COMPARATIVE EXPOSURE CHARACTERIZATION

The State of the Science of Alternatives Assessment Methods

2nd International Symposium on Alternatives Assessment

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21 Century Exposure Agenda

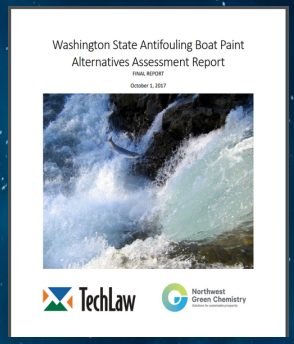
- Exposure, exposure everywhere…What is exposure….?!
- How does comparative exposure assessment fit into Alternatives Assessment (AA)?
- Why incorporate comparative exposure assessment into AA?
- What changes are needed to foster use of comparative exposure assessment?
- How can you propel yourself into the exposure assessment realm?
  - Steps to get yourself into orbit here at the AA Symposium!
  - Steps to remain in orbit after the AA Symposium!

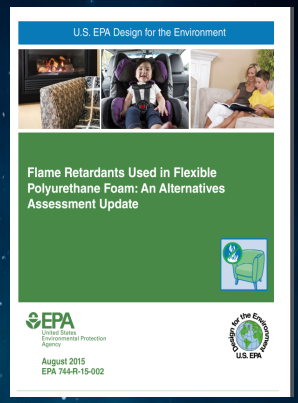
Introduction

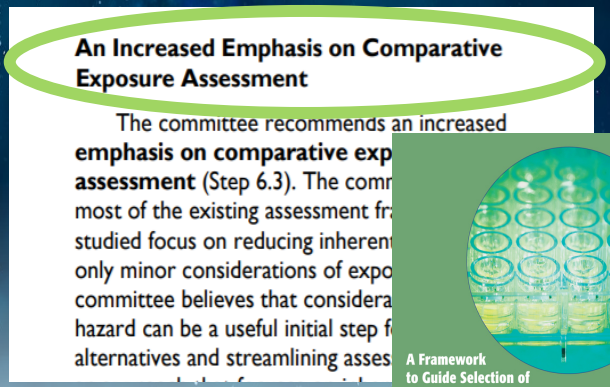
- I am a toxicologist with 25 years of experience at work at ToxServices
- ToxServices is a 15-year old, U.S.-based consulting firm comprising expert toxicologists, chemists, engineers, and environmental scientist
- Relevant areas of expertise:
  - Third Party Reviews Under Numerous Ecolabels
  - Hazard, Exposure, Alternatives, and Risk Assessments
    - California Proposition 65 Safe Harbor Evaluations
    - Cosmetics/Personal Care Product Assessments
    - Medical Device Biocompatibility Assessment
    - Assessment of Products, Components, Materials, Biologics, and Discrete Chemicals

Alternatives Assessments and Exposure Assessment: Where on Earth are We Now?

- Most completed AAs are hazard-based rankings
- Most AAs don't address differences in human and/or ecosystem exposure
- Four AA frameworks (BizNGO, CA SCP, IC2, REACH) include exposure assessment as a part of their methodology
- **Lift off has not yet begun!!**

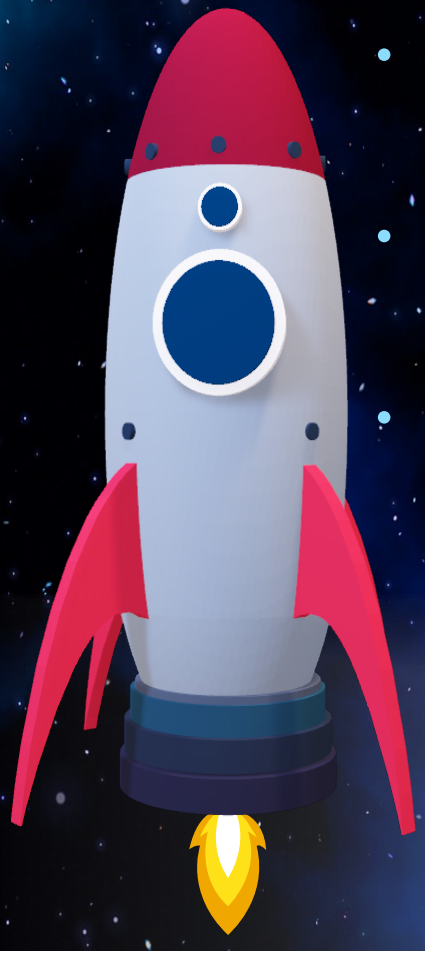




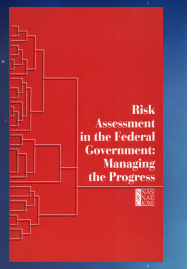


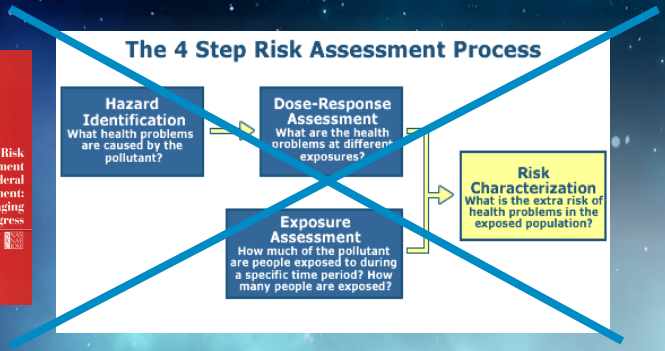
NAS 2014

Definitions: Exposure-Related Jargon



- **Exposure** is defined by the IPCS as a **c**oncentration or amount of a particular agent that reaches a target organism, system, or (sub)population in a specific frequency for a defined duration.
- **Exposure assessment** is the process of considering and estimating the extent of exposure among human and ecological receptors
- **Comparative exposure assessment** estimates relative exposure differences between potential alternatives and the original chemical of concern



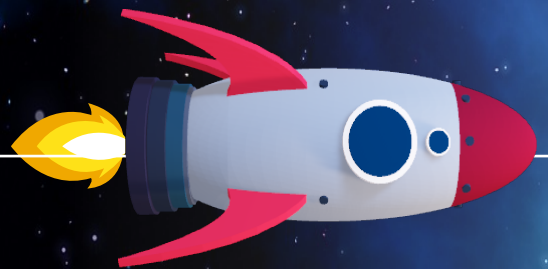


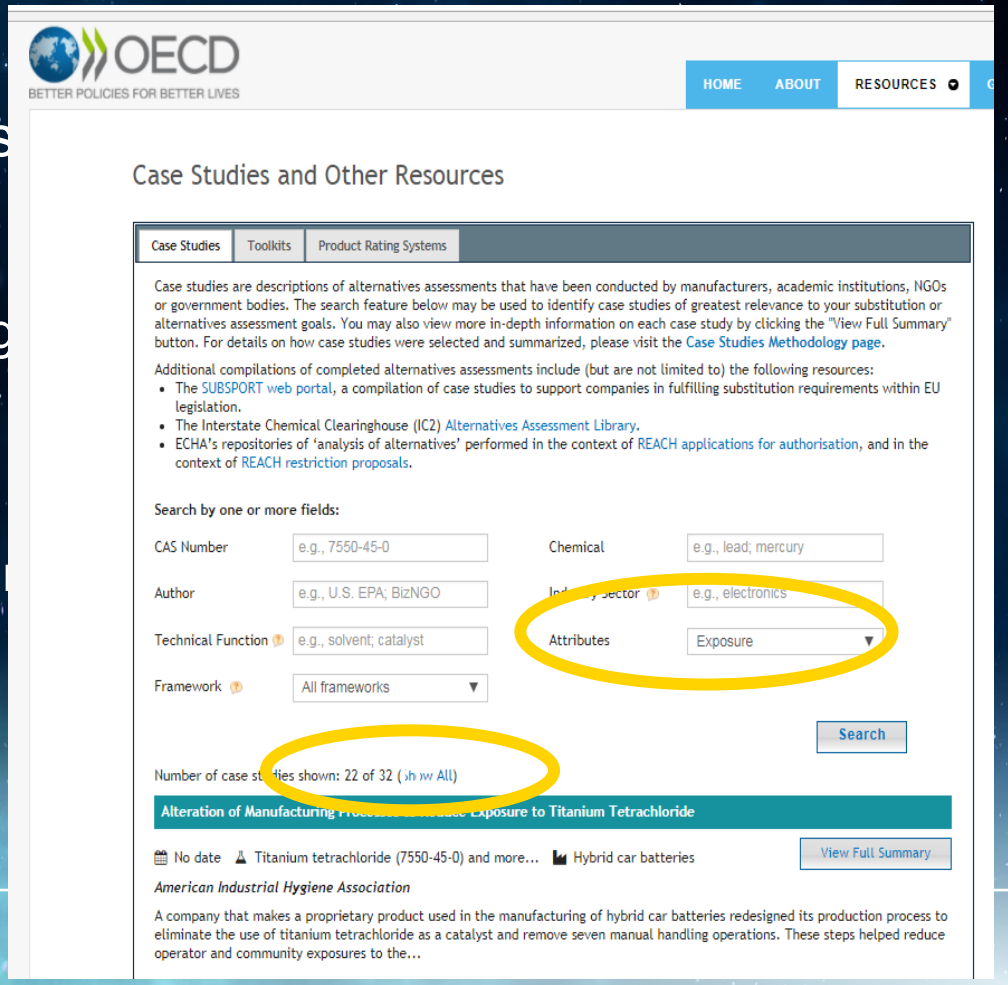
An AA exposure assessment is NOT the same thing is an exposure assessment conducted in a risk assessment!

Exposure: Coming Late to the AA Party

Why such limited exposure in AAs performed to date?

- Many AA frameworks have a *stated principle* to prevent harm by focusing first on inherent toxicity rather than controlling exposure
- Example:
  Of the 32 AA case studies available in the OECD AA Toolbox, only 22 AAs incorporate exposure rigorously





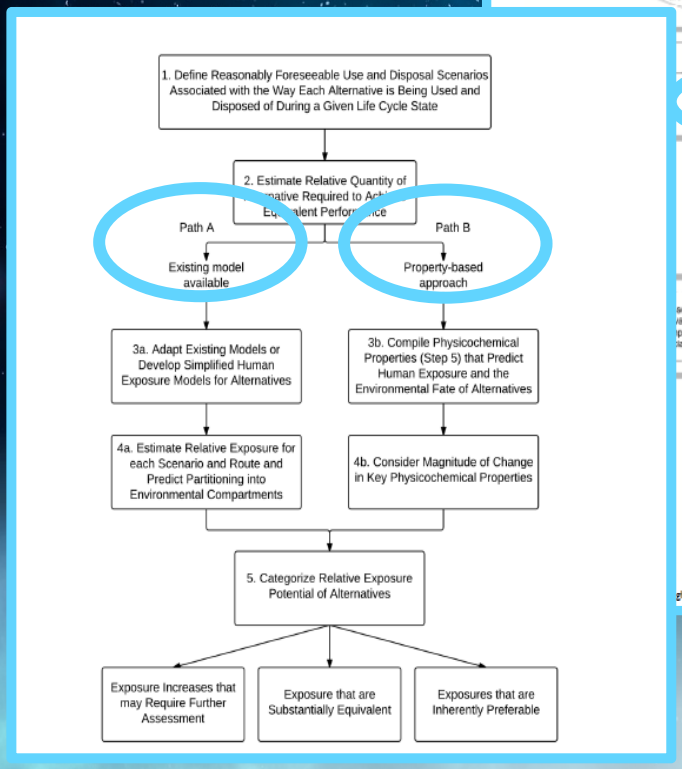
What is Comparative Exposure Assessment?

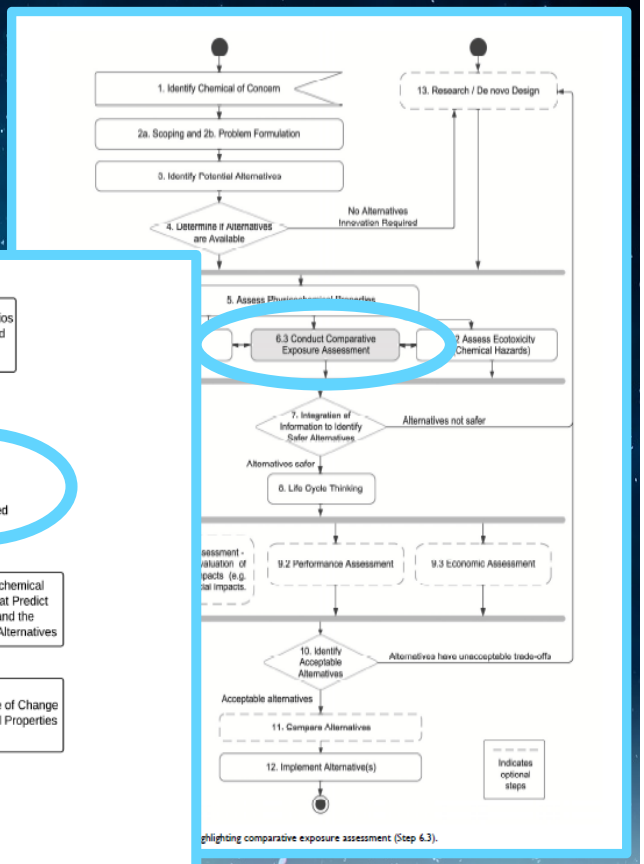
- **Comparative exposure assessment** estimates relative exposure differences between potential alternatives and the original chemical of concern
- Chapter 6 of the NAS (2014) AA framework report outlines two approaches for a *comparative* exposure assessment
- Exposure in the NAS framework is not to demonstrate “safe” levels of exposure (so, different than a risk assessment)
- Instead, exposure is ***comparative*** and is focused on intrinsic potential for exposure without physical or administrative

What is Comparative Exposure Assessment?

The NAS (2014) report outlines 2 approaches for ***comparative*** exposure assessment

- **Path A** is a quantitative approach, employing models and applying them to foreseeable use and disposal for a product containing an ingredient and its potential alternatives
- **Path B** is a property-based approach, comparing physical/ chemical properties to predict human exposure and environmental fate while considering foreseeable use and disposal.





Challenges with Hazard-Based Tools

A comparison of two solvents reflects some of the challenges:

- Methylcyclohexane is a GreenScreen Benchmark™ 2 chemical ("Use but Search for Safer Substitutes"), while 3-Ethoxyperfluoro(2-methylhexane) is a GreenScreen Benchmark™ 1 chemical ("Avoid – Chemical of High Concern")
- Methylcyclohexane is more toxic than 3-Ethoxyperfluoro(2-methylhexane) in terms of human health hazards —particularly to workers, so just selecting based on hazard only may not be the best choice

Additional information such as conditions of use, exposure, and life cycle considerations should be considered to support informed substitution

Hazard Summary Table for Individual Solvents

Chemical	CAS #	Group 1 Human Health					Group II and II* Human Health									Ecotox.		Fate		Physica		GreenScreen® Benchmark Score
		Carcinogenicity	Mutagenicity	Reproductive	Developmental	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic	Chronic Aquatic	Persistence	Bioaccumulation	Reactivity	Flammability	
								s	r*	s	r*											
Methylcyclohexane	108-87-2	*L*	**L**	**M**	**L**	DG	**M**	**H**	**L**	**M**	**L**	**L**	*L*	**H**	**L**	**vH**	**vH**	*L*	**L**	*L*	**H**	**BM 2**
3-Ethoxyperfluoro(2-methylhexane)	297730-93-3	*L*	**L**	*L*	*L*	DG	**L**	**L**	**L**		*L*	**L**	*L*	**L**	**L**	*L*	*vH*	*vH*	**vH**	*L*	**L**	**BM 1**

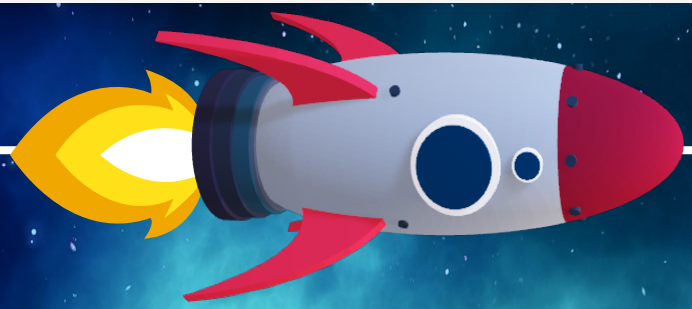
Goal of Comparative Exposure Assessment

- The goal of a comparative exposure assessment is to identify potential exposure for each alternative to assess whether each is:
  a) substantially equivalent
  b) inherently preferable, or
  c) potentially worse than a chemical of concern

- If exposure is substantially equivalent between an alternative and the chemical of concern, then determination of “safer” can be limited to the relative hazard of the chemicals

- Comparative Exposure Assessment is best suited for products with discrete end uses

- Challenging to assess exposure to chemicals that don’t have clearly defined end uses



Blast Off: Comparative Exposure Assessment at the Symposium

Today's afternoon session: Comparative Exposure Evaluation and Consideration of Life Cycle Impacts

We have seven exposure-focused presentations this afternoon!

Qualitative Approach to Comparative Exposure in Alternatives Assessment

Addressing Exposure to 8000+ Chemicals in Consumer Products with Quantitative High Throughput Methods for Alternatives Assessment

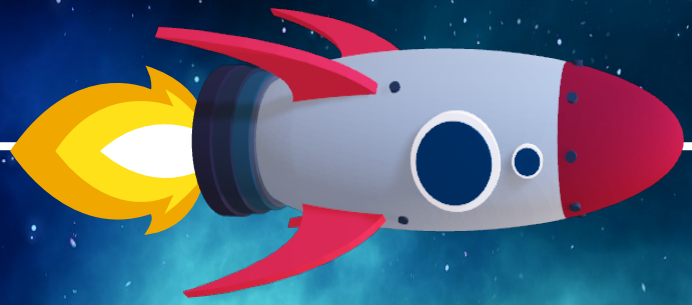
Bridging Life Cycle and Exposure Ontologies to Enable Integration of Data Streams for Rapid Exposure Estimation and Comparative Exposure Assessment

The Supply Chain Dimensions of Alternatives Assessment

Future Focus: Comparative Exposure Assessment

The focus of AAs over the next five years should be the incorporation of comparative exposure assessments

Small steps, such as incorporating qualitative exposure assessments into AAs will strengthen our ability to move away from hazardous substances and avoid regrettable substitution



Staying in Orbit: Get Your Training Spacesuit On!

- Dr. Marie Fortin (a big advocate of AA) is holding a two day boot camp on January 10 and 11, 2019 at Rutgers University
  - The course is free, although they would appreciate donations to their grad student travel fund **https://pharmacy.rutgers.edu** >> Donate tab
- The focus is on risk assessment methods, but many of the concepts and tools are relevant for Comparative Exposure Assessments
- Our goal as an AA community should be to hold an AA Boot Camp course annually!

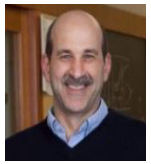
RUTGERS
Environmental and Occupational Health Sciences Institute | EOHSI

Risk Assessment Boot Camp

January 10 and 11, 2019

Sign up for a 2-day Boot Camp on Risk Assessment in the Environmental and Occupational Health Sciences Institute at Rutgers University. Topics will include risk analysis, systematic review, data quality, weight of evidence, hazard identification, susceptible populations, exposure pathways, point-of-departure, reference values, and more. Case studies and hands-on exercises will provide real world scenarios for application of content. Lunch will be provided both days. There are no costs to participants.

Register at https://goo.gl/wcWP7E



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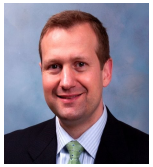

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Thank You and Enjoy the Symposium!

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