



Using the RISK21 Roadmap and Webtool to Categorize Pesticides Slated for Re-evaluation Regarding Human Health

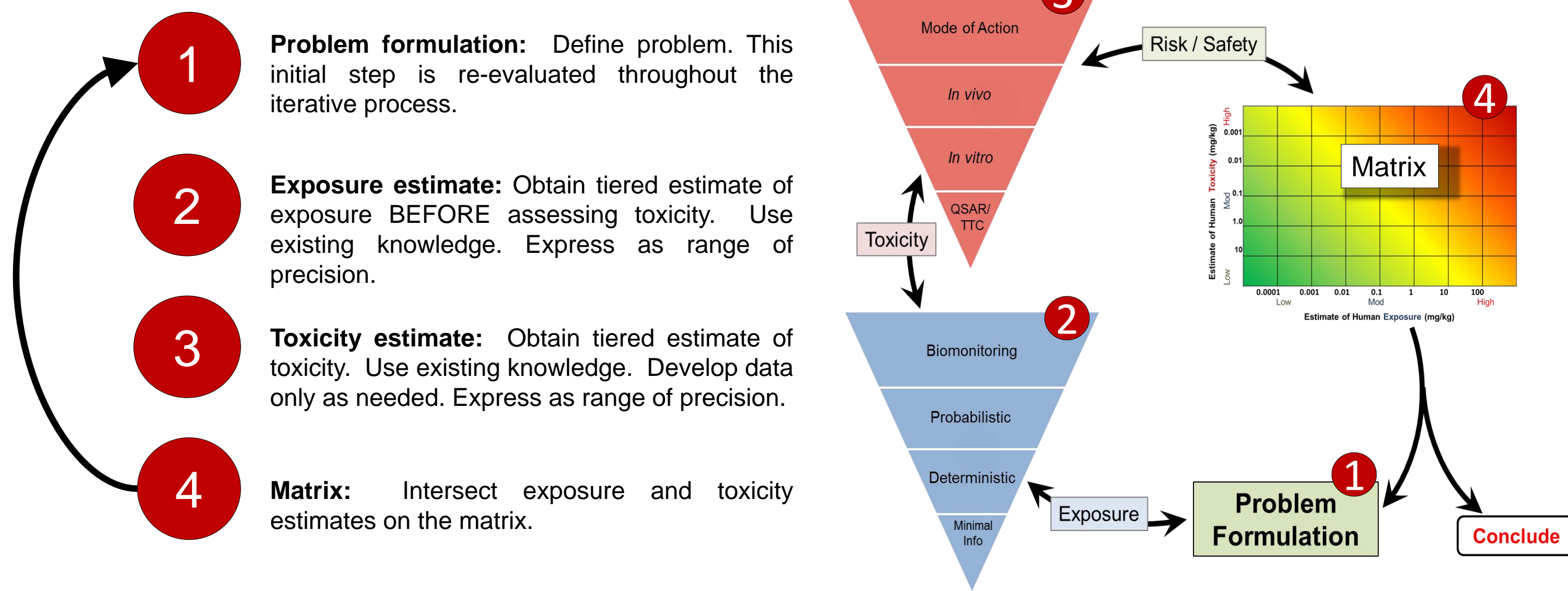
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RISK21 Principles

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.

The RISK21 Roadmap



RISK21 Matrix Webtool: www.risk21.org



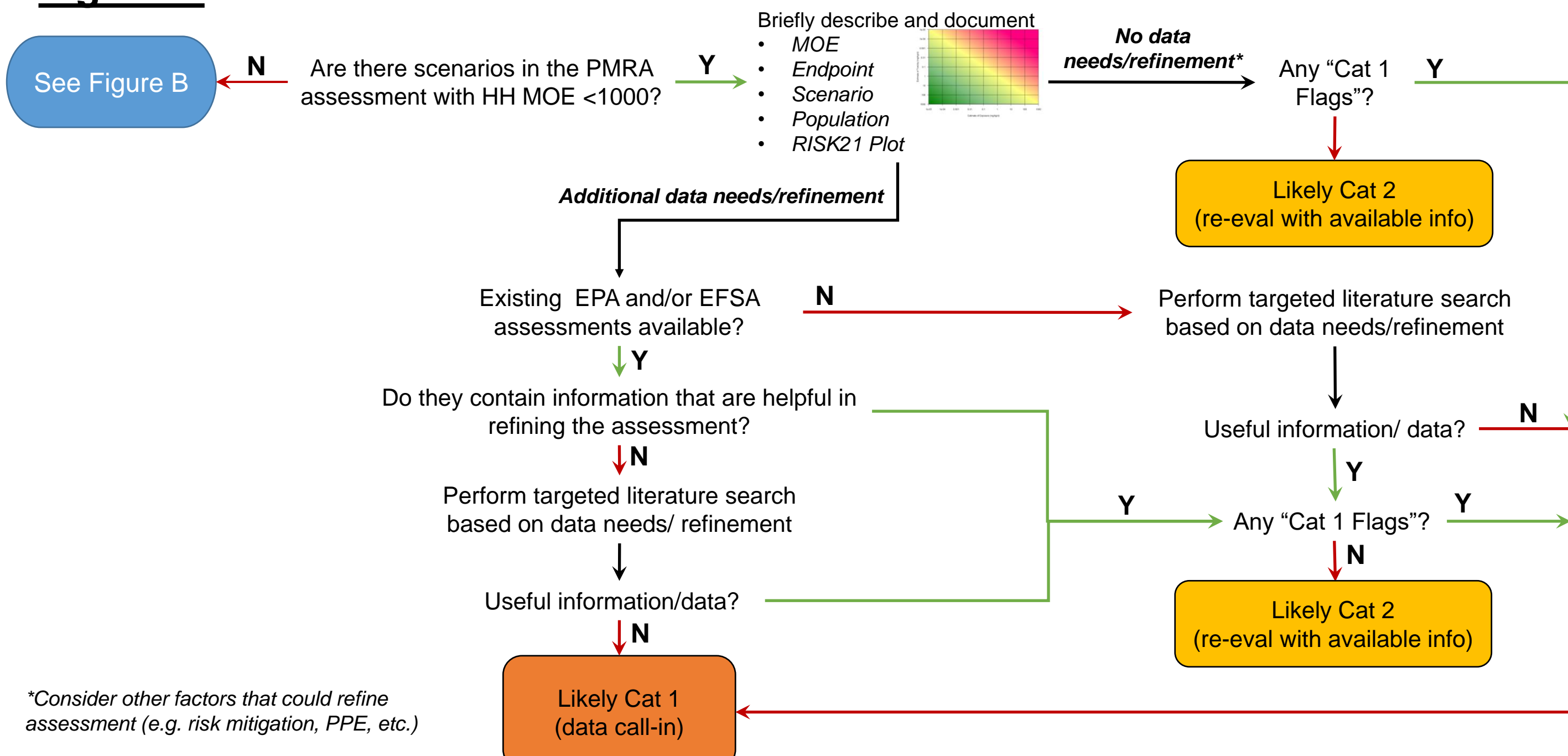
- Users can interact with the RISK21 webtool application to visualize their own risk data, creating a custom plot which will be displayed on the screen.
- Users can input estimated exposure and toxicity data for each chemical, and the tool will automatically intersect these toxicity and exposure distributions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

Using RISK21 for Categorization

- The RISK21 approach can be used to categorize a group of chemicals, in this example pesticides, using existing risk assessments
- In order to simplify the categorization process, a flowchart was developed in collaboration with Health Canada's Pesticide Management Regulatory Agency (PMRA) based on margins of exposure (MOE) and data needs and refinements
- The RISK21 Webtool Matrix can then be used to communicate the human health risk and help make evidence-informed decisions
- For the purpose of this example, PMRA risk assessments were used in order to show a real-world application of the RISK21 categorization process
- This categorization process allows for an easy and transparent approach leading to the ability to rapidly prioritize financial and staffing resources within an agency regarding the pesticide reevaluation process

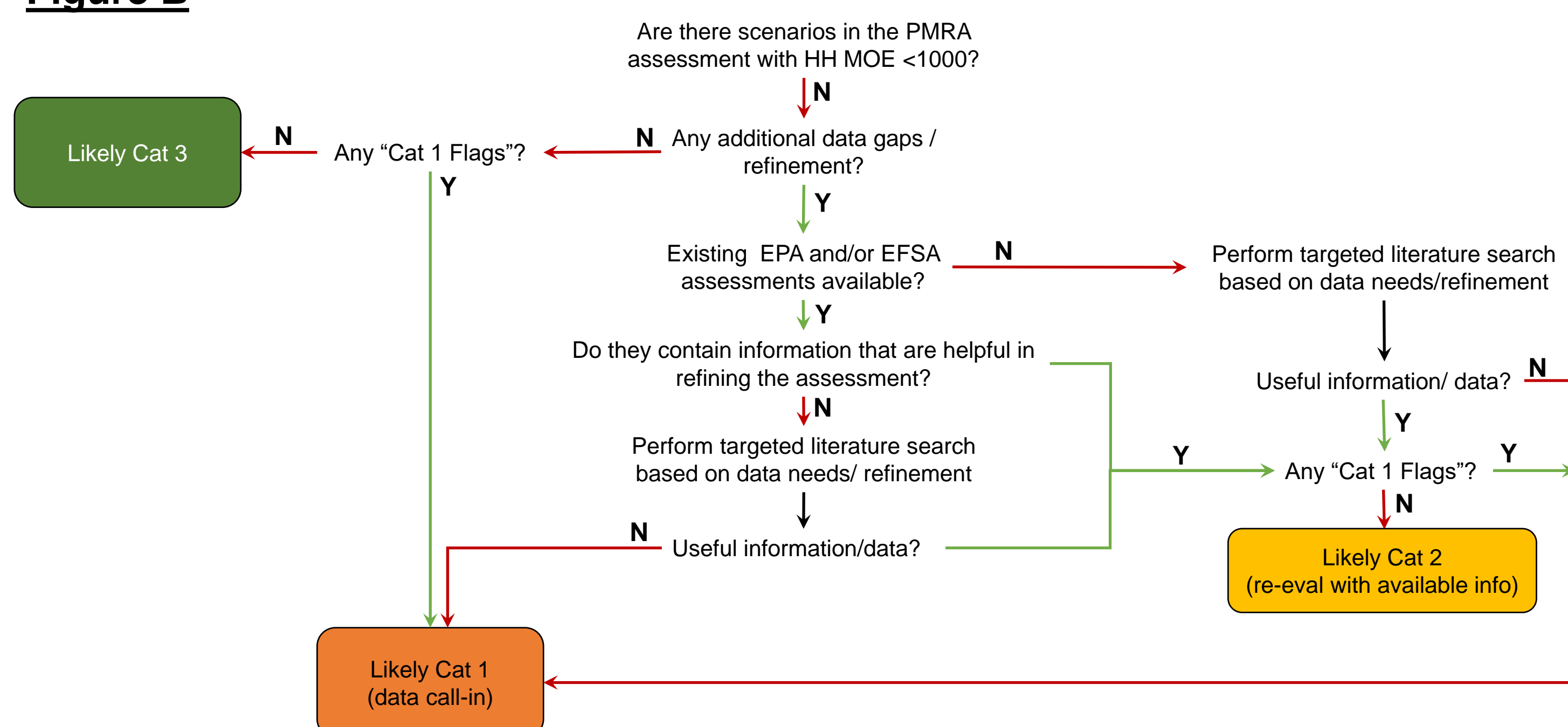
Human Health Re-evaluation Flowchart

Figure A



*Consider other factors that could refine assessment (e.g. risk mitigation, PPE, etc.)

Figure B



Exposure and Toxicity Information

Pesticide	Dietary Toxicity	Occupational Toxicity	Exposure: Occupational Application (MOE)	Exposure: Occupational Post Application (MOE)	Exposure: Bystander (MOE)	Exposure: Dietary (MOE)	Data Gaps
Spinosad ¹ (A)	2.7 mg/kg bw/d (UF=300)	5 mg/kg bw/d (UF=300)	0.0043 mg/kg bw/d (1,163)	0.068 mg/kg bw/d (73)	1.27 mg/kg bw/d (4)	0.0072 mg/kg bw/d (375)	Additional studies needed on post-application exposure assessment
Triticonazole ² (B)	Acute: 5 mg/kg bw/d (UF=300) Chronic: 2.5 mg/kg bw/d (UF=300)	1000 mg/kg bw/d (UF=300)	0.0211 mg/kg bw/d (119)	0.17 mg/kg bw/d (5,560)	N/A	Acute: 0.00204 mg/kg bw/d (2,450) Chronic: 0.00108 mg/kg bw/d (2,315)	N/A
Florasulam ³ (C)	5.0 mg/kg bw/d (UF=100)	1000 mg/kg bw/d (UF=100)	0.0025 mg/kg bw/d (400,000)	N/A	N/A	0.005 mg/kg bw/d (1,000)	N/A

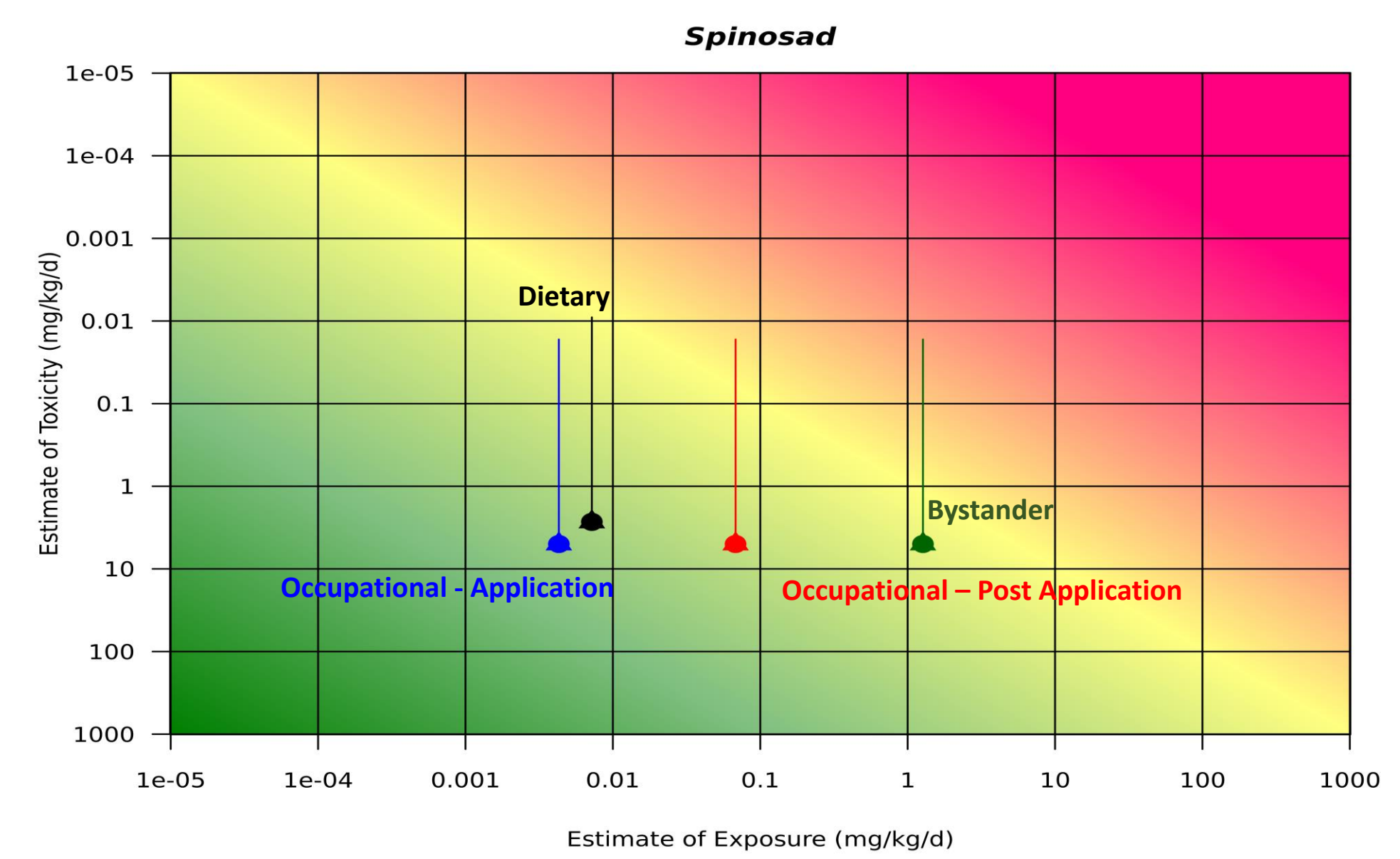
¹Health Canada PMRA, 2001. Spinosad Regulatory Note. REG2001-10.

²Health Canada PMRA, 2004. Triticonazole Proposed Regulatory Decision Document. PRDD2004-06.

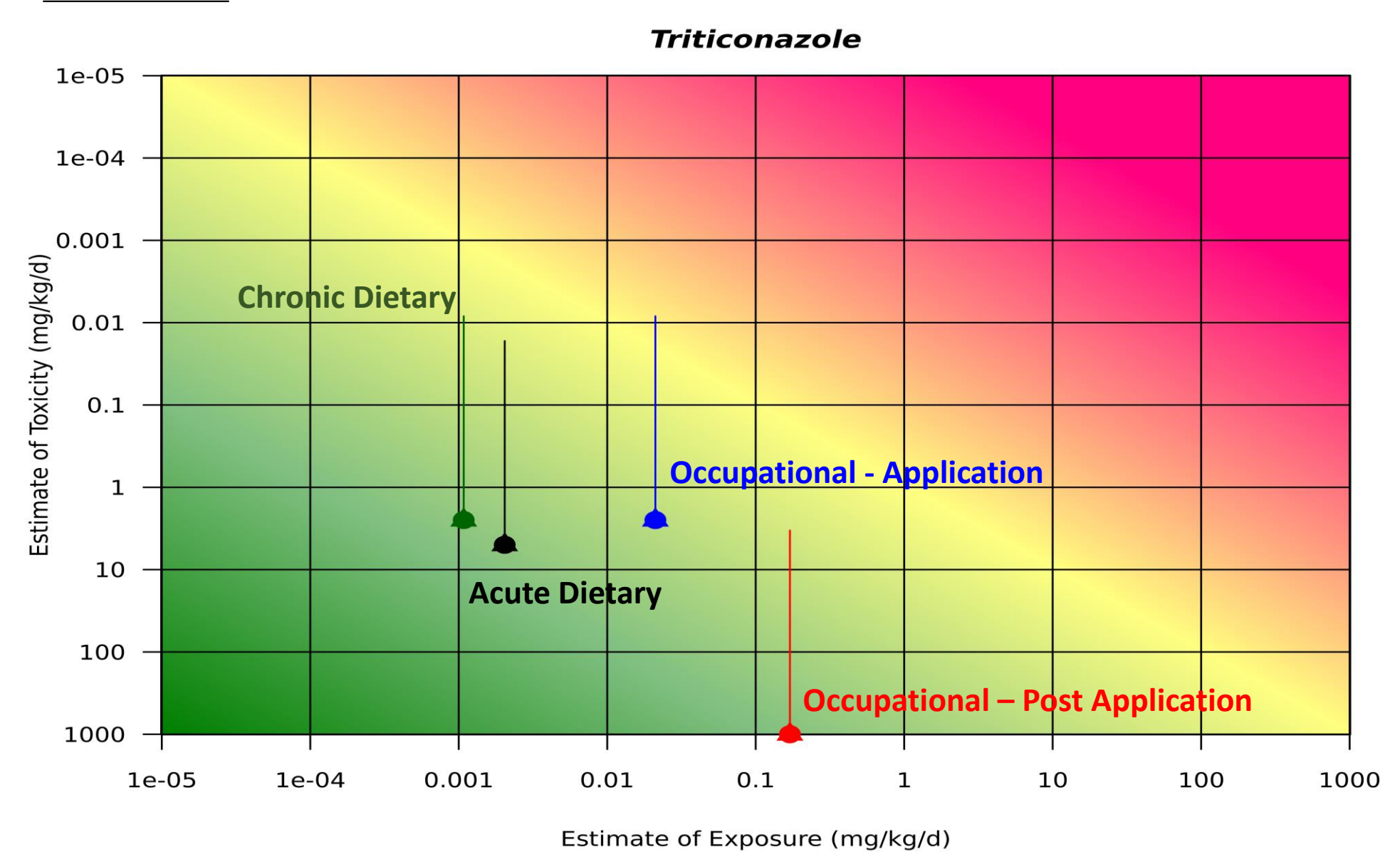
³Health Canada PMRA, 2001. Florasulam Regulatory Note. REG2001-12.

RISK21 Matrix Plots

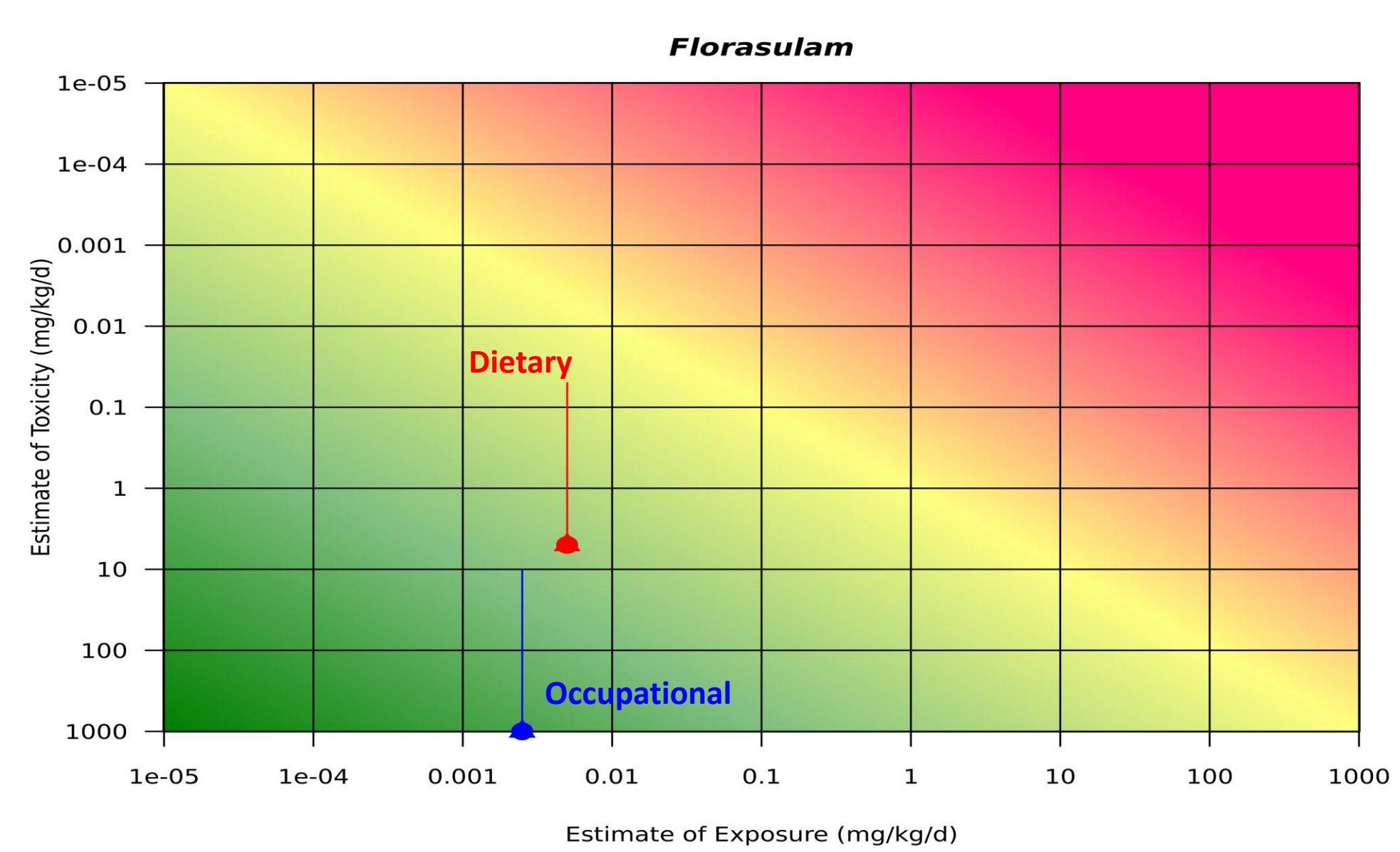
Plot A:



Plot B:



Plot C:



Categorization

Category	Description	Categorization Conclusions
Category 1	Data call-in. Longest projected time frame and a data call-in is required. The data call-in can be satisfied by a variety of means including new studies or revisions of toxicological end points.	Spinosad (A): scenarios where MOE < 1000, bystander and occupational post application exposure are of concern; additional studies needed to refine post-application exposure assessments.
Category 2	Reevaluation with available information. Do not require a data call-in but may require an evaluation of certain aspects of the risk assessment using current assumptions.	Triticonazole (B): scenarios where MOE <1000, review existing assessments from other agencies, and perform literature search to re-evaluate with existing data
Category 3	New evaluation unwarranted. All components are adequately addressed in the previous assessment, and a new evaluation is not warranted.	Florasulam (C): no data gaps, all MOE >1000 previous assessment adequately addresses risk
Category 1 "Flags"	"Flags" to consider. Agency dependent – some examples of "flags" from PMRA: PCPA, endocrine effects, dietary metabolites, and water modeling.	If the risk assessment for the pesticide contained any Category 1 "Flags", the pesticide would then have to be categorized as Category 1 regardless of MOE or data gaps