developed to describe dose metrics for key events across range of observation from genomic to community.
- Internal EPA and Federal collaboration will leverage expertise and resources effectively.

Impact

These tasks are developing a complete suite of exposure, dosimetry and health assessment methods to support efficient and informed prioritization, risk screening, and ultimately, risk assessment, and to ensure that Agency assessments remain state of the science. This project brings to bear evolving methods to support rapid and robust evaluation of chemicals.