The right work at the right time for the right reason to enhance efficiency in decision-making.

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Solution

Application of problem formulation and exposure driven principles for determining knowledge generation.

For new AIs, re-registration and to resolve issues.

Framework for communication, to enable focused data generation, and decrease the likelihood of unanticipated issues.

Problem formulation: what problem is being addressed?

Original Approach from the 1970's (what we still do):

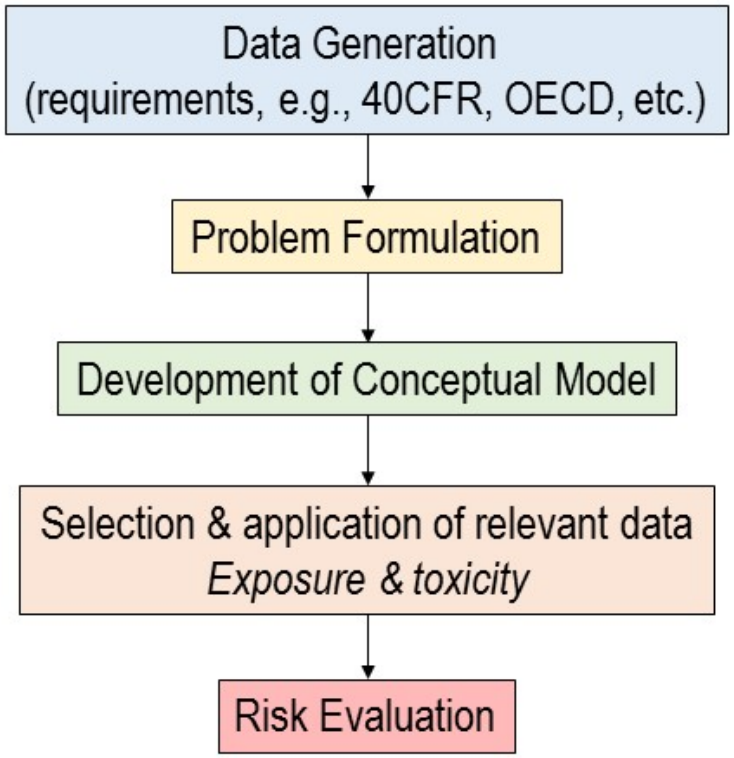
Identify the hazards a chemical could cause and prevent them by eliminating the chemical use.

What we should be doing:

Identify and characterize the **context** in which a chemical could result in an adverse effect so that appropriate **risk management** measures can be taken to safeguard human health and the environment.

What are we trying to accomplish with our safety testing?

Current Paradigm



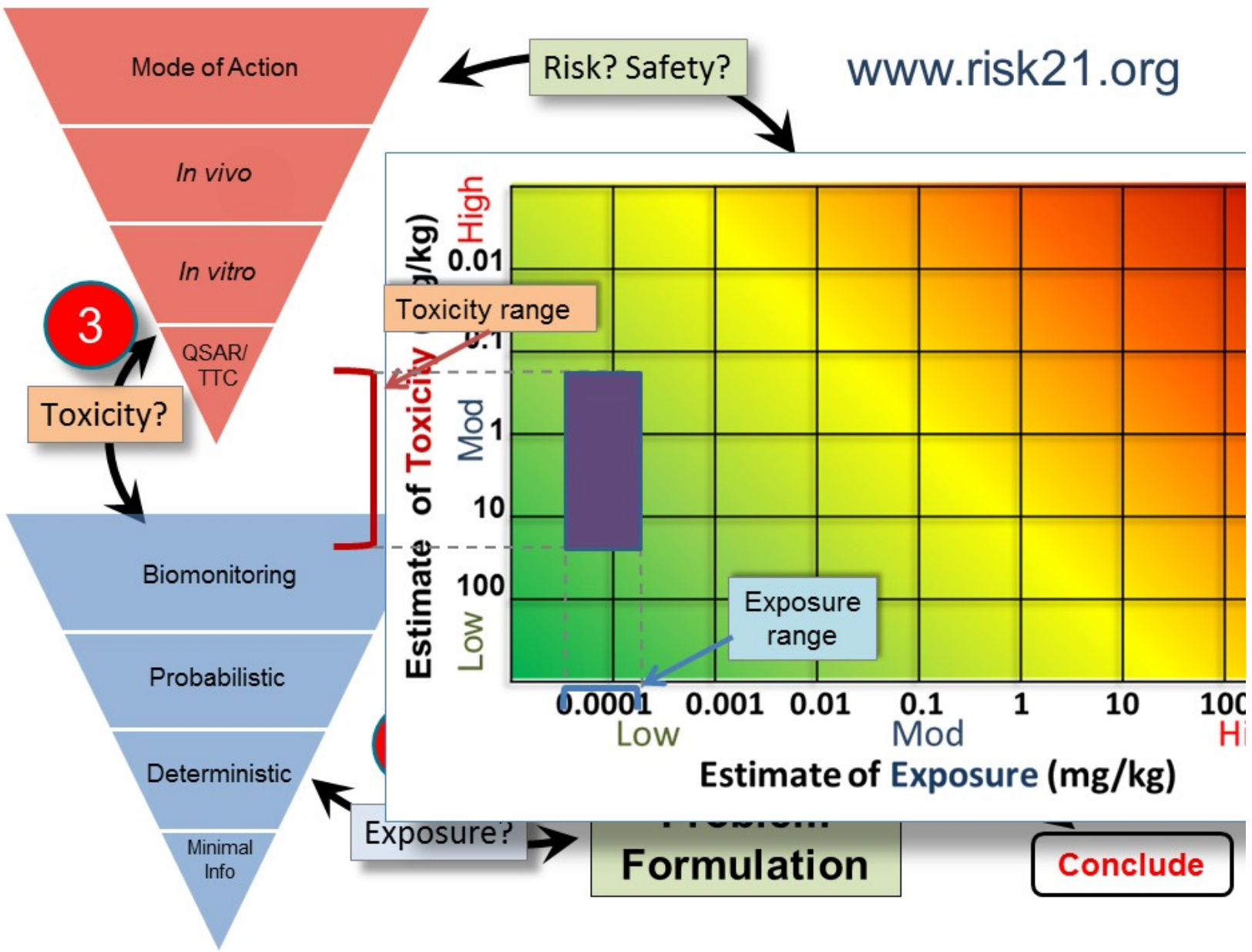
We should be trying to **prevent** adverse health outcomes

not predict all possible adverse effects.

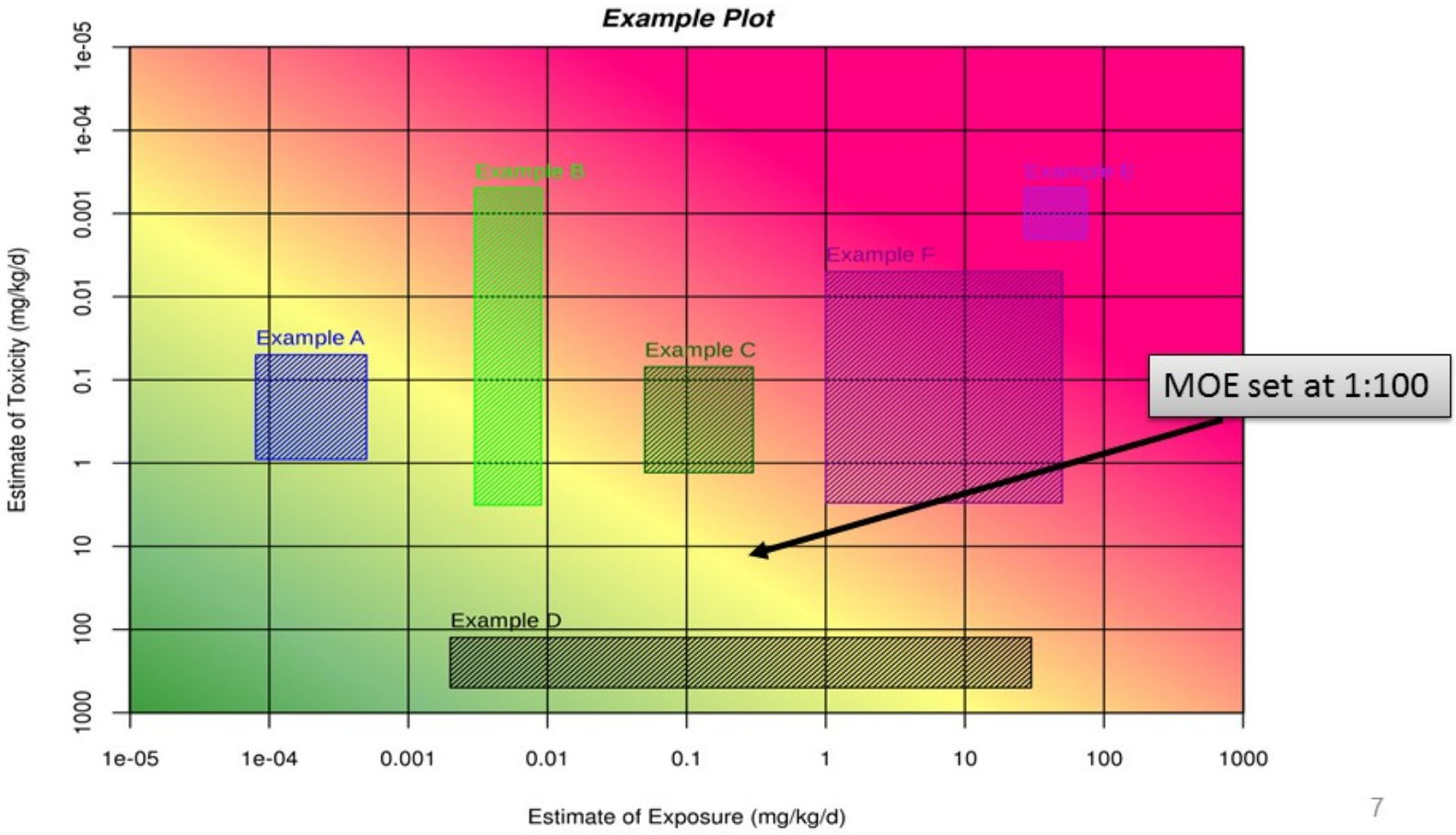
Change in Orientation and Conceptual Model

An integrated evaluation strategy that provides the **necessary** scientific knowledge to make a regulatory determination of the potential for an adverse impact, from the use of a chemical, on public health and the environment with speed, efficiency and accuracy.

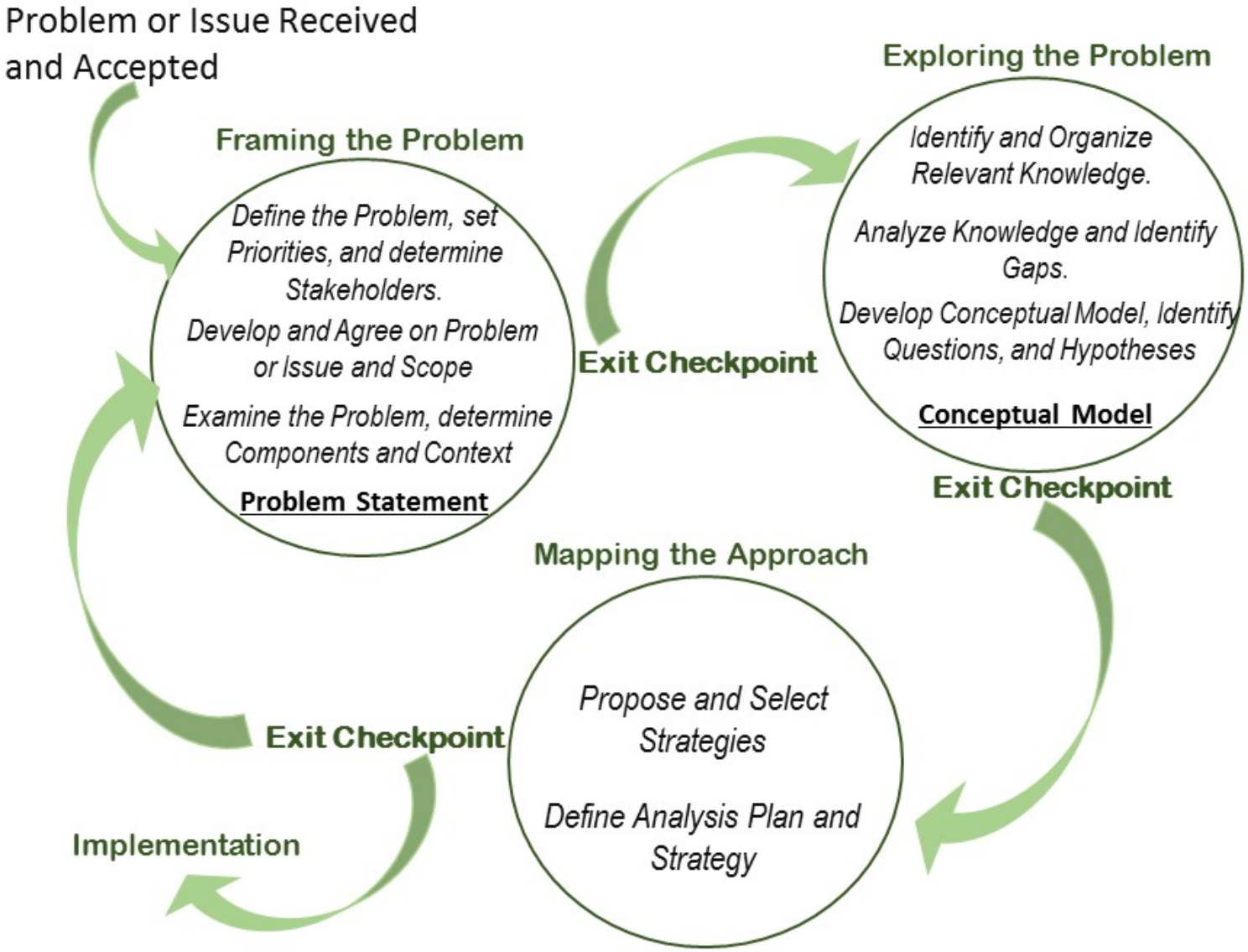
"The difficulty lies, not in the new ideas, but in escaping from the old ones"
John Maynard Keynes (1883–1946), British economist


Mode of Action
In vivo
In vitro
QSAR/
TTC
3
Toxicity?
Biomonitoring
Probabilistic
Deterministic
Minimal
Info
Risk? Safety?
www.risk21.org
Toxicity range
Exposure
range
Estimate of Toxicity
High
Mod
Low
0.01
1
10
100
0.0001
0.001
0.01
0.1
1
10
Low
Mod
Estimate of Exposure (mg/kg)
Exposure?
Formulation
Conclude

Use of RISK21 Matrix



Problem Formulation Framework

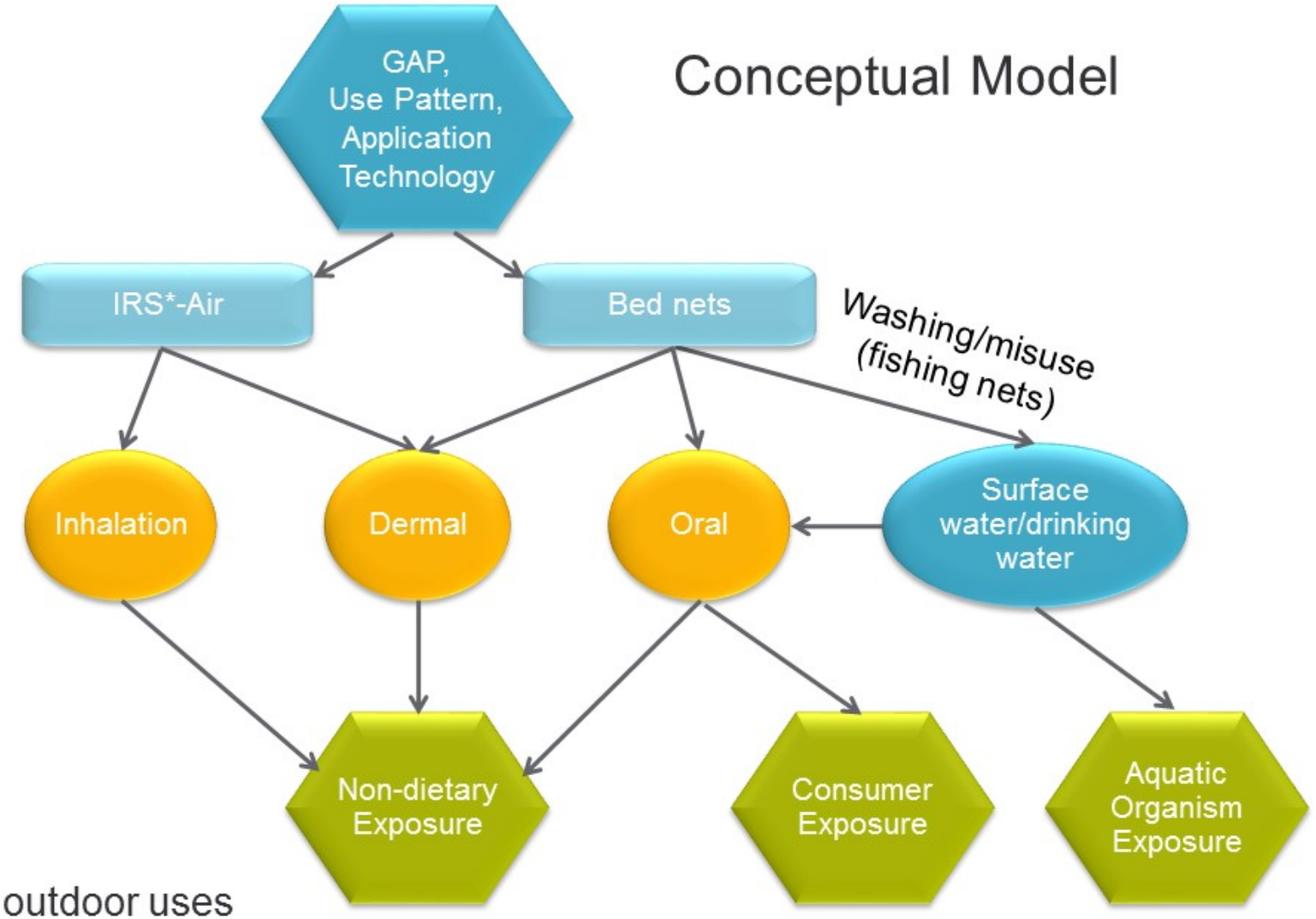


Vector control project

- Project is for vector control only
  - For mosquitos transmitting malaria
- No crop protection uses and no outdoor uses

- Applications
  - Indoor residual spraying (IRS)
  - Long lasting Insecticide treated bed nets

Conceptual Model



* No outdoor uses

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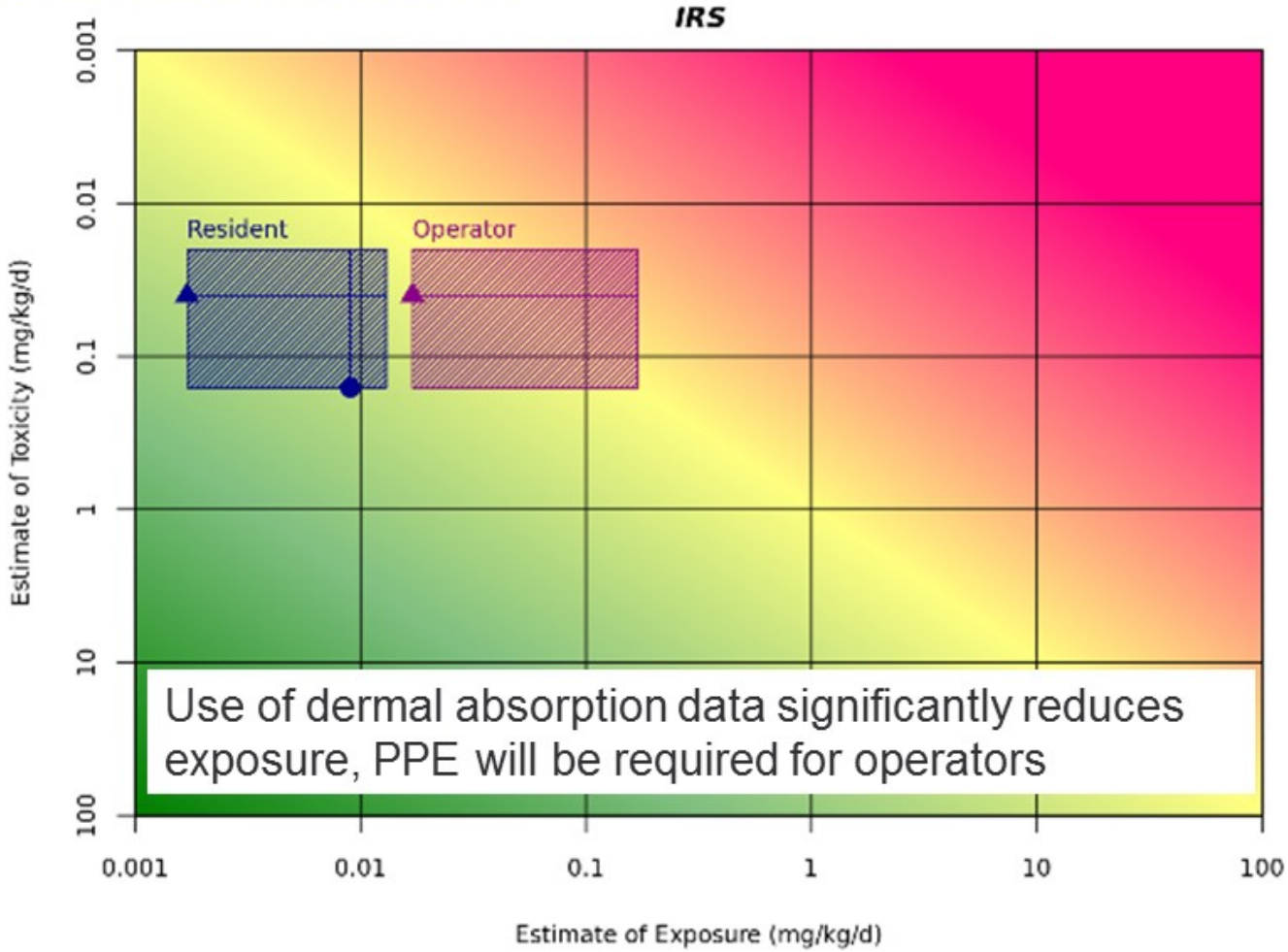
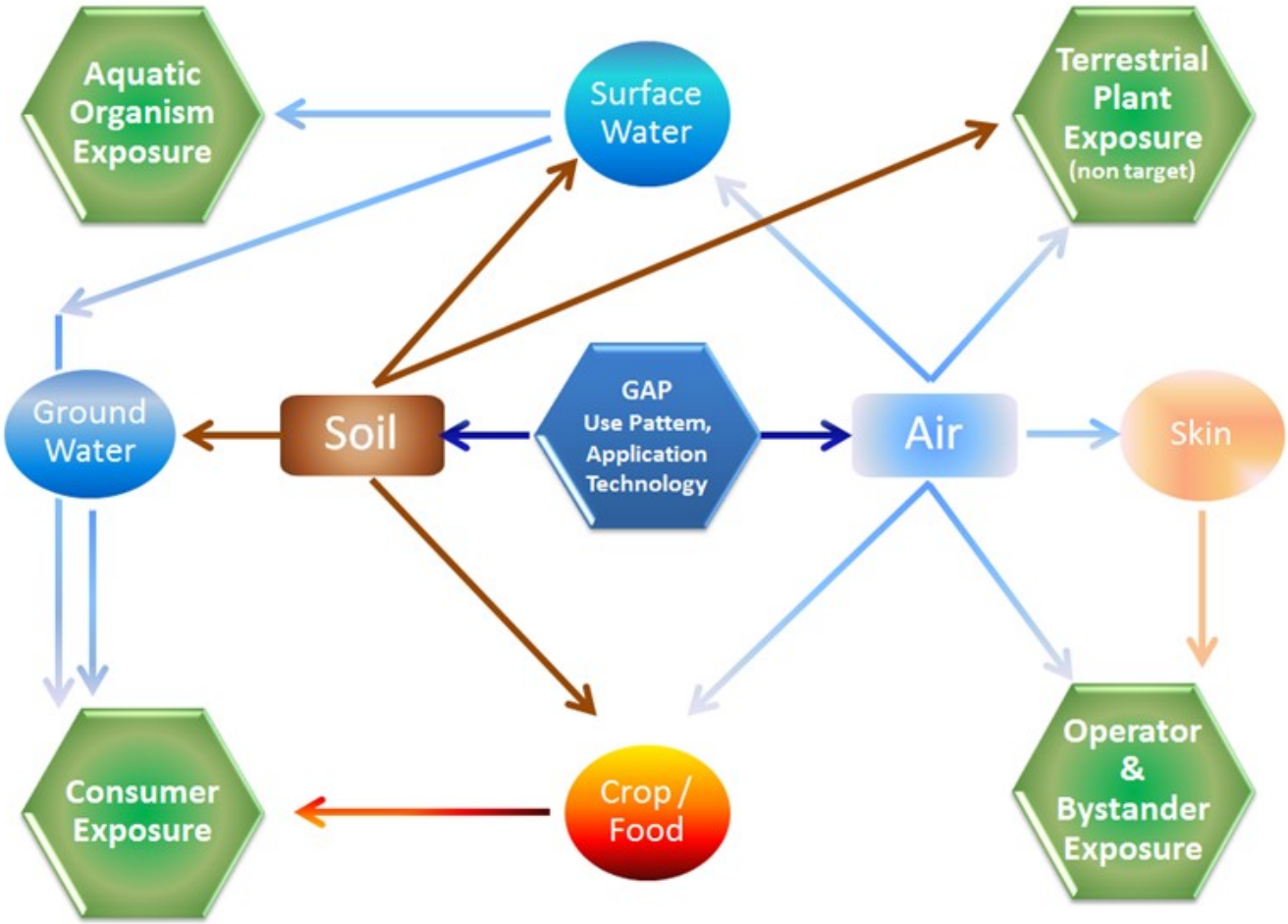
Risk 21 Evaluation



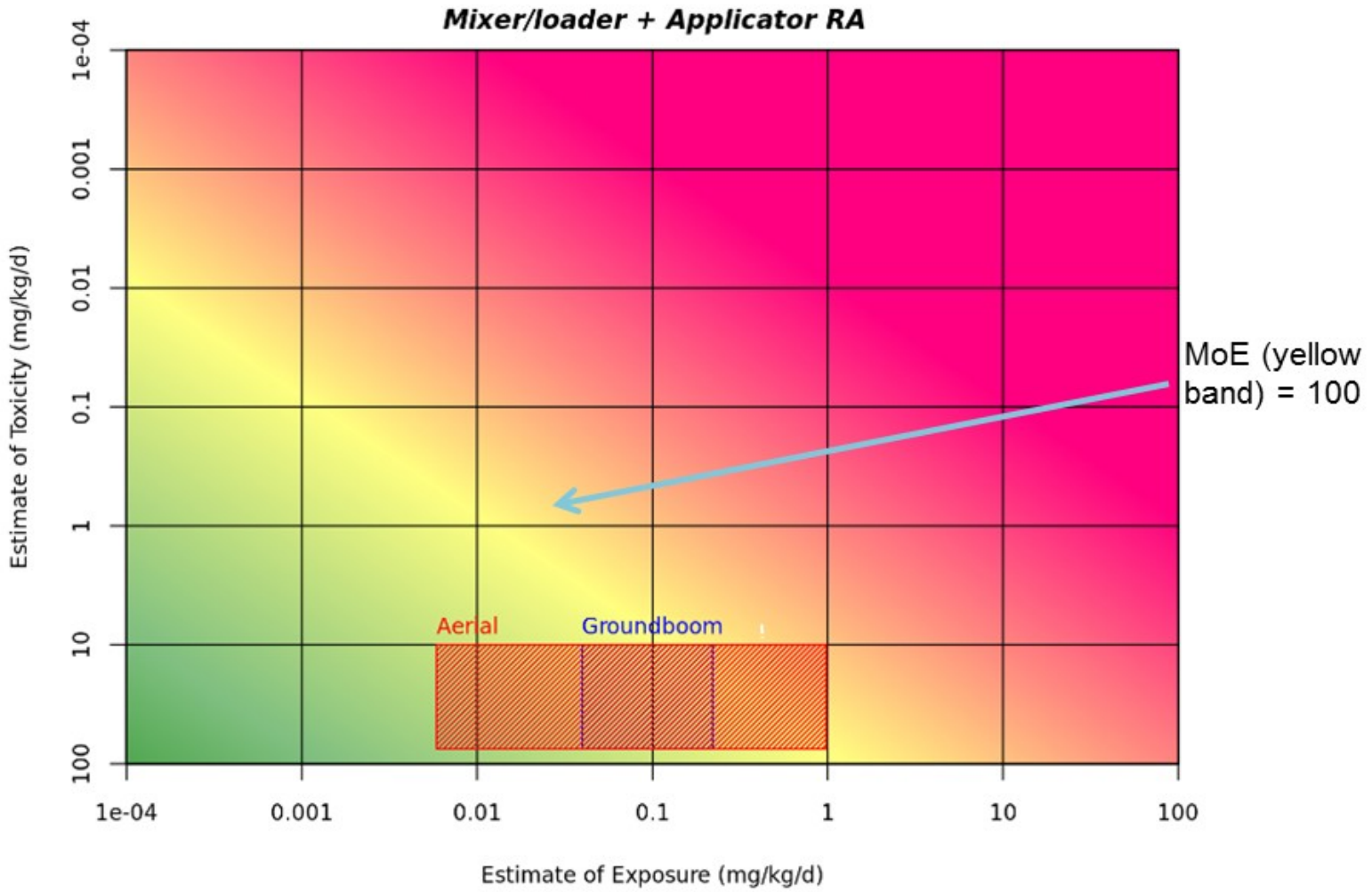
Problem Statement

How do we reliably advance a pre/early-post emergence herbicide through the development and regulatory approval process by conducting necessary and appropriate testing to demonstrate safe use?

Conceptual Model Outlining Exposure Scenarios From a Given Use.



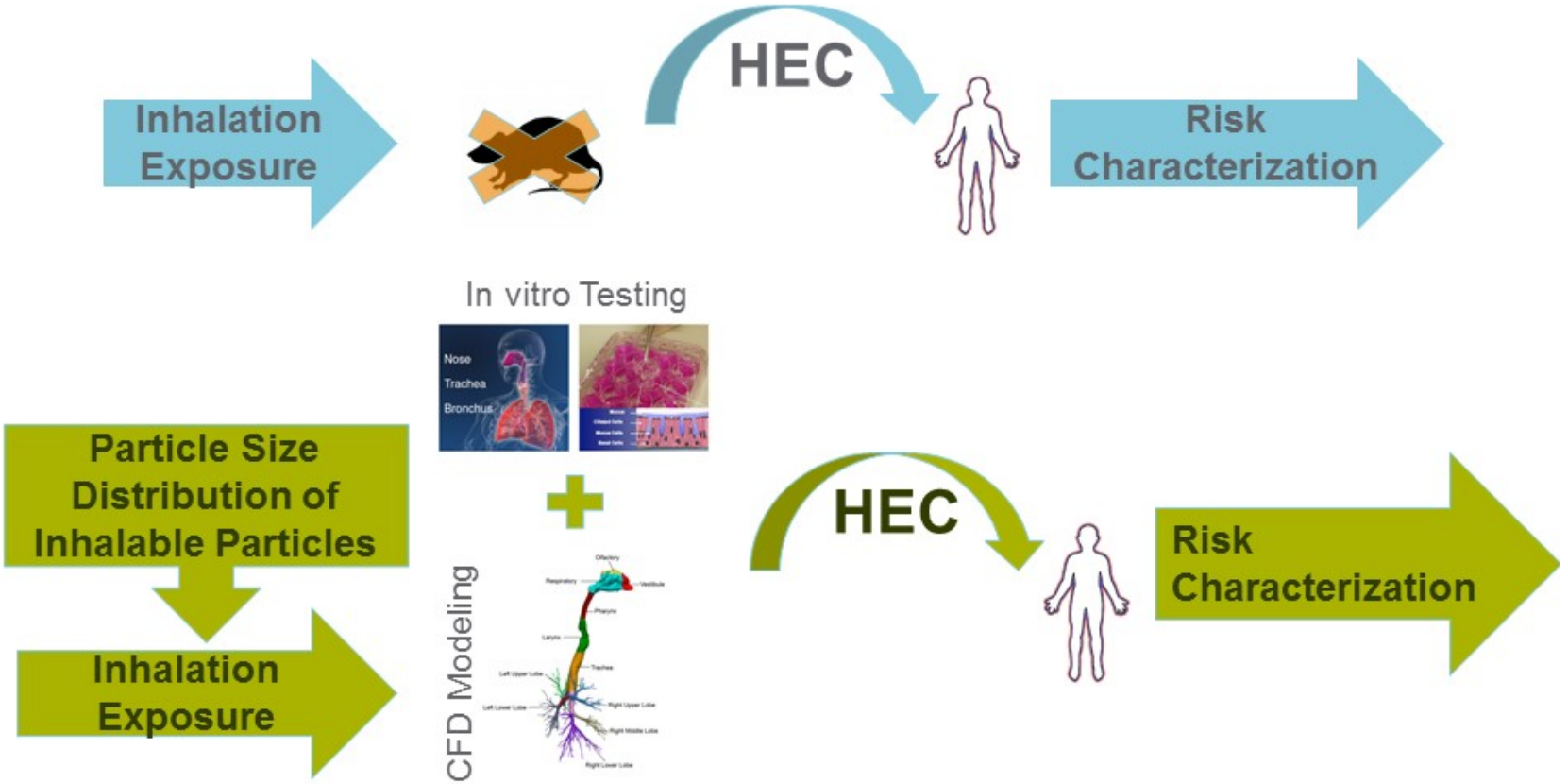
RISK21 Evaluation of Operator Exposures



Problem Statement

A “smarter testing”/alternative approach can be developed and would be suitable to inform inhalation toxicity in lieu of a subchronic inhalation study.

Conceptual Model



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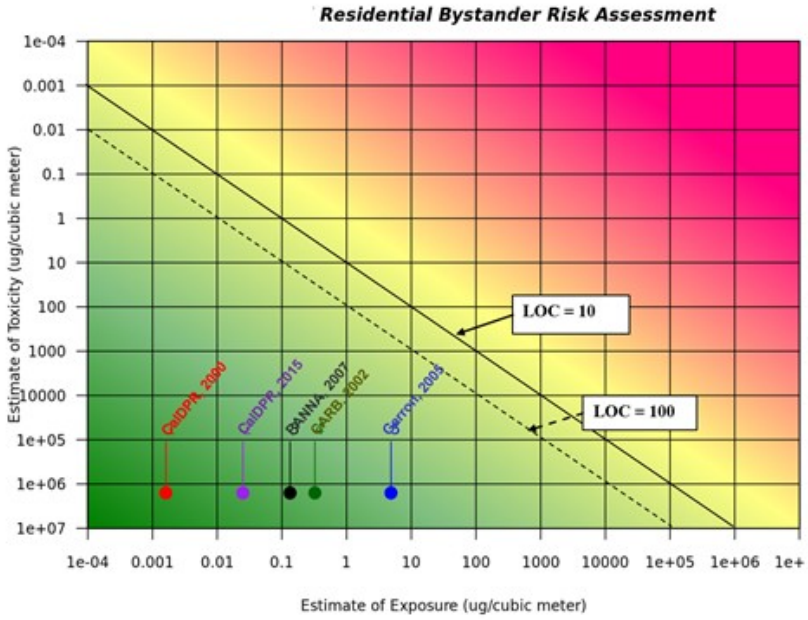
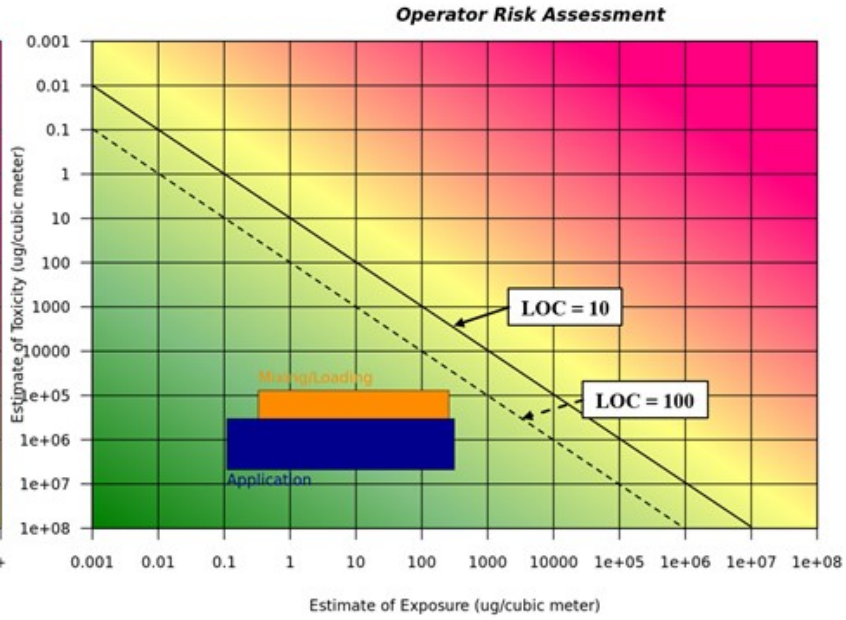
Risk Assessments





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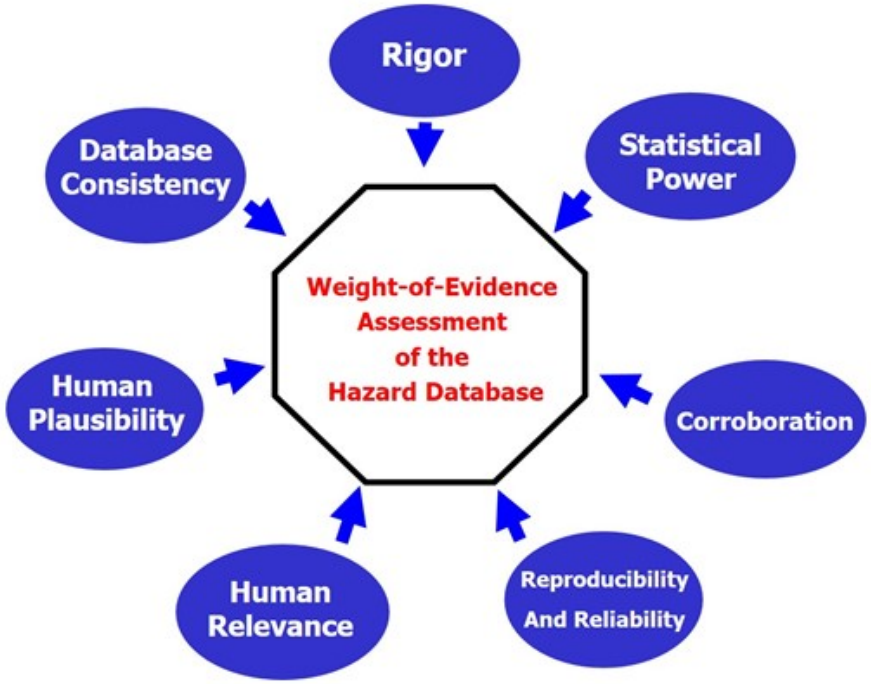
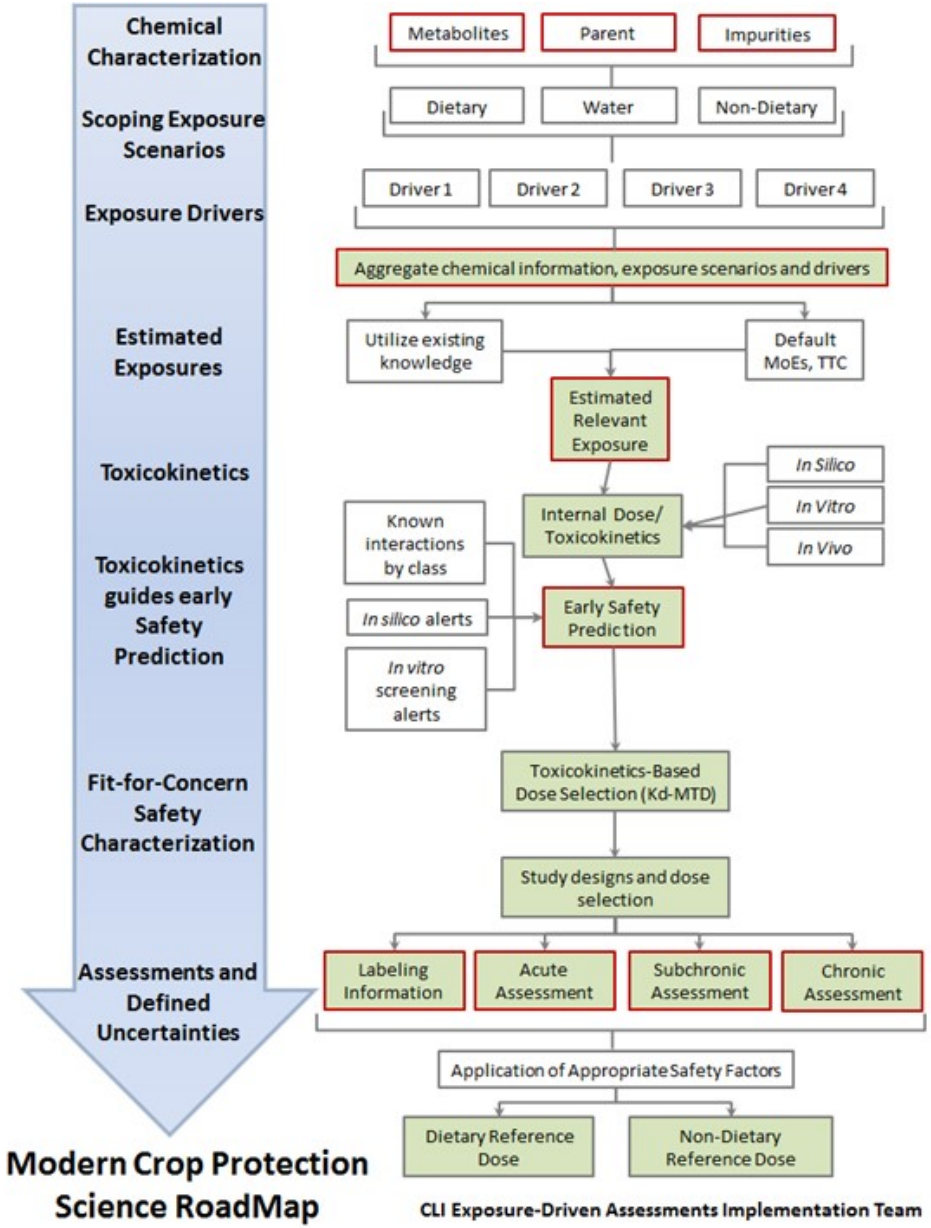
Waiving Studies Based on Adequate Knowledge

- Promote full use of existing knowledge to focus on scientifically sound and credible characterization of a pesticide's risk profile.
- Determine data needs required to reliably support the safety of the Active Ingredient and remain protective of public health and the environment.
- Avoid unnecessary use of time, data generation costs, and animal testing.



Waiving Studies Based on Adequate Knowledge

Waivers Considered by EPA's Office of Pesticide Programs (12/2011-2/2017)				
Type of Study	**~Number of Animals/Study**	**Waivers Granted**	**~Number of Lives Saved**	**Total # of Requests**
Inhalation	96	222	21,312	288
Neurotoxicity	80	163.5	13,080	186
Dermal	80	50	4,000	57
Developmental	1700	39	66,300	48
DNT	880	15	13,200	18
Subchronic Dog	32	11	352	14
Reproductive	880	32	28,100	38
Immunotoxicity	40	207	8,280	223
Chronic/ Carcinogenicity	480	24	11,520	28
Subchronic Rat	80	10	800	12
			>166,000	

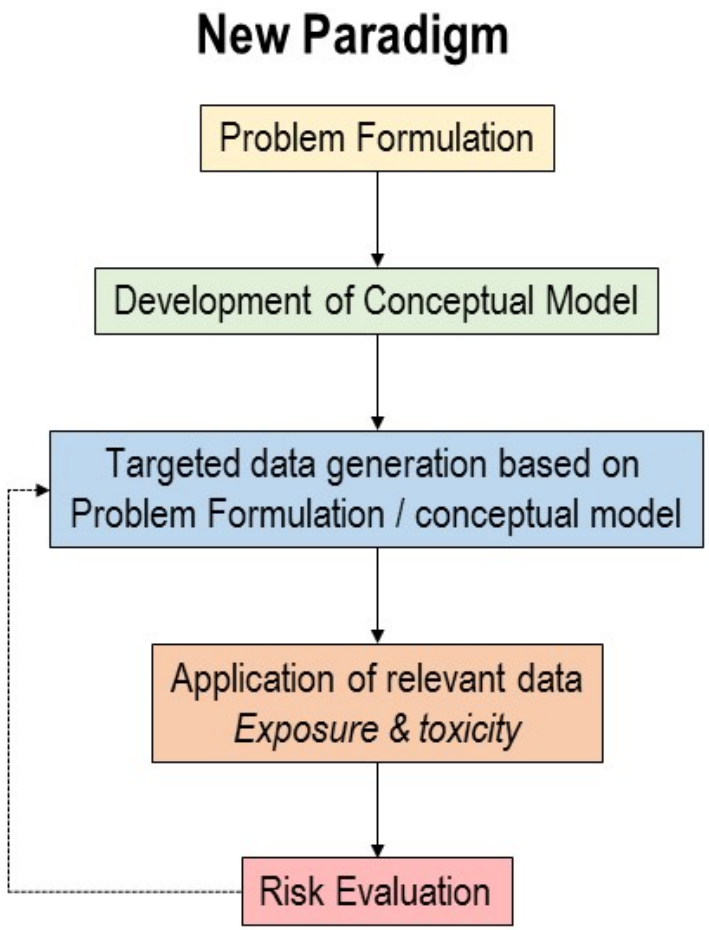


Roadmap for Exposure-Driven Assessments for Modern Crop Protection

Vision: Implementation of globally harmonised RA-based approach for regulatory decision-making

Outcome

Globally harmonized science-based approach **centered on a risk assessment and management** paradigm for decision-making that results in the elimination of studies not relevant or used for human health risk assessment.



"To innovate is not to reform"
Edmund Burke (1729–1797), Irish philosopher, statesman.