



RISK21: A 21st Century Roadmap for Human Health Risk Assessment



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What is RISK21?

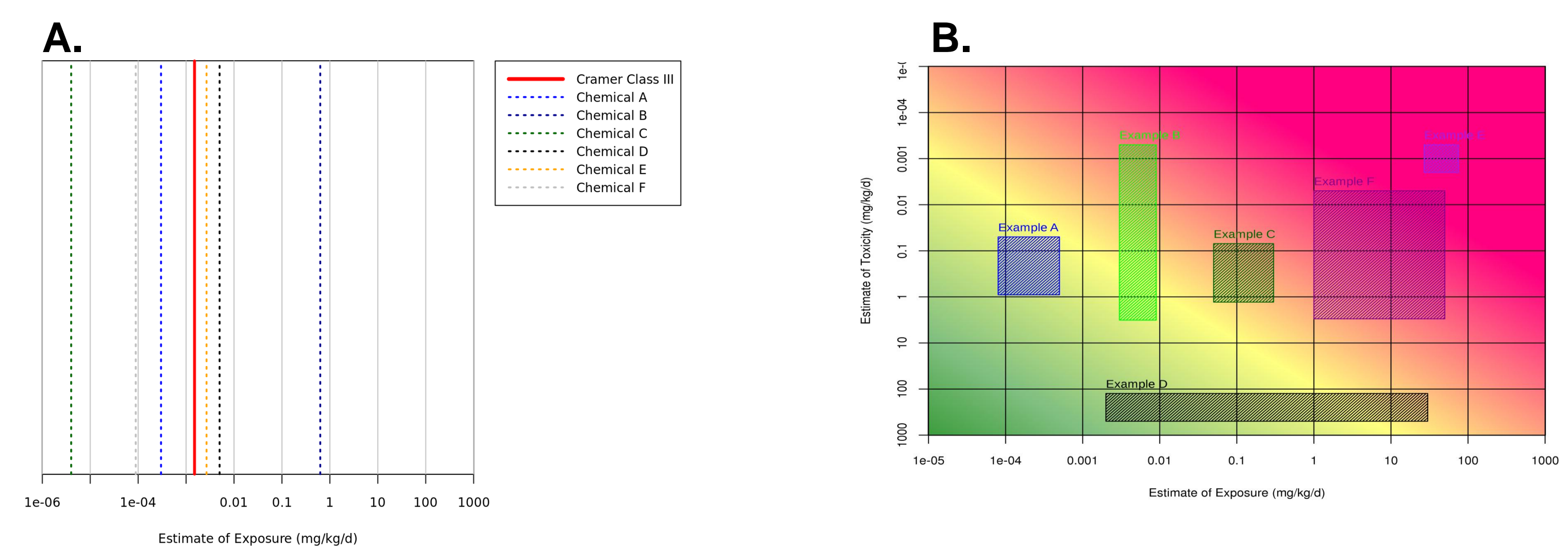
RISK21 is a scientific, transparent, and efficient framework approach developed by international scientists from government, industry, academia, and NGOs that emphasizes problem formulation and a tiered approach to the evaluation of exposure and toxicology data for risk assessment purposes. The RISK21 roadmap and matrix promote applicable, accurate, and resource appropriate approaches to today's complex risk assessment problems.

RISK21 Principles

RISK21 is a transparent framework for knowledge synthesis to enable effective decision-making that is:

- **Problem formulation-based:** An iterative process that establishes purpose, scope, and a plan for collecting and evaluating information.
- **Utilizes existing information:** Applies information on inherent chemical properties as well as existing exposure and toxicity information before generating additional data.
- **Exposure-led:** Considers relevant exposure estimates up-front to prioritize and determine data needs.
- **Tiered:** Optimizes use of resources.
- **Flexible:** Allows one to make an informed decision on human health safety as soon as sufficient evidence is available.

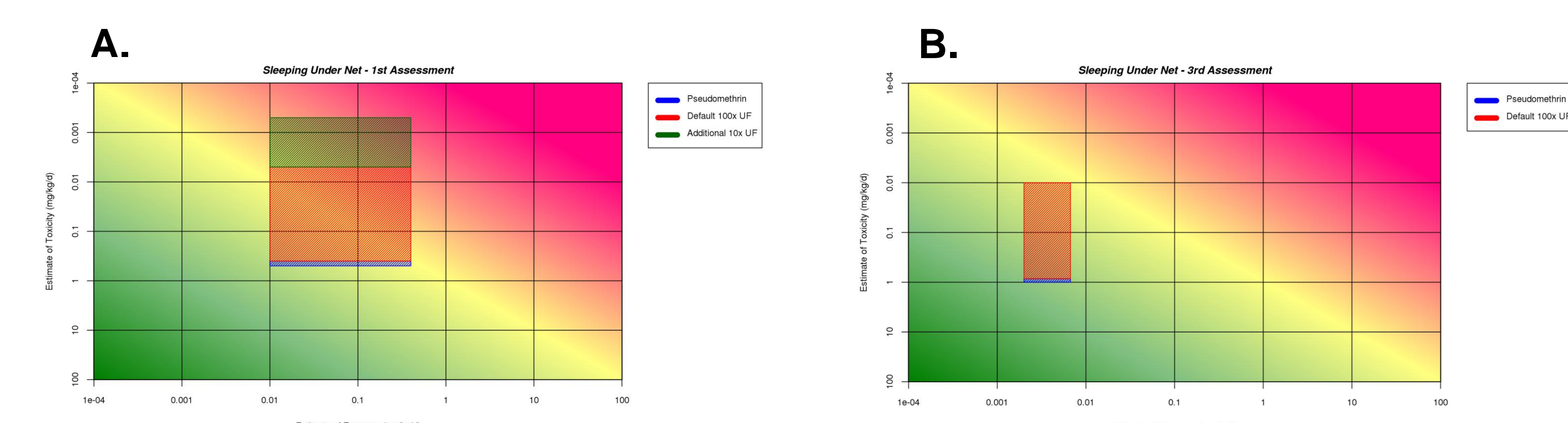
Webtool Example Plots



Illustrative examples of the RISK21 visualization matrix used for priority setting. (A) Adapts the matrix to apply the Threshold of Toxicological Concern (TTC) as a low-tier prioritization and screening approach, using only chemical structure and exposure information. (B) Illustrates how the RISK21 matrix could be used for six chemicals for which both exposure and toxicity information is available.

Pyrethroid Case Study

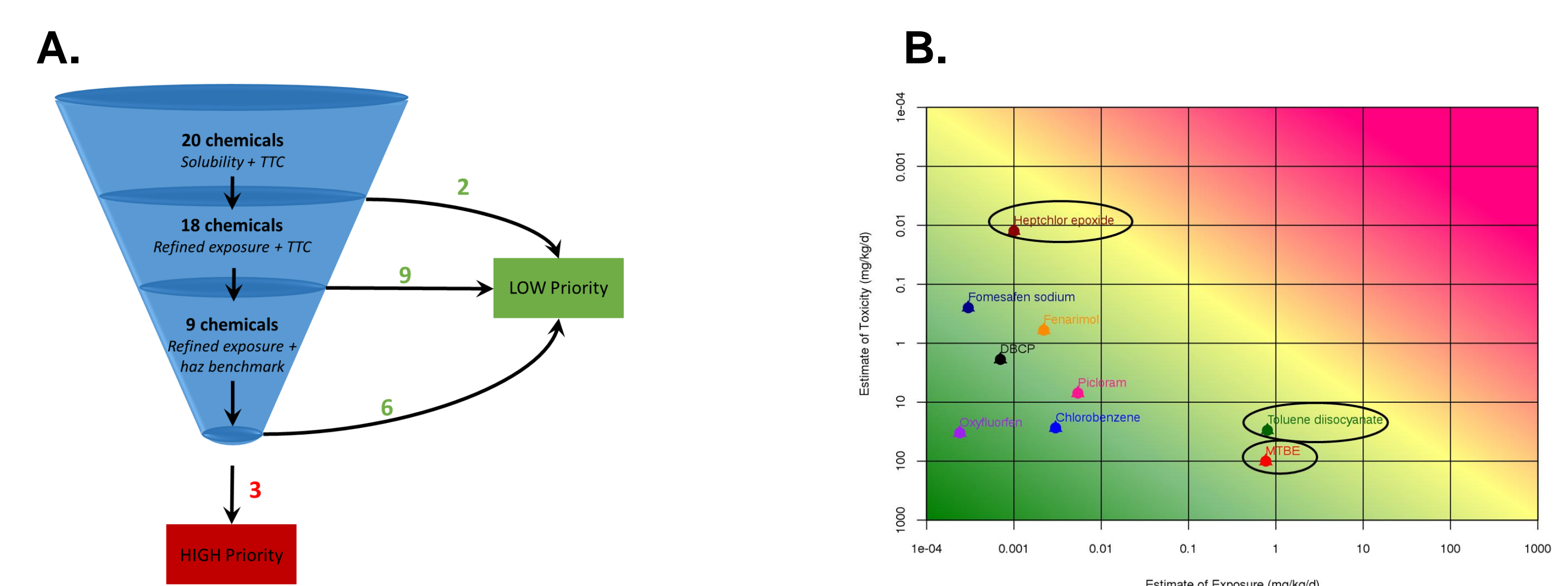
- A new 'nth' in class pesticide (termed 'pseudomethrin') to be used in mosquito netting.
- Used existing information from other pesticides in the same chemical class, as well as knowledge of use patterns, to inform decision making.
- Only 24 animals used.



Application of the ranges for exposure and toxicity on the RISK21 matrix to form the exposure/toxicity intersect area for sleeping under the net for first assessment (A) and the third and final assessment (B). The area to the left of the yellow shading indicates where exposure is below the human safe level for toxicity.

Drinking Water Case Study

- 20 chemicals found in ground and surface water that could potentially be found in drinking water
- Prioritized chemicals of highest potential concern.
- Of 20 chemicals, 17 were eliminated using a tiered approach and 3 were quickly identified as being of concern.
- No animals used.



Illustrative Water Case study figures. Overview of the case study evaluation steps (A); Matrix plot of the nine remaining chemicals (point estimates for both exposure and toxicity). Those circled are the three designated high priority for further evaluation based on proximity to the yellow zone (B).

Publications

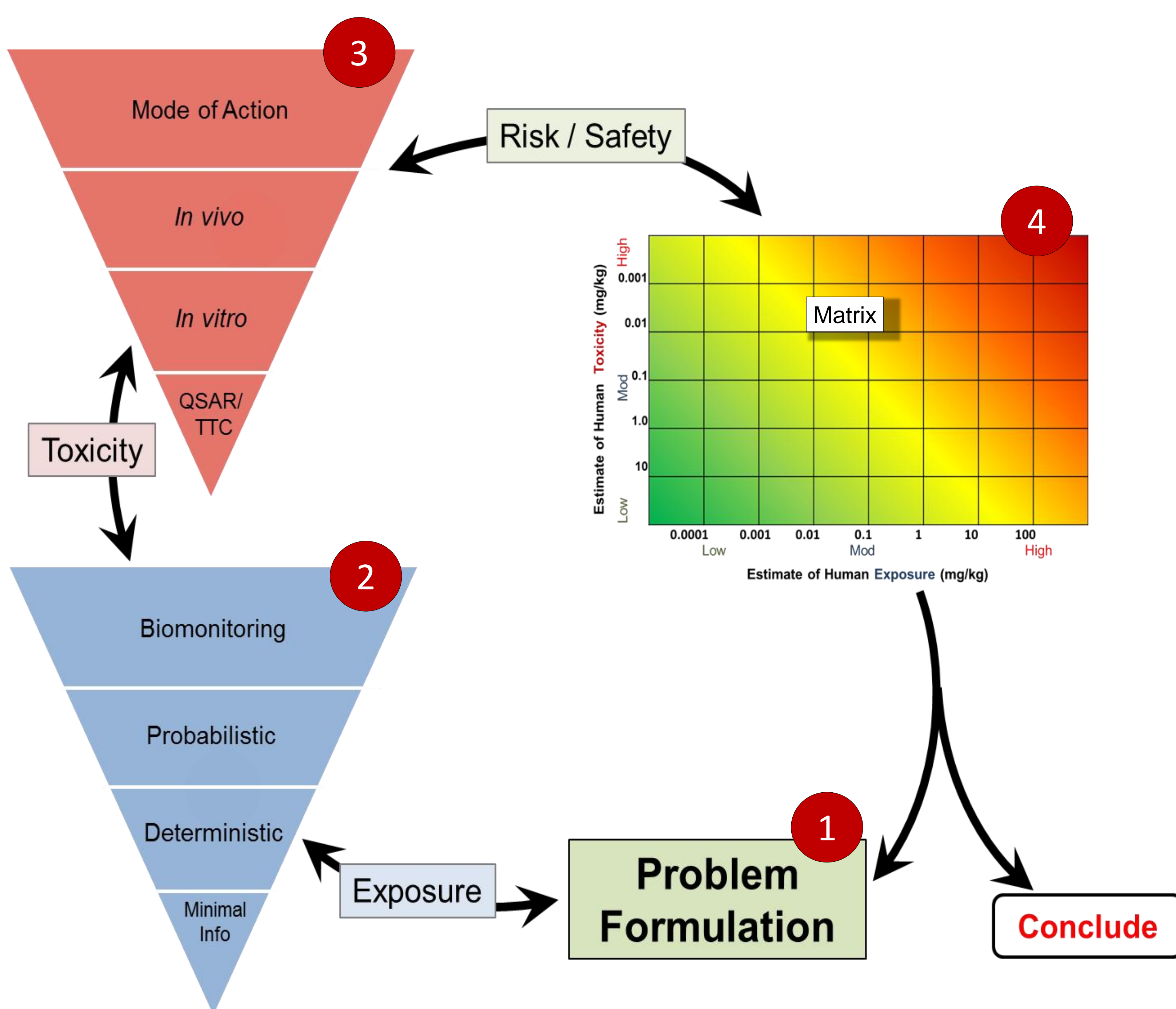
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www.RISK21.org

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The RISK21 Roadmap



- 1 **Problem formulation:** Define problem. This initial step is re-evaluated throughout the iterative process.
- 2 **Exposure estimate:** Obtain tiered estimate of exposure BEFORE assessing toxicity. Use existing knowledge. Express as range of precision.
- 3 **Toxicity estimate:** Obtain tiered estimate of toxicity. Use existing knowledge. Develop data only as needed. Express as range of precision.
- 4 **Matrix:** Intersect exposure and toxicity estimates on the matrix.

RISK21 Matrix Webtool: www.risk21.org



- Users can interact with the RISK21 webtool application to visualize their own risk data, creating a custom plot which will be displayed on the screen.
- Users can input estimated exposure and toxicity data for each chemical, and the tool will automatically intersect these toxicity and exposure distributions and plot the intersection area, overlaying a risk matrix represented as a heat map.